Principles of Specialty Nursing
Under the Auspices of the *European Specialist Nurses Organisations (ESNO)*
Series Editor: Ber Oomen

Françoise Charnay-Sonnek
Anne E. Murphy *Editors*

Principle of Nursing in Oncology

New Challenges

ESNO
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The role of the specialist nurse in Europe is still not clearly defined. Despite the fact that there have been formal training programs – e.g. for nurse anaesthetists, operating room nurses, intensive care and mental health nurses – for years now, the practices, status, duration and content of training can vary greatly from country to country. Some other specialist roles, e.g. for Diabetes, Dialysis, Urology and Oncology, have successfully been established in Europe with the help of professional transnational collaborations. Moreover, advances in medical technologies and more sophisticated treatment will not only require specialist nurses in order to ensure quality and safety of care, but will also call upon them to assume new roles in their professional field to compensate for physician shortages. Most of the available literature on specialty nursing practice currently comes from the USA, Canada, and Australia, and accordingly reflects evidence-based nursing in these countries. Therefore, there is a need to establish European evidence-based practice on the basis of different clinical experiences. This series, which encompasses textbooks for each specialty, shapes evidence-based practice in Europe, while also integrating lessons learned from other continents. Moreover, it contributes to clarifying the status of the specialist nurse as an advanced practice nurse. Each volume is dedicated to a specialty such as Mental health and Pyschiatry, firstly published, Oncology, Gastroenterology/Endoscopy, Anesthesia, Critical Care etc. and for most of them, textbooks are supported by ESNO member societies.

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Editors
Françoise Charnay-Sonnek
Unicancer
Paris
France

Anne E. Murphy
University Hospital of Geneva
Geneve
Switzerland

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Foreword

Florence Nightingale was one of the most famous nurses in the history. Nowadays, she is still remembered as a founder of modern nursing. You can hardly open a book about nursing where the achievements of Florence Nightingale are not mentioned. In her times, patient care was becoming more and more important, and today, this trend is still developing.

Cancer is becoming a chronic disease, and the aging population in Europe means we can expect more patients living with and after cancer. The diagnosis is set earlier than ever before due to modern techniques, and healthcare programs are modernized. The treatment of cancer has improved and survivorship rate has grown in the last decades.

The needs of patients will be different and also the nurse occupation will evolve. This also means new challenges for the nursing profession. How can the patient and the nurse meet each other in their own needs, and what is the best way to approach the relationship? Patients are more empowered today and want to participate in decision-making with the healthcare professional. Multidisciplinary care and patient co-decisions will grow in important in the coming years.

In Europe, there are a lot of effective initiatives on how to improve nursing practice and creating better quality of care for cancer patients. Taking the stage of the disease and cultural differences into account, we are able to learn from each other and share best practices. Collaboration across Europe and creating common goals involving patients and nurses are essential for the improvement of the practice.

The Association of European Cancer Leagues (ECL) believes that collaboration between different cancer societies can generate best quality of care. The role of the (oncology) nurse is very important, and studies show that patients put a lot of confidence in nurses. The ECL Patient Support Working Group endorses this book as an excellent example of how many interventions and initiatives are taken in the field to develop the role of the oncology nurse in an ever-changing environment. A nurse is more than just a caregiver in a hospital but a person patients can rely on with their needs and, as this book suggests, serving multiple functions within the oncology team.

ECL
Association of European Cancer Leagues

Brussels, Belgium

Alrik Meesen

Preface

The purpose of this book is to produce evidence-based nursing in oncology from a European perspective including international literature. With my coeditor, we have been thinking a long time on how to compose the table of contents we wanted as exhaustive as possible. We were conscient that we could not include all themes of oncology in a predefined framework. We had to make a choice and focus on the themes we estimated to be the most relevant introducing a chapter written by a patient about her experience of the disease. In fact, can we care today without involving the patient in the process? The response is definitely no, we cannot.

Caring patient with cancer evolves. Patients are not restricted to an organ anymore. A patient has to be considered as a global person with his or her private, social, and professional environment, a person who codecides what will happen with him or her in terms of treatments and care. He is an actor, a collaborator.

This concept changes completely the way of working for the healthcare professionals, who are not anymore in an authority position telling what to do with *no point of return*. Healthcare professionals have to compose and adapt according to the patient and his environment. A lot of evidences highlight that patient involvement in the treatment and decision-making can benefit the adherence to the treatment and its efficiency. It requires new skills based on communication, interpersonal communication, and education.

Thanks to advances in medicine, people with cancer can be cured and live longer than they could have done years ago. The treatments are increasingly sophisticated and personalized and target specific receptors in the chain reactions of the functioning of the cancer cell. The big trend is immunotherapy, which restores the immune system's ability to respond to cancer cells and is often associated with more traditional treatments. In addition, drugs that mitigate the adverse effects of therapies have evolved considerably and allow patients to tolerate much better their treatment and for some to continue their professional activity during this period of their life.

Therapeutic education, which is from a very long time used in chronic disease such as diabetes, applies now to oncology, especially with the increasing number of oral medications, 1-day treatments, and outpatient surgery. Care is increasingly moving to the patient's home, and it becomes essential that it is provided correctly by competent professionals to avoid any inadvertent hospitalization and above all *ensure* secure and quality care. So, cancer treatment is switching from a hospital care setting to a home care setting embracing in the process of care the healthcare professionals at home. The network enlarges, and both systems in the hospital and at home must closely work together in order to make the patient care path as fluid as possible. The nurse coordinator has a huge role to play, and almost all chapters of this book underline her or his pivotal place.

Supportive care, which is now very well established, provides a high level of care based on the supportive needs of the person going beyond the effects of cancer or its treatments. It implies a pluriprofessional approach, which is nowadays essential.

The more we advance in the study of cellular functioning, the more the mechanisms become more complex and the more treatments will take into account this new knowledge. And the further we go, the more we feel we know less. The body in its infinitely small form is comparable to space in its infinite grandeur. It’s a never-ending job of great detail.

Thanks to the sequencing of the genome, we can identify specific characteristics of each cancer and/or hereditary genetic predispositions to certain cancers. Molecular biology is becoming increasingly important in diagnosis and therapeutic decision. The future of tomorrow will focus on treatments based on genetic abnormalities that would be identical for different diseases (not just cancer). All of these present and future discoveries will certainly change medicine and how to care for patients.

eHealth is growing, new electronic tools are created in a very fast manner, telemedicine enhances reality, etc. This is another point and a crucial one to be considered in our vision of care, but it requires also from the healthcare professionals to be aware of those changes and willing to adopt those new tools. On one hand, it means fantastic progress; on the other hand, it might lead to unequal access of care and a gap between rich and poor: rich people living in the cities being more easily educated and connected than the poor living in the countryside.

Robotic surgery brings new perspectives permitting to operate a patient at distance with surgeons situated at in a different place in the world, but it also means new challenges for nurses.

Finally, we can observe that cancer disease has always been a concern for competent authorities all around in the world. Initiatives taken by governments, at local and national level, and by international organizations contribute to enhance the caring of the patient with cancer.

We wanted this book not to be stowed on the shelf and taking the dust; we wanted it easy to read, bringing knowledge but also driving a reflection on everyone’s own practice.

It reflects oncology nursing in Europe. Some countries are more advanced than others, some chapters are more developed from a scientific point of view, and others have a more practical point of view, but they are all based on founded literature. Actually, this approach reveals a very complementary aspect. Research is not apart on a distant planet but closely correlated with the practice. Without the practice, research is an empty vase. Without research, practice cannot progress.

Nurses can do both but taking in mind that their first role is “caring.”

Etterbeek, Belgium, Paris, France
Geneve, Switzerland

Françoise Charnay-Sonnek
Anne E. Murphy

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About the Editors

Françoise Charnay-Sonnek has studied foreign languages, nursing, pedagogy, and management. She graduated as a nurse in 1992 from the School of Nursing at the University Hospital in Heidelberg, Germany. She worked as a nurse in oncology and hematology in Germany and moved to France in 1998. She had been nurse manager in the Strasbourg University Hospital and later in the Strasbourg comprehensive cancer center. Françoise was Education Head for the continuous training in oncology at the FNCLCC-EFEC School of Oncology in Paris, and in January 2018, she moved to a new job within Unicancer as Education Coordinator.

She was engaged in different professional nursing associations. She was a board member of AFIC (French Association of Oncology Nurses) before joining the EONS executive board (from 2007 to 2013). In addition, she became an active member of the EAU (European Association of Urology) guidelines panel team on “pain management and palliative care” from 2012 to 2014. She represented EONS at the board of ESNO (European Specialist Nurse Organistions). She became the president in 2014. Her mandate ended in December 2017 after 5 years leadership.

Anne E. Murphy is currently working as a nurse and genetic counselor in Geneva University Hospital. She graduated as a nurse in 1981 and has been working in Geneva and abroad with "Doctors Without Borders." Since 1991, she is active in the field of oncology and has been involved in the Swiss Oncology Nursing Association. She was a member of the EONS education group from 1993 to 1997 and accreditation committee from 1997 to 2005. She represented Europe at ISNCC (International Society of Nurses in Cancer Care) from 2000 to 2004. After a bachelor's degree in Education and a master's in genetic counseling, she has been active in the creation of the Oncogenetics Unit of Geneva University Hospital. Since 2014, she is involved in the first Swiss Helpline for rare diseases. She is currently member of the AFCG (French Association of Genetic Counselors) and President of the Swiss Association of Genetic Counselors.

Contributors

Cathie Amrhein University Hospital Strasbourg, Strasbourg, France

Claude Bertrand King Albert II Institute for Cancerology and Haematology, Cliniques Universitaires Saint-Luc, Brussels, Belgium

Inma Bonilla Nuclear Medicine Department, Hospital Universitary of Bellvitge, Barcelona, Spain

Richard Booth Arthur Labatt Family School of Nursing, Western University, London, ON, Canada

Pascale Breton PREVIA, Paris, France

Ryan Chan Arthur Labatt Family School of Nursing, Western University, London, ON, Canada

Andreas Charalambous Cyprus University of Technology, Limassol, Cyprus

University of Turku, Turku, Finland

Françoise Charnay-Sonnek Unicancer, Paris, France

Patrick Crombez Department of Hematology and Hematopoietic Stem Cell Transplantation, Jules Bordet Institute, Brussels, Belgium

Loïc Dagorne Réseau Ile-de-France d'Hématologie Oncologie Pédiatrique (RIFHOP), Paris, France

Maria Goreti da Rocha Rodrigues School of Health Sciences, HES-SO University of Applied Sciences and Arts Western Switzerland, Geneva, Switzerland

Julio C. de la Torre-Montero Comillas Pontifical University, Madrid, Spain

Complutense University of Madrid, Madrid, Spain

University of Salamanca, Salamanca, Spain

Paz Fernández-Ortega Nursing Research Institute Català d'Oncologia, University of Barcelona, Barcelona, Spain

Faith Gibson Centre for Outcomes and Experience Research in Children's Health, Illness and Disability (ORCHID), Great Ormond Street Hospital for Children NHS Foundation Trust, Faculty of Health and Medical Sciences, University of Surrey, London, UK

Bente Thoft Jensen Department of Clinical Medicine, Aarhus University & Chair of Bladder Cancer SIG-Group, European Association of Urology Nurses, Aarhus, Denmark

Sultan Kav Faculty of Health Sciences, Başkent University, Ankara, Turkey

Susanne Vahr Lauridsen Department of Urology, Copenhagen University Hospital & Chair of the European Association of Urology Nurses, Copenhagen, Denmark

Delphine Lesoin Home Care Geneva, Geneva, Switzerland

Danuta Lichosik European Institute of Oncology, Milan, Italy

Claire Llambrich Institut Curie, Paris, France

Marion Lucas Department of Oncology for Child and Adolescent with Cancer and Young Adult Transversal SPIAJA Team, Gustave Roussy, Villejuif, France

Helena Sofia Azevedo de Oliveira Magalhães Day Hospital of Hemato-Oncology, Portuguese Oncology Institute, Lisbon, Portugal

Clotilde Messin Ecole Santé sociale Sud Est, Lyon, France

Marie Met-Domestici University Hospital of Lausanne, Lausanne, Switzerland

Adam Morse Arthur Labatt Family School of Nursing, Western University, London, ON, Canada

Anne E. Murphy University Hospital of Geneva, Geneva, Switzerland

Carine Musete Auto-entrepreneur Consultante en formation, Pontault-Combault, France

Séraphine de Senlis hospital Les Murets, La Queue-en-Brie, France

Maria Parsonage Respiratory Medicine, Wirral University NHS Hospital Trust, Wirral, UK

Chulja J. Pek HPB Surgery, Erasmus University Hospital, Rotterdam, The Netherlands

Sylvie Perrin Centre Léon Bérard, Lyon, France

Christine Remacle King Albert II Institute for Cancerology and Haematology, Cliniques Universitaires Saint-Luc, Brussels, Belgium

Suzanna Winston Cliniques Universitaires Saint-Luc, Université Catholique de Louvain, Brussels, Belgium

Maya Zumstein-Shaha Division of Nursing, Department of Health, Bern University of Applied Sciences, Bern, Switzerland

1 Basis of Carcinogenesis

Anne E. Murphy and Françoise Charnay-Sonnek

Abstract
We can define cancer as a genetic, multistep, and clonal disease, but we will see later in this chapter that this perspective is changing.

This chapter is dedicated to normal cell biology and how cells become malignant.

Keywords
Genome · Genotype · Phenotype · Telomerase · Hallmarks of cancer · Tumor cell environement · Angiogenesis · Immune process

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History

The name "cancer" comes from the Greek word "Karkinos".

A legend tells us that during the second battle of Hercules, the goddess Era put before him a hydra named Karkinos who seized one of Hercules's legs with one of its coils. He defended himself by decapitating the nine heads of this enormous water serpent. On dying, the hydra created the Cancer constellation in the sky.

A. E. Murphy (✉)
University Hospital of Geneva, Geneva, Switzerland
e-mail: anne.murphy@hcuge.ch

F. Charnay-Sonnek
Unicancer, Paris, France

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In a second legend, attributed to the Greek physician Paul d'Egine (in the seventh century after JC), the term cancer refers to the idea that once a crab has grabbed an organ, it will not release it.

Historically, we can see that cancer as a disease has a long existence. The skeleton of a prehistorical man from the Iron Age and Egyptians mummies shows signs of cancer. Furthermore, Mesopotamian, Indian, and Persian writings talk about cancer.

In the fifth century before JC, Herodote described the breast tumour of Atossa, Cyrus's daughter and wife of Darius. Hippocrates (460–370 before JC) defines carcinome as being an invasive tumour leading to an inevitable death; he describes skin, breast, stomach, and cervix cancers. Celsus, a Roman physician, defines the stages of the disease according to its growth: cacoethes (early-stage tumour), which is considered as pernicious, malign, carcinoma without ulceration, and carcinoma with an exuberant lesion. He also defines the treatments according to the evolution of the disease: excision, cauterization, and ointments. Galien (130–201 after JC) describes cancer as a tumour, due to excessive mood, a disorder of the black bile for which treatments comprised specific diets, purges, drugs, bleedings, and of course lesion's excision. These treatments have been in use for the last 1500 years.

We also know that, being the disease of the cell, it has always existed even in plants and animals.

Over the past 30 years, we have made tremendous advances in understanding the role of genes in normal cell function and structure but also on how genetic modifications are implicated in the development and evolution of malignancies.

Firstly, it is important to know that a cell can be altered through several factors: environmental, lifestyle, personal, and hereditary factors. The main risk factor for cancer is age.

To begin with let us start with the description of a normal cell.

Normal Cell Biology

The Cell

The cell is the fundamental unit of life, and it is estimated that the human body contains about 100 trillion cells of different types. Every group of cells has a specialised function with a specific structure according to its function. For example, a nerve cell contains structures transmitting neural impulses, while lymphocytes B cells have a structure that is capable of producing antibodies.

Human cells are composed of a plasma membrane, the cytoplasm, and the nucleus. The *plasma membrane* envelopes the cell and regulates the movement of substances in and out of the cell. The *cytoplasm* is a fluidlike substance, enclosed by the plasma membrane, in which organelles or "little organs" are suspended. The *nucleus* is the largest organelle and is located in the centre of the cell. The majority of cells in human body are eukaryotic cells meaning that they contain one nucleus. Mature red blood cells are an exception since they have no nucleus.

The nucleus contains *DNA* (deoxyribonucleic acid) which is a structural component of chromosome.

The majority of human cells possess 46 *chromosomes* (22 pair of autosomes plus one pair of gonosome or sexual chromosomes [XX for women, XY for men]). Diploid cells contain two sets of homologous chromosomes and two copies of each gene, whereas haploid cells, like gamete or sex cell, contain only one set of chromosomes.

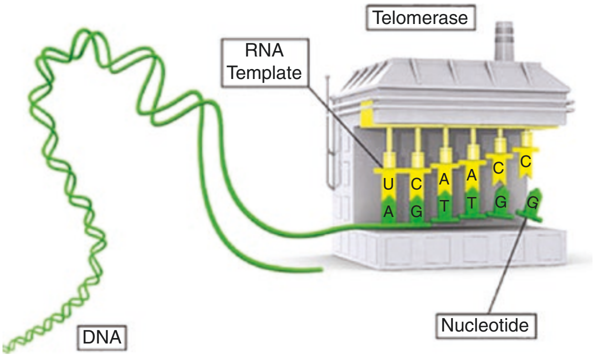
Each of our 46 chromosome comprises two long and tightly coiled strands of *DNA* twisted together to form a DNA double helix that contains all the genetic information for an individual, called the genotype. DNA is made up of four different bases or nucleotides: adenine (A), thymine (T), cytosine (C), and guanine (G). These nucleotides are present in DNA in base pairs (A-T or C-G), with the order of these base pairs differing from one DNA molecule to the next. Each nucleotide is composed of a phosphoric acid and sugar (deoxyribose) backbone, with an associated nitrogenous base (A, T, C, or G). In DNA, these nucleotides are linked together in recurrent sequences.

Genes are sections of DNA and are the core units of heredity defined by the sequence of bases/nucleotides. Each gene can contain a chain of as many as 1000 pairs of nucleotides. The length of DNA sequences are described according to the number of units of base pairs (bp) or thousands of base pair or kilobase pairs (kp) [1]. Genes are present in a cell in two copies or alleles, one maternal and the other paternal.

The Telomeres

The telomeres are the terminal portions of chromosome and sustain its stability. Telomeres shorten with each cell division and thus contribute to cell senescence (the ageing of cells).

The Telomerase



A telomerase is an enzyme in eukaryotic organisms that adds a structure to the endings of each telomere during DNA replication to maintain the length of the chromosome. It is produced from an RNA template with the repeating sequence TTAGGG (*T, thymine; A, adenine; G, guanine). It is present during embryogenesis, in germinal and haematopoietic cells. It is absent in other adult tissues. It is important to note that in most cancer cells, telomerase activity is observed, which explains why the proliferation capacity of cancer cells appears to be unlimited.

The Genome

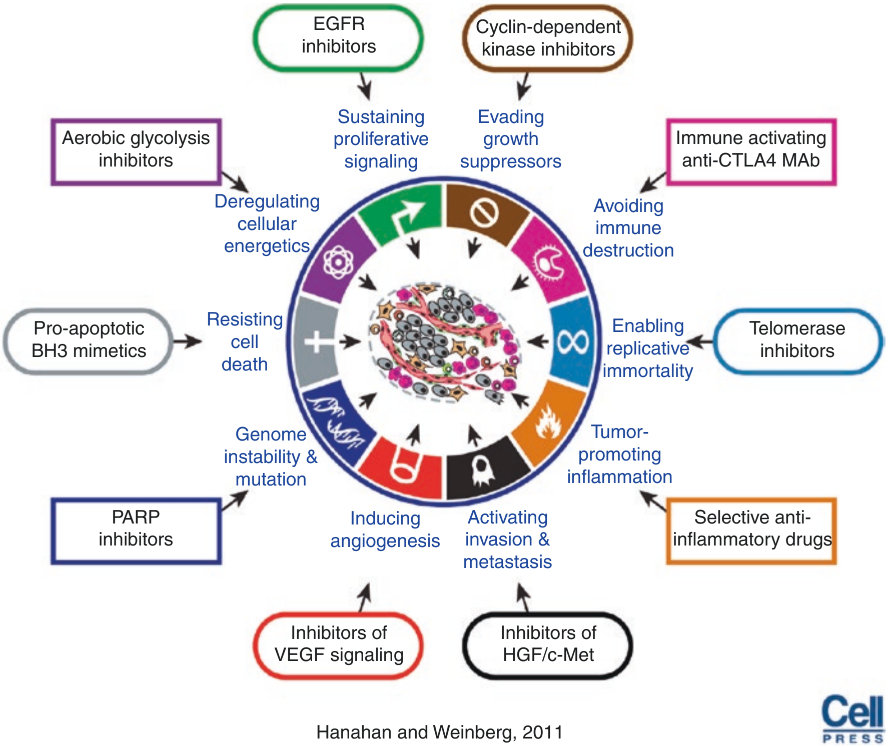
It is the complete set of instructions contained in all our chromosomes; it is also referred to as the “master blueprint” of the human body. It is estimated that only 10% of the genome contains the protein-coding sequences in exons, whereas 90% of the genome is made of noncoding sequences called introns [2].

The transmission of genetic information from one cell generation to another occurs through a base-pairing reaction: the nitrogenous base A pairs with T and G pairs with C. This specific pairing ensures that the new strand of DNA is an exact copy of the original and reduces the risk of errors. This mechanism of DNA replication is highly accurate with the possibility of removing the incorrect nucleotides. However, genetic mistakes or *mutations* can occur and can have very important consequences for cell functioning. Mutations are known to be implicated in several complex diseases such as autoimmune diseases, neurodegenerative disorders, and especially cancer.

Hallmarks of Cancer

Nowadays, progress in human biology and especially human genetics have led to a better comprehension of the sequence of steps that transforms a normal cell to one that is cancerous.

Hanahan and Weinberg [3] described that “the hallmarks of cancer comprise ten biological capabilities acquired during the multistep development of human tumors. (…)



They include sustaining proliferative signaling, evading growth suppressors, avoiding immune destruction, enabling replicative immortality, promoting tumour inflammation, activating invasion and metastasis, inducing angiogenesis, allowing genome instability and mutation, resisting cell death and deregulating cellular energetics" (Cf. Fig. 1.1).

Generally, a cell will be expulsed when detected abnormal by the organism. A cancer cell has acquired specific characteristics, including the capacity to multiply in an anarchical way and to appear to be immortal. Cancer cells also inhibit the immune system so that it will not be recognized as abnormal. Furthermore, it resists apoptosis/normal cell death and senescence (ageing of the cell): the physiological process leading to a slow degradation of the body's functions. The cancerous cell continues to multiply in an autonomous way due to growth factors and interacts with the extracellular environment called the stroma. Its growth permits it to penetrate the epithelial barrier and invade organs in the proximity. A cancerous cell also has the ability to create blood vessels ensuring that it will receive the nutriments required and allowing the cancer to disseminate via the blood and lymphatic system to others organs of the body.

Before we go into more detail concerning cancer, it is essential that we review normal cell biology in order to understand the genetic basis of cancer pathogenesis [4].

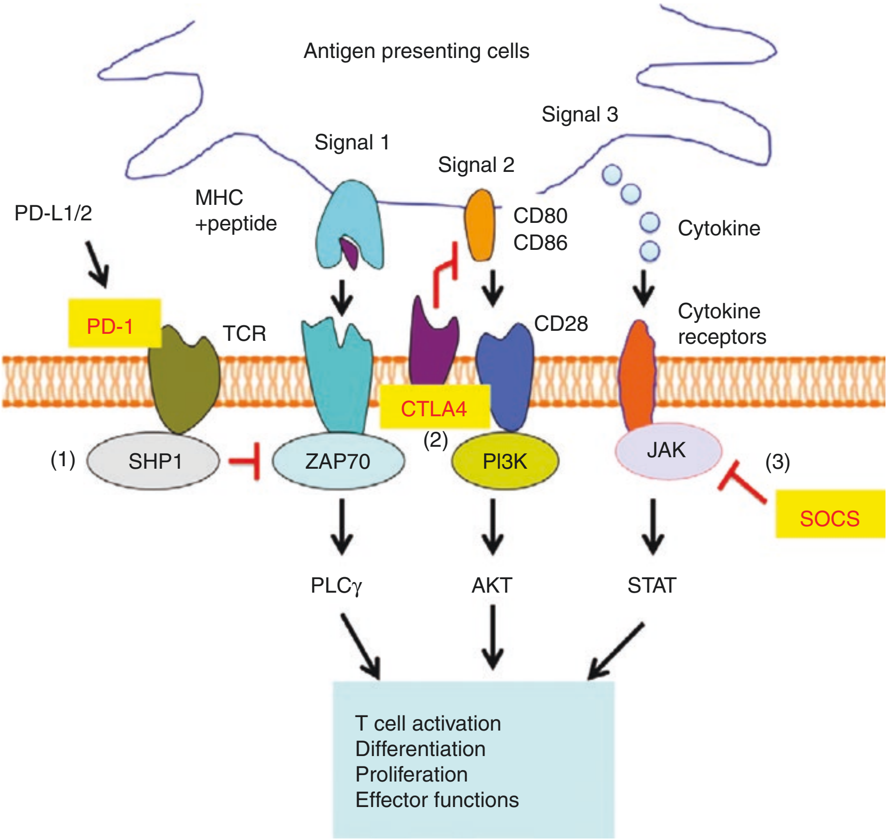


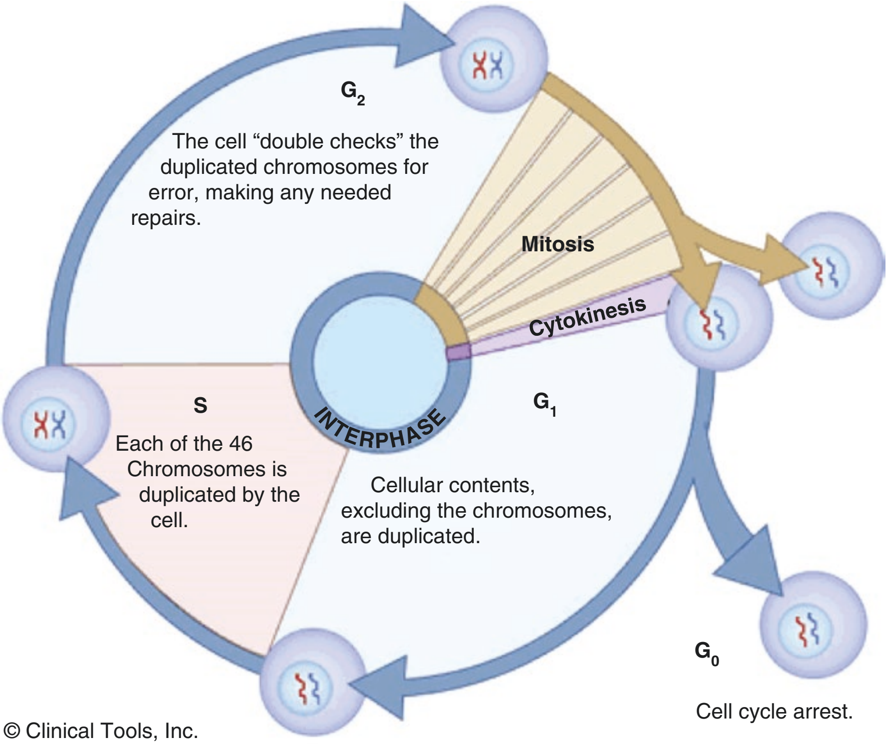
Fig. 1.1 T cell immune checkpoints for antitumour immunity. There are three major T cell activation signals, signal 1, signal 2, and signal 3. Signal 1 is MHC-antigen-peptide complex-TCR signal that activates tyrosine kinases including ZAP70. Signal 2 is the co-stimulatory signals from CD28, in which mostly PI3 kinase is involved. Signal 3 is the cytokine receptor signals that activate the JAK/STAT pathway. T cell activation by TCR, co-simulators, and cytokines is blocked by (1) PD-1, (2) CTLA4, and (3) SOCS (Chikuma et al. [15], p. 6)

Gene expression has been referred to as the "central dogma" of molecular biology and genetics. Each gene encodes and provides the cell with information to produce a specific protein. Generally, genes and the protein they encode have the same name, e.g. the *p53* gene encodes for the p53 protein. The protein synthesis process comprises two steps: *transcription* and *translation*.

During transcription, RNA copies the specific information contained in the DNA in the cell nucleus. The appropriate section of double-stranded DNA separates thus exposing the sequence of nucleotides. With the base pairs exposed, these DNA nucleotides pair with *RNA* nucleotides present in the nucleus. This pairing generates the messenger RNA (*mRNA*). This mRNA contains the code from the DNA necessary to produce a protein. The mRNA exits the nucleus into the cytoplasm to start translation, the second step of protein synthesis. During the translation, ribosomes present in the cell are brought into contact with the mRNA using *tRNA* (transfer RNA), as well as, ribosomal RNA and enzymes to produce a sequence of amino acids forming a protein (Sallas, Beth / S2L2 a&b – Cell Cycle, https://goo.gl/images/kB5M13).

In normal tissue, the number of new cells is equivalent to the number of dying cells. This equilibrium is maintained through cell proliferation and regulation. Cell growth and the transfer of genome from one cell to its progeny are guided by genetic expression. If an error or mutation in the genetic expression occurs, it can alter the growth and the reproduction of the cell and may eventually lead to cell death. These errors and mutations are implicated in several diseases, such as cancer, autoimmune diseases, neurodegenerative disorders, and viral infections.

Cell Cycle



The cell cycle is a multistep process leading to the duplication of the cell's contents forming two identical cells. This mechanism is essential in human cells since it serves to replace the cells that have been lost by "general wear and tear" or have died. Each cell proliferates and grows to reach a programmed size and extent (e.g. a nervous cell), then matures, and eventually dies. To maintain the same number of cells in the body, an adult human has to manufacture millions of new cells each second.

The aim of the cell cycle is to produce two genetically identical daughters' cells by copying DNA from the parent cell. This process equally divides the chromosomes between the two daughter cells and duplicates the cytoplasm from the parent cell. The cell cycle comprises four phases:

- G1 (Gap 1)
- S (synthesis)
- G2 (Gap 2)
- M (mitosis)

G1 is the beginning of the cycle and is the phase in which the cell prepares all the necessary components for division. In phase S (synthesis), the DNA replicates by doubling of the DNA and forming chromatin forming two identical sets of chromosomes (chromatids). In G2, the cell grows before the final phase mitosis or cell division.

The Cell Cycle Control System

The four phases are regulated by two molecular controls:

1. Cascade of cyclin (cell cycle proteins), cyclin-dependent kinases (CDKs), and CDK inhibitors
2. Checkpoints that monitor the molecular activities of each phase and delay the progression to the next phase if a problem is detected. These checkpoints have an essential role: they avoid the accumulation of genetic mistakes during the cell cycle.

Prior to these phases, the cell is in a quiescent period, either it has finished its differentiation or it is in a nonreproductive mode. Mitogens, nutrients, and growth factors can stimulate a cell to move from this quiescent mode to the G1 phase of the cell cycle.

What Is Cancer?

Cancer is the dysregulation or loss of equilibrium in the control of the cell cycle. This results in the proliferation of cells that can be localized to an organ and a region or can spread throughout the body.

The mechanism of this transformation that results in changes in the genes involves three groups of genes: the (proto)oncogenes, the tumour suppressor genes, and the DNA repairing genes. It is estimated that we have around 342 genes associated with somatic mutations and 70 genes associated with germline mutations [5].

DNA is believed to consist of approximately 30,000 genes, among which about 30 are proto-oncogenes and 300 are tumour suppressor genes.

The proto-oncogene is the result of a modification or overexpression of a normal gene. It is involved in the cell division and activates an excessive proliferation of cells: the first step in oncogenesis. One mutation is sufficient to activate this process.

Research on oncogenes has permitted a better understanding of the reasons why some individuals are more predisposed to develop a cancer. The explanation is that they are more susceptible to convert their oncogenes into proto-oncogenes.

Tumour suppressor genes are negative regulators of cell proliferation. They inhibit mechanisms leading to oncogenesis or activate mechanisms that inhibit oncogenesis. During oncogenesis, tumour suppressor genes are not activated.

An initial mutation transforms a normal cell into a cancerous cell; while a second mutation inevitably leads to cancerogenesis.

The gatekeeper gene Rb which inhibits cell growth is an example of a tumour suppressor gene, and the gene TP53 is a gene protecting the cell against aggressions.

More and more publications suggest that genes are mutable and can evolve in a negative or positive manner. Changes in lifestyle may have a real impact on behaviour and may deeply impact genetic patrimony

Genotype and Phenotype

The genotype is the inherited genes (patrimony), and the phenotype is actually the expression of the genotype. The phenotype includes physical appearance, biochemical processes that take place in the body, and the genetic determined behaviour.

The relationship between genotype and phenotype is mediated by environmental inputs on gene expression, trait development, and phenotypic integration.

One of the characteristic of cancer cells is their phenotypic plasticity, the fact that they are able to change state according to environmental fluctuations [6].

Today cancer is studied more from the perspective of dysregulated pathways rather than as a disease resulting from individual gene mutation. In fact, with a pathway-centred view, we acknowledge different genomic profiles from different cancer patients with the hypothesis that mutated genes from the same pathway are likely to produce similar disease phenotypes. A pathway-centred approach helps finding genotypic causes of diseases, classifying disease subtypes, and identifying drugs [7].

Metabolism and Cancer Cell

In this section we will discuss cancer cell metabolism and how this differs from that of healthy cells. Different components are involved in this process.

The Role of Glucose: Warburg Effect

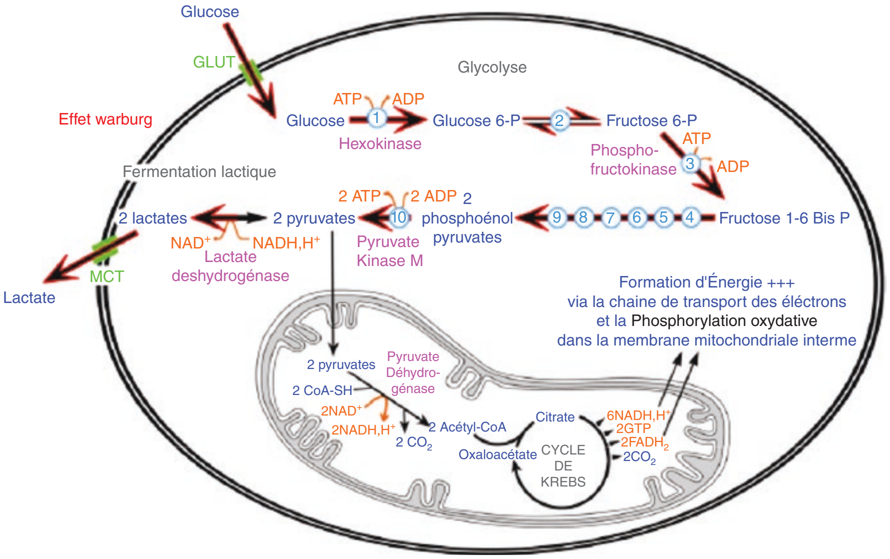
Otto Warburg in the early 1930s described the process by which cancer cells obtain their energy, essentially from glucose through glycolysis.

In the presence of oxygen, most differentiated (healthy) cells change glucose into pyruvate in the cytoplasm and then into carbon dioxide. Through this reaction, a maximum of ATP (adenosine triphosphate) is produced and that of lactate is limited. This reaction is only possible in the presence of oxygen and is referred to as aerobic glycolysis.

In a cell the energy is produced in the mitochondria where lipids are changed into glucose. Glucose is fundamental; in addition to ATP, it also provides the metabolic intermediates required for anabolic reactions. Glucose and glutamine are two essential energy sources.

By comparing healthy liver cells with tumour liver cells, Warburg noticed that tumour cells needed more glucose. By measuring the level of oxygen, he observed that compared to healthy cells, tumour cells consumed less oxygen, metabolized ten times more glucose, and produce more lactic acid, the by-product of glycolysis.

According to Warburg's theory, an irreversible change of the respiratory process in the mitochondria results in cell death. However, some cells like tumour cells can adapt their metabolism to an anaerobic one, thus needing substantially less oxygen to growth. Consequently, the cell morphology changes and growth becomes anarchical.

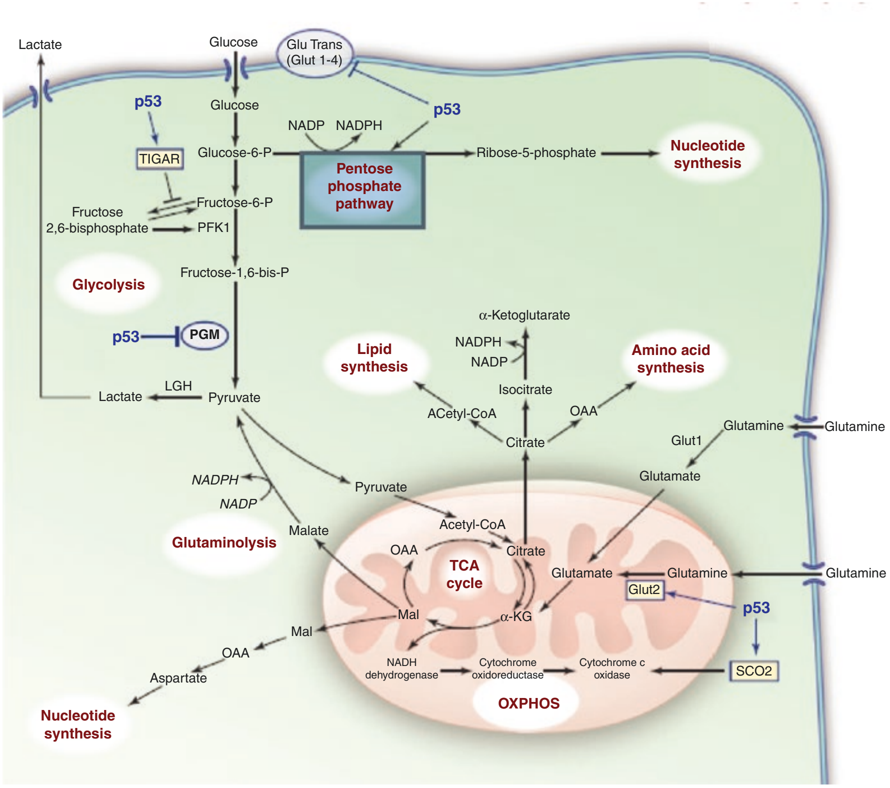


The theory developed by Warburg could only be completely validated with the development of molecular biology and its discoveries. Today, substantial evidence for this theory exists which is referred to as the "Warburg effect".

Further research has shown that mitochondria are able to function in tumour cells. Finally, Warburg did not discover why healthy cells become malignant, but he did identify one of the most important characteristics of tumour cells. His research provided important insights, crucial for understanding complex metabolic diseases.

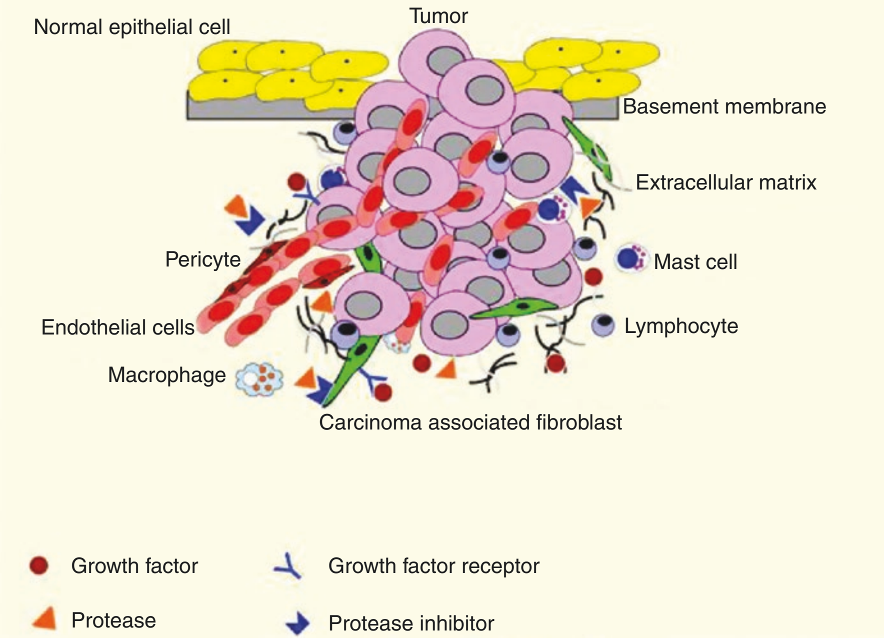
Levine and Puzio-Kuter identified different intermediates implicated in cell growth and division. They also showed that oncogenes and tumour suppressor genes regulated key cancer-producing pathways [8].

The metabolism of the cancer cell may have an impact on the therapeutic target. Indeed, we can see that the energy production is fundamental for growth, proliferation, and cell survival. The energy production by the cell is a source of oxidation which might influence the mutation process by changing the bases of the DNA and damage the lipid membrane. Obesity and diabetes increase the risk of cancer, while calorie restriction reduces it. As an example, a large animal with a low metabolic level (In body mass) has a lower risk of developing cancer.



Tumour Cell Environment

Cancer development results not only from the dysregulation of cells but also from complex interactions between the tumour tissue and the peri-tumoural stroma [9].



The stroma consists of a compilation of cells, including fibroblasts/myofibroblasts, glial, epithelial, fat, immune, vascular, smooth muscle, and immune cells along with the extracellular matrix (ECM) and extracellular molecules. The cells constituting the stroma are not malignant, but their direct or indirect interaction with cancer cells may alter their functioning and their phenotype.

In normal tissue, fibroblasts play a very important role and produce the noncellular scaffolds, the extracellular matrix (ECM), and contribute to the basement membrane production by secreting collagen and laminin. The cellular/tumoural environment is not static and is continually being remodelled. Fibroblasts serve as scaffolds and secrete increased levels of ECM proteins, growth factors, and chemotactic factors. Thereby, they coordinate the influx of inflammatory cells and vascular progenitor cells, as well as supply the scaffold for cell growth and proliferation [10].

In the tumour microenvironment, fibroblasts are the main component of the tumour stroma. In some cancer, there are more fibroblast cells than cancer cells. Fibroblasts within tumours have an activated phenotype and behave like fibroblasts in wound healing. Cancer-associated fibroblasts (CAFs) are functionally and phenotypically distinct from normal fibroblasts (in the same tissue). CAFs are distinctly different from physiologically activated fibroblasts in that they are always in action: neither reverting to their original normal phenotype nor undergo apoptosis (programmed cell death) and elimination.

This abnormal interplay between tumour and stroma cells, combined with active molecular signal transfers, drives the cancer stroma phenotype and may result in permanent alterations in cell function. Growth factors and chemokine produced by fibroblasts and immune cells are damaged, thus stimulating tumour cell growth and recruitment of precursor cells, which themselves respond with abnormal growth and proliferate. Malformed tumour vessels contribute to tumour hypoxia, acidosis, and increased interstitial fluid pressures.

This interplay between the tumour cells and the microenvironment has and continues to be an area of considerable interest for the development of targeted therapies.

Angiogenesis

Angiogenesis is the process by which a new vascular tree is formed from an existing one. This vascularisation supplies cells with oxygen and nutrition and removes carbon dioxide and waste products.

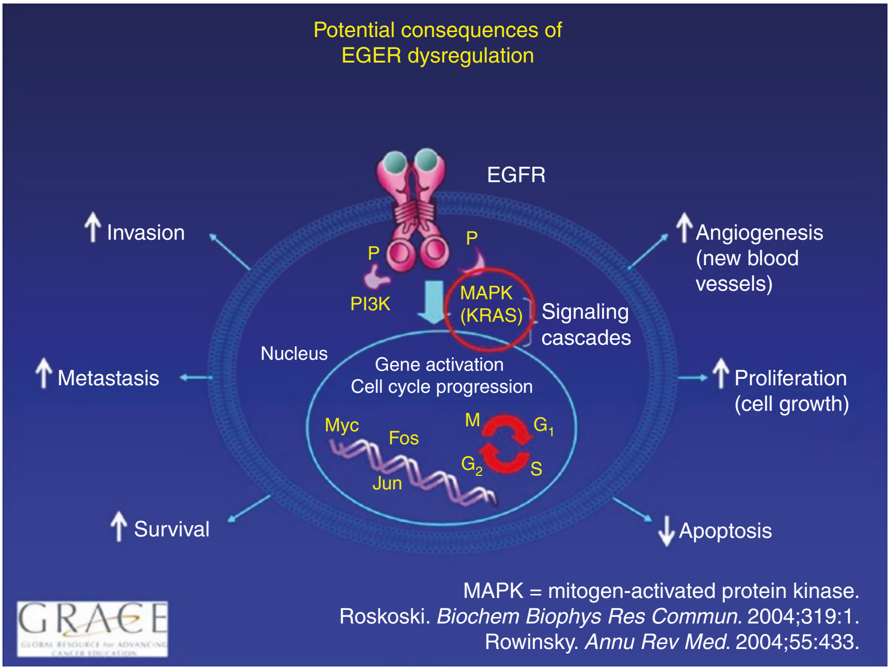
Capillaries are needed in all tissues for exchange diffusion of nutrients and metabolites. Changes in metabolic activity lead to proportional changes in angiogenesis and, hence, proportional changes in capillarity. Oxygen plays a pivotal role in this regulation. Haemodynamic factors are critical for survival of vascular networks and for structural adaptations of vessel walls.

Interestingly, scientists were investigating angiogenesis even before the dawn of the twenty-first century. In 2669 BC, Chinese medicine considered that the heart controlled the blood. In 1550 BC, vessel tumours were described in Ebers Papyrus. Hippocrates of Cos (460–370 BC) observed that the building of tumour was associated with swollen blood vessels around the tumour giving the impression of the claws of a crab. He thus named this type of tumour, karkinos and karkinoma. Later in ca. 200 AD, Galen of Pergamum, a Greek physician in the Roman Empire, described blood vessels related to tumour growth. Islamic medicine between ca. 1000 and 1300 AD, especially Avicenna, brought new knowledge of the cardiovascular system. During the renaissance period, the understanding of anatomy and vascular the system developed [11].

John Hunter, anatomist and surgeon in the eighteenth century was the first to bring insight in angiogenesis. Despite never citing the word angiogenesis in his work “the treatise” published in 1784, he was the first to describe the formation of new vessels during wound healing. More recently Judah Folkman (1933–2008), considered by many as the modern father of angiogenesis partly because of his pioneering studies, showed that tumour growth is angiogenesis-dependent.

Tumour cells need active angiogenesis to be able to growth. In tumour cells, there is an overexpression of angiogenic molecules (VEGF and FGF) and a reduction of the anti-angiogenesis factor expression. Tumours send signal, such as VEGF, that drives the proliferation of neighbouring blood vessels.

*VEGF: vascular endothelial growth factor
*FGF: fibroblast growth factor



Potential consequences of
EGER dysregulation

EGFR

↑ Invasion

↑ Angiogenesis
(new blood
vessels)

P

P

PI3K

MAPK
(KRAS)

Signaling
cascades

Nucleus

↑ Metastasis

Gene activation
Cell cycle progression

↑ Proliferation
(cell growth)

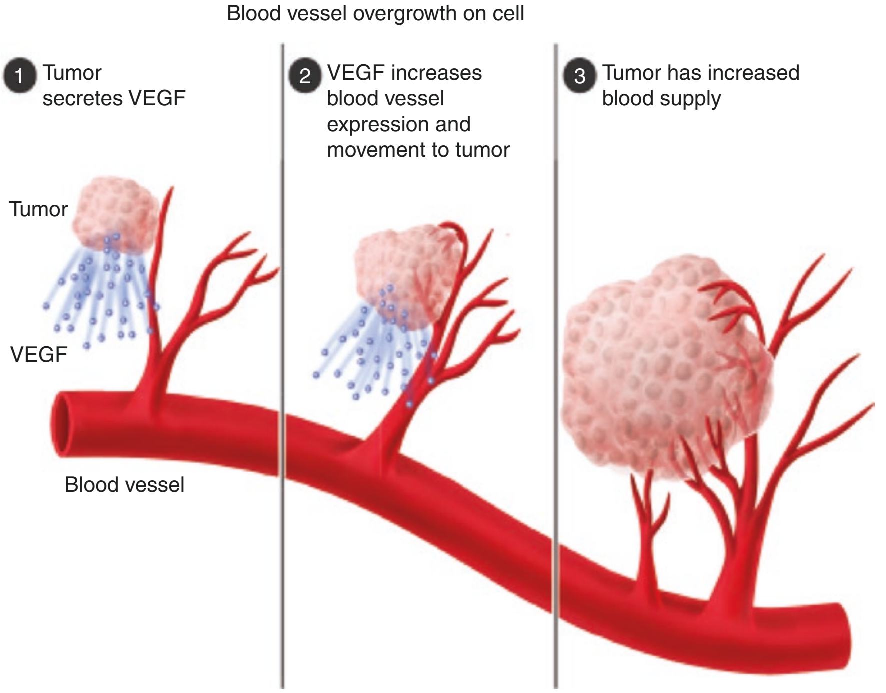
Myc
Fos
Jun

M
G_1
G_2
S

↑ Survival

↓ Apoptosis

MAPK = mitogen-activated protein kinase.
Roskoski. *Biochem Biophys Res Commun*. 2004;319:1.
Rowinsky. *Annu Rev Med*. 2004;55:433.



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The recognition that the control of angiogenesis could be of therapeutic value has stimulated research over the past 40 years. On one side, stimulation of angiogenesis can be therapeutic in ischemic heart disease, peripheral arterial disease, and wound healing. On the other side, decreasing or inhibiting angiogenesis can be therapeutic in cancer, ophthalmic conditions, rheumatoid arthritis, and other diseases.

A recent publication [12] shows how the branched peptide NT4 reduces angiogenesis and the invasiveness of tumour cells.

Anticoagulants (heparin derivatives) have an inhibitory role on tumour cells and procoagulants (thrombin), rather an activator role of proliferation, migration, and invasion. In the last few years, the relation between the peptide NT4 and heparan sulphate proteoglycans (HSPGs) has been extensively investigated. HSPGs are composed of a core protein, an O-glycosylated with a glycosaminoglycan (GAG). HSPGs are able to interact with a variety of proteins, such as those in the extracellular matrix (ECM): macromolecules; growth factors, such as fibroblast growth factors (FGFs); chemokines; morphogens; enzymes; heparin-binding epidermal growth factor-like growth factor (HBEFG); platelet-derived growth factor (PDGF); and many others. Most of the proteins that engage with HSPGs have a heparin-binding site that interacts with the sulphated GAG chains of HSPGs. NT4 binds to HSPGs and selectively targets cancer cells and tissues.

So, this peptide provides evidence of interplay with tumour invasion pathway and should continue to be used in studies related to links between coagulation and tumour progression involving HSPGs (Bracci et al. [12], p. 5).

Immune Process

Cancer should be considered, by our immune system, as an aggressor and therefore should be recognized as an intruder and be destroyed. However, cancer cells through different mechanisms escape detection by our immune system.

The tumour microenvironment (TME) that contains stromal cells and immune cells shapes cancer development and impact the response to tumour therapy (Hanahan and Weinberg [3]; Palucka and Coussens [13]). Intratumoural immune cells include lymphocytes, such as T, B, and natural killer (NK) cells, as well as a variety of myeloid cells (granulocytes, monocytes, macrophages, and dendritic cells).

T cells require glucose for proliferation and survival. Naïve or quiescent T cells require extrinsic cytokine stimulation to maintain glucose uptake for normal functions. Activated T cells require substantially more energy to grow, proliferate, and perform effector functions required of an activated lymphocyte. Energy production in the activated T cell may initially rely on AMPK activity for maximal ATP production and later, rely on changes in Glut1 expression, glucose uptake, and aerobic glycolysis. Without enough energy, activated T cells undergo apoptosis [14].

On one hand, T cells are activated through antigen recognition by the T cell receptor (TCR) and co-stimulatory signals such as CD28. On the other hand, the inhibitory signals for T cell activation (i.e., immune checkpoints) are very important to maintain self-tolerance and prevent autoimmunity and an excessive immune responses.

Under self-tolerance, we understand the absence of an immune response directed against a person’s own tissue’s antigens.

We should make the distinction between central tolerance and peripheral tolerance depending on where the state is originally induced, in the thymus and bone marrow (central) or in other tissues (lymph node [peripheral]). The mechanisms by which these forms of tolerance are established are distinct but the resulting effect is similar.

For antitumour therapy, Th1 cells that produce interleukin-2 (IL-2) and interferon-c (IFNc) play an activating role, while CD4+ regulatory T cells (Tregs) suppress antitumour immunity.

So, immune checkpoints are inhibitory pathways connected to the immune system that are crucial for maintaining self-tolerance.

The two immune checkpoint receptors that have been most actively studied in the context of clinical cancer immunotherapy, cytotoxic T-lymphocyte-associated antigen 4 (CTLA4, also known as CD152) and programmed cell death protein 1 (PD1, also known as CD279), are both inhibitory receptors.

The T lymphocyte recognizes the tumour cell through the binding of its receptor to its antigen; the contact of PD-1 with PD-L1 prevents the T lymphocyte from recognizing the tumour cell as an invader/foreign cell which results in immune tolerance.

The clinical efficacies of antibodies that block either of these receptors provide evidence that antitumour immunity can be enhanced by inhibiting immune checkpoints. The expression and activation of immune checkpoint proteins are important immune resistance mechanisms of tumours. A number of other immune checkpoints are promising targets for therapeutic blockade based on preclinical experiments with inhibitors for many of these currently under development.

In addition to TCR and co-stimulatory signals, T cell activation requires a third signal: signals from the cytokine receptors (Fig. 1.1) [15]. For example, IL-2 is necessary for the proliferation of T cells, and IL-12 and IFNc are important for Th1 differentiation and CTL activation.

SHP1 Phosphatase

ZAP70: A protein normally expressed near the surface membrane of T cells and natural killer cells. It is part of the T cell receptor and plays a critical role in T cell signalling. It is a member of the protein-tyrosine kinase family.

PI3K: A type of enzyme that transmits signals in cells and that helps control cell growth. Some tumours have higher-than-normal levels of PI3K.

CD80-CD86: Cluster of differentiation (CD) 80 and 86 are proteins found on dendritic cells, activated B cells, and monocytes that provide a co-stimulatory signal necessary for T cell activation and survival. It is the ligand for two different proteins on the T cell surface: CD28 (for autoregulation and intercellular association) and CTLA-4 (for attenuation of regulation and cellular disassociation).

JAK: Janus kinase (JAK) is a family of intracellular, non-receptor tyrosine kinases that transduce cytokine-mediated signals via the JAK-STAT pathway.

(SOCS) suppressors of cytokine signalling are major negative regulators of the JAK/STAT pathway.

The immune checkpoints like CTLA4 or PD-1/PL-L1 are those which have been studied most to be use as therapy. The inhibitors of PD-1 and PD-L1 prevent the binding of the receptor with the corresponding antigen allowing the T lymphocyte to recognize the tumour cell with subsequent destruction by the immune system.

In this first chapter, we can see how complex a single cell is. New discoveries, with more and more precise technology, will more than likely uncover an even more complex system with new pathway that can be targeted for cancer treatments.

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Epidemiology and Prevention

2

Anne E. Murphy

Abstract

Incidence (see final page for Glossary) and *mortality* due to cancer have increased gradually since the nineteenth century and represent an enormous burden in the world. As already mentioned, the risk of cancer increases with age, and it has been observed also that the incidence of cancer and mortality due to the disease increases because of the population growth (National Cancer Institute. Cancer risk factors and protective factors. www.cancer.gov/about-cancer/causes-prevention/risk/age. (Accessed May 1 2018)). This situation is observed of course in the developed countries but also in the developing part of the world since nearly 44% of cancer cases and 53% of cancer deaths occur in countries at a low or medium level of the *Human Development Index* (International Agency for Research on Cancer and Cancer Research UK. World Cancer Factsheet. Cancer Research UK, London, 2014).

Keywords

Epidemiology · Cancer statistics · Early detection · Cancer screening · Risk factors

Introduction

Incidence[1] and *mortality* due to cancer have increased gradually since the nineteenth century and represent an enormous burden in the world. As already mentioned, the risk of cancer increases with age, and it has been observed also that the incidence of cancer

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[1] See final page for Glossary.

A. E. Murphy (✉)
University Hospital of Geneva, Geneva, Switzerland
e-mail: anne.murphy@hcuge.ch

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Principles of Specialty Nursing, https://doi.org/10.1007/978-3-319-76457-3_2

and mortality due to the disease increases because of the population growth [1]. This situation is observed of course in the developed countries but also in the developing part of the world since nearly 44% of cancer cases and 53% of cancer deaths occur in countries at a low or medium level of the *Human Development Index* [2].

Human suffering caused by cancer is enormous, and the cost of care and treatment is certainly an important part of the rising amounts involved in health-care services and social insurance in the world.

To illustrate the scope of the problem, international epidemiology surveys and data presented in this chapter are available from several organizations such as:

- The International Agency for Research on Cancer (IARC)
- World Health Organization (WHO)
- US Surveillance, Epidemiology and End Results (SEER)
- National Cancer Institute (NCI)
- National Cancer Registries

Epidemiology and Cancer Statistics in Europe and in the World

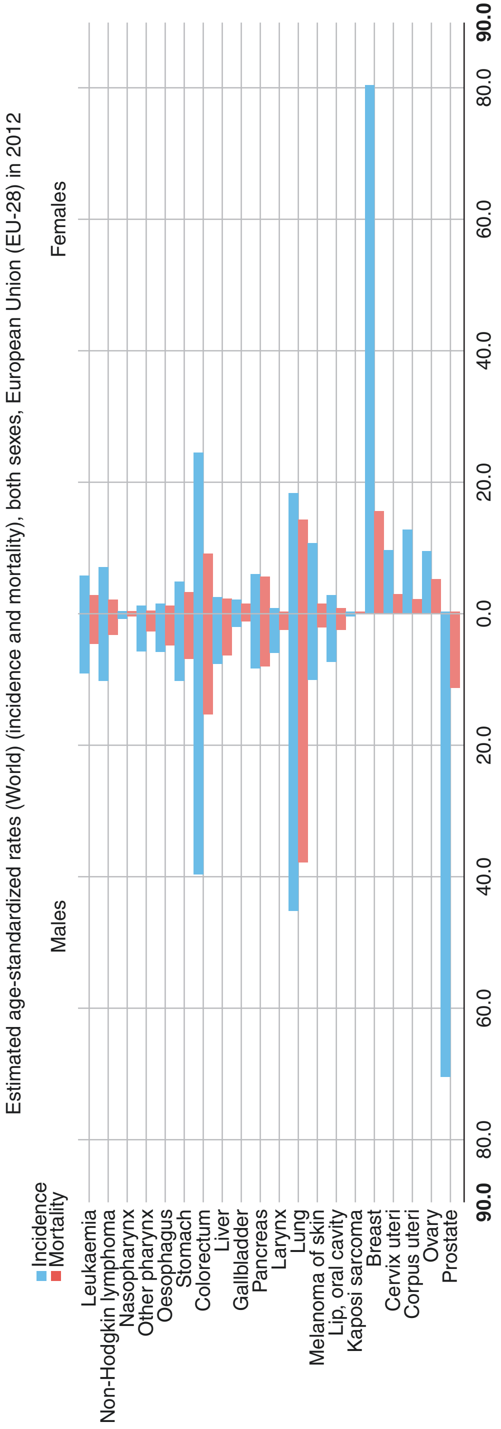
According to the American Cancer society, one out of every two men and one out of every three women will develop cancer during their lifetime. And in 2012, the burden of cancer in the 28 Member States of the European Union (EU) was 1.43 million new cases and 0.71 million deaths among men and 1.2 million new cases and 0.55 million deaths among women[3]. Cancers of the breast, cervix and colorectum were the most frequent ones in the European Union with 0.26 million deaths [3]. In the world, an estimated 14.1 million new cancer cases have occurred in 2012. And lung, female breast, colorectal and stomach cancers represent more than 40% of the cancers diagnosed in the world. Lung cancer was the most common cancer (16.7% of all new cases) in men, whereas breast cancer was the most common in women with 25.2% of all new cases (Fig. 2.1) [3].

As illustrated by Fig. 2.2, differences between the types of cancers observed in the world certainly reflect life habits and in particular the effect of screening for cervix cancer and the smoking habits for lung cancer (Fig. 2.3).

The risk of developing cancer before age 75 is estimated in the world at 21% for men and 16.4% for women, and the risk of dying from cancer before age 75 is 12.7% for men and 8.4% for women [3]. In Europe, those risks are higher with 29.5% for men and 21.5% for women, and also the risks of dying before age 75 are superior with 15.7% for men and 9.3% for women. Those differences are being clearly linked to ageing of the population, lifestyle factors and also the fact that infectious disease are less prevalent in Europe.

Being a disease of ageing, there is a great variation between young and adults with a peak of incidence from 50 to 80 years of age as shown in the figure below (Fig. 2.4).

A difference in the type of cancer is also observed with the youngest portion of the population being more at risk of developing testis, leukaemia, brain or thyroid cancer, and the oldest part of the population more at risk for breast, colorectal and lung cancers [5].



Data source: GLOBOCAN 2012
Graph production: Global Cancer Observatory (http://gco.iarc.fr/)
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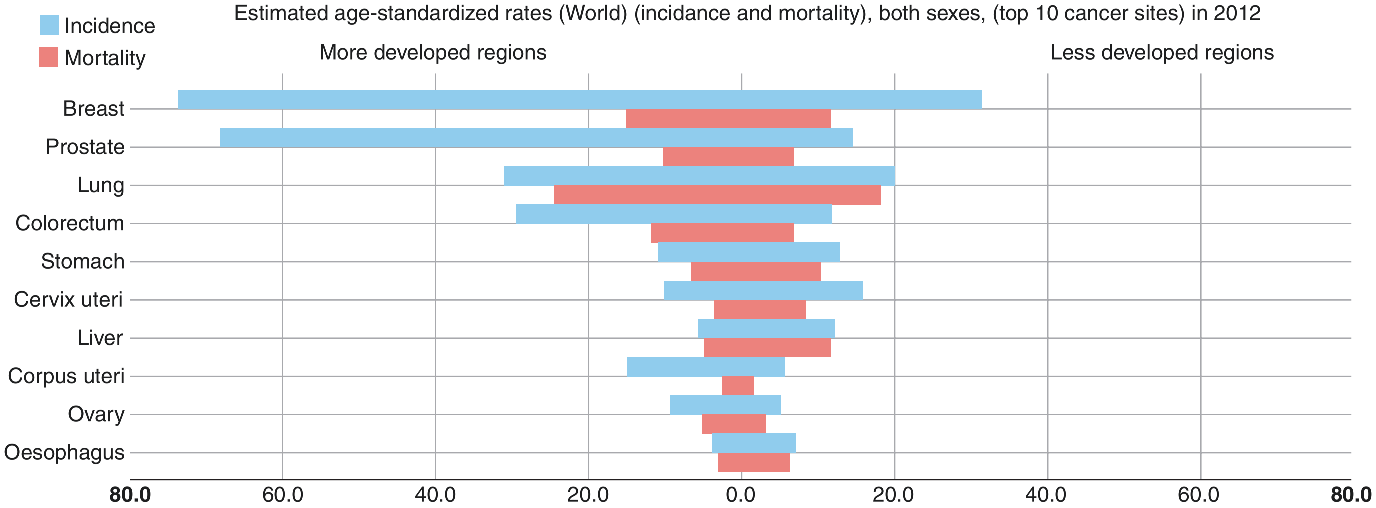
Fig. 2.1 Differences between men and women in EU in 2012



Data source: GLOBOCAN 2012
Graph production: Global Cancer Observatory (http://gco.iarc.fr/)
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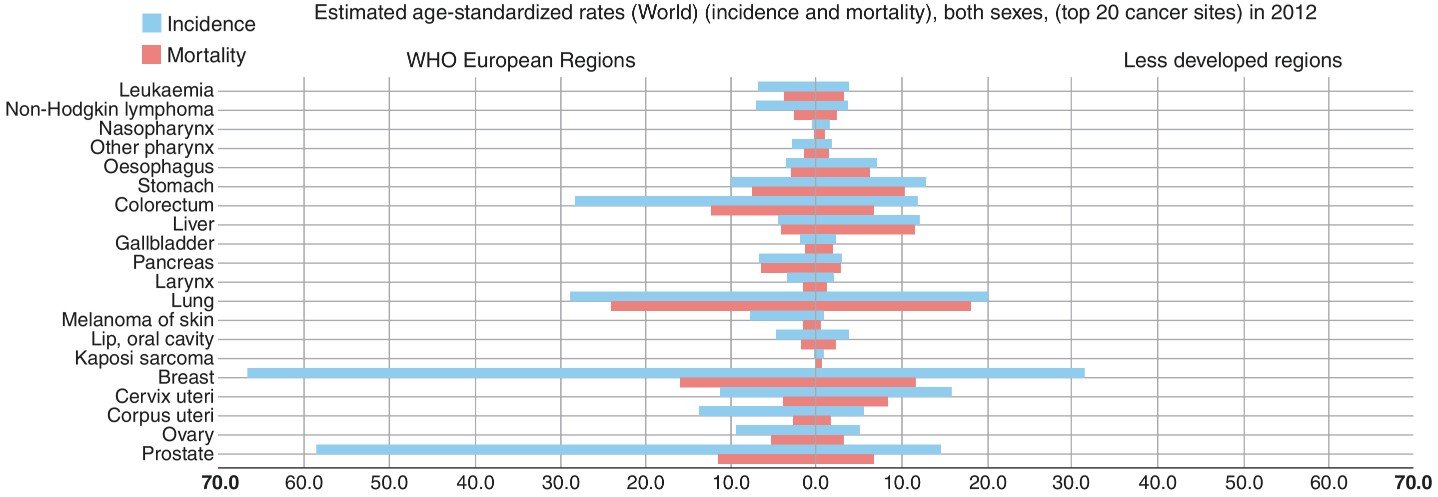
Fig. 2.2 Differences between developed and less developed regions in 2012



Data source: GLOBOCAN 2012
Graph production: Global Cancer Observatory (http://gco.iarc.fr/)
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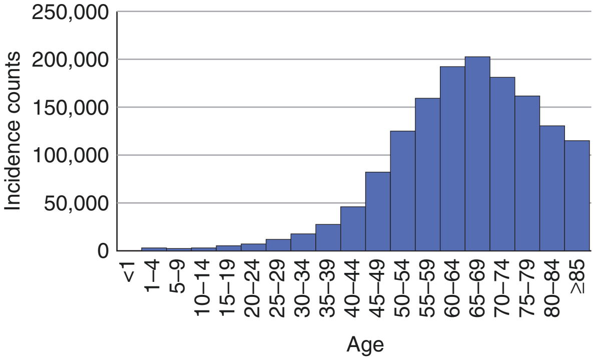
Fig. 2.3 Differences between European regions and less developed regions

Fig. 2.4 Invasive cancer incidence, by age, in the USA, 2009 [4]



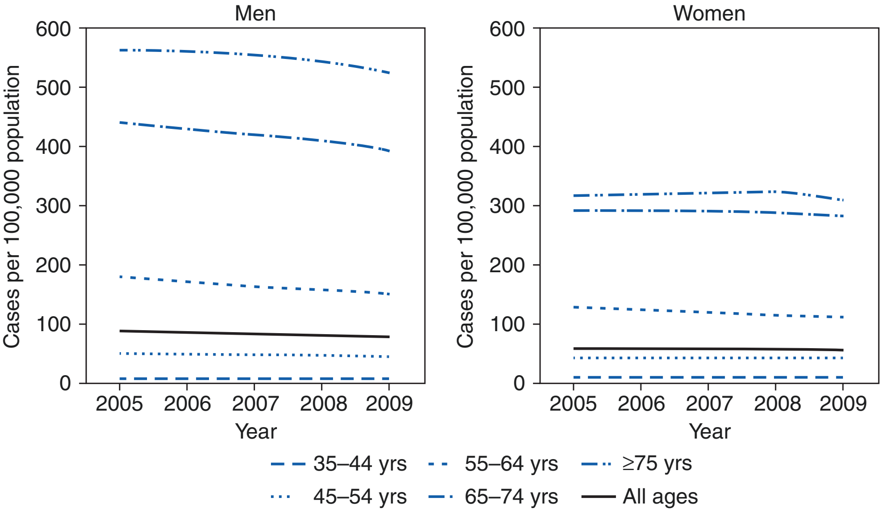


Fig. 2.5 Rate (lung cancer incidence per 100,000) of invasive lung cancer cases among men and women, by age group. United States, 2005–2009 [6]

But the variation in the incidence of cancer between different countries and sometimes regions, and also mortality rates, can certainly be explained by changes in the environmental factors and lifestyle, as well as benefits from early detection and screening measures. The example of the decrease of lung cancer in the USA for men aged ≥75 years and both men and women from 2005 to 2009 illustrates the cessation of smoking in this population (Fig. 2.5).

Cancer Versus Other Diseases

Non-communicable diseases (NCDs), such as cardiovascular diseases (heart attacks and stroke), cancer, diabetes and chronic lung disease, kill 40 million people each year in the world, representing 70% of all deaths globally. And 15 million people die between the ages of 30 and 69 every year from a NCD, and over 80% of these "premature" deaths occur in low- and middle-income countries.

The NCD diseases tend to be chronic and the result of a combination of genetic, physiological, environmental and behavioural factors. Children, adults and the elderly are all vulnerable to the risk factors contributing to NCDs, such as unhealthy diets, physical inactivity and exposure to tobacco smoke or the harmful use of alcohol.

Cardiovascular diseases (CVD) account for most of those NCD deaths, with 17.7 million people annually, followed by cancers (8.8 million), respiratory diseases (3.9million) and diabetes (1.6 million) [7].

Cancer is generally considered as the second leading cause of death in the developed countries, after cardiovascular disease (CVD), but a recent study conducted in Europe in 2016 [8] showed that "CVD mortality rates have been falling by as much as 25 to 50% over the past 10 years. Along with this decline, 12 countries now record more deaths from cancer each year for men, and two countries for women (Israel and Denmark) – despite cancer accounting for less than half the number of deaths than CVD in Europe as a whole. Transition from CVD to cancer as the most common cause of death in men was seen first in France and then in Spain".

Effect of Therapy on Cancer Survival

To assess the impact of intervention on cancer, survival rates over a fixed period of time after initial diagnosis are the most common method used. The 5-year survival rate is a common arbitrary measure obtained from population-based cancer studies and is an optimum method to assess and monitor the effectiveness of patient care. Its variation will provide useful information of the impact of treatment, diagnostic techniques and awareness or screening strategies between countries.

Globally, treatment of cancer has shown an effect on overall survival rates in the world since more than 40 years, but international comparison reveals differences that can certainly be attributed to the differences in access to early diagnosis and optimum treatment. For example, in the USA, the number of cancer survivors continues to grow although incidence is declining for men and is stable for women [9]. The CONCORD Working Group has also showed that 5-year survival from colon and breast cancer has increased in most developed countries and can reach up to 85% for breast cancer in some developed countries [10].

And more than one-half (56%) of survivors in the USA have been diagnosed within the past 10 years, and 47% are over 70 years of age [10].

Oncology nurses in particular but also nurses working in other fields and especially with people older than 70 years will be facing a large number of survivors. Those individuals have been through a difficult period of acute treatment but generally have a good quality of life and very low or even no side effects.

Risk Factors

Actually, it is not possible to know why a person will develop cancer and another will not. And it is not possible to control ageing, which is the major risk factor for cancer, or change one's family history. But several risk factors have been identified through epidemiology studies in which scientists studied large groups of individuals and compare those who develop cancer with those who did not. These studies showed that individuals who develop cancer had different behaviours or exposition to certain substances than those who did not develop cancer as, for example, smoking in lung cancer.

But from a patient's perspective, no study can prove that a specific behaviour or consumption of a substance has been the unique cause of his or her cancer.

Identification of risk factors and a better knowledge of the carcinogenesis multistep process give public health authorities useful tools to lower cancer incidence, but unfortunately, avoidance of known risk factors remains a challenge.

Reasons to avoid risk factors such as tobacco, overweight and alcohol use are also linked to the fact that there are also implicated in the main chronic diseases, such as heart disease, stroke, chronic respiratory disease and diabetes.

According to the American Association for Cancer Research (AACR), the main preventable risk factors in 2012 were:

- Tobacco (33%)
- Excess weight and obesity (20%)
- Diet (5%)
- Lack of exercise (5%)
- Occupation (5%)
- Viruses (5%)
- Family history (5%)
- Alcohol (3%)
- UV and ionizing radiations (2%)
- Prescription drugs (1%)
- Reproductive factors (3%)
- Pollution (2%)
- Unknown (11%)

WHO has established in 2012 that excess body mass index increases the risk of several cancer types such as postmenopausal breast (24%), uterine (22%), colon (18%), kidney (13%), gallbladder (6.7%), pancreatic (5.6%), rectal (5.2%), oesophageal (3.6%) and ovarian (1.9%) cancer. And the American Cancer Society estimates that this excess body weight combined with physical inactivity and excess of alcohol consumption and poor nutrition account for 20% of all cancers and could be prevented.

Regarding infectious agents, a study conducted in 2016 [11] has identified five different agents implicated in the development of cancer in the world for both sex. The first is *Helicobacter pylori* for 36% and then human papillomavirus (29%), hepatitis B virus (19%), hepatitis C virus (7.7%) and other agents for 8.1%. Different cancers due to infectious agents could be prevented through vaccination or the treatment of the infection but also with behavioural changes.

And many of the skin cancer cases due to excessive sun exposure and use of indoor tanning devices could be prevented by avoiding those risk factors.

Prevention and Early Detection

Prevention of cancer can be defined as specific measures aiming at preventing its development or occurrence and having a marked effect on mortality rates.

Three levels are generally defined:

- *Primary prevention* includes a set of measures aiming to avoid cancer occurrence and so to reduce cancer incidence.
- *Secondary prevention* or early detection includes measures aiming to reduce cancer prevalence and screening measures to detect cancer as early as possible. It includes also access to optimal care.
- *Tertiary prevention* includes measures such as prophylactic mastectomy for women at high risk of breast cancer but also chemoprevention or management of recurrence or treatment complications and its after-effects (Fig. 2.6).

Nurses clearly have a key role to play in those different levels of cancer prevention, by identifying individuals at risk but also in promoting healthy lifestyle and regular screening measures.

Regarding the *primary prevention* level, several measures have already been described, but in Europe, the European code against cancer has established 12 recommendations based on those known factors with the aim of preventing cancer by helping people to adopt healthier lifestyles and of boosting cancer prevention. It is estimated that almost half of all deaths due to cancer in Europe could be avoided if everyone followed these recommendations.

The European code against cancer was prepared by cancer specialists, scientists and other experts to increase the awareness of European citizens about efficient ways to prevent cancer. The first edition of the code was published in 1987 (Fig. 2.7).

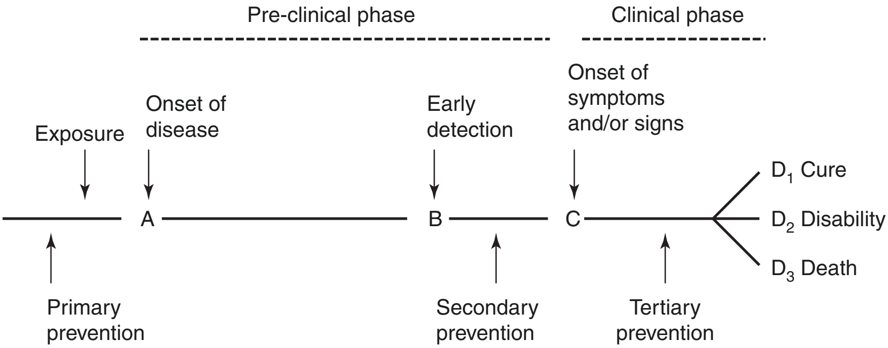
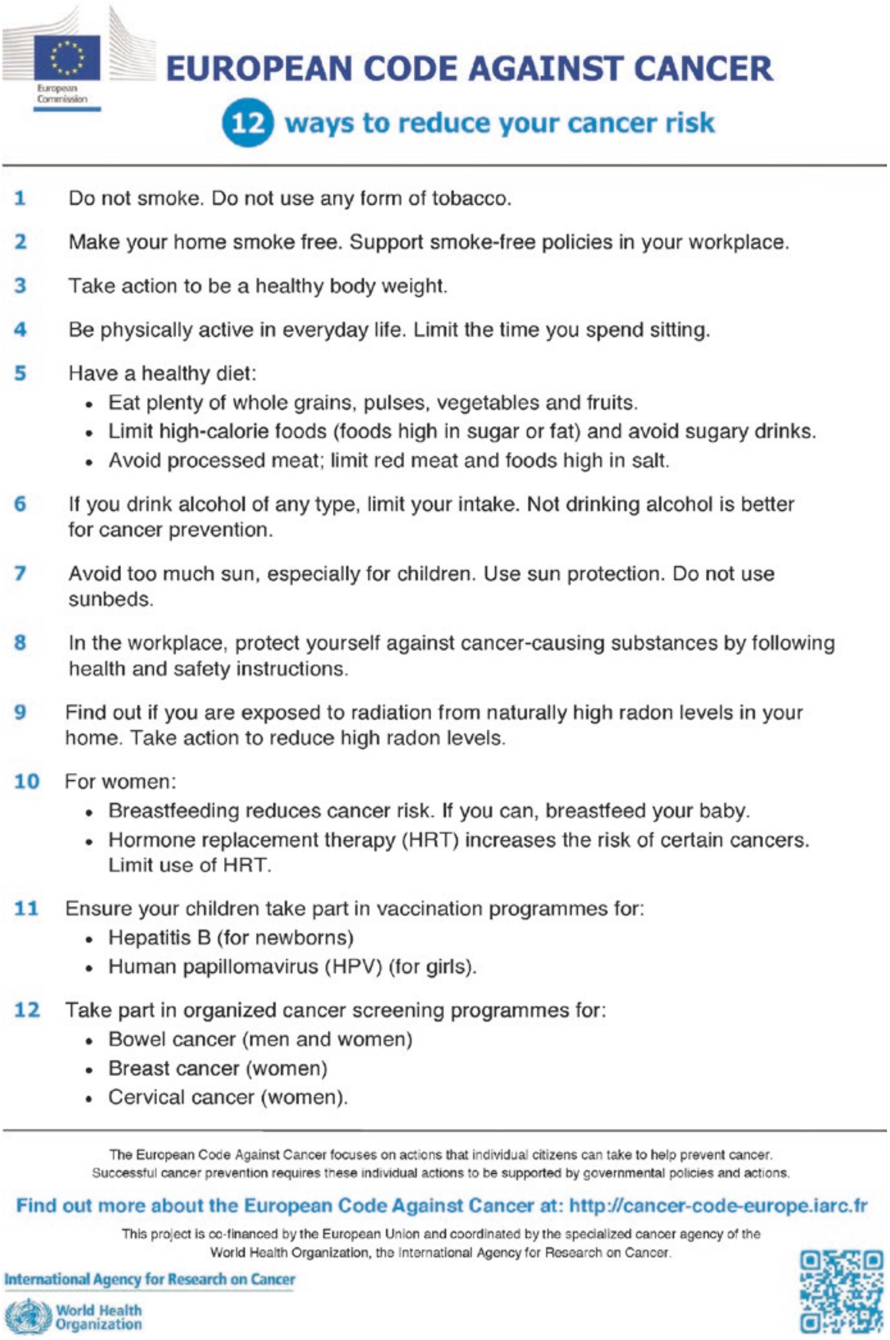


Fig. 2.6 Natural history of cancer and levels of prevention [12]



European Commission

EUROPEAN CODE AGAINST CANCER

12 ways to reduce your cancer risk

1 Do not smoke. Do not use any form of tobacco.

2 Make your home smoke free. Support smoke-free policies in your workplace.

3 Take action to be a healthy body weight.

4 Be physically active in everyday life. Limit the time you spend sitting.

5 Have a healthy diet:
- Eat plenty of whole grains, pulses, vegetables and fruits.
- Limit high-calorie foods (foods high in sugar or fat) and avoid sugary drinks.
- Avoid processed meat; limit red meat and foods high in salt.

6 If you drink alcohol of any type, limit your intake. Not drinking alcohol is better for cancer prevention.

7 Avoid too much sun, especially for children. Use sun protection. Do not use sunbeds.

8 In the workplace, protect yourself against cancer-causing substances by following health and safety instructions.

9 Find out if you are exposed to radiation from naturally high radon levels in your home. Take action to reduce high radon levels.

10 For women:
- Breastfeeding reduces cancer risk. If you can, breastfeed your baby.
- Hormone replacement therapy (HRT) increases the risk of certain cancers. Limit use of HRT.

11 Ensure your children take part in vaccination programmes for:
- Hepatitis B (for newborns)
- Human papillomavirus (HPV) (for girls).

12 Take part in organized cancer screening programmes for:
- Bowel cancer (men and women)
- Breast cancer (women)
- Cervical cancer (women).

The European Code Against Cancer focuses on actions that individual citizens can take to help prevent cancer. Successful cancer prevention requires these individual actions to be supported by governmental policies and actions.

Find out more about the European Code Against Cancer at: http://cancer-code-europe.iarc.fr

This project is co-financed by the European Union and coordinated by the specialized cancer agency of the World Health Organization, the International Agency for Research on Cancer.

International Agency for Research on Cancer

World Health Organization

Fig. 2.7 European code against cancer

Cancer Screening

Cancer screening is the *secondary* and sometimes *tertiary* level of prevention and aims to detect, as early as possible, and in the absence of symptoms, lesions (skin, polyps) that could or be a cancerous lesion or could evolve towards cancer. Screening is the possible identification of the disease or defects by the use of specific procedures (tests, examinations).

Screening can be done on an individual basis and is named opportunistic or can be organized as a population-based screening and must fulfil a certain number of criteria. According to WHO [13], a NCCP (national cancer control programme) is a "public health programme designed to reduce the number of cancer cases and deaths and improve quality of life of cancer patients. This is done by implementing systematic, equitable and evidence-based strategies for prevention, early detection, diagnosis, treatment and palliation using available resources".

But some factors have to be taken into account when choosing a screening technique:

- Sensitivity: effectiveness in detecting cancer for individuals who have the disease
- Sensibility: extent to which a negative result really corresponds to individuals who are free of the disease
- Positive predictive value: extent to which individuals have the disease in those with a positive result
- Negative predictive value: extent to which individuals are free of the disease in those with a negative result
- Acceptability: extent to which the targeted population agrees to be tested

Successful population-based screening programme should also:

- Target a common cancer, with high morbidity and mortality and remaining at a preclinical stage for a long time and possible to treat at an early stage.
- Ensure that an effective treatment is available.
- Check that test procedures are acceptable, safe and not too expensive.

But screening programmes have to take into account the potential psychological and economic consequences of false positive or false negative results and avoid overdiagnosis and treatment [14]. Physicians and nurses are willing to have an effective communication with their patients and present screening procedures with their potentials benefits and harms [15].

At a national level, it is essential that the organization of the screening programme allows a large proportion of the target group to be screened and that individuals presenting abnormalities will receive appropriate diagnosis and therapy. Guidelines should be agreed by all the actors of the programme, especially for:

- Frequency and ages of screening
- Quality control for the screening tests
- Established procedure for referral and treatment when needed
- Specific information guidelines inviting the target population for the screening but also recall individuals for the next test, follow those with abnormalities, but also monitor and evaluate the programme.

Such structured programme is actually not available in each country in the world, with a difference between developed and less developed countries.

When evaluating screening procedures, some common biases have to be taken into account, and they include information bias and selection bias. In the case of information bias, data is not accurate, and this could be due to faulty instruments or wrong data, whereas in selection bias, the population studied is not representative of the larger population, because a lot of individuals are lost during the follow-up or because of inadequate sampling process.

Four biases appear in screening for cancer [16], which are [17]:

- *Lead time* bias corresponds to the systematic error of apparent increased survival from detecting disease in an early stage.
- *Length time* bias is the systematic error from detecting cancer with a long latency or preclinical period.
- *Detection* bias meaning the detection of insignificant disease.
- *Referral/volunteer* bias being the systematic error from detecting the disease in individuals who have a propensity to seek health care.

In 2003, the European Council recommended population-based screening programmes for three cancers corresponding to the criteria already mentioned, and it was breast, colon and cervical cancer. Three following measures were recommended:

- Mammography for women aged 50–69 years
- Faecal occult blood test (FOBTs) for men and women aged 50–74 years
- Papanicolaou testing for women from 20 to 30 years.

Following those recommendations, a recent study [18] has shown a global improvement in access to screening in a large number of Member States of the European Union and especially a remarkable progress for colorectal cancer screening since, compared to 2007, the number of men and women having access to population-based colorectal screening in 2016 has almost doubled (57.9 million *vs.* 110.3 million).

But there are still ongoing discussion concerning screening tests, especially how to choose those who have demonstrated a reduction in cancer deaths, which is the final aim of such test.

We will now describe the “pros and cons” of some specific screening procedure for the most common cancers:

Breast Cancer

Mammography is considered as the most important procedure for breast cancer detection and diagnosis, and the EUSOBI (European Society of Breast Imaging) in collaboration with Europa Donna – The European Breast Cancer Coalition has established in 2017 the following information for all women [19]:

- Direct digital mammography should be preferred to film-screen or phosphor plates.
- Screening (in asymptomatic women) should be distinguished from diagnosis (in symptomatic women).
- A breast symptom has to be considered even after a negative mammogram.
- Digital breast tomosynthesis increases cancer detection and decreases the recall rate.
- Contrast-enhanced spectral mammography can help in cancer detection and lesion characterization.

The European guidelines recommend a 2-year interval for women aged 50 to 70 years of age. Depending on national or regional programmes, mammography can be offered from 40 and be extended until 75 years. Those differences are being attributed to cultural differences, economic situation, technical limits and also breast cancer prevalence.

Between 40 and 50 years, it is recommended to perform the exam every year up to 45–50 because of the high density of the breast. Extension of screening after 70 years is of course depending on the general health condition of the women.

Mammography, like other screening procedure, is not perfect, and two main limits have to be cited, the first one being its limit in the diagnostic performance with an actual estimate of up to 28% of breast cancer not seen [20] and especially in younger women with dense breasts and the second one being overdiagnosis. As established by the Euroscreen Working Group in 2014, “for every 1000 women screened from 50 to 69 years of age, 7–9 breast cancer deaths are avoided, 4 breast cancers are over-diagnosed, 170 women have at least one recall followed by noninvasive assessment with a negative result and 30 women have at least one recall followed by invasive procedures with a negative result [21]”.

Screening by MRI (magnetic resonance imaging) is reserved to women who carry *BRCA1/BRCA2* mutations or with a strong family history.

Colon Cancer

In contrast with screening of breast cancer, different tests can be used to screen for polyps and for colorectal cancer. The American Cancer Society [22] encourages any men and women at an *average risk*[2] to be screened and makes a distinction between:

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[2] See Glossary.

(a) Tests that can find polyps and cancer:
    - Colonoscopy
    - Virtual colonoscopy
    - Flexible sigmoidoscopy
    - Double-contrast barium enema

(b) Tests that mainly find cancer:
    - Faecal immunochemical test (FIT)
    - Guaiac-based faecal occult blood test (gFOBT)
    - Stool DNA test every 3 years

A combination of those tests starting at age 50 is detailed as follows [23]:

- Faecal occult blood test (FOBT) – every year
- Flexible sigmoidoscopy – every 5 years
- Faecal occult blood test (FOBT) – annually – and flexible sigmoidoscopy every 5 years
- Double-contrast barium enema (DCBE) every year
- Colonoscopy every 10 years

Recent studies have shown that all these tests are effective at reducing mortality from colorectal cancer and that all are acceptable. Concerning the FOBT test, which implies a diet before performing it, the FIT (faecal immunochemical test) is more patient-friendly since there are no dietary restrictions to follow.

As for other screening procedure in the general population for individuals that do not have any symptoms of the disease, compliance remains the greatest challenge.

Specific guidelines with colonoscopy only are designed for individuals at high risk. The surveillance will start at a younger age, and a yearly exam can be recommended, in families with a history of FAP (familial adenomatous polyposis) or Lynch syndrome.

Cervical Cancer

Although cervical cancer is less frequent in developed countries, it still affects women in the Western world being, for example, the 10th most frequent cancer in France and causing 1100 deaths per year [24] in this country. Cervical cancer is also the most preventable malignancy among human cancer since its genesis is essentially linked to an infection of the cervix due to HPV (human papillomavirus) [25].

But since four decades, incidence of cervical cancer and mortality has decreased in Europe and North America with the introduction of screening for asymptomatic women. This population-based screening is done with regular Pap (Papanicolaou) tests consisting in a microscopic exam of the cells from the cervix. This exam will result negative with no intraepithelial lesion or malignancy or showing epithelial abnormalities or malignant cells.

This screening with the Pap test is recommended for women from around 20 years, with an interval that can vary from a country to another but is generally of 3 years if there have been two normal exams at 1-year interval.

New knowledge about HPV has also led the American Cancer Society to recommend using HPV DNA test in combination with the Pap test but only for women aged 30 years and older and for women who have abnormal Pap test results.

Although controversial like other vaccine, vaccination with HPV is recommended by several heath authorities and should be given to girls and boys at age 11 or 12. But since the HPV vaccine does not prevent against all types of HPV viruses, women who have received the vaccination still need to have regular Pap tests.

Prostate Cancer

Despite the fact that prostate cancer grows slowly and that there is time for early detection and effective treatment, the benefit of a population-based screening for prostate cancer has not been established. Similar results have emerged from two studies conducted in Europe (ERSPC [26]) and the USA (PLCO [27]) showing that there is no sufficient evidence to assess the balance between benefits and risks in men younger than 75 years. The main result of the PLCO study was that "after 7 to 10 years of follow-up, the rate of death from prostate cancer was very low and did not differ significantly between the group being screened annually and the control group". Treatment-related complications, such as incontinence or impotence, are particularly in disadvantage of screening even more in cases of overdiagnosis.

So screening recommendations from various organizations now differ but are still discussed on an individual basis and consist of digital rectal examination and PSA testing.

Melanoma

Skin cancers such as melanoma and basal and squamous cell carcinoma cannot be screened on a population-based programme [28]. Basal and squamous cell carcinomas are called the nonmelanoma skin cancer and represent the vast majority of skin cancer but do not lead to death. Concerning melanoma, its incidence, mortality and survival rates in Europe are variable and certainly linked to inequalities in the access to skin cancer early detection and prevention and also case registration [29].

Early detection by visual skin evaluation by a clinician does not have good sensitivity and specificity to detect melanoma and cannot be considered as a tool for population screening. Regarding primary prevention, such as avoiding risk factors, there is a lack of national programmes and insufficient registration of skin cancers to document the reality of the situation.

Actually, there is a consensus to pursue information campaign for the general population and insist on minimizing exposure to ultraviolet radiation especially for children, adolescents and young adults.

Another way of preventing skin cancer is to raise awareness on the risk factors for melanoma:

- Personal or familial history of melanoma
- Fair complexion
- Use of indoor tanning beds
- Sunburn history or previous skin cancer
- >2 dysplastic naevi
- Multiple naevi (>40)
- Atypical mole (dysplastic naevus)

If a person has one of those risk factors, clinical examination by a dermatologist should be done using the ABCDE rule meaning looking for asymmetry, border irregularity, nonuniform colour, diameter >6 mm and evolution over time. Videoscopy with digital computer-aided evaluation is sometimes used on an individual basis.

Lung Cancer

Three screening procedures can be used to detect a lung cancer, generally in a heavy smoker or former smoker:

- Cytology of a sputum
- Chest X-ray
- Low-dose spiral CT scan

Whereas cytology and chest X-ray are used for early symptoms, low-dose spiral CT scan can be considered as a screening for a healthy individual. The National Lung Screening Trial (NLST) conducted by the American College of Radiology Imaging Network and the National Cancer Institute has taken place in the USA since 2002 and has showed a reduction in deaths from CT screening compared to X-ray [30]. But those encouraging results have not been repeated in another study published in 2011 [31].

Those controversial findings make actually the CT screening a possibility to be discussed on an individual basis, but of course, the best way to avoid lung cancer is not to smoke or quit smoking.

To conclude, it is essential to stress that even though progresses will be made in cancer prevention with chemoprevention or new tools such as DNA analysis and easy to access screening procedures, the primary prevention and especially the avoidance of the known risk factors is one of the keys to reduce the global burden of cancer in the world.

Glossary

Age-standardized rate (ASR) Age-standardized rate is the rate that a population would have if it had a standard age structure [2]. It is necessary to use standardization when comparing several populations with differences in regard to age since age is an important risk factor of developing a cancer.

Average risk Average risk for colon cancer is a man or a woman aged from 50 years and with no previous history of adenoma or colon cancer, no previous inflammatory disease of the colon and no family history (one parent from the 1st degree or two parents from the 2nd degree).

Human development index (HDI) Human development index is a composite index of three dimensions of human development: (i) life expectancy (based on life expectancy at birth); (ii) educational attainment (based on a combination of adult literacy rate and primary to tertiary education enrolment rates) and (iii) income (based on GDP per capita adjusted for purchasing power parity (PPP US$)). Countries were grouped into four levels of HDI according to the United Nations Development Programme estimates for 2012: very high HDI, high HDI, medium HDI and low HDI.

Incidence Incidence is the number of new cases in a specified population during a given period and is generally expressed for a population of 100,000 persons yearly.

Morbidity Morbidity refers to having a disease or [32] a symptom of disease or to the amount of disease within a population. Morbidity also refers to medical problems caused by a treatment.

Mortality Mortality is the number of persons who died from the disease in a given period in a specified population and is given as an absolute number of deaths per year or as a rate standardized per 100,000.

Prevalence Prevalence of a specific cancer is the number of individuals who have been diagnosed with that type of cancer in a defined population during a fixed time and who are still living at the end of this given year. It is usually given as a number and a percentage of 100,000 persons.

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3

Evidence-Based Nursing in Basic Anticancer Treatment: Management of the Most Important Side Effects

Clotilde Messin and Cathie Amrhein

Abstract

Every cancer is unique. Each patient will benefit from the best therapeutic strategy adapted to their situation. Surgery, radiotherapy, and chemotherapy remain essential treatments. Used alone or in combination, the goal will be the same: to kill all cancerous cells while sparing, as much as possible, healthy tissues to limit undesirable effects. These rapid, cumulative, or delayed side effects have an impact on the entire body of the patient. In this chapter, we address only the main effects, hematological disorders, digestive disorders, alterations of body image, fatigue, and sexual health disorder. It is the responsibility of nurses to respect and empower patients by providing personalized counseling and developing their education. Today, cancer pathology is increasingly considered chronic. This chronicity implies long-term follow-up of the person affected.

Keywords

Side effects · Chronicity · Patient education · Body image · Fatigue · Sexuality Teamwork

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C. Messin
Ecole Santé sociale Sud Est, Lyon, France
e-mail: messin@essse.fr

C. Amrhein (✉)
University Hospital Strasbourg, Strasbourg, France
e-mail: Cathie.Amrhein@chru-strasbourg.fr

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Introduction

The complexity of tumor diseases and the multiplicity of possible treatments require multidisciplinary collegial decisions. In addition, not all tumors are sensitive to the same therapeutics: this requires the implementation of protocols in a medical collective known as a multidisciplinary collaborative meeting [1].

Every cancer is unique. Each patient can benefit from the best therapeutic strategy through a personal care plan. These strategies are based on the recommendations of the National Comprehensive Cancer Network (NCCN), the National Intergroup Thesauri. (International references based on works done by recognized professional organizations), and the Standards and Recommendations (SOR) [2] of the Institut National du Cancer (INCa) in France.

Therapeutic strategies are:

- Essential to ensure that the patient benefits from the best of each treatment by limiting toxicities
- Designed to ensure the greatest chance of recovery from the outset
- Reviewed at the time of relapse to extend the survival time and maintain comfort

A study has shown that management of cancer diseases is much better performed through a multidisciplinary team (MDT) decision [3]. Furthermore, patients should be actively integrated into the MDT process to ensure that they have an informed choice regarding their treatment and to ensure that the recommendations are based on the best available patient-based and clinical evidence [4].

Generalities Regarding the Main Treatments

Let us start first by reviewing the generalities of the main anticancer treatments.

Surgery was the first therapeutic method locally used in the treatment of cancers and still retains a place of choice nowadays.

This treatment has several indications:

- *Exploratory surgery* is diagnostic surgery. Collection of anatomopathological samples of the tumor allows us to make the diagnosis of cancer with certainty and to define its characteristics (histology, chemosensitivity, radiosensitivity, doubling time), which will be taken into account for the therapeutic strategy. This surgical procedure makes it possible to evaluate the extension of the tumor locally, the invasion of the surrounding tissues, and the risk of lymphatic extension.
- *Curative surgery* consists of performing total excision of the tumor with a margin of safety in the surrounding healthy tissue to leave no cancer cells. It can sometimes be mutilating and cause disruption of the body image. For some cancers that are detected early or easily accessible, surgery can be the only treatment

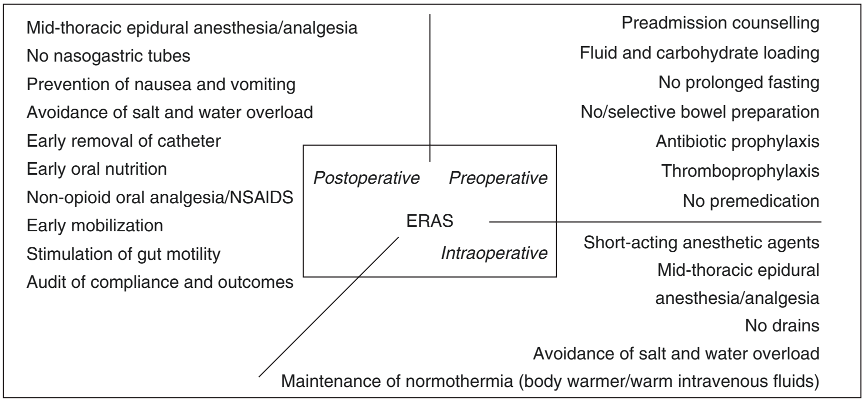
used to treat the cancer. Sometimes, the goal is to reduce the tumor volume to facilitate the second step of treatment with radiotherapy or chemotherapy.
- *Restorative or plastic surgery* can correct mutilations that have been necessary following total removal of an organ.
- *Palliative surgery* is aimed at restoring function (e.g., by performing a colostomy or ureterostomy), ensuring comfort (e.g., by removing a necrotic, ulcerated, or compressive tumor), and/or reducing pain by interrupting pain sensitivity pathways.

All current operative techniques have their place, but we can observe that less invasive intervention and ambulatory surgery are increasingly preferred. Moreover, studies show that a large proportion of patients would prefer to walk to the operating theater for their operation if they have the choice. Such a process enhances patient autonomy and may reduce delays in transferring patients to the theater [5]. This highlights the fact that having the choice between two options, patients feel more empowered in the decision making and more willing to adopt change [6].

Hospitals such as the Gustave Roussy Institute in Paris apply this process for patients with breast cancer and have observed reductions in patients' anxiety and need for premedication [7].

Enhanced recovery after surgery (ERAS)—a "fast track" program initiated in the 1990s by Professor Henrik Kehlet—has returned to center stage. This program is aimed at modifying physiological and psychological responses to surgery. It results in reduced complications and a shorter hospital stay, earlier return of bowel function, and earlier resumption of normal activities. This program is based on a multiprofessional collaboration [8].

Melnyk et al.



Radiotherapy is a local treatment, which attempts to destroy cancer cells by damaging the DNA with radiation: electrons, photons, or protons. In France, 50% of cancer patients are treated with radiotherapy [2].

The more the tissue is oxygenated via blood vessels, the more successful the radiation will be. Tissues with fewer blood vessels are less radiation sensitive.

Different techniques exist:

- *Transcutaneous*: brachytherapy for tumors that are easily accessible (via an interstitial needle or endocavity mold)
- *Metabolic*: through the oral pathway (radioactive iodine)

This treatment has different indications:

- *Curative radiotherapy*: exclusive or associated with surgery or/and with chemotherapy
- *Palliative radiotherapy*: to relief pain in bone and liver metastases, or to remove compression by brain or spinal metastases

The challenge of this treatment is to not touch the healthy surrounding cells, which would lead to side effects. Significant progress has been made in this regard, and the areas where radiation will be delivered (i.e, the tumor) can be better targeted in three dimensions. Moreover, fourth-generation ratiotherapy is a controlled radiotherapy can irradiate a moving lung tumor while protecting healthy tissue [9].

To reduce side effects, we have to wait until the tissue regenerates. That is why the treatment is divided into a certain number of sessions spread over 5–7 weeks.

Undesirable effects can occur early and/or be inconvenient but without gravity: cutaneous disorders (of variable intensity, from erythema to exudative epidermitis) and fatigue linked to cell destruction, with increased anabolic processes, and also linked to travel to the treatment center.

Other effects are more specific to the irradiated area:

- Xerostomia and dysgeusia with irradiation of the ear, nose, and throat (ENT) sphere
- Cystitis, proctitis, diarrhea, nausea, and vomiting with irradiation of the abdominopelvic sphere

With regard to the doses and duration of the irradiation, patients may also suffer late side effects, which can appear 6, 12, or 18 months after treatment: radiation hail (damage of small intestine due to radiation), pulmonary fibrosis, radiation pericarditis, etc.

Flash radiotherapy is a very promising technique in which the usual radiation dose is delivered within 200 ms, versus a duration of minutes with the classical technique. In a comparison of the flash technique with the conventional one in the treatment of lung cancer, it has been observed that no fibrosis appears after a radiation dose of under 20 Gy delivered via the flash technique, while fibrosis may be observed 6–8 months after irradiation with the conventional technique [9].

Cancer chemotherapy is a general treatment that affects all cells in the body: it is aimed at all cancer cells, regardless of where they have spread to, and metastases.

The treatment can be administrated intravenously, subcutaneously, intra-arterially, intrathecally, intrapleurally, intraperitoneally, or orally, with combinations of different drugs to combine different toxic modes of action and/or complementary actions to potentiate the curative effects.

It has been estimated that by 2020, 50% of patients will receive oral chemotherapy at home [10].

Oral chemotherapy can reduce certain side effects such as infection associated with the injection site, the risk of extravasation, treatment costs, hospitalization, and travel. Moreover, the patient has the advantage of receiving his or her treatment at home.

Chemotherapy has several indications:

- Curative chemotherapy: adjuvant or neoadjuvant therapy
- Palliative chemotherapy: the goal is to relieve pain after a benefit/risk evaluation for the patient

These drugs kill both cancer cells and healthy cells during cell multiplication. Hence, if a cell is resting, it will not be affected by the drug. Therefore, it is necessary to repeat the treatment.

Chemotherapy causes a large number of side effects, which are specific to each molecule that is part of the protocol. We talk about early, cumulative, or late side effects.

Since chemotherapy acts on all cells during division, rapidly dividing ones will be affected first—such as hematopoietic cells, digestive epithelial cells, or gonadal cells—which explains the main undesirable effects:

- Hematological toxicities, causing anemia, fatigue, infectious risk, hemorrhagic effects
- Toxicity to integuments, alopecia, brittle nails, mucositis
- Digestive disorders, nausea, vomiting
- Sexual health disorders

In general, chemotherapy dehydrates the body. It is necessary to involve the patient in daily monitoring of this. At an early stage we advise the patient to drink a bottle of water (and follow any medical recommendations regarding fluid intake), to moisturize the face and body with a moisturizer containing sun protection factor, and to moisturize the lips with a hydrating lip balm.

Surgery, radiotherapy, and chemotherapy are often used in association either successively or in parallel. Other therapies—such as targeted therapies, hormone therapy, immunotherapy, vaccination, gene therapies, monoclonal antibodies, radiofrequency therapy, or cryotherapy for metastases—may complete the proposed therapeutic strategy.

Today, cancer is increasingly considered a chronic disease. This supposes that there will be variations in the physical and psychological states of the patient over time. This chronicity implies the need for long-term follow-up of the affected person. Chronic illness requires education and coping strategies.

According to J.M. Lubkin, “Chronicity is a state of malaise produced by a disease or an invalidity requiring medico-social interventions affecting several aspects of the life of the persons concerned” [11]. Chronicity comprises absence of healing, and this perspective changes the caregiver’s type of care. Caregivers talk about care pathways, while patients talk about their life to come; the two parties do not have the same vision.

With the growth in ambulatory services, patients return home earlier and have to care for themselves, away from the watchful eye of hospital health care professionals but with backup ensured by specially trained professionals. Nurses have a very important role to play in patient education to promote quality care.

Management of Prevalent Side Effects

Anticancer treatments induce a large number of side effects, which are specific to each treatment. We are talking about early, cumulative, or delayed side effects. Anticancer therapies also produce so-called indirect side effects, which have a significant impact on the entire body of the patient but are not due to the treatment itself—for example, anxiety, impaired body image, fatigue, anorexia, or sexual health disorders.

In the following sections we discuss the main adverse effects of anticancer therapies. This discussion is intentionally not exhaustive; other chapters in this volume treat those subjects in depth. The goal here is to stick to the mainstream and focus on nursing.

Hematological Toxicity: Myelotoxicity

Myelotoxicity results from the destruction of rapidly dividing hematopoietic stem cells. It is the major toxicity of cancer treatments, causing the earliest and most common complications. It concerns all anticancer drugs except for bleomycin.

Myelotoxicity is reversible but may be a limiting factor, especially in chemotherapy treatment, as it can put the patient at risk. Monitoring of the blood formula count is therefore mandatory before the start of any chemotherapy treatment and also during follow-up after radiotherapy. This assessment will be a key element in getting the “green light” to start treatment.

Myelotoxicity varies according to the molecules used and the doses and duration of the treatment. By the fourth day of treatment, white blood cell and platelet counts begin to fall. This decrease continues, and the nadir is usually reached between days 8 and 12. A return to normal is expected during the third week; hence, certain chemotherapy protocols are administered every 21 days. These attacks of myelotoxicity sometimes necessitate transfusions of globular concentrates or platelets.

The combination of several cytotoxic drugs increases the toxicity. All blood lines are affected by the destruction of hematopoietic stem cells, resulting in pancytopenia (reductions in the counts of all three blood cell lines: white blood cells, red blood cells, and platelets). This toxicity is poorly understood by patients because it is not visible. It therefore necessitates therapeutic education on the effects to be monitored, and also good reading of blood tests (Tables 3.1 and 3.2).

Table 3.1 World Health Organization hematological toxicity rating scale [12]

Hematological parameters	Toxicity				
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Hemoglobin (g/L)	<110	95–109	80–94	65–79	<65
Leukocytes (10^9/L)	>4	3.0–3.9	2.0–2.9	1.0–1.9	<1
Granulocytes (10^9/L)	<2	1.5–1.9	1.0–1.4	0.5–0.9	<0.5
Platelets (10^9/L)	<100	75–99	50–74	25–49	<25
Hemorrhage	None	Petechiae	Light bleeding	Important bleeding; transfusion indicated	Massive hemorrhage

Table 3.2 Summary of side effects due to myelotoxicity [13]

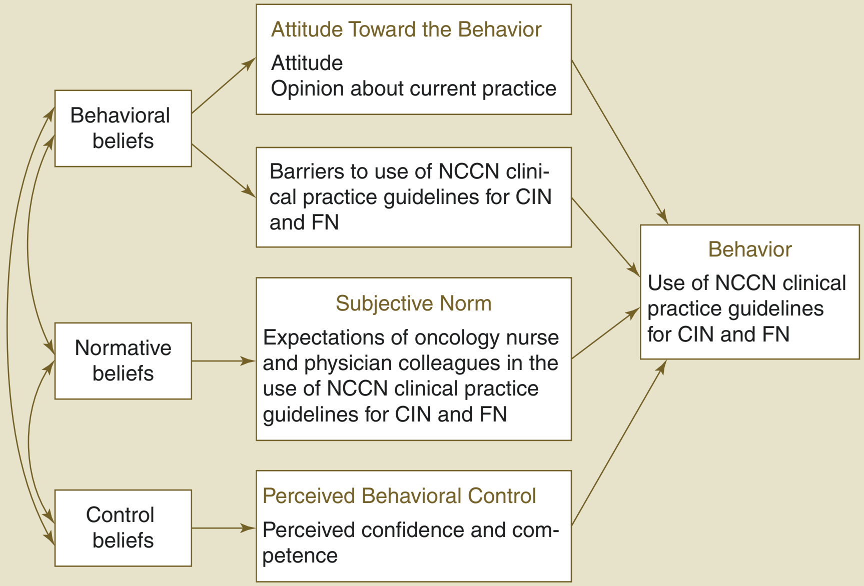
	Neutropenia	Anemia	Thrombopenia	Aplasia
Generalities	First manifestation of myelosuppression; it varies in severity and duration	Progressive after several weeks of treatment		Complication of pancytopenia or major pancytopenia Heavy chemotherapy
Norms	Neutropenia if the polynuclear neutrophil count is <500/mm^3	Anemia if the hemoglobin level is <11 g/dL in women or <12 g/dL in men	Bleeding risk if the platelet count is <20,000	White blood cell count <1000/mm^3 with polynuclear neutrophil count <500/mm^3
Signs	Hyperthermia	Cutaneomucosal, asthenia, polypnea, tachycardia, hypotension, headache, vertigo	All traces of blood: epistaxis, rectal bleeding, petechiae, hematuria, etc.	Blood sample Hyperthermia = febrile aplasia
Complications	Complication risks: 5% in the ambulatory care setting, 34% in the hospital care setting The most frequent cause of death (90% of cases) is bacterial infection		Bleeding	Major risk of infection Mortality

(continued)

Table 3.2 (continued)

	Neutropenia	Anemia	Thrombopenia	Aplasia
Patient education	Regular control of body temperature Hyperthermia = potential infection No self-medication (caution: antipyretics and/or corticosteroids); simple hygiene rules: hand washing, body washing, washing of underwear, oral hygiene Avoid injuries and treat them quickly Screening for signs of anemia/thrombocytopenia Adapted nutritional and liquid components of the diet Food education: no eating of raw food or leftovers Avoid public places and transport Avoid cut flowers Attention to the environment (animals)	With regard to signs of anemia: ensure that the patient is vigilant; assist in establishing the diagnosis; enable rapid intervention	Soft toothbrush on prescription, or mouthwash No self-medication (note: aspirin) Avoid cuts: gardening, sport, blows, etc. No electric shaver use, no hair removal Beware of sharp foods: rusks, small bones, fries, etc. Report any traces of blood: epistaxis, rectal bleeding, petechiae, hematuria	Neutropenia
Nursing role	Prevention by monitoring of blood tests If hyperthermia occurs: blood cultures + other samples (cytobacteriological urine analysis, nose and throat swabs, KT (venous katheter), etc.) Rigorous asepsis of care Evaluation of patient education	Monitoring with blood sampling and clinical observation for potential signs	Attention to the cuff of the Dinamap®: risk of hematoma Compression point after blood test Prohibition of intramuscular and subcutaneous injection	In this case and according to the supported profiles, protective isolation in a sterile setting, with positive pressure flows, laminar flow, etc. Strict guidelines in terms of food (lack of raw products), visits, etc.

The NCCN guidelines are worldwide references for physicians and nurses in managing anticancer treatment–induced myelotoxicities. In an article published in 2010, Nirenberg et al. [14] highlighted the need for oncology nurses to use the NCCN clinical practice guidelines for chemotherapy-induced neutropenia (CIN) and febrile neutropenia (FN). Since oncology nurses deliver cancer treatments to patients on an outpatient basis, they should therefore be able to identify risk factors and instruct patients and their families about how to do so at home.



CIN—chemotherapy-induced neutropenia; FN–febrile neutropenia; NCCN—National Comprehensive Cancer Network

Digestive Toxicity

This toxicity results from the destruction of epithelial cells. These cells are among those most affected by chemotherapy. This side effect is so well known and feared that the patient believes it is “normal” and some patients go so far as to think that the absence of nausea is synonymous with inefficient treatment.

These various disorders may also be observed as a result of radiotherapy on the abdominal sphere [12].

Nausea/Vomiting

In 1978, 90% of patients presented with this side effect, but in 2018, only 10–20% did so, thanks to preventive administration of antiemetic treatment [15].

We can identify four grades of toxicities (see Table 3.3 [12]).

Table 3.3 World Health Organization digestive toxicity rating scale [12]

Digestive parameters	Toxicity				
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Vomiting	None	1 episode	2–5 episodes/day Intravenous fluid required	>6 episodes/ day Intravenous fluid required	Uncontrollable—life threatening
Diarrhea	None	Increase of <4 stools/day	Increase of 4–6 stools/day	Increase of >6 stools/day Intravenous fluid required	Life threatening Hemorrhage diarrhea Dehydration
Constipation	None	Occasional or intermittent	Persistent symptoms with regular use of laxatives	Subocclusion	Occlusion

Table 3.4 Different types of chemotherapy-induced nausea/vomiting

Description of vomiting	Characteristics
Acute	Occurs within the first 24 h after chemotherapy injection
Delayed	Occurs >24 h after chemotherapy injection (without an end limit)
Refractory	Occurs despite good treatment
Anticipated	Occurs before chemotherapy

The risks of nausea and vomiting are individual and variable according to people's sensitivity to certain risk factors (e.g., a history of nausea/vomiting during pregnancy, history of motion sickness, or history of migraines):

- Variation by sex: greater sensitivity in women than in men
- Variation by age: greater sensitivity in people aged ≤55 years than in older people
- Variation according to the evolution of the disease: brain metastases, digestive obstruction, cerebral edema, etc.
- Variation according to anxiety and apprehension, or a history of nausea/vomiting during previous treatment

Different types of vomiting can be identified (Table 3.4).

The adaptation of antiemetics will be based on the factors of variability and the molecules used.

- If we identify central toxicity of chemotherapy by stimulation of the thalamus, neuroleptics, anxiolytics, and corticosteroids will be effective.
- When peripheral toxicity induces disorders of the motility of the intestine or an alteration of its wall, andosetron, setron will have an action on early and delayed vomiting.
- Anticipatory nausea and vomiting are not directly related to molecules but are related to anxiety; they can be effectively treated with anxiolytics and corticosteroids.
- Aprepitant (Emend®) is used for the most "at risk" molecules.

– Delayed nausea is often underestimated by caregivers and is considered normal toxicity. The constant arrival of new treatments with longer half-lives provides an effective response, as do combinations of corticosteroids [15] (Table 3.5).

Diarrhea and Constipation

These intestinal disorders are variable according to the type of chemotherapy that is used. They can cause diarrhea (fluorouracil (5-FU), Campto®), while other drugs used as antiemetics can induce constipation. This is related to toxicity to the intestinal mucosa or acceleration of motility. It is necessary to exclude a cause other than chemotherapy: infectious colitis, intestinal tumor foci, tumor compressing the intestinal wall, etc.

Early signs are weight loss, asthenia, anorexia, tachycardia, hypotension, and disturbances of consciousness (Table 3.6).

In some cases of severe diarrhea or constipation, it is necessary to introduce an adjuvant treatment, adapt the cytotoxic doses, or even stop the treatment.

Table 3.5 Nursing role in treating nausea and vomiting

Nursing role	Patient education
Identification of the type of nausea/vomiting (acute, delayed, anticipated) and its cause (other drugs, pain, etc.) Evaluation of the nutritional status of the patient by data collection during interchange Adaptation of antiemetics favoring appropriate routes of administration (rectal, sublingual, intravenous) Anticipation of delayed nausea and vomiting Dehydration monitoring Supportive care: arrange access to a dietitian, complementary medicine, sophrology, hypnosis, homeopathy, etc.	Correct misconceptions; nausea is not synonymous with effective treatment The patient must be able to describe his digestive state on the days following the chemotherapy, so that antiemetic treatment can be suitable adapted; this should be documented in a notebook Avoid fasting chemotherapy sessions: light meals should be eaten on the day before the treatment and on the morning of the day of treatment Mouth care after each food intake Beware of unsuitable dental prostheses Fresh and carbonated drinks: favor cola Meals: small amounts, snacks, easy to digest Warm or cold food Avoid tobacco, alcohol, and rich or spicy foods The patient should not force himself or herself to eat Do not go to bed immediately after eating; go to bed 2–3 h later

Table 3.6 Nursing role in treating diarrhea and constipation

Nursing role	Patient education
Stool evaluation Detect any signs of low bleeding Dehydration monitoring and loss compensation Weight monitoring Hygiene and dietary advice Supportive care: arrange access to a dietitian	Constipation: drink in large quantities outside of meals, drink a glass of fresh water upon waking every morning, favor foods rich in fiber (such as green vegetables, fruits, and prunes); activity is encouraged, as is belly massage (except in cases of peritoneal carcinomatosis) Diarrhea: usual dietary advice, such as drinking plenty of fluid; avoiding fruits, dairy products, cereals, and green vegetables; favoring rice, starchy foods, carrots, and bananas; progressive replenishment

Taste Disorders

The cells for taste (taste buds) and those for smell are some of the rapidly dividing cells that may be transiently affected by certain chemotherapies. Locally situated mainly on the tongue and in the nose, they are useful for analyzing the flavor of food in the mouth. This affects 50% of patients on chemotherapy, and 90% of patients receiving radiation therapy in the throat and mouth have problems with taste and Hyposialia during treatment [16].

These disorders are manifested by a change in the taste sensation of food. This may be quantitative—i.e., either a decrease (hypogeusia or ageusia) or an increase (hypergeusia)—or it may be qualitative (dysgeusia), manifesting as a bitter taste, metallic taste, cardboard taste, etc., in the mouth.

Patients will describe:

- An aversion to eating—the feeling that “nothing happens” for lack of taste.
- Extreme sensitivity to flavors, leading to either a new desire for certain dishes or a disgust for previously favored foods.
- A decrease in the perception of flavors that makes foods taste bland.
- Changes in tastes and flavors that “denature” foods. People sometimes speak of a metallic or bitter taste and too-sweet or too-salty flavors.
- Hypersensitivity to cooking odors (Table 3.7).

Mucositis

Mucositis is an inflammation of the lining that covers the inside of the digestive tract, from the mouth to the anus. Often located in the mouth, the signs are burns of the mouth or throat, mouth ulcers, fungal infection, decreased salivary flow,

Table 3.7 Nursing role in treating taste disorder

Nursing role	Patient education
Inform patients of these disorders Supportive care: arrange access to a dietitian	For smells: Avoid foods with a smell the patient finds unpleasant (e.g., cabbage, onion) Favor cold dishes Use a straw in a closed cup, if needed Avoid fatty foods and fried foods Avoid foods with an altered taste, especially foods that the patient normally likes, to avoid creating a permanent aversion to them For a bland diet: Use spices or sauces Add flavor enhancers (e.g., flavored salts, aromatic herbs) Avoid adding more sugar or salt to adjust the taste of a meal, as this will not make them more flavorful and will have the disadvantage of causing unwanted effects (e.g., water retention, increased blood sugar) If the food seems too sour, add some cream For a metallic taste while eating meat: Replace meat with eggs, fish, soy, or lentils

desquamation of the mucosa turning into ulcerations, and necrosis. These disorders can be major and painful because the mouth is very innervated.

This disorder affects 40% of patients undergoing chemotherapy and 80% of those undergoing bone marrow transplants. Severe mucositis is experienced by 60% of patients treated with radiotherapy/chemotherapy for ENT cancers and is the primary reason for hospitalization in hematology.

Mucositis induces many complications: dysphagia with denutrition, dysgeusia, dysphonia, decreased saliva (which causes dental cavities and a high risk of bacterial or fungal infections), and anorexia.

The World Health Organization (WHO) and the National Cancer Institute (NCI) grade mucositis as follows:

0 = None
2 = Erythema: unpleasant feeling, pain
3 = Patchy ulcerations or pseudomembranes: pain but still capable of eating
3 = Confluent ulcerations or pseudomembranes, bleeding with minor trauma: pain making it impossible to eat solid food, only liquid food possible
4 = Tissue necrosis, spontaneous bleeding, life threatening: intolerable pain causing an inability to eat or drink, or to speak; need for enteral or parenteral nutrition (Table 3.8)

All of these digestive disorders cause patients to experience a risk of deficient food intake or denutrition. They have been described as “a real additional disease to cancer” [18].

> The prevalence of undernutrition in oncology represents, on average, 40% of cases; however, it is often underestimated by patients and their caregivers [18].

According to Bruno Raynard, President of the Inter-Clan (Food and Nutrition Liaison Committee) of all French Centers Against Cancer, “Patients over 70 years

Table 3.8 Nursing role in treating mucositis

Nursing role	Patient education
Daily visual monitoring of the mouth: the slightest change can be identified Schedule use of mouthwash If necessary: antifungals, analgesics, cryotherapy, laser therapy [17] Amifostine® [17] Nutritional evaluation Adaptation of the texture of the diet; favor soft foods, mixed food Supportive care: arrange access to a dietitian	Oral hygiene prevention: brush teeth at least 3 times daily with a soft brush/gargle Consult a dentist Understand the importance of using mouthwashes based on bicarbonate (or even cola): 3–6 times/day If there is a dental prosthesis, remove it for mouthwashing and at night, or wear it as little as possible Avoid foods that are too spicy, too acidic (e.g., vinegar, lemon, mustard), nuts, Gruyère cheese Increase fluid intake, suck ice Moisturize the lips Reduce tobacco and alcohol use Chew gum for saliva maintenance with an antiseptic role

old have an increased prevalence of 45%, three quarters suffer from anorexia and half of them loss of taste."

During their illness, 80% of patients will develop an episode of undernutrition [18].

If undernutrition is related to the adverse effects of chemotherapy and radiotherapy treatments, depending on the area, other causes—such as hypercatabolism, hypermetabolism of certain tumors, or the localization of certain tumors (including digestive tumors (involving the pancreas or stomach), ENT tumors (involving the oropharynx, hypopharynx, or larynx) and, in patients over 70 years of age, involvement of the pancreas, lung, breast, or prostate)—will increase this risk.

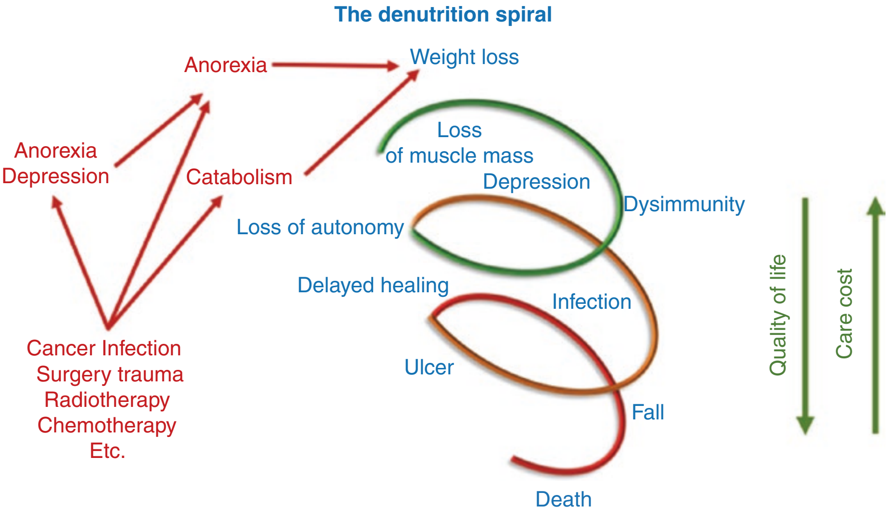
Pain, fatigue, and depression associated with the disease can also make any food intake difficult.

The evaluation of this undernutrition is based on:

- The speed of weight loss: more than 5% in 1 month and more than 10% in 6 months
- A body mass index (BMI) <21 in an adult aged over 70 years or <18 in people aged under 70 years
- A decrease in the rate of albuminemia

This denutrition has major impacts on the patient.

Adaptation of the denutrition spiral created in 1993 by Monique Ferry, geriatrician



Denutrition leads to increased hematological toxicity (anemia) induced by chemotherapy.

The continuation of the therapeutic program may be compromised, and there is a greater risk of treatment being stopped or fewer benefits being obtained.

Table 3.9 Nursing role in treating denutrition

Nursing role	Patient education
Create a nutritional balance as soon as the disease is diagnosed (weight/size, food intake, taste, no taste, etc.) Blood test, albumin dosage, prealbumin Evaluation of ingesta on at least 3 consecutive days Take into account and treat all symptoms that reduce food intake (nausea, disgust, mucositis, pain, etc.) Adapt the diet to the habits and preferences of the patient, e.g., "food pleasures" and "food at will"; solicit the participation of the family Improve the presentation of meals (presentation on plate, with half portions, allows the patient to have the satisfaction of "emptying" the plate) Allow time for the patient to eat in a quiet environment Suggest eating in the company of other patients or the patient's family Evaluate and regularly plot the weight of the patient with objective data on an even scale in the same conditions Supportive care: personalized dietary advice for the patient but also for those around the patient An increase in energy intake to 30 kcal/kg/day and increased protein intake are recommended	Help the patient to understand the issues of diet (impact on treatment, less fatigue, maintenance of autonomy, survival, etc.) Avoid the feeling of satiety: drink between (rather than during) meals, split inputs, provide snacks, limit stimulants (e.g., coffee) that reduce hunger Enrich the meal with milk powder, egg yolk, grated cheese, cream, semolina, etc. Have meals away from chemotherapy or radiotherapy Physical activity is advised to allow the patient to preserve or regain muscle mass

Chemotherapy is more effective in people who eat, because it works during cell division; thus, if patients eat less, there are fewer cell divisions.

Thirty percent of cancer patients die from undernutrition. There is also the question of calculating the chemotherapy dose in relation to the body surface area (BSA) and not in relation to the BMI [19] (Table 3.9).

If the nutritional needs are not covered by the diet, additional contributions will be prescribed:

- Oral nutritional supplements are recommended to be used between meals and should be ingested while fresh, slowly, and in small quantities because they lead to a rapid onset of satiety. It must be ensured that the taste and texture are suitable.
- As long as the digestive tract remains functional, enteral nutrition will be maintained for as long as possible. One month of enteral nutrition will always be more effective than 3 months of parenteral nutrition [20].
- Parenteral nutrition exposes the patient to an increased risk of infection, especially in oncology, because patients are immunocompromised.

When it is still possible, it is important to combine artificial nutrition with an oral diet so that the patient does not lose the reflex of eating.

Impairment of Body Image

This is certainly the most feared consequence for patients. It is linked to mutilating surgical procedures (removal of an organ, stoma) and also to alopecia induced by chemotherapy, and weight loss or gain.

This trauma, in addition to its physical repercussions, will also have psychological and sociological impacts on self-esteem, self-confidence, and even personal identity.

Mutilation

The removal of a breast—which is a strongly invested organ, symbolizing femininity and motherhood, and associated with sexuality—can lead to patient apprehension regarding their partner's gaze and decreases in seductive appeal and libido. Between 14% and 24% of women suffer from postmastectomy depression [20].

Laryngectomy leads to a renunciation of not speaking "as before," and loss of the verbal personality, which contributes to the feeling of authority and virility—"to lose face". As described by Reich, a tracheostomy represents "the hole that spits in the faces of others" [21] and is difficult to mask.

Patients with stoma will experience leaks and odors. Insecurity regarding stool or urine control refers to the dimensions of anality with the learning of sphincter control and the attainment of cleanliness. Patients may feel disfigured by the material applied to the belly, and they may no longer feel whole.

These alterations cause apprehension with regard to people looking at each other and being observed. A process of mourning will be necessary to accept this body, which is no longer aesthetically correct in a society where appearing is more important than being.

The attitude of the clinical team during the first days after the surgical intervention can play a determining role. Some patients will be waiting for reassurance and will want to be carried away by words of comfort and thoughtful gestures. In this role, the nurse can inspire the patient with a new positive perception of his or her transformed image (Table 3.10).

The patient will develop effective coping strategies when he manages to take care of him- or herself, without embarrassment or disgust, finding his or her own solutions to physical problems (loss of voice, gas, etc.) and resuming a social life. For that, time works wonders.

The proportion of women diagnosed with breast cancer who have not undergone a reconstruction at 4 years is strongly associated with age and the presence of comorbidities [22]. in France, the proportion of women who opt for breast reconstruction is less than 20% [20]. The patient's choice will be respected even if it runs counter to normative prejudices—prejudice that we must go beyond as caregivers.

Table 3.10 Impairment of body image-nursing role

Nursing role	Patient education
Establish a relationship of trust, help, and empathy to encourage the person to express their feelings and put into words their emotions (anger, sadness, frustration, guilt, etc.) Listen to the patient's singular experience Evaluate any major depressive episode Invite the patient to ask questions Invite the patient to look at and touch the area operated on, gradually and without forcing adaptation to the patient's new image Integrate loved ones into care education Offer supportive care: Psychological support or antidepressant treatment Speech therapy for speech and swallowing Socioaesthetic therapy to provide camouflage strategies, scarves, and makeup tips Contact with associations or former patients who can testify to and share their experiences	Correct any misconceptions: There are currently techniques for stoma enemas and colonic irrigation that prevent stool release by the ostomy pouch for 48 h; this makes it possible to use a smaller pouch during this period, allowing swimming practice, for example A tracheostomy does not hinder the patient from living normally, with leisure and work, but under certain conditions: not all sports are permitted, no bathing, caution with trades and activities that generate dust; include aspiration equipment in the patient's daily organization Encourage the patient to maintain a social life: visiting friends, associative activities, etc.

Alopecia

Alopecia is total or partial loss of hair, including eyelashes and pubic hair: it begins between the tenth day and 3 weeks of chemotherapy. More or less complete baldness appears after 1–2 months. It is a common but reversible side effect, and its intensity will depend on the drugs used. The regrowth is slow: about 1 cm/month, depending on the person. Patients should be warned that the texture and color of the hair may be changed on regrowth.

Alopecia is a known toxicity and is clinically the least serious, but it is the toxicity most feared psychologically by patients. Alopecia after chemotherapy is the ultimate visible mark of the disease; it is the straw that breaks the camel's back.

There are five grades describing the degree of alopecia, depending on the molecules used:

- Grade 5: severe alopecia
- Grade 4: moderate to severe alopecia
- Grade 3: moderate alopecia
- Grade 2: little to moderate alopecia
- Grade 1: little alopecia
- Grade 0: no alopecia

The grades experienced as the most difficult are the “intermediate” grades: the hair falls out in a piecemeal and unsightly way, and becomes sparse.

A refrigerant helmet can be offered in some cases. The goal is to apply hypothermia to the scalp, cause vasoconstriction, and reduce the flow of the chemotherapy product to the germ cells of the hair. This will not necessarily prevent hair loss, but the helmet can slow down the loss of the hair and preserve hair bulbs to facilitate regrowth.

The contraindications to refrigerant helmet use are:

- Tumors or brain metastases; bronchial tumors
- Bone metastates at the level fo cervical vertebra
- Scalp wounds
- Leukemia, lymphoma
- Infusions that are too prolonged (inefficiency)
- A history of migraines

Possible side effects of refrigerant helmet use are:

- Eye or cervical pain
- Migraines
- Pressure ulcers in the helix of the ear

Shin et al. performed a meta-analysis of different interventions in the literature, involving more than 1000 participants, most of whom were women with breast cancer treated with doxirubicin- or epirubicin-containing chemotherapy. Scalp cooling—a popular intervention—significantly reduced the risk of chemotherapy-induced alopecia (CIA) while other methods did not have a significant effect. These data underscore the efficacy of scalp cooling as a preventive treatment for CIA, but the authors urged that more studies be conducted to establish the long-term safety of the method [20] (Table 3.11).

Table 3.11 Alopecia-nursing role

Nursing role	Patient education
Inform the clinical team promptly about the presence or absence of this side effect Inform the patient of the reversibility of this side effect Accompany patients during this difficult step Free speech; allow the patient to express his or her feelings Propose a progressive cut of the hair Offer a refrigerant helmet Supportive care: socioaesthetic therapy to help with application of scarves, a hair prosthesis, temporary or semipermanent makeup	Do not wash the hair too often, use no friction, use a tooth comb gently for detangling No hair dryers, heating curlers, or accessories that can pull hair out No hair lacquer or dye No use a shampoo that tighten the hair scales Anticipate the need for purchase of a hair prosthesis and turbans before hair loss occurs, if the patient wishes

Sexual Health

Sexual health is a taboo in our society, with an underestimated multifactorial involvement when a person is sick. Cancer treatments rarely cause a change in sexual capacity or desire.

Sexual health is defined as a state of physical, emotional, mental, and social well-being associated with sexuality [23]. Sexual health is a central aspect of the person throughout his or her life, which includes sex, gender identity and role, eroticism, pleasure, intimacy, and reproduction. It is a positive and respectful approach to sexuality (Table 3.12).

Caregivers have a fundamental role to play: patients have the right to be informed and helped. We must reduce resistance to the major information needs of patients. Such resistance is shared by both patients and caregivers. The importance of sexual health is secondary, considered a minor problem in relation to cancer. Talking about cancer and sexuality is an oxymoron! In our societal representations, cancer is synonymous with death, while sexuality is synonymous with life.

Table 3.12 Consequences of anticancer drugs

For women	For men	For both women and men
Disturbance of the menstrual cycle Absence of menstruation Hot flashes Vulvovaginal itching Early menopause Vaginal dryness, which can lead to fissures of the vaginal wall Falling libido Disturbance of female identity and body image Short- or long-term hypofertility Teratogenic effects	Oligospermia or azoospermia Falling libido Incapacity Disturbance of male identity and body image following disfiguring surgery	Representations of the disease: on the part of the patient or the people around him or her Tiredness Anxiety, fears, apprehensions Pain A decrease in solicitations by the partner for fear of being intrusive or of causing hurt, of being unable to cope with the situation, etc. Modification of intimacy: hospitalizations, modification of the living environment, etc. Following side effects of treatments: nausea, transit disorders, drought, etc. Alteration of the general state Modification of the body’s appearance with alteration of self-image Binding apparatus (e.g., a stoma or probe) A feeling of being a “secondary subject” Implications of a drop in libido for quality of life Creation of embarrassment between the couple, shame about what the patient has become, because of bodily modifications or mutilations Altered emotions, relationships, or even communication

Table 3.13 Sexual health-nursing role

For women	For men	For both women and men
Hydration advice: increase fluid intake Lubricants Regular sexual activity for maintenance of vaginal secretions Strengthening of the perineum Ovule or estrogen gel for dryness and during use of barrier contraception Approval to attempt pregnancy 18 months to 2 years after the end of treatment	Recommendation of a sperm deposit (e.g., at CECOS) Drugs that promote erections	Breaking the silence and talking freely about sexual health problems: inform, advise More in the sens of giving confort reinsurrance Reframe what the patient might read, hear, or see on the internet: restore "truths" and correct misconceptions Regular sexual activity to promote self-esteem and maintain sexual health Explore a change in practices (e.g., new positions) Meet the partner to spread the word, explain the side effects, and advise them Allow relative privacy during long hospitalizations: avoid frequent intrusions into the room, inform the team, put a sign on the door, signal the time when care is required, etc. Supportive care: psychologist, socioaesthetician, gynecologist, urologist, sexologist

CECOS Centre d'Etude et de Conservation du Sperme Humain

Caregivers must anticipate this topic and demonstrate that it can be approached easily. This requires knowing how to communicate on the subject, having answers to provide, addressing the possibility of a different sexuality, and knowing how to refer the patient for appropriate supportive care. Although no sexual activity may be possible (as is the case at certain stages of critical or terminal illness), intimacy and physical warmth remain important. A hug or a massage can be really satisfying. It is the proximity of loved ones that bring pleasure and recovery of self-confidence.

The caregiver will demonstrate triple competence: theoretical knowledge, knowledge to be, and know-how, without going beyond the need—coming to the fact without being intrusive, while remaining within a state of competence and legitimacy as a caregiver (Table 3.13).

All patients are concerned, but also so are their partners, whatever their age and the idea the caregiver can make of the sexuality of others. Inclusion of the patient's partner will help to raise questions and frustrations that penalize the couple's dynamic and therapeutic alliance [24]. Being able to talk about the issue and be listened to often solves most problems that are mentioned.

Taking care of sexual health gives meaning to life by allowing the patient to find a climate of security and communication within a couple. It brings new self-confidence and acceptance of the gaze and the touch of others.

Fatigue

It is only in about the last 10 years that the medical profession has taken into account fatigue—not out of ignorance but for lack of suggestions regarding ways to resolve it. Fatigue is the first side effect evoked very early in patients. This symptom occurs before nausea, depression, or pain; indeed, it is the one for which no therapy can be proposed, unlike the other three [25]. It is considered to be the most feared, most severe, and most affecting symptom in patients' daily lives. Yet, trying to do anything about fatigue is often considered futile it is a symptom heard but not recognized, and something inevitable in oncology, whether on the side of patients or caregivers.

There are multiple definitions of fatigue. Fatigue can be defined as a subjective and multidimensional phenomenon without a physiological component [26]. The North American Nursing Diagnosis Association defines fatigue as an overwhelming and prolonged sense of exhaustion that reduces the usual ability to work physically or mentally. Fatigue is the first and last symptom cited by patients.

In patients with tumor pathology, asthenia is present in:

- 50–75% of patients at the time of diagnosis
- 75–95% of patients receiving chemotherapy
- 60–80% of patients undergoing radiotherapy
- 80% of patients during time away from treatment
- 13–35% of patients 6 months after their initial treatment
- 40–75% of palliative care patients [27] (Table 3.14)

There are four main dimensions to fatigue [29]:

1. Physical: a feeling of physical exhaustion or lack of energy
2. Cognitive: difficulties in concentration
3. Emotional: a state of discomfort and decline in motivation
4. Behavioral: inhibition of activities

Table 3.14 Causes of fatigue in cancer patients [28]

Linked to the patient	Linked to the disease	Linked to treatments	Linked to the environment and the context
Stress Fear of the future Sleep problems Reactive depression	The disease itself The type of cancer The severity of the cancer Induced pain and its treatment Induced weight loss	The treatments themselves Side effects: anemia, leukopenia, infections, fever, anorexia, slimming, vomiting, diarrhea, etc.	Social problems: job loss, family imbalance, isolation, etc. Unsuitable housing: stairs, distance between the bedroom and bathroom, etc. Expectations before different consultations Travel and need to use multiple forms of transports Hospitalizations

Two types of fatigue have been identified: physical fatigue due to asthenia in the evening and late in the afternoon, and mental fatigue due to asthenia when waking up, often accompanied by psychopathological disorders. It should be noted that a person with psychopathological disorders is often tired, but a tired person does not always have psychopathological disorders.

The first intention of the caregivers will be to remove pathological elements and to correct them:

- Correction of anemia
- Management of pain
- Prevention of undernutrition
- Detection and resolution of psychopathological disorders

Fatigue is often misrepresented: it is often associated with disease and especially cancer. The first advice given by the medical profession and the clinical team is "Rest!" Forty-five percent of patients think that nothing can be done about their fatigue—that it is related to the cancer itself and then to the treatments [30]. This welcome and welcome rest has dramatic consequences for the organization.

Rest causes a cascade of consequences; this is called a deconditioning or mismatching effort.

Deconditioning

Deconditioning is defined as a state of diminished physical performance involving all organs and functions. It is one of the main causes of fatigue related to cancer, when the body becomes unaccustomed to making a physical effort. It is a self-aggravating phenomenon; everything contributes to deconditioning. The less the patient does, the less he or she will be able to do. The consequences are multiple: deconditioning amplifies vulnerability and physical maladjustment, causes muscle wasting, devalues the self-image, increases the loss of self-confidence, and degrades the quality of life, with a high risk of disability.

The medical and paramedical team can take care of the patient's fatigue. However, it is necessary, first of all, to identify the elements that favor this fatigue and the resources of the patient that will allow therapeutic education to be established (Tables 3.15 and 3.16).

Adapted Physical Activity

These different elements that are put in place must be complementary to adapted physical activity (APA). APA is the setting in motion of people who—because of their physical, mental, or social condition—cannot practice physical activity under normal conditions. APA is any bodily movement that produces a marked increase in energy expenditure in relation to the expenditure at rest: it is not limited to sports activity and includes all of the activities of daily life: domestic tasks, work, transport, leisure, etc.

Table 3.15 Deconditioning-nursing role

Factors that promote fatigue	Resources in favor of therapeutic education
Bad prognosis Partner and other people around the patient Ubiquitous symptoms or minimization of symptoms Depressive syndrome Feelings of wear, helplessness, weariness Feeling of guilt Acquired beliefs: from the internet or other people, bad information given by a trusted medical professional Cancer/fatigue representations Religious beliefs Unavailability of the team/lack of listening Chronicity Reduced cognitive abilities Addiction Lack of spirit, liveliness Lack of information Family situation/disruption of family dynamics Fear of becoming Duration or multiplicity of hospitalizations	Helpful partner Ease of expression by the patient/participation Identification of representations Dynamic patient/athlete Healthy lifestyle already present Availability of professionals/medical team/sensitivity and confident by using the method Patient follow-up in time/continuity of care Communication tool/facilitating EVA Applicant patient: informed about possible management of fatigue Spiritual beliefs Will Compliance Trust

Table 3.16 Deconditioning-nursing role

Nursing role	Patient education
Allow the patient to talk about it Listen Identify the patient’s representations concerning fatigue Encourage verbalization of symptoms Avoid evoking a certain “inevitability” Take into account the fatigue by evaluating it with the help of an analog visual scale or another more comprehensive (but more complex) scale (e.g., the Piper fatigue scale or the FACT-F scale) Reassure the patient Address causes that can be treated: anemia, pain, nausea, insomnia, undernutrition, depression, etc. Propose techniques favoring the saving of energy; any such initiative of from the team, the patient, or people around the patient will be favorable and welcome Involvement of people around the patient Organization of care during hospitalization to respect the patient’s rest time Supportive care: social worker, adapted physical activity teacher–educator, physiotherapist, occupational therapist, dietitian, complementary medicine therapist, relaxation therapist, stress management coach	Avoid resting too much, but arrange breaks during the day: split activities Prioritize daily goals and limit noncore activities Delegate certain tasks: administrative, shopping, meetings Divide housework over the week or delegate it Nutritional balance between energy intake and expenditure; have fun Adapt the habitat: place chairs at various places in the house, avoid stairs, put grab bars in place, etc. Assessment of the quality of sleep: mattress, room temperature, pillow, noise, fixed hours, etc. Protection from the cold and from the sun Avoid unnecessary trips Avoid major work Avoid public transport and large shopping environments; get items delivered Simplify the gestures of everyday life: use a bathrobe rather than a towel, shower gel rather than soap, an electric shaver and electric toothbrush, clothes that are easy to put on, etc. Encourage activities to restore concentration: reading, excursions, leisure, cultural outings, etc. Adapted physical activity

FACT-F Functional Assessment of Cancer Therapy—Fatigue

Over the past decade, studies on this topic have multiplied, and all have demonstrated the effectiveness of APA in improving the general condition of the patient in oncology. We are talking not about sport but about physical activity adapted to each person in each situation. The level of scientific evidence is high, as shown in several consistent analyses [31].

Adapted Physical Activity Is the Only Validated Treatment for Oncology Fatigue

APA significantly reduces cancer fatigue. Overall, APA decreases fatigue (regardless of the time of care) by 27%, including fatigue during treatment (which is decreased by 23%) and including distance fatigue occuring after the treatments (which is decreased by 44%). Thanks to APA, there is a significant reduction in depressive symptoms, an improvement in body image, a decrease in anxiety, an improvement in sleep quality, and a decrease in psychotropic intake [31].

APA is possible in most cases, whatever the patient's age, stage of disease (including during treatment), type of cancer, and previous physical activity. On the other hand, there may be contraindications such as wounds, risky bone lesions, metastases, a decrease in immune defenses, severe thrombocytopenia, or heart disease. Thus, there will be a need for a medical certificate from the oncologist.

APA must be supervised by an APA teacher–educator with specific training. This activity must be progressive, personalized, and preferably carried out in groups. To be effective, the pace of APA should be 3–5 times weekly with sessions of 20–50 min. The activity must be aerobic, progressive, of moderate intensity, and adapted for the patient's needs.

To date, it is recommended not to advise patients to stop their activities and not to rest during the period of cancer treatments. It will be necessary to plan APA from the beginning of cancer care, and the treatments must not constitute a brake on APA.

The benefit of APA is not limited to control of fatigue. APA improves quality of life, improves tolerance of and adherence to treatments, regulates weight gain, and has a proven role in preventing a relapse or second cancer [32]. In the survival of patients with breast cancer and colon cancer, APA is associated with a 35–40% lower risk of relapse. The data are similar in patients with glioblastoma or prostate cancer [33].

The role of health care professionals is to inform patients about the benefits of APA, to encourage its practice, to eliminate any treatable cause that might prevent or discourage the patient from following the course of the recommended APA, to detect limiting factors, and to establish the patient's aptitude.

Conclusion

Cancer is a challenging disease that affects the person and those around the patient. The treatment is a period of fighting to lead.

While most side effects are temporary, some patients may experience later effects. Three out of five people reportedly experience sequelae for 2 years after a diagnosis of cancer, including pain, chronic fatigue, motor or vision problems, psychological difficulties, memory and attention disorders, or impaired fertility [34].

Every effort must be made to preserve the quality of life after healing on the personal, family, and socioprofessional levels. After the acute phase of treatment, patients may feel a sense of disorientation, loneliness, a great emptiness, or abandonment—it is a period of withdrawal of treatment.

The time after cancer is a new period of care, in the long run. It must be adapted to the unique needs of patients and revisable over time. It includes elements of global monitoring of the patient, including support and access to supportive care. It must specify and emphasize the modalities of joint surveillance between hospital teams and health professionals in the community.

It is the responsibility of nurses to respect and promote patient independence throughout the process by providing personalized counseling and developing education. E-health (which is discussed in another chapter in this volume), is a real challenge for health professionals. The new digital tools used in remote monitoring of patients will radically change our approach to care—the goal being to support patients who are connected, informed, and involved in their treatment. These are new skills for the health professionals of tomorrow to develop [35, 36].

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4

The Patients' Journey with Targeted Therapies

Christine Remacle

Abstract

Oral targeted therapies have become central in the management of advanced cancer since they delay the progression of the disease and extend overall survival of the patients. Targeted therapies, despite inducing some dramatic response, rarely eradicate cancer but rather switch it to a chronic state. This implies that the treatments are taken chronically over several months or years with consequences on compliance. This is of particular importance since these drugs have also specific side effects that can greatly affect patients' quality of life. In the present chapter, the main side effects of targeted therapies, their management from the angle of specialised nursing care, and several prophylactic measures have been reviewed. The nurse indeed plays a critical role in guiding and supporting patients receiving oral treatments. A multidisciplinary and multi-professional approach involving physicians, pharmacists, and paramedical staff guarantees a better efficiency. In addition, properly educated patients will improve their adherence to treatment.

Keywords

Targeted cancer therapy · Treatment adherence · Therapeutic education · Side effects · Guidelines · Quality of life

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C. Remacle (✉)
King Albert II Institute for Cancerology and Haematology,
Cliniques Universitaires Saint-Luc, Brussels, Belgium
e-mail: christine.remacle@uclouvain.be

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Introduction

The number of patients affected by chronic diseases, including cancer, continues to grow. Over the past two decades, the median age at diagnosis of cancer has increased around 70 years of age, as a result of a generally better life expectancy. Healthcare services will have to adapt to the increased number of cancer patients presenting with age-related comorbidities and chronic disease. The development of many oral agents, mostly targeted therapy, is shifting the cancer care point of care from the hospital, where chemotherapy and invasive treatments are administered, to an ambulatory setting and ultimately to home care. In contrast to chemotherapy that has a broad and relatively non-specific spectrum of cytotoxicity, targeted therapies specifically block or enhance a specific intracellular pathway involved in the development and promotion of a specific tumour type. Targeted therapies rarely eradicate cancer but rather switch them to a more chronic state, delaying the progression and ultimately extending overall survival. This implies that targeted therapies are taken chronically for often an extended period of time. Because they target specific physiological pathways, usually redundant in cancer and normal cells, targeted therapies are very specific and have varied side effect profile. It is therefore essential to provide a support system for the patient and his specific therapeutic environment that responds to this major change. In addition to their anticancer treatment, many patients are also receiving multiple medications for other diseases, with multiple drug interactions, ranging from reducing the anticancer agent activity to critically increasing toxicity causing severe side effects or even death of the patient. Hence, health professionals have to pay particular attention to the co-medications. Another critical conundrum of oral agents is the compliance/adherence issue. When prescribing injectable agents, physicians control precisely the dose and administration schedule. In case they prescribe oral drugs, they rely on the patient adherence and compliance to achieve a correct therapeutic target.

According to the World Health Organization (WHO 2003 report), the proportion of patients affected by chronic disease that complies with their treatment is only about 50% [1]. Health professionals have in the past believed that adherence to treatment of cancer patients was better than most patients with chronic disease because of the fear of the recurrence or the death. Contrary to these beliefs, different studies have shown that this compliance is far from being optimal [2]. Noteworthy, the patient is not only the source of compliance's issue, the role of providers being also important. A system approach of compliance and adherence is therefore required. According to the WHO report, a single-factor approach might be expected to have limited effectiveness. The most effective approaches have been shown to be a multilevel – targeting more than one factor with more than one intervention (e.g. education in self-management; pharmacy management programmes; nurse, pharmacist, and other non-medical health professional intervention protocols; counselling; behavioural interventions; and follow-up and reminders, among others). Several programmes have demonstrated good results using multilevel team approaches, involving multidisciplinary and multi-professional models. The WHO recommends applying therapeutic education, a support helping the patients to become autonomous (to be empowered), to take care of themselves in order to maintain or improve their quality of life, their well-being. Education is a main part of nurse's support role of patients taking oral treatments. Education of patients receiving anticancer oral treatment aims at their empowerment to secure their journey, to improve the efficiency of the treatment, and to preserve their quality of life. Transversal and multi-professional care pathways, involving physicians, nurses, pharmacists, dietitians, psychologists, other related healthcare professionals, and properly educated patients, will secure an efficient delivery of the medication.

General Measures

Before prescribing oral drugs and initiating treatment, the following general measures should be considered by healthcare professionals. According to Goodin et al., they should provide patients and caregivers with education and training to understand how to take treatment safely. Patient documentation and other educational materials should be continuously evaluated to ensure accurate and up-to-date information. The patient's consent for oral anticancer treatment should be obtained. The ability of patients to take oral treatment and to comply with their treatment plan should be evaluated. Patients should also be informed of all issues related to safe handling. The drug interactions of the usual treatment should be examined. Interference with diet and clear instructions on dosage should be provided, including what to do when a dose is missed or when vomiting occurs. During prescription referrals, any potential drug and food interactions should be reassessed and discussed with the patient or caregiver. The patient should be made aware of the required surveillance arrangements by having access to the written protocol and treatment plan of the facility where treatment was initiated [3].

The main side effects that can significantly impact the patient's health and quality of life, especially in the case of new targeted agents that are sometimes prescribed continuously over long periods of time, must be known by the physician and the patient. The identification of the main classes of drugs, the exhaustive knowledge of their side effects, proper monitoring, and in-depth education of nurses and patients are key elements to secure the efficacy of these therapies.

Main Side Effects of Targeted Therapies and Their Management

We have summarised the most frequent side effects within four main groups: dermatological, cardiovascular, oral and upper gastrointestinal, and metabolic toxicity, including fatigue. The most commonly used classification is the Common Terminology Criteria for Adverse Events (CTCAE) [4].

Dermatological Side Effects (Table 4.1)

Many targeted therapy drugs cause skin reactions. They usually develop slowly after a few days or weeks and can range from mild (minimal skin changes or Grade 1) to severe (painful ulcerative dermatitis or Grade 3). They are not signs of a drug allergy, which often includes other serious symptoms such as difficulty breathing, dizziness, tightness in the throat or chest, or swelling of the lips or tongue.

Patients have to be informed about the skin symptoms that might occur during the course of their treatments before they have started the treatment to help prevent skin changes or at least try to keep them under control. Preventive as well as symptomatic measures have to be advised to optimise quality of life and improve treatment compliance. It is essential to identify whether the skin symptom is related to antineoplastic therapy or not. Cancer patients are often presenting with inflammatory, infectious, and specific skin lesions as well as graft-versus-host disease-related rash. They regularly also take multiple drugs, and it is not easy to know which one is responsible for the skin condition. Another critical point is to evaluate the serious skin reactions that require treatment discontinuation and/or specific management.

Skin changes frequently occur as a result of the targeted agent mode of action, the skin being a very sophisticated environment controlled by regulatory pathways largely similar to the cancer pathways. Drugs such as EGFR inhibitors (e.g. cetuximab (Erbitux®), panitumumab (Vectibix®), erlotinib (Tarceva®)) target the epidermal growth factor receptor (EGFR) protein, which tells the cancer cells to grow and divide. The normal skin's homoeostasis heavily relies on the EGFR pathway, so that

Table 4.1 General prophylactic measures to keep the patient skin in a good condition [5]

Advise the patient to
Use very mild soaps, body washes, and shampoos that do not contain alcohol, perfume, or dye
Take baths instead of showers and try oatmeal bath products to soothe the skin
Bathe with cool or lukewarm (instead of hot) water and avoid hot, humid places
Moisturise skin at least twice a day with a thick emollient cream that has no alcohol, perfumes, or dyes. The best time to do this is right after the bath, while the skin is still damp
Wear loose, soft clothing
Keep nails short, avoid biting nails or false nails
Use laundry detergents or fabric softeners without strong perfumes
Avoid as much as possible exposure to sunlight, because sunlight seems to trigger and/or worsen rashes in some people. This also applies to exposure to sunlight behind the glass, such as in a car or at home. Wear a hat and clothes with long sleeves outside during the day. Use a broad-spectrum sunscreen with SPF of at least 30 and zinc oxide or titanium dioxide at least 1 hour before going out
Do not use acne medicines. Though the rash may look like acne, acne medicines don't work. They can even dry it out and make it worse
Try gel shoe inserts if the soles of the feet are tender
Wear shoes that fit well and aren't too tight. Thick, soft socks may help
Use certain kinds of makeup (skin-friendly and liquid). Water-based makeup can cover rashes without making them worse
Use only steroid creams, ointments, or gels (even those that don't require a prescription) as directed by doctors

drugs targeting the EGFR pathway can switch off the signal for skin cells to grow normally and make it harder for them to retain moisture, leading to dry skin.

Dry skin (*xerosis*) can start within the first few weeks after the first intake of the targeted therapy drugs and is reported in about one third of the patients after 1–3 months. It is observed in almost all the patients treated with EGFR inhibitors. But nearly everyone getting targeted therapy has dry skin after 6 months of treatment. The skin can become dry, itchy, scaly, and brittle and may even crack open. Hands and feet are especially concerned [6]. Dry skin is best controlled by using emollients applied on humid skin to be more effective.

Fissured dermatitis of the finger pulp or heels can be treated with vitamin A- or urea-based ointments.

Prophylactic Measures for Dry Skin To keep the skin in a good condition, it is essential:

- To moisturise the skin at least twice a day with an unscented greasy cream
- To use mild shower/bath oils, moisturising and preferably unperfumed without alcohol because of its drying effect
- To apply cream on the skin as clean as possible, especially after washing, showering, or bathing

Rash (Papulopustular Rash/Folliculitis of the Seborrheic Areas) It usually appears during the first week of treatment at various degrees and is often described as acneiform while differing from acne in the absence of retentional lesions or presence of comedones. In most people, the rash is mild, but nevertheless profuse eruption may occur, and it is described as uncomfortable and sometimes painful [7, 8]. It is worth informing the patient that the occurrence and intensity of this eruption is associated with a better tumour response and overall survival. The hypothesis is that some polymorphisms of EGFR might be associated with the appearance of cutaneous signs and a better antitumor response. Another hypothesis is a better bioavailability of the drug in the skin and the tumour as well as a beneficial effect of the inflammatory/immune reaction in the skin and perhaps also in the tumour [9]. These authors also pinpoint the importance to differentiate moderate rash from serious hypersensitivity reactions such as drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome or Stevens-Johnson syndrome usually associated with mucosal involvement, bullous lesions, and systemic and biological signs.

Management of Rash

- *Mild skin changes (Grade 1)* may not need treatment. They include rashes that are only in a limited area, that are not causing any distress, and that are not infected. Moisturising creams or ointments that contain no alcohol, perfume, or dye can sometimes help with dryness. Other, more symptomatic lesions need topical treatment relying on local antibiotics (erythromycin, clindamycin, metronidazole) and copper- and zinc-based antiseptic creams. When antibiotics are not sufficient, topical corticosteroids are usually effective. Camouflaging the lesions with appropriate non-comedogenic makeup (water-based) is allowed.

- *Moderate skin changes (Grades 2–3)* include a rash over a larger area of the body or skin changes causing mild distress from itching or soreness, but with no signs of infection. It will be advised to watch closely to see if the rash gets better or worse. Systematic treatment such as cyclins (doxycycline, 100–200 mg/day) is used at first-line therapy for 4–8 weeks longer if needed. The dose of the targeted therapy drug usually does not need to be changed for moderate skin problems.
- *Severe skin changes (Grade 3)* are bad rashes that cover a lot of skin, cause itching and soreness affecting the quality of life (such as sleep problems or pain), and are likely to get infected. A dose reduction is advised if the treatment is poorly tolerated by the patient. If the rash doesn't get better within about 2 weeks, the targeted drug is often stopped until the skin changes improve. The symptoms rapidly attenuate after reduction or interruption of treatment and do not always recur upon resumption of the drug. The treatment may then be restarted with continued skin care. Treatment is much more likely used for moderate changes, including creams or gels, as well as systematic oral antibiotic. Along with this, a course of corticosteroid pills is often given [10].

Prophylactic Measures Antibiotics might reduce the relative risk of severe rash associated with EGFR-targeted agents by 42–77%. Vitamin K cream is also identified as having a potential role in the management of EGFR-targeted agent-induced rash [11].

The hand-foot syndrome (HFSR) is a typical feature of angiogenesis inhibitors targeting the vascular endothelial growth factor (VEGF) axis, including, for example, the anti-VEGF bevacizumab (Avastin®), tyrosine kinase inhibitor sorafenib (Nexavar®), sunitinib (Sutent ®), pazopanib (Votrient®), and axitinib (Inlyta®). VEGF helps the tumour to build and keep a blood supply, but they also seem to be important to the very small blood vessels in the hands and feet. Blocking these proteins leads to damage in these tiny blood vessels with the drugs leaking out damage and causing the hand-foot syndrome.

The earliest symptoms of HFSR are sensitivity, tingling, numbness, and pain in the hands and feet. The palms of the hands and the soles of the feet become red. In some cases, the redness looks like sunburn with blisters. The blisters can open up and become sore in severe cases. The lesions are located on pressure or friction areas, they can rapidly become hyperkeratotic, and this phenomenon is often bilateral and symmetrical. HFSR can be very painful. This side effect can affect the ability to walk and to do normal activities [12].

Management of HFSR [13]

- *Mild (Grade 1) HFSR* can be controlled by simple symptomatic measures including moisturising creams, keratolytic agents such as 40% urea, and/or creams or ointments containing 1–10% salicylic acid on the calloused areas.

- *Grade 2 HFSR.* In addition to the symptomatic measures recommended for Grade 1 HFSR, topical corticosteroids (clobetasol) can be initiated for a few days on inflammatory lesions. If needed, analgesic treatment should be prescribed. In some cases, a dose reduction of 50% should be considered.
- *Grade 3 HFSR.* Symptomatic measures should be prescribed as well as antiseptic treatment of blisters and erosions. Treatment should be interrupted for a minimum of 7 days and until toxicity has resolved to Grades 0–1. The resumption of treatment should be begun at a reduced dose for a minimum of 7 days. After a second or third occurrence of Grade 2 or Grade 3, resumption or dose re-escalation should be based on clinical judgement and patient preference. No systematic therapy is recommended.

Preventive measures include removal of pre-existing areas of hyperkeratosis calluses by mechanical or chemical keratolytic treatment (topical 10–50% urea, 2–5% salicylic acid ointments). The patient should be advised to wear comfortable and flexible shoes with padded or gel- or foam-based shock absorber insoles, avoid friction and trauma arising from exercise, and reduce exposure of the hands and the feet to hot water. They should treat dryness and cracking areas with emollients, moisturising creams, or ointments.

Paronychia is the appearance of red and sore cuticles, the areas around the nails. Paronychia is less frequently observed than rash and occurs after at least a month of treatment. It can look like an inflammation of the periungual folds or resemble an ingrown nail. It more often affects the large toes than the fingers (thumbs). Swollen, red, and painful sores can appear around the fingernails and toenails. These sores may become infected and can affect the ability to walk. Nails may also become brittle and grow more slowly [14].

Management of paronychia is aimed at reducing the extent of the granulation tissue using either topical corticosteroids, chemical cautery with liquid nitrogen (silver nitrate or trichloroacetic acid), or even surgical excision followed by the application of phenol.

Prophylactic measures include advising patients to avoid too much pressure on the shoes when jogging, walking, jumping, etc. They have to be informed to avoid friction-traumas-manipulations and to wear wide, open shoes.

Changes in Hair or Skin Colour Targeted therapy-related hair modifications are underreported in the literature. Some targeted drugs can turn the skin or hair in a yellowish colour during treatment (e.g. with pazopanib (Votrient®) and sunitinib (Sutent®)). For a few people, the hair and/or skin gets darker. This tends to go away once treatment ends. Almost all the patients treated with kinase inhibitors or blocking antibody drugs have a change in hair texture (e.g. the hair on the head becomes thin, dry, straw-like and brittle, or even curly) after 2–3 months. Long-term use may lead to bald patches or alopecia (with sorafenib slightly less with sunitinib and pazopanib). Sores on the scalp and on other hairy areas can appear. Scars caused by these sores may keep hair from growing back after treatment. Facial hypertrichosis for both men and women may grow faster than usual, including longer, thicker, and curly eyebrows and eyelashes. But in some men, facial hair growth slows down. Eyebrows may thin out as well. These changes may usually be noticed later on a course of treatment [15].

Prophylactic Measures Advise patients to use hair conditioners, to wax their facial hair, and to regularly trim their eyelashes to prevent conjunctiva and keratitis. Patients with trichomegaly who complain about symptoms of eye irritation should be seen by an ophthalmologist, because other ocular conditions such as conjunctivitis and keratoconjunctivitis sicca can complicate anti-EGFR therapy (e.g. erlotinib (Tarceva®)). Trimming and epilation have been found to be satisfactory, safe therapeutic options [16]. It would be the role of the nurse to suggest a list of recommended wigmakers.

Oedema may occur in the periorbital areas in the morning and inferior parts of the body in the evening. They appear very frequently on an average of 6 weeks after initiation of anti-kit, platelet-derived growth factor receptor (PDGFR) treatment (e.g. imatinib (Gleevec®)) [17]. The eyes may burn and become red or dry. In some people, the eyelids get red, tender, and swollen, and the lashes may become crusty. Sometimes the eyelids may turn inwards or outwards. Distorted eyelids or prolonged dryness can damage the cornea.

Management of Oedema Moderate periorbital oedema does not require any treatment. Severe and/or diffuse oedema can be alleviated by diuretics and electrolyte monitoring. If the eyelids are crusty or swollen, careful cleansing and clean, warm, wet clothes laid over closed eyes may help.

Cardiovascular Side Effects

Most targeted therapies and combination treatment are associated with an increased risk of cardiovascular toxicity [18].

Cardiomyopathy and Left Ventricular Dysfunction

Targeted therapy (type II agents) such as trastuzumab (Herceptin®) and the tyrosine kinase inhibitors sunitinib (Sutent®), lapatinib (Tyverb®), and imatinib (Glivec®) have shown to induce cardiomyopathy. However, in contrast to type I agents, which include chemotherapy like anthracycline, mitoxantrone, or cyclophosphamide, that induce irreversible myocardial damage, type II agent cardiomyopathy is potentially reversible [19].

Coronary Artery Disease

Antiangiogenic drugs have been shown to induce coronary events mainly via two different mechanisms: coronary artery vasospasm and arterial thrombotic events by inhibition of the vascular endothelial growth factor (VEGF).

Cardiac Arrhythmia

Most arrhythmias are not clinically significant. The most concerning is the prolongation of the QT/QTc interval with the associated increased risk of torsade de pointes. This is common among patients treated with multi-targeted kinase inhibitors and angiogenesis inhibitors. Early detection by regular ECG and appropriate treatment is essential to avoid life-threatening arrhythmias [20].

Hypertension

Hypertension is very common after initiation of anti-VEGF therapy by multi-targeted tyrosine kinase inhibitors (sunitinib, sorafenib, axitinib, cediranib, telatinib, etc.) or monoclonal antibodies (bevacizumab). Different mechanisms of action are involved in the rapid increase in blood pressure including vasoconstriction caused by the inhibition of the VEGF pathway and a decrease in nitric oxide levels and endothelial cell apoptosis, which causes a reduction in capillaries and increase overall vascular resistance [21, 22]. Hypertension is usually reversible within 2 weeks of treatment discontinuation.

It is important that the patient is informed that targeted drugs, especially those called angiogenesis inhibitors, can raise blood pressure to the point that specific medication may be needed. It may be useful to educate the patient about monitoring his blood at home so that any onset of hypertension is quickly reported to the nurse or to the treating physician.

Venous Thromboembolic Disease

Drugs such as thalidomide and erlotinib are associated with an increased incidence of venous thromboembolism events, probably due to an increased platelet aggregation and a direct effect on the endothelium.

Prophylactic measures for cardiovascular health include before all the identification of a risk factor and an early referral to a cardiologist. Cancer patients indeed often underestimate cardiovascular risk factors. They should be informed that cardiovascular monitoring is required during and after anticancer treatment. Early involvement of a cardiologist should be encouraged in patients with a pre-existing heart condition such as hypertension, hypercholesterolaemia, type II diabetes, and hypertriglyceridemia. Prior to cancer treatment initiation, cardioprotective measures or modifications to the proposed treatment regimen should be proposed to individuals at high risk. Any anticancer agent should be immediately discontinued at occurrence of a cardiovascular event such as a significant decrease in LVEF or a significant prolongation of the QTc (>500 ms.) [23].

Oral and Upper Gastrointestinal Side Effects

Xerostomia (dry mouth) and dysgeusia (taste loss or disturbance), stomatitis, and mucositis (oral ulceration) are common with mTOR inhibitors such as everolimus (Afinitor®) or temsirolimus (Torisel ®). Stomatitis refers to painful inflammation of the mucous lining of the mouth, whereas mucositis is rather a painful inflammation and ulceration of the mucous membranes lining the digestive tract [24]. Dysgeusia affects almost half of the patients. A decrease in the perception of acid taste is noticed, and an increase in the perception of sweet taste is observed. The modification of bitter and salty tastes is less frequent. Red and infrared low-level laser therapy (LLLT) can partially prevent oral mucositis and also significantly reduce pain, severity, and duration of symptoms [25].

Prophylactic measures include:

- Regular use of mouthwashes.
- Advise eating soft, creamy, and unctuous foods.
- Avoid irritant food: dry, hard, too salty, too spicy, and acidic foods, alcohol, and soft drinks.
- Moisturising with ice, the use of a fogger, and artificial saliva can be helpful to treat xerostomia.
- Sucking acidulous and mint candies may help reduce the feeling of dry and pasty mouth.
- Taking a spoon of cream at the beginning of the meal to help swallow.
- Rinse the mouth with mouthwashes or acidulous sparkling water (sparkling water + lemon juice) before each meal to enhance the taste of food in case of dysgeusia.

Gastrointestinal perforation is rare and has been reported in association with targeted agents, with the highest rate being with bevacizumab [26]. Gastrointestinal perforation is an indication for immediate discontinuation of therapy.

The most important *prophylactic measure* is to conduct an in-depth anamnesis before starting the treatment. Treating physician and nurse should pay specific attention on history of past diverticulitis or ulcers, previous radiation exposure, recent sigmoidoscopy or colonoscopy, gastrointestinal obstruction, and multiple previous surgeries.

Diarrhoea is the most common side effect of targeted drugs. This adverse event has been often described with tyrosine kinase inhibitors. The pathophysiological mechanism is secretory by inhibition of EGFR effects on chloride secretion. The management of diarrhoea is essential because of its negative impact on social life and the potentially life-threatening outcomes.

Treatment and Management

Mild diarrhoea may be managed with diet to decrease the frequency of stools. A BRAT (banana, rice, apples, toast) diet can be helpful [27].

Loperamide remains the standard therapy for uncomplicated cases. Chronic low- to intermediate-grade (Grade 1–2) symptoms can be managed with continued loperamide. Early recognition of the warning signs of complicated cases of diarrhoea should be performed. In some aggressive cases, the addition of antibiotics is necessary [28]. Dose adjustments of the anticancer agent or even discontinuation is required for Grade 3 or Grade 4.

Prophylactic measures include:

- Maintaining an abundant liquid and salt intake. Ideally the drinks should contain starches and/or sugars, sodium, and some potassium. Molasses and other forms of raw sugar can be used; they contain more potassium than white sugar. The WHO advises a home-made oral rehydration solution: stir a mixture of 1 L of water with 2.5 mL (1/2 level teaspoon) of salt and 30 mL (6 level teaspoon) of sugar until dissolution. Traditional remedies such as carrot soup, rice water, gruels (diluted mixtures of cooked cereals and water), weak tea, and green coconut water are suggested.
- Encouraging to keep dietary measures and avoid drug interactions.
- Avoiding diets high in fibre or lactose that may aggravate diarrhoea.

Weight Loss

Weight loss may result from a loss of appetite caused by cancer such as from treatment-related nausea, vomiting, dysgeusia, diarrhoea, pain, and mechanical obstruction, among others. Anorexia can result from the loss of appetite. The related symptoms are fatigue, weakness, and distress. They have a negative impact on health-related quality of life. In case of severe cachexia, pharmacologic intervention may be required.

Recommendations and Prophylactic Measures

Different screening and assessment tools are available. The MSTC (malnutrition screening tool for cancer patients) is appropriate for nurses [29]. The MNA (Mini Nutritional Assessment) is a practical tool for identification of nutritional status in geriatric practice [30].

A simple nutritional assessment programme and early counselling by a dietitian are essential to guide nutritional support and to alert the physician to the need for intervention [31]. Nurses should advise patients to keep at least three daily meals, preferably six small meals to split the intake and decrease the quantities. They are advised to eat in a calm, friendly place, at usual times, to adapt cutlery, to remove bad smells, and to adapt the textures of food. Rich food adapted to the tastes is preferable while avoiding hot or spicy food.

Fatigue and Metabolic Toxicities

Fatigue is considered by cancer patients as the most impacting side effect on their quality of life. It is a major cause on non-adherence to treatment, and it may compromise the efficacy of the treatment [32]. Fatigue results from multiple causes. It can be cancer-related, treatment-related, and, as often seen with targeted therapies, related to other conditions including anaemia, hypothyroidism, sleep disturbance, depression, or pain [33].

Recommendations and Prophylactic Measures It is important to understand the plausible underlying causes of fatigue before providing any recommendation.

Hypothyroidism is a very common side effect of patients treated with TKIs. Detection and treatment of pre-existing hypothyroidism before starting TKI treatment are advised. Initially monthly TSH dosage should be performed, but there is no clear consensus on the frequency of thyroid function monitoring. Hyperglycaemia is a very common side effect of the mTOR inhibitors [33]. Before initiating mTOR treatment, the monitoring of the fasting serum glucose is indicated and periodically thereafter.

Treatment and management of fatigue should be based on daily assessment (using reliable and simple tools), patient information, identification and treatment of causal aetiologies, anti-inflammatory therapy when needed, and education and psychological support.

Adherence to Treatment: An Indicator of the Patient's Empowerment

Therapeutic education is a major component of building a strong therapeutic alliance with the patient, and as such it is a very important part of the nurse role. A therapeutic alliance is built around and in agreement with the educated person. It includes an assessment of needs, available resources, and educational objectives or goals with a choice of tools, intervention planning, and evaluation.

Concretely, optimising a safe and efficient administration of an oral anticancer therapy starts with an exhaustive information and education plan. It serves the purpose of securing that the patient knows and understands his disease and his treatment, as well as the importance of taking the pills. Counselling how to take the drugs safely and how to recognise and to manage side effects is a key element to provide patients with the necessary skills to manage their treatment in a complete autonomy. The adherence process includes tools such as notebooks, folders, computer applications, and smart goal choices, among others. Too much information, however, does not guarantee an optimal adherence. To trigger an action consistent with health, the information must either adhere to the beliefs and representations of the patient or change them [34]. Hence, nurses have to adapt the information to each individual patient, information being not only to talk but also, if not more, to listen to the patients. Ask patients open-ended questions because these are more likely to uncover patients' concerns and help determine what the patients might need. When needed, the patients should be referred to specialised colleague's psychologist, dietitians, physicians, and general practitioners. In the end it is about tailoring the process to each individual patient [35].

A prior assessment is essential. In order to ensure the patient's adherence to the treatment, the multidisciplinary group has to assess the ability (cognitively, psychologically) of the patient to take his/her treatment appropriately and follow the recommendations and after that to propose appropriate supportive care. An exhaustive exchange of information between the care team and the patient will open to a relationship of trust indispensable to an adherence process. In addition, healthcare professionals should keep in mind that the daily administration schedule impacts on compliance, less frequent dosing regimens resulting in better compliance across a variety of therapeutic classes [36].

General Recommended Information for Establishing an Education Programme

According to Mc Cue, a comprehensive oral anticancer education should contain the following information: drug and indication, dose, dosing schedule, start date, administration, what to do for missed doses, food and drug interactions, side effects and management, clinic contact information, and safe handling instructions [37].

The Multinational Association of Supportive Care in Cancer (MASCC) has developed an Oral Agent Teaching Tool (MOATT) that includes four steps to help patient education [38]. This tool is available online at http://www.mascc.org/MOATT. These steps are (I) key assessment questions, (II) patient education, (III) drug-specific education, and (IV) evaluation. These steps focus on special considerations health professionals might have when assessing, educating, and evaluating patients receiving oral agents for cancer is considered.

Key Assessment Questions

When educating a patient, it is recommended to adapt the teaching to accommodate special considerations such as age, feeding tubes, vision problems/colour blindness, dietary issues, and mental problems (dementia, depression, cognitive impairments).

The key assessment questions proposed by MOATT are related to what the patient has been told and knows about this treatment plan with oral medication. It secures that the patient knows that these oral agents are for cancer and are taken by mouth. The patient has to be asked about what other medications or pills he/she is taken by mouth. It is advised to go over the list of patient medicines prescribed or not, herbs, complementary, and other treatments, with the patient. A particular interest should be directed towards the ability of the patient to swallow pills or tablets and to understand the concerned problems. The ability of the patient to read the drug label/information sheet and to safely handle the medicines, bottles, or packages needs to be evaluated. To find out if there were any problems taking the medicine or any other event such as adverse events, the following question is suggested: "Have you taken other pills for your cancer?" "Are you experiencing any symptoms that would affect your ability to keep down your pills, for example, nausea or vomiting?" In some countries patients can have delay in obtaining the oral treatment because of insurance problems. Paying attention and asking the patient if he/she had problems with insurance who interfere with obtaining the medication should be assessed.

Patient Education

Improvement of the patient's knowledge, skills, and responsibility will be performed by making the patient aware of the importance to consider the following items:

- Inform any other healthcare provider, doctor, and dentist about the treatment taken.
- Keep the pills/tablets away from children and pets.
- Keep the pills/tablets in the original container unless otherwise directed. Do not mix with other pills.
- Wash hands before and after handling the pills/tablets.
- Avoid crushing, chewing, cutting, or disrupting pills/tablets unless directed otherwise.
- Store pills away from heat, sunlight, or moisture as it may degrade the pills/tablets potentially making them less effective.
- Build a system to take the pills/tablets correctly.
- Make sure the direction about what to do is known if a dose is missed.
- Contact a doctor or a nurse immediately if too many pills are taken accidentally or if someone else has taken pills/tablets.
- Ask a nurse or a pharmacist advice about what should be done with any pills that have not been taken or are outdated.
- Carry at all time a list of medicines that they are taken, including the cancer pills/tablets.
- Let the prescribing doctor or the nurse know if they have a problem with paying for or getting the pills/tablets.
- Plan ahead for travel, refills, and weekends.

Drug-Specific Information

The following references are proposed by the MOATT tool:

- The official product package insert or prescribing information for countries of the European Union can be found on the EMA website: http://www.ema.europa.eu.
- The "We are Macmillan Cancer Support" website: http://www.cancerbackup.org.uk/Treatments/Chemotherapy/individualdrugs.
- Micromedex: https://www.micromedexsolutions.com/home/dispatch.
- The drug information website of the American Society of Hospital Pharmacist (AHFS): http://www.ahfsdruginformation.com.

This list is not exhaustive and should be completed with any local or national official source of information.

It is recommended that whichever tool is used to educate the patient, the physician and nurse include the following drug-specific information:

- Drug name (generic and trade).
- What the drug looks like.
- Dose and schedule (How many different pills? How many times a day? For how long?).
- Where to store the drug. The patient needs to have concrete advises. Be specific, for example, away from heat (not in the kitchen), humidity (not in the bathroom), and sun (not on the window sill).
- What are potential side effects and management of them? Include lab evaluations or any medical tests that will be used for drug monitoring.
- Are there any precautions?
- Are there any food interactions?
- When and whom to call with questions? Give names and phone numbers.

Evaluation

By the end of the education process, patient may have retained only part of the information. It is thus critical to perform an evaluation and review the key points before the patients start the treatment. An easy way to conduct that evaluation is to have the patient and/or caregiver answer the following questions to ensure that they understand what information has been given:

- What is/are the name(s) of your cancer pill(s)/tablet(s)?
- At what time(s) of the day will you take your cancer pill(s)/tablet(s)?
- Does it matter if you take this pill(s)/tablet(s) with food or not?
- Where do you plan to keep it?
- When do you call the doctor or nurse?
- Do you have other questions?
- When is your next appointment?
- Who should you contact in case of problems?

Psychological Aspects

The needs of any cancer patient will evolve over the different psychological stages according to their personality, to their representations, as well as to their beliefs and experience. Distress is frequently related to the uncertainty of the disease. Difficulty in facing the disease and complying to the treatment is very often a consequence of experiencing side effects that alter the quality of life.

Nurses play a key role supporting the patients in their coping process regarding the repercussions of the disease and treatments in their daily life and detecting any frailty the patient might have. The use of the Distress Thermometer might be helpful to assess distress [39]. Prompt reference to a psycho-oncologist is required when distress is identified.

Summary

Several oral targeted therapies effectively prolong the duration and the quality of life. However, because these drugs are administered over a long period of time, patients have to face with side effects that can severely affect their quality of life. Preventive and symptomatic measures are key to optimise treatment compliance and improve quality of live. Management of these associated side effects has become a central role of nursing care. This engages the nurse to support the patient in coping with his treatment plan. This requires adapted information and personalised education throughout all the treatment plan. This unfortunately can be standardised until a certain level only. Indeed, it is essential to take into account the personality of the patient and the factors that influence informative and educational support over time.

Finally, there is space for an appropriate care that takes into account various factors of influence. There is the place for a clinical sense in the support role which includes the adapted information and the education in a process of therapeutic alliance, in order to make the patient becomes an actor in his/her treatment plan. This is the primary function of a multidisciplinary and multi-professional team in which each discipline and health professional takes care of the patient with the knowledge of his expertise.

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Immunotherapy: New Challenges for Nursing

5

Claude Bertrand

Abstract

Anticancer immunotherapy brings a radical change in oncology for two major reasons.

The first one is of scientific nature because the therapeutic target is from now on the immune system, while the other anticancer treatments used to target the cancer cell.

Immunotherapy makes the patient the main actor of its fight against cancer by using its own immune system as a weapon [1]. The second one is of clinical order. Indeed, antibodies of immunotherapy are given intravenously and do not require premedication.

The side effects, new in oncology, are unpredictable and will require on behalf of the patient and of the nursing team real challenges for their identification and their management.

Big hopes were born with immunotherapy. The latter gets a profit in terms of global survival and especially in terms of quality of life, ending in a chronicity of the disease.

Immunotherapy evolves in a lightning way with new therapeutic indications, and "it is the first time that it is possible to treat so many different cancers with the same molecule" [2].

So it is necessary to be able to rely on a nursing staff having been trained specifically.

An advanced nurse practitioner or referent or coordinator can be responsible for these various missions.

C. Bertrand (✉)
King Albert II Institute for Cancerology and Haematology, Cliniques Universitaires Saint-Luc, Brussels, Belgium
e-mail: Claude.bertrand@uclouvain.be

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Having an extensive knowledge on the disease and the treatment, this person will thus be the central interlocutor for the patients and his/her family and friends as well as for the doctors and the nursing staff in the interdisciplinary team [3].

Keywords
Immunotherapy · Chronicity · Therapeutic education · Side effects Interdisciplinarity

Introduction

Immunotherapy is an important track of the current cancer research. Several immunotherapy treatments are already available. Immunotherapy has become the nurse's daily concern and is often involved in a long-term process of stable or progressive chronic diseases, and also upsets the way we look at cancer [4]. To accompany this therapeutic revolution, it is necessary to change the mentalities.

Immunotherapy radically changes the way cancer is looked at.

The increasing importance of treatments raises the question of the impact of those therapies on patients and on health system organization, in particular in terms of equity of access.

We also wonder as for the opportunities and challenges which will result from it to improve the quality of care. Particularly through the importance of the patient follow-up.

New less well-known side effects appear and require a totally other approach from the nursing staff.

Thus, here we all embark for new challenges.

Challenges for the Patient

Cancer and its chronicity remain a difficulty to live with; treatments and controls are an important constraint for the daily organization of the patient and his close relatives. One of the challenges involves integrating a long-term treatment as well as its side effects into the daily life.

The patient becomes the own actor of his health. It is thus agreed to include him as well as his close relatives in the system of care; we speak here about patient-nursing partnership or pilot-co-pilot.

Problems related to the long-term disease will be better resolved if there is an active implication and an understanding in the management of the symptoms.

The communication with the health-care team must be fluid. Indeed today the patients are better equipped with regard to their pathology (Internet), so we can't leave them alone with all these informations.

Hospital is offering more and more expertise, excellence in the treatments and the patients are more and more at home.

Challenges of the Multidisciplinary Work

Every team member has to play his own role while knowing those of the others. Everyone has to know who will act and when in order to reach the goals clearly defined by the team. This is certainly an added value in terms of productivity for a medical team who has to work toegether to maximize the by-product from a global action for the patient while avoiding the duplications, the overlapping and the useless waste of time [5].

This is why it's so important to have a well trained team about immunotherapy and especially as the field of prescription of these molecules is going to grow in oncology and that interdisciplinary management of this dysimmunitary toxicity represents a real issue.

It will therefore be important for the entire team to be continuously trained and informed about immunotherapy, especially as the field of prescription will widen in oncology and as the interdisciplinary management of these dysimmune toxicities represents a real challenge.

Challenges for the Nursing Team

It is advisable to adapt the management of patients under immunotherapy: we are not any more in the information but well in the therapeutic education which has to join the process of care all along with the therapeutic path.

The nursing team needs the patient to be the actor of his/her health as a partner but also as an autonomous patient. Therefore the nursing team has to know the person and his/her environment (his/her close relations and friends, story, place of life, social situation, etc.).

It's even more true since the hospitalization's time has been reduced to 1 hour every 15 days or 3 weeks. This situation put the patient and his/her close relatives in the front line [6].

Patient's demand today is not only to be "seen" by a member of the team. They ask for more information, explanation and answers to their query.

The written or phone exchange is appropriated to these requests of time for the nursing team; written allows to deepen, to reread and to complete, not to forget [7].

The relation with the professional is then focused on themes chosen by the patient, thus on his/her own concerns.

The digital tracks, mobiles' applications, will allow the patients and their relatives to feel more involved in their treatment due to the fact that they have themselves access to certain data and receive more feedback [3].

What Is Immunotherapy?

Unlike targeted therapies, chemotherapy, radiotherapy or surgery, immunotherapy is a treatment consisting in using the patient's immune system to fight directly or indirectly the cancer.

The immune system is all the organs, tissues and cells protecting us against germs (viruses, bacteria, parasites) but also against tumours. To do so, the immune system has specialized cells: the *lymphocytes* (a type of white cell) which are able to recognize the molecules and the *antigens*, which are present on the aggressors and on the abnormal cells. The immune system is active everywhere in the human body and concentrates its action in the sites where the aggression is taking place. It can also adapt its action over time. It is then well armed against tumours in order to fill the gaps in other treatments.

Lymphocytes are white cells responsible for the recognition of antigens. They are two types. The *lymphocytes B* produce and liberate *antibodies* which are proteins that attach themselves to antigens external to cells (either free or attached to the surface of the cells). *T lymphocytes* recognize another type of antigens, which are issued from the interior of the cell. Those antigens are little fragments of proteins (peptides) appearing on the surface of the infected cell. T lymphocytes are able to stick to the cells presenting those antigens and kill them, for example, cells infected by a virus or cancerous cells. The action of the immune system is very efficient: it is able to recognize a wide diversity of antigens and to face numerous aggressions. Its action is also very specific: it targets the foreign elements and the abnormal cells by distinguishing them from normal cells and tissues that it leaves intact. Besides, a part of the B and T lymphocytes that has reacted will persist in the body for several years, standing by to react much more quickly in the case of a new aggression. It's the *immunity memory*.

Generally, cancerous cells have few external antigens distinguishing them from normal cells. B lymphocytes from a patient with cancer and the antibodies he is producing have little or no effect against those cancerous cells. However, cancerous cells have a certain number of internal antigens since they have genetic anomalies which cause many abnormal peptides to appear on their surface making them targets for the T lymphocytes. Human tumours are often infiltrated by T lymphocytes, and those which have a lot often have a slower and favourable evolution than those which have a few of them.

Nevertheless, the majority of tumours increase in size even though they are infiltrated with T lymphocytes, which shows that the immune response is not efficient enough to control them. In fact, some tumours adapt themselves in eliminating a part of the tumour cells but without having much effect on the rare resisting cells, which end up taking over. In other cases, immunity cells are inhibited. Inhibitors are securities that prevent too strong or too persistent immune response to prevent damage to inflamed tissues. Tumours take advantage from those inhibitors to avoid being destructed. Some of those inhibitors have been identified. They can be neutralized with new medicines, like immunomodulatory antibodies (often called "immune checkpoint inhibitors").

The Main Treatment in Cancer Immunotherapy: Immunomodulatory Antibodies

PD-1 is a receptor appearing on T lymphocytes when they are activated. Those will become inactive ("go back to sleep") if their PD-1 receptor meets the PD-L1 protein, when it is present in the inflamed tissue or if it is present on the tumorous cells. The sleeping T lymphocyte cannot kill the tumorous cells, and the tumour can grow without any limit. The PD-1/PD-L1 is the link we were talking about.

The main immunomodulatory antibodies will bind to PD-1 (or PD-L1) and prevent, by blocking the PD-1/PD-L1 liaison, the falling asleep of the lymphocyte which can maintain its killing activity against the tumour. Around 30–40% of patients with metastatic melanoma answer the treatment with a PD-1 antibody. An important fact is that a lot of those patients have a prolonged remission and are probably cured, what no treatment at the moment would allow to obtain. This treatment acts also in other types of cancers, such as lung, bladder or renal, and head and neck cancers and Hodgkin's lymphoma.

The efficacy of this medication is explained by its mode of action which targets not only the cancerous cells directly to kill them but rather the immune cells to stimulate them. The lymphocytes waken up by those therapies will attack the tumour by recognizing several different antigens, which renders it more vulnerable and impairs it to become resistant. In addition, immune reaction is active all over the body (where there can be metastasis in several places) and persists on a long-term basis, thanks to its memory effect, which impairs more delayed recurrence [8].

Anticancer immunotherapies targeting the immune checkpoints PD1, PD-L1 and CTLA4 are now essential in the management of cancers, and their number does not stop to increase in research [9].

The response to the treatment is not always immediate and can take weeks or months before noting a benefice.

But there are setbacks. First, a great number of patients do not answer to those treatments, for still poorly understood reasons, and side effects can be serious.

Research is advancing at big steps; tomorrow other pathologies will be validated, and immunotherapy will become an adjuvant treatment for certain indication.

We can also note that other immunotherapy approaches exist such as:

Bispecific antibodies which are composed of two identical halves, each of them recognizing the same antigen. The first bispecific antibody has just been approved for the treatment of certain lymphomas and leukaemia.

The adoptive transfer of lymphocyte T: Here, lymphocytes are obtained from the blood or a metastasis of a patient with cancer. The T lymphocytes "enriched" are then reinjected in a great amount to the same patient.

Main Therapeutic Indication (Table 5.1)

Table 5.1 Immune checkpoint-blocking antibodies approved by the Food and Drug Administration[a]

Drug	Target	Indication
Ipilimumab	CTLA-4	Melanoma
Nivolumab	PD-1	Melanoma, non-small-cell lung cancer, renal cell carcinoma, hepatocellular carcinoma, classic Hodgkin's lymphoma, squamous cell carcinoma of the head and neck, urothelial carcinoma, colorectal cancer with high microsatellite instability or mismatch repair deficiency
Pembrolizumab	PD-1	Melanoma, non-small-cell lung cancer, classic Hodgkin's lymphoma, squamous cell carcinoma of the head and neck, urothelial carcinoma, gastric cancer, solid tumours with high microsatellite instability or mismatch repair deficiency
Atezolizumab	PD-L1	Non-small-cell lung cancer, urothelial carcinoma
Avelumab	PD-L1	Merkel cell carcinoma, urothelial carcinoma
Durvalumab	PD-L1	Urothelial carcinoma

Source: Weber et al. [25, p. 785]

[a] *CTLA-4* cytotoxic T-lymphocyte-associated protein 4, *PD-1* programmed cell death protein 1 and *PD-L1* programmed-death ligand 1

Management of the Side Effects Linked to the Immune Response

Main Consideration

The new immunotherapy molecules *immune checkpoint blockers* have led to new adverse effects called dysimmunitary.

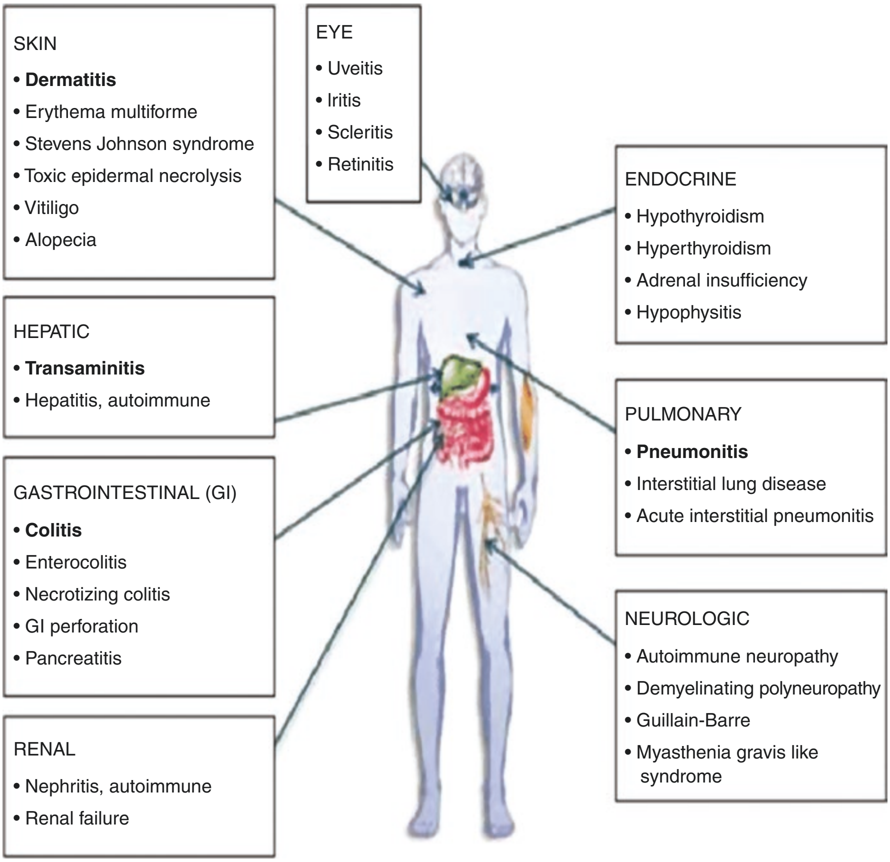
Indeed those molecules, by their mode of action allowing the lifting of ways of inhibition of the immune system, caused an increased activation of the lymphocytes, favouring the occurrence of manifestations similar to auto-immune diseases which can affect all the systems and the organs, with a high interpersonal and chronological variability. It is important to know and to recognize those side effects, to inform patients about it when starting the treatment and to detect them systematically during this one.

Those secondary effects (SE) can appear at any time during the treatment, and even 1 year after the end of it, the patient's participation is thus crucial knowing that those secondary effects are reversible with the introduction of therapy with corticoid.

Depending on the checkpoint, those dysimmunitary effects can be more frequent and more severe with the antibodies CTLA-4 than with the inhibitors of PD-1 or PDL-1.

Secondary Effects

Non-exhaustive List of the SE of Immunotherapy



The more frequent serious complications appear in bold type.

Source: Bridgen [26]

Although some SE occurs much more frequently than others, it is important to note that any organ or tissue can be involved.

Others are less frequent but can be very serious, even mortal, such as neurological disorders and a myocarditis.

The association of two immunotherapy increases the risk of the SE all grades combined (Figs. 5.1 and 5.2).

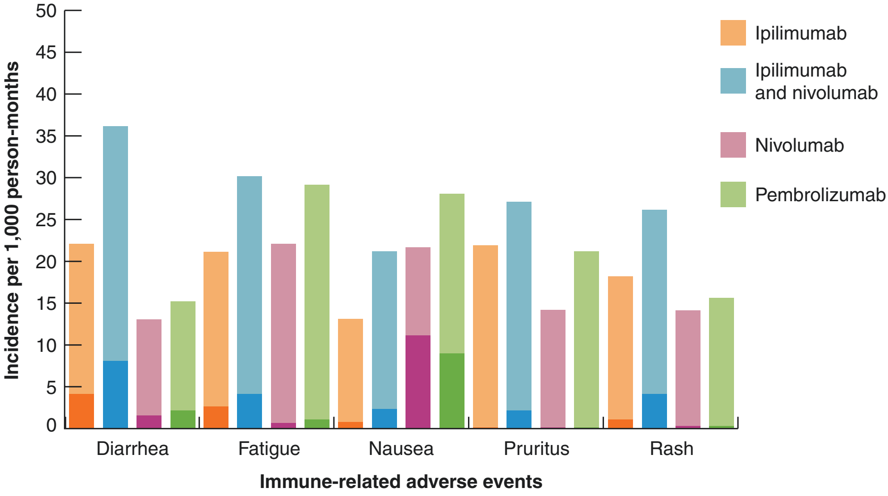


Fig. 5.1 Most common adverse events with immune checkpoint inhibitors. Note: Adverse events of grades 1–2 are represented by lighter shades, and adverse events of grades 3–5 are represented by darker shades. (From Boutros et al. [27]. Copyright 2016 by Macmillan Publishers Ltd. Adapted with permission)

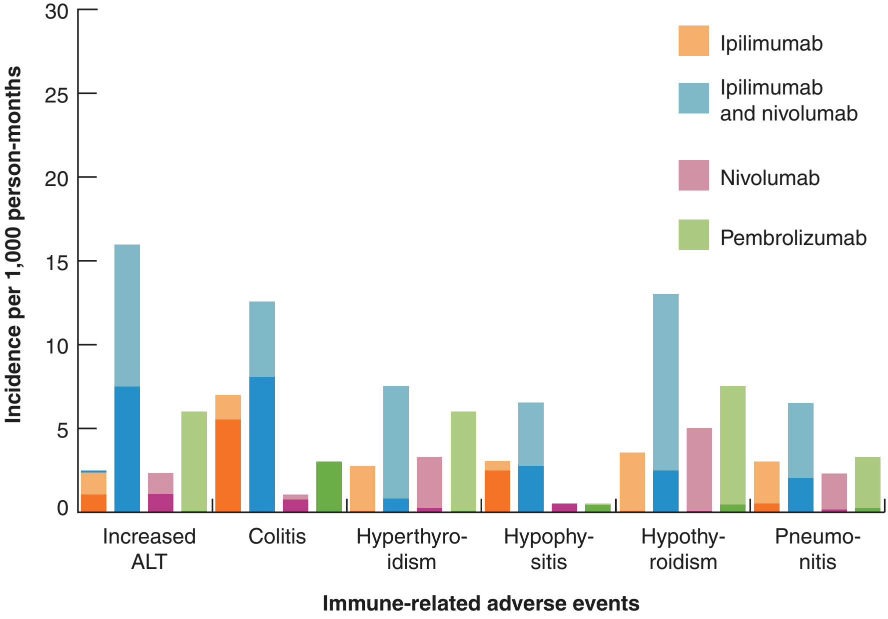


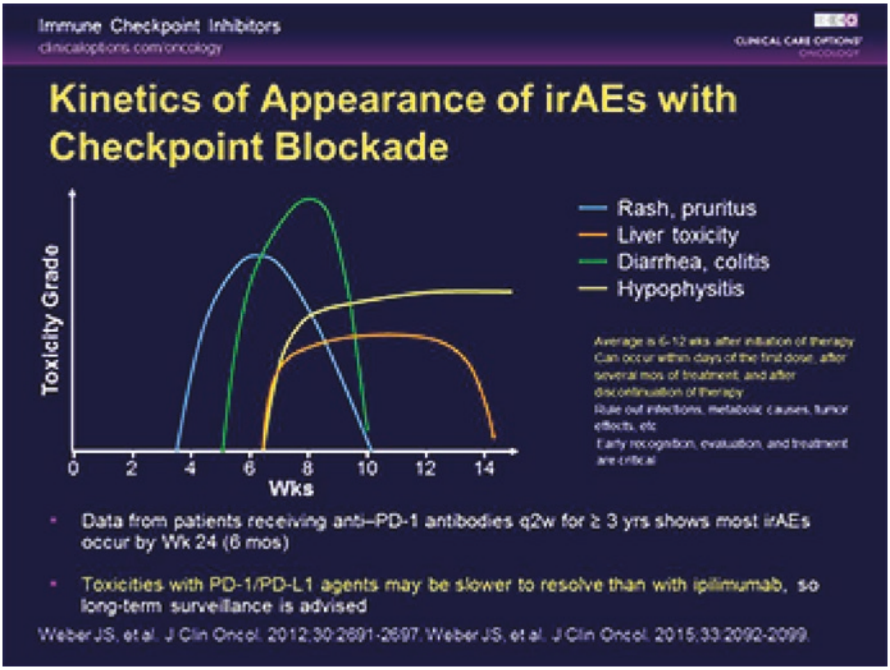
Fig. 5.2 Adverse events of special interest associated with immune checkpoint inhibitors. ALT, alanine aminotransferase. Note: Adverse events of grades 1–2 are represented by lighter shades, and adverse events of grades 3–5 are represented by darker shades. (From Boutros et al. [27]. Copyright 2016 by Macmillan Publishers Ltd. Adapted with permission)

Frequency of Occurrence of the SE and Their Resolution

Some SE occurs more prematurely; this is the case for toxicity in the skin, the liver or on the gastrointestinal system.

Some SE such as endocrinopathy toxicity will resolve later.

It is not possible to predict the occurrence of the SE.



Immune Checkpoint Inhibitors
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Kinetics of Appearance of irAEs with Checkpoint Blockade

Average is 6-12 wks after initiation of therapy
Can occur within days of the first dose, after several mos of treatment, and after discontinuation of therapy
Rule out infections, metabolic causes, tumor effects, etc
Early recognition, evaluation, and treatment are critical

- Data from patients receiving anti–PD-1 antibodies q2w for ≥ 3 yrs shows most irAEs occur by Wk 24 (6 mos)
- Toxicities with PD-1/PD-L1 agents may be slower to resolve than with ipilimumab, so long-term surveillance is advised

Weber JS, et al. J Clin Oncol. 2012;30:2691-2697. Weber JS, et al. J Clin Oncol. 2015;33:2092-2099.

Source: Weberj et al. [25, p. 787]

General Guidelines for the Management of the Secondary Effects of Immune Origin

Management of SE is done according to the grades "Common Terminology Criteria for Adverse Events" (CTCAE) [10].

We will analyse here the nursing role for the more frequent SE.

For complementary information concerning other side effects, we invite you to consult the Management of Toxicities from Immunotherapy: ESMO Clinical Practice Guidelines [11].

Those very practical recommendations concern at the same time the more frequent toxicities and the more known (cutaneous, endocrines, digestives, pulmonary, hepatic) but also the more rare (central and peripheral, neurological, cardiac, ocular, rheumatological, haematological, renal).

We will analyse here the nursing role for the more frequent SE.

Following recommendations are general. For the treatment of secondary effects of specific immunological origin of certain organs, it is recommended to refer to the summary of the characteristic of the product [12].

Severity—CTCAE grade	Ambulatory inpatient care	Corticosteroids	Other immunosuppressive drugs	Immunotherapy
1	Ambulatory	Not recommended	Not recommended	Continue
2	Ambulatory	Topical steroids or systemic steroids, oral 0.5–1 mg/kg/day	Not recommended	Suspended temporarily[a]
3	Hospitalization	Systemic steroids, oral or IV 1–2 mg/kg/day for 3 days, then reduce to 1 mg/kg/day	To be considered for patients with unresolved symptoms after 3–5 days of steroid course (organ specialist referral advised)	Suspended and discuss resumption based on risk/benefit ratio with patient
4	Hospitalization, consider intensive care unit	Systemic steroids IV methylprednisolone 1–2 mg/kg/day for 3 days, then reduce to 1 mg/kg/day	To be considered for patients with unresolved symptoms after 3–5 days of steroid course (organ specialist referral advised)	Discontinue permanently

Source: Lonchay [28]

Cutaneous Toxicities

Skin maculopapular rashes, pruritus and rash are the most frequent secondary effects and are generally the first ones to appear [13].

Itchy eruptions are more frequent in anti-CTLA-4 treatments.

Skin rashes with or without pruritus are generally low to mild and can be treated easily with a rapid treatment.

Vitiligo can be observed by the patients treated for a melanoma.

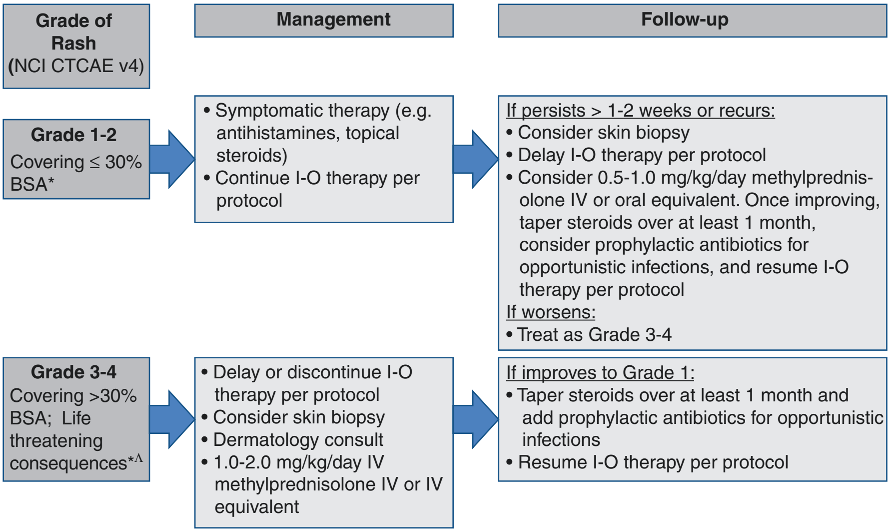
Clinical Nursing Evaluation

Signs and Symptoms

- General condition of the patient
- Clinical examination of the skin
- Redness, itching, eruption
- Oedema, pruritus, xerosis, rash
- Change in the pigmentation or the colour of the skin

Identify

- A pre-existing dermatitis
- A pre-existing psoriasis
- Haematological anomalies coherent with another aetiology (eosinophil, hepatic anomalies)



Grade of Rash (NCI CTCAE v4)	Management	Follow-up
Grade 1-2 Covering ≤ 30% BSA*	• Symptomatic therapy (e.g. antihistamines, topical steroids) • Continue I-O therapy per protocol	If persists > 1-2 weeks or recurs: • Consider skin biopsy • Delay I-O therapy per protocol • Consider 0.5-1.0 mg/kg/day methylprednisolone IV or oral equivalent. Once improving, taper steroids over at least 1 month, consider prophylactic antibiotics for opportunistic infections, and resume I-O therapy per protocol If worsens: • Treat as Grade 3-4
Grade 3-4 Covering >30% BSA; Life threatening consequences*^	• Delay or discontinue I-O therapy per protocol • Consider skin biopsy • Dermatology consult • 1.0-2.0 mg/kg/day IV methylprednisolone IV or IV equivalent	If improves to Grade 1: • Taper steroids over at least 1 month and add prophylactic antibiotics for opportunistic infections • Resume I-O therapy per protocol

Source: *Bristol Myers Squibb Management algorithms for immuno-oncology agents*

Cutaneous rash is a generic term.

Nurses have raised awareness to the patients with regard to the cutaneous SE by encouraging them to implement auto-care strategies.

Strategies for auto-care are use of gentle cleaning products respecting natural PH of the skin, use of hydrating creams and also use of high-level sun protective cream. It is mainly preventive intervention, even more for at-risk patients (dermatitis, xerosis).

If patients develop cutaneous toxicities, the nurse has to put a grade on this toxicity, propose adequate support care and work in team for their management. The role of treatment and use of topic and oral steroids and also antihistaminic are discussed with the multidisciplinary team, and a reference dermatologist could be solicited. Oral or intravenous corticotherapy will be the treatment to symptom resolution [14].

Vigilance is necessary throughout the treatment to recognize rapidly the first signs such as skin rashes, oral lesions, a folliculitis or other symptoms of the syndrome of Stevens-Johnson or toxic epidermal necrolysis which represent medical emergencies usually requiring hospitalization.

Gastrointestinal Toxicities

Gastrointestinal toxicities are the second most frequently observed secondary effects with immunotherapy, going from light diarrhoea to severe colitis and intestinal perforation, leading to death in some rare cases.

For the severe form of diarrhoea, a consultation with a gastroenterologist is often necessary.

Clinical Nursing Evaluation

Signs and Symptoms

- Weakness
- Fatigue
- Fever
- Loss of appetite
- Loss of weight
- Dehydration
- Modification of the frequency of stools and modification of their consistence; rectal bleeding, mucus or phlegm
- Abdominal pain

Identify

- Blood anomalies
- Dehydration
- Infectious cause
- Perforation’s signs (pain, bloating)

Grade of Diarrhea/ Colitis (NCI CTCAE v4)	**Management**	**Follow-up**
Grade 1 Diarrhea:< 4 stools/day over baseline; Colitis: asymptomatic	• Continue I-O therapy per protocol • Symptomatic treatment	• Close monitoring for worsening symptoms. • Educate patient to report worsening immediately If worsens: • Treat as Grade 2 or 3/4
Grade 2 Diarrhea: 4-6 stools per day over baseline; IV fluids indicated <24 hrs; not interfering with ADL Colitis: abdominal pain; blood in stool	• Delay I-O therapy per protocol • Symptomatic treatment	If improves to grade 1: • Resume I-O therapy per protocol If persists > 5-7 days or recur: • 0.5-1.0 mg/kg/day methylprednisolone or oral equivalent • When symptoms improve to grade 1, taper steroids over at least 1 month, consider prophylactic antibiotics for opportunistic infections, and resume I-O therapy per protocol. If worsens or persists >3-5 days with oral steroids: • Treat as grade 3/4
Grade 3-4 Diarrhea (G3): ≥7 stools per day over baseline; incontinence; IV fluids ≥24 hrs; interfering with ADL Colitis (G3): severe abdominal pain, medical intervention indicated, peritoneal signs G4: life-threatening, perforation	• Discontinue I-O therapy per protocol • 1.0 to 2.0 mg/kg/day methylprednisolone IV or IV equivalent • Add prophylactic antibiotics for opportunistic infections • Consider lower endoscopy	If improves: • Continue steroids until grade 1, then taper over at least 1 month If persists > 3-5 days, or recurs after improvement: • Add infliximab 5 mg/kg (if no contraindication). Note: Infliximab should not be used in cases of perforation or sepsis

Source: *Bristol Myers Squibb Management algorithms for immuno-oncology agents*

The nursing role is essential in the early recognition and graduation of those toxicities compared to the basis anamnesis.

Because simple diarrhoea can evolve quickly towards colitis and severe forms, it is important that the patient reports any gastrointestinal modification however small it is.

For moderate to severe diarrhoea, corticotherapy is the key to manage the symptoms.

Resolution of the problem is often fast and also the reintroduction of immunotherapy.

Hepatic Toxicities: Hepatitis

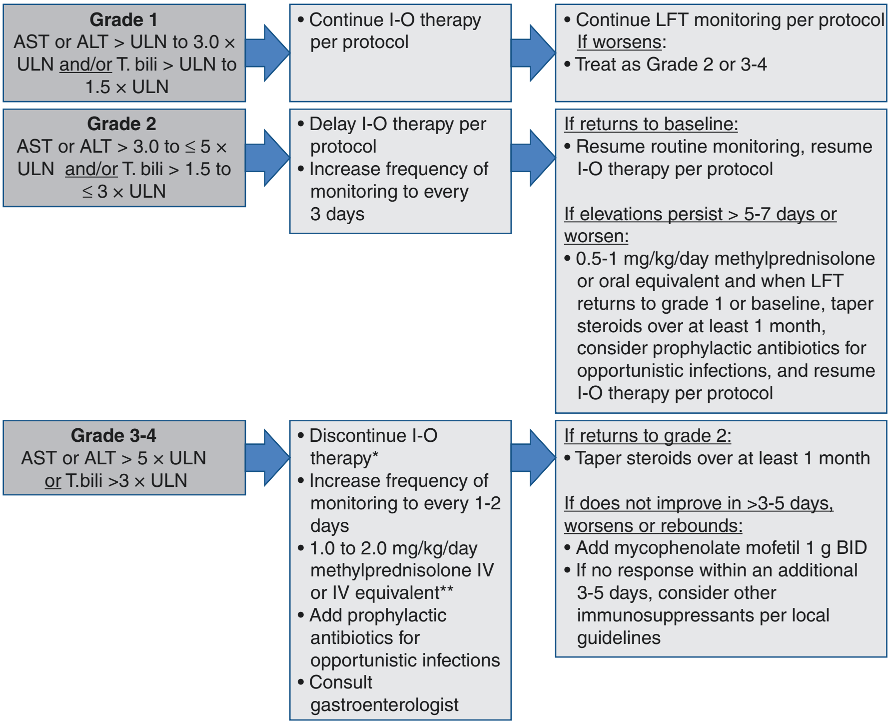
Clinical Nursing Evaluation

Signs and Symptoms

- Fatigue
- Diminution of energy level
- Bruises
- Jaundice
- Modification of the colour of the stools
- More frequent bleeding
- Darker urines
- Increased perspiration

Identify

- Blood anomalies: rising of the transaminase
- Augmentation of total bilirubin
- Alteration of the gastrointestinal function
- Jaundice
- Ascites
- Infectious aetiology linked to other pathologies



Grade 1 AST or ALT > ULN to 3.0 × ULN and/or T. bili > ULN to 1.5 × ULN	• Continue I-O therapy per protocol	• Continue LFT monitoring per protocol If worsens: • Treat as Grade 2 or 3-4
Grade 2 AST or ALT > 3.0 to ≤ 5 × ULN and/or T. bili > 1.5 to ≤ 3 × ULN	• Delay I-O therapy per protocol • Increase frequency of monitoring to every 3 days	If returns to baseline: • Resume routine monitoring, resume I-O therapy per protocol If elevations persist > 5-7 days or worsen: • 0.5-1 mg/kg/day methylprednisolone or oral equivalent and when LFT returns to grade 1 or baseline, taper steroids over at least 1 month, consider prophylactic antibiotics for opportunistic infections, and resume I-O therapy per protocol
Grade 3-4 AST or ALT > 5 × ULN or T.bili >3 × ULN	• Discontinue I-O therapy* • Increase frequency of monitoring to every 1-2 days • 1.0 to 2.0 mg/kg/day methylprednisolone IV or IV equivalent** • Add prophylactic antibiotics for opportunistic infections • Consult gastroenterologist	If returns to grade 2: • Taper steroids over at least 1 month If does not improve in >3-5 days, worsens or rebounds: • Add mycophenolate mofetil 1 g BID • If no response within an additional 3-5 days, consider other immunosuppressants per local guidelines

Source: *Bristol Myers Squibb Management algorithms for immuno-oncology agents*

It is recommended that nurses closely monitor hepatic values before and during the treatment.

Specialized advice will be required in case of grade 2 or grade 1 persisting for more than 2 weeks, in the absence of obvious aetiology [15].

Endocrine Toxicities: Endocrinopathy

This term encompasses mainly the following inflammation: hypothyroidisms, hyperthyroidisms, adrenal insufficiency, hypophysitis and diabetes.

Endocrinopathy under immunotherapy occurs because the immune system, hyperactive, causes damage to the endocrine organs by imitating the auto-immune process.

Endocrinopathies are less frequent than the cutaneous or gastrointestinal SE, but they can have severe consequences if they are not recognized and correctly treated [16].

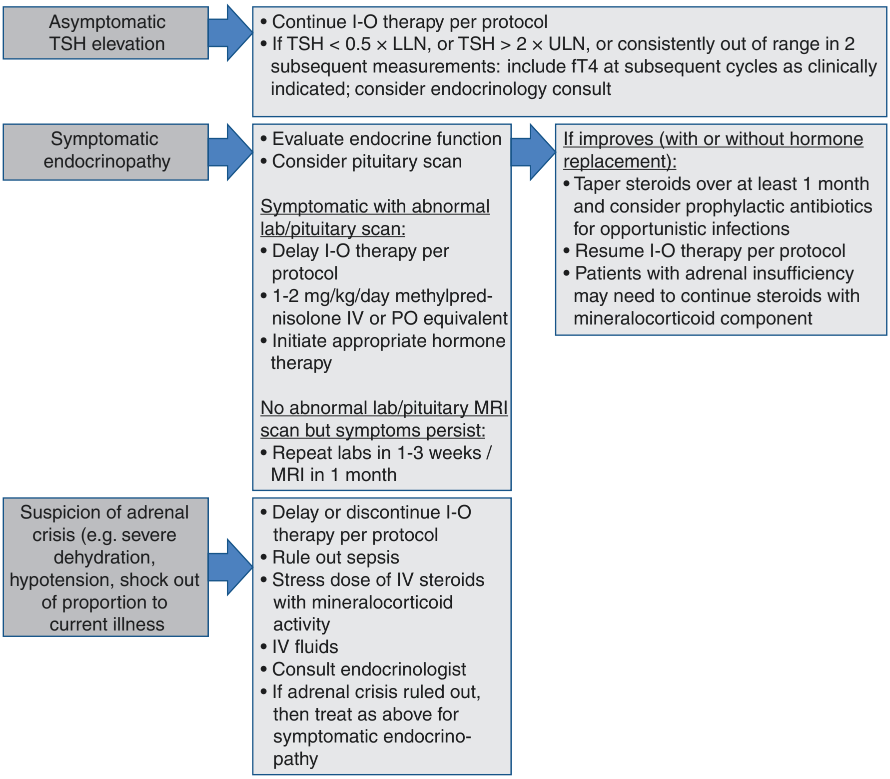
Clinical Nursing Evaluation

Signs and Symptoms

- Fatigue
- Loss of energy
- Weight modification
- Palpitation
- Headaches
- Excessive thirst
- Frequent urination
- Modifications of the mental state
- Abdominal pain
- Unusual intestinal transit
- Hypotension
- Feeling of hot/cold

Identify

- Symptoms of diabetes: rising of the blood glycaemia
- Hyper- or hypothyroidism (modification of free TSH-T4)
- Hypophysitis: reduced hormonal rate (ACTH-TSH-FSH-LH-GH), reduced rate of cortisol
- Infection
- Other diagnoses such as depression



Asymptomatic TSH elevation

- Continue I-O therapy per protocol
- If TSH < 0.5 × LLN, or TSH > 2 × ULN, or consistently out of range in 2 subsequent measurements: include fT4 at subsequent cycles as clinically indicated; consider endocrinology consult

Symptomatic endocrinopathy

- Evaluate endocrine function
- Consider pituitary scan

Symptomatic with abnormal lab/pituitary scan:

- Delay I-O therapy per protocol
- 1-2 mg/kg/day methylprednisolone IV or PO equivalent
- Initiate appropriate hormone therapy

No abnormal lab/pituitary MRI scan but symptoms persist:

- Repeat labs in 1-3 weeks / MRI in 1 month

If improves (with or without hormone replacement):

- Taper steroids over at least 1 month and consider prophylactic antibiotics for opportunistic infections
- Resume I-O therapy per protocol
- Patients with adrenal insufficiency may need to continue steroids with mineralocorticoid component

Suspicion of adrenal crisis (e.g. severe dehydration, hypotension, shock out of proportion to current illness

- Delay or discontinue I-O therapy per protocol
- Rule out sepsis
- Stress dose of IV steroids with mineralocorticoid activity
- IV fluids
- Consult endocrinologist
- If adrenal crisis ruled out, then treat as above for symptomatic endocrinopathy

Source: *Bristol Myers Squibb Management algorithms for immuno-oncology agents*

Nursing role in the identification of endocrinopathy is not always easy since endocrinopathy often presents with vague and diffuse symptoms (e.g. fatigue, headache, depression, drowsiness) that require a deeper evaluation and a reference to basis anamnesis before every perfusion.

If needed, it is necessary to initiate a substitution hormone therapy in a way that is often irreversible [17].

Collaboration with an endocrinologist can be essential in order to respond to the requirements of those conditions.

Pulmonary Toxicities: Pneumonitis

Pneumonitis is a less frequent disease but can potentially be fatal. Inflammatory or interstitial severe pneumopathy can be observed. Such as endocrinopathy the pneumonitis tends to occur lately than the other SE associated to immunotherapies [18].

Pulmonary toxicities are more frequent in the patients affected with a lung cancer.

The importance of a deep basis anamnesis will help us as for the evolution of the symptoms and will allow us to detect a problem from its installation.

Clinical Nursing Evaluation

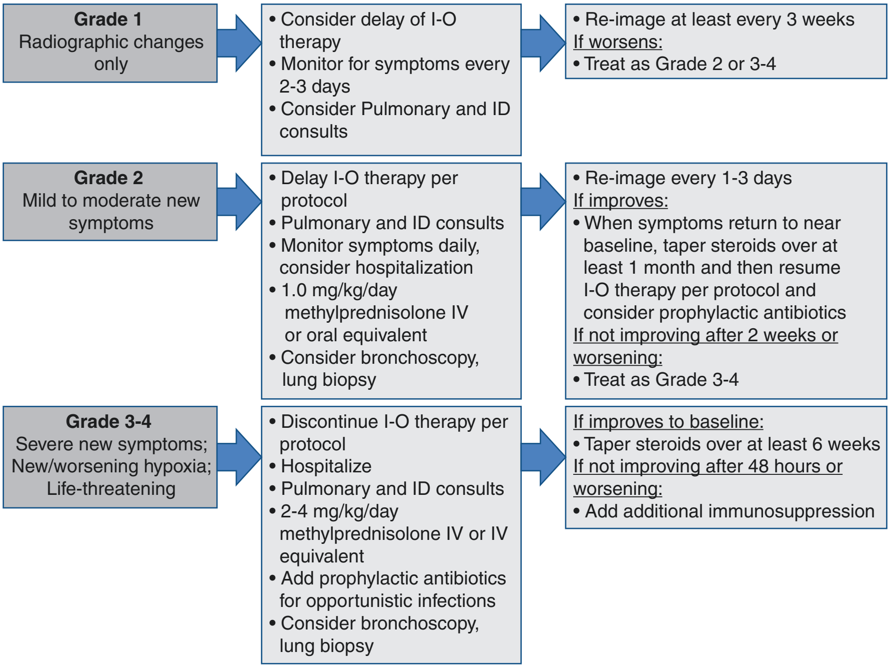
Signs and Symptoms

- Dyspnoea
- Respiratory despair
- Coughing
- Expectoration
- Fatigue
- Wheezing
- Fever

Identify

- Is O2 saturation lower than at basis anamnesis?
- Is there a respiratory background: asthma, bronco-pulmonary?
- Chronical pathology, tobacco, sarcoidosis?
- Radiotherapy before?
- Pulmonary infection?

It is always necessary to look for another cause: infection, pulmonary embolism, progress of the disease.



Grade 1
Radiographic changes only

- Consider delay of I-O therapy
- Monitor for symptoms every 2-3 days
- Consider Pulmonary and ID consults

- Re-image at least every 3 weeks

If worsens:
- Treat as Grade 2 or 3-4

Grade 2
Mild to moderate new symptoms

- Delay I-O therapy per protocol
- Pulmonary and ID consults
- Monitor symptoms daily, consider hospitalization
- 1.0 mg/kg/day methylprednisolone IV or oral equivalent
- Consider bronchoscopy, lung biopsy

- Re-image every 1-3 days

If improves:
- When symptoms return to near baseline, taper steroids over at least 1 month and then resume I-O therapy per protocol and consider prophylactic antibiotics

If not improving after 2 weeks or worsening:
- Treat as Grade 3-4

Grade 3-4
Severe new symptoms; New/worsening hypoxia; Life-threatening

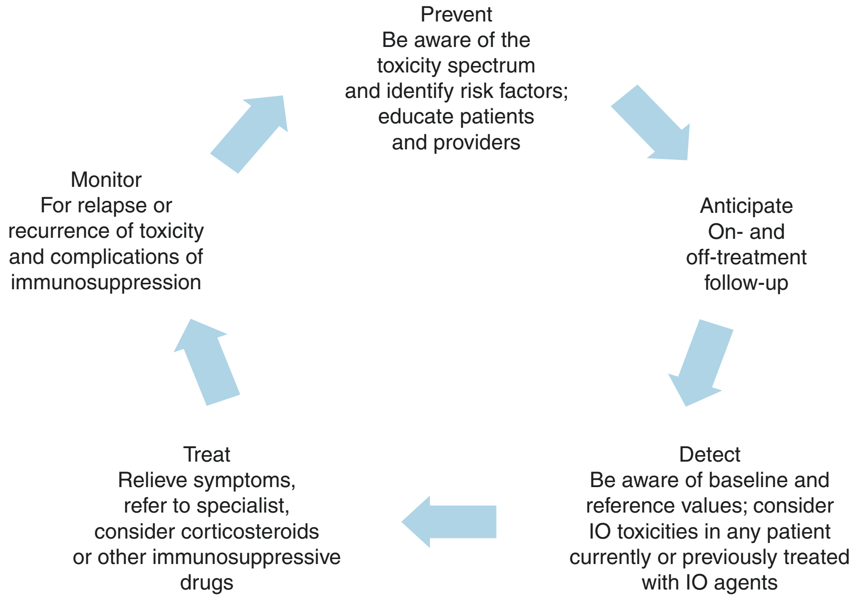
- Discontinue I-O therapy per protocol
- Hospitalize
- Pulmonary and ID consults
- 2-4 mg/kg/day methylprednisolone IV or IV equivalent
- Add prophylactic antibiotics for opportunistic infections
- Consider bronchoscopy, lung biopsy

If improves to baseline:
- Taper steroids over at least 6 weeks

If not improving after 48 hours or worsening:
- Add additional immunosuppression

Source: *Bristol Myers Squibb Management algorithms for immuno-oncology agents*

Five Pillars to Help the Management of Toxicities



Prevent
Be aware of the toxicity spectrum and identify risk factors; educate patients and providers

Anticipate
On- and off-treatment follow-up

Detect
Be aware of baseline and reference values; consider IO toxicities in any patient currently or previously treated with IO agents

Treat
Relieve symptoms, refer to specialist, consider corticosteroids or other immunosuppressive drugs

Monitor
For relapse or recurrence of toxicity and complications of immunosuppression

Adapted from Champiat et al. [19]

(A) Prevent

It is crucial that all the team knows the spectrum of toxicities and be trained to manage the SE.

Before starting any treatment with immunotherapy and after having informed and educated the patient to the secondary effects, it is essential that he/she is aware of when, how and who to contact in case of a suspicion of SE or any other question related to his/her treatment and pathology.

It is necessary to stress on any "early detection". Indeed, as mentioned before, a SE taken at a starting grade can be reversible and will allow the continuity of treatment. It is important that an anamnesis specific to immunotherapy be completed. This anamnesis is a real snapshot of the patient's initial state.

It will also be participative. Indeed the auto-evaluation from the patient will reinforce his/her role as an actor in the process [19].

Side effects
Explain condition
How do you evaluate your health?
Are the treatments creating a worry in your life's organization?
Would you like to communicate us with anything?
What is your level of energy?
To which degree would you describe the fatigue you have now?

Side effects
What is your appetite?
Do you have sleeping difficulties?
What is your weight? Height?
Digestive system
Are you experiencing diarrhoea or an increase in bowel movement?
Are you experiencing any nausea?
Have you experienced abdominal pain or tenderness?
Have your stools changed in colour?
Skin
Is your skin dry or itchy?
Is your skin peeling?
Lungs
Are you experiencing shortness of breath or chest pain?
Do you have a new or worsening cough?
Liver
Have you noticed yellowing of the skin or eyes?
Have you noticed right-sided abdominal pain?
Do you bleed or bruise more easily?
Kidneys
Have you experienced a decrease in urine production or change in the colour of your urine?
Are your ankles swollen?
Hormonal change
Are you feeling hungrier or thirstier than usual?
Are you feeling more tired than usual?
Are you feeling colder or warmer than usual?
Have you experienced headaches, dizziness or fainting?
Are you constipated?
Is your voice deeper?
Have you or your family members noticed any changes in your mood or behaviour?

Physical examination [20]:
  - Weight
  - Height
  - Blood pressure measurement
  - Cardiac frequency
  - Measure of O2 saturation
  - Temperature

Medical history:
  - Identify dysimmunitary risk factors
  - Personal and familial history of auto-immune diseases
  - Psoriasis, thyroiditis, Crohn's disease, pancreatitis, lupus, polyarthritis, type 2 diabetes
  - Chronic infections: viral hepatitis, tuberculosis, HIV
  - Notion of toxicity linked to anterior immunotherapy

Surgical medical records

Laboratory testing:
  - Complete blood biology
  - Reference imaging: thoracic scan

At the end of the therapeutic education process, it is appropriate to ensure the good comprehension from the patient and his/her relatives. In order to do this, there are some examples of questions that will allow you to evaluate the level of comprehension of the patient.

- What would you do if you see some sores in your body?
- When do you have to call your doctor or nurse?
- Do you know who you have to call in case of necessity?
- Have you got others questions to ask?

The general practitioner, physical therapist and pharmacist have to be informed of the treatment followed by the patient, and he/she has to be in possession of an "alert card" with destination to other carers. This card will contain the main information about the treatment.

(B) Anticipate

Anamnesis has to be readapted before each perfusion; the situation has to be re-evaluated.

Examples of Questions for the Patient
- Would you like to share about a change, even small, that appeared since your last treatment?
- How do you evaluate your tolerance to the treatment?

Physical Examination
- Weight
- Height
- Blood pressure measurement
- Cardiac frequency
- Measure of O2 saturation
- Temperature
- Complete clinical evaluation
- Blood test before each perfusion: renal function, COFO, hepatic enzymes, TSH and proteinuria (1x each 2 months)

A medical check-up (scanner and more complete blood) will take place every 3 months, apart from the first medical check-up that takes place after 2 months.

(C) Detect

Refer to the basis anamnesis.

When an event appears, there are three possibilities:

1. It is a tumour progression.
2. It is a fortuitous event (differential diagnosis).
3. It is really an auto-immune toxicity: it's necessary to grade the SE in order to treat it in an appropriate way.

When there is a doubt on a dysimmunitary affection (cough, diarrhoea, biological perturbations), propose a complementary check-up as soon as possible [21].

(D) Treat

A symptomatic treatment should be established for the low to moderate grades.

A majority of SE are reversible if treated at an early stage.

The treatment with corticoids, oral or intravenous, will be made according to the grade.

Grades 3 and 4 often require hospitalization.

Corticoids will be gradually decreased, and the immunotherapy will be reintroduced from reduction of the symptoms in grade 1.

In case of resistance to corticoids, we shall administer an immune-suppressor treatment.

The definitive stop of immunotherapy will be done for grade 4 or grade 3, severe or recurrent.

It is necessary to remain vigilant permanently; there is always a risk of relapse or a new SE.

It is from then on important to have a specialist network of resource in case of toxicity.

(E) Monitor

Time of resolution varies according to the secondary effect.

(Ref. Kinetics of appearance irAEs).

When corticotherapy is administrated on a long period of time, it is convenient to prescribe to the patient a prophylactic antibiotherapy against germs [22].

Conclusion

New treatments in immunotherapy allow today a considerable extension of the length of life and quality of life of the patients.

Thanks to their knowledge on the pathology and treatments in immunotherapy, nurses in oncology can have a positive impact on the continuity of the treatment, by educating the patients on the importance to indicate immediately any changes of their health, by supplying a support for the patients throughout the treatment process and, finally, by estimating the observance and the understanding at the treatment in several stages of their therapy. The nurse serves as a link between the patient, his/her relatives, the medical team and the referent doctors.

The term interdisciplinarity takes all its meaning: the efficiency of care is increased by the implementation of a professional frame favouring the work in interdisciplinarity.

This way of working is not easy; "it needs a great communication and an active collaboration. It's working together with the same objectives" [23].

The research is advancing quickly therefore the knowledge of the medical staff must be constantly updated. Indeed, new targets will be identified to improve the efficacy of those treatments, to decrease the side effects and to be able to make it available to more patients [24].

The future is promising! Tomorrow, the immunotherapy can be administrated at home, it will be associated with other treatments, and the duration between perfusions will be longer. If our patient will be more and more at his home, our role as for him will always be very present!

There is still a long way to go and a lot of pages in the history of immunotherapy to write.

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6

Robotic Surgery

Danuta Lichosik

Abstract

Throughout the history of nursing, the discoveries and system of belief of yesterday have served as a platform for the innovations of today. That is especially true for minimally invasive surgery (MIS) approach; exactly indeed perioperative practitioners have been challenged to stay abreast of technology in a field that is a constantly changing landscape of new techniques and improved instruments and equipment. The “laparoscopic revolution” of the 1980s propelled and encouraged the changes toward a less invasive approaches and new techniques, such as modern robot-assisted surgery. Science and technology are advancing at an incredible pace. Over the last several decades, there has been technological advancement in the operating room. The use of robotics is expanding rapidly in the medical arena. The evolution of robotics in surgery is presented within the context of virtual reality, telepresence, telemanipulation, and passive (i.e., master-slave) robotic surgical systems. A critical analysis of these new developments becomes a duty in the perioperative nursing.

Minimally invasive surgeries, including robotic-assisted surgeries, are performed in many hospitals in the world, especially in genitourinary, gynecology, general, pediatric, cardiothoracic, head and neck, and breast surgery.

Nursing care for patients undergoing robotic surgery has crucial importance. The target is to reduce the risk during surgical procedures by adequate perioperative nursing for patients undergoing robotic procedure. The nursing team needs to strictly follow the protocols and specific procedures. Working tools must be shared and followed by all team members.

D. Lichosik (✉)
European Institute of Oncology, Milan, Italy
e-mail: danuta.lichosik@ieo.it

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Starting a robotic surgery program implies an organizing effort that has to be evaluated. The program can be challenging as multiple members of the team are learning the technology and their own personal roles on the team. Important is to point out that robotic surgery program needs frequent update and audit regarding efficiency, outcomes, and patient satisfaction.

Keywords

Robotic surgery · da Vinci Surgical System · Robotic surgery program Multidisciplinary approach · Nurses' roles · Challenges and opportunities for OR nurses · Education · Training · Learning curve · Perioperative nursing care Patient advocacy

Introduction

Robotic surgery, computer-assisted surgery, and robotically assisted surgery are terms for technological developments that use robotic systems to aid in robotic procedures. Robotically assisted surgery was developed to overcome the limitations of pre-existing minimally invasive surgical procedures and to enhance the capabilities of surgeons performing open surgery. Due to these techniques, there is reduced duration of hospitalization, blood loss, transfusions, and use of pain medication and less of surgical scars.

Robot-assisted surgery has recently changed the face of surgery, and robotic technology has been in constant fluctuation over the last 20 years. Robotic surgery has been standard procedure in many large hospitals in the world. Robot-assisted surgery has given perioperative nurses the opportunity to adapt and renew their practice, think creatively, and develop efficient practices to care for the patients undergoing robotic surgery procedures.

Serious complications may occur in any surgery, including da Vinci® Surgery; individual surgical results may vary. Patients should talk to their doctor to decide if da Vinci Surgery is right for them. Patients and doctors should review all available information on nonsurgical and surgical options in order to make an informed decision.

Evolution of Surgical Robots

Robotic systems for minimally invasive surgery have been developed or are under development to enhance the precision and extend the capabilities of surgeons in many surgical specialties as cardiothoracic surgery, abdominal surgery, urology, gynecology, pediatric surgery, breast surgery, head and neck surgery, neurosurgery, orthopedics, ophthalmology, and other surgical fields. Compared with other minimally invasive approaches, robot-assisted surgery gives the surgeon better view of surgical site and better control over the surgical instruments. The three-dimensional view with depth perception is a marked improvement over the conventional laparoscopic camera views. Hand tremors are filtered out by the robot's computer software, and finally, surgical robotic system can continuously be used by rotating surgery teams.

The Key Elements that Contribute to Raise a Successful Robotic Program

- Development of the business plan requires an evaluation of the direct costs such as:
  - *Buying the robotic system and of the associated material.*
  - *Operating room (OR) modifications could be necessary.*
  - *Staff recruitment and/or staff training.*
- The cost analysis – we need to evaluate the following items:
  - *The cost of robot-assisted procedures surgery*
  - *Reimbursement (according to the different health systems)*
- Starting a robotic surgery program implies an organizing effort that has to be evaluated. Robotic surgery program needs frequent update and audit regarding efficiency, outcomes, and patient satisfaction. High surgical volume center can have an impact in terms of variable costs reduction. The best chance to increase surgical volume and therefore to reduce costs is to share the use of the da Vinci system with many surgical teams and specialties.

Brief History

In the mid-to-late *1980s*, a group of researchers at the National Aeronautics and Space Administration (*NASA*) Ames Research Center working on virtual reality became interested in using this information to develop telepresence surgery. This concept of telesurgery became one of the main driving forces behind the development of surgical robots. In the early 1990s, several of the scientists from the *NASA*-Ames team joined the Stanford Research Institute (*SRI*). Working with *SRI* are other roboticists and virtual reality experts; these scientists developed a dexterous telemanipulator for hand surgery. While these robots were being developed, general surgeons and endoscopists joined the development team and realized the potential these systems had in ameliorating the limitations of conventional laparoscopic surgery.

In 1985, a robot, the *PUMA 560*, was used to place a needle for brain biopsy using CT guidance. Three years later, the same robotic system has been used to perform a transurethral resection.

In 1987, these technological advancements led to the first laparoscopic surgery, laparoscopic appendectomy performed by German gynecologist Dr. Kurt Semm, and laparoscopic cholecystectomy in 1987 by French surgeon Dr. Philippe Mouret.

Some literature mention that first laparoscopic cholecystectomy was performed in 1985 by the German surgeon Erich Mühe.

In 1988, the *PROBOT*, developed at Imperial College London, designed specifically to aid in the prostatic tissue. The system has image guide, model based, with simulation and online video monitoring.

In 1990, the Automated Endoscopic System for Optimal Positioning (*AESOP*) system produced by Computer Motion became the first system approved by the Food and Drug Administration (*FDA*) for its endoscopic surgical procedure.

In 1992, the *ROBODOC*, from Integrated Surgical Systems (*ISS*), has been introduced in orthopedic surgery to mill out precise fittings in the femur for hip replacement. This system made a medical history as a first robot assisting in a human total hip arthroplasty (*THA*).

The first application of robotics in abdominal surgery dates back to 1993, when Yulin Wang succeeded in developing the first *FDA*-approved robotic device for use in general surgery. Automated Endoscopic System for Optimal Positioning (*AESOP*) consisted of a table-mounted articulating arm that was used to control the movements of the camera during laparoscopic surgery. Originally, the *AESOP* was manipulated by hand or foot controls, but the later version was capable of utilizing voice commands and incorporated voice control of the endoscope and operating room lights.

In 2001, introduction of the *ZEUS* system (Computer Motion Inc., Santa Barbara, CA) represented the real step toward the modern concept of robotically assisted laparoscopic surgery. This platform allowed the surgeon to control a robotic slave device that was docked to the patient remotely from a console. The *ZEUS* robotic system had a camera arm that was voice controlled (*AESOP System*), along with two other operating arms that provided four degrees of freedom and were able to hold a variety of instruments that were telemanipulated with joysticks from the surgical console. Jacques Marescaux utilized the *ZEUS* system, in *2001*, to perform a robot-assisted cholecystectomy on a patient in Strasbourg, France, who was 4000 km away from the surgeon in New York. This procedure, nicknamed "Operation Lindbergh," was a demonstration of telepresence in surgery. This means that specialists can perform a surgery on patients whom is very far away without either of them having to travel.

In 1995 was founded Intuitive Surgical International in California. This group of researchers was able to develop the first Food and Drug Administration (*FDA*)-approved fully robotic system for application in laparoscopic surgery with licensed technologies from MIT, IBM, and Stanford Research Institute (*SRI*). Computer Motion Inc., Santa Barbara, CA with the *ZEUS* Robotic Surgical System carried out further development of robotic systems and Intuitive Surgical with the introduction of the *da Vinci Surgical System*.

In May 1998, Dr. Friedrich-Wilhelm Mohr using the da Vinci *surgical robot* performed the first robotically assisted heart bypass at the Leipzig Heart Centre in Germany.

In September 1999, Dr. Randall Wolf and Dr. Robert Michler performed the first robotically assisted heart bypass in the USA at The Ohio State University.

In 2000, the *da Vinci Surgical System* broke new ground by becoming the first robotic surgery system approved by the Food and Drug Administration (*FDA*) used in both adult and pediatric robotic surgery procedures in the following areas:

- *Urological surgeries*
- *Gynecological surgeries*
- *General laparoscopic surgeries*
- *General non-cardiovascular thoracoscopic surgeries*
- *Thoracoscopically assisted cardiotomy procedures*

This was the first time the Food and Drug Administration (*FDA*) approved an all-encompassing system of surgical instruments and camera/scopic utensils. The da Vinci robotic surgery system's three-dimensional magnification screen allows the surgeon to view the operative area with the clarity of high resolution. Robotic surgery system da Vinci removes the need to leverage the sides of the incision walls. This advancement allows for less contact between exposed interior tissue and the surgical device, greatly reducing the risk of infection. The "endowrist" features of the operating arms precisely replicate the skilled movements of the surgeon at the controls, improving accuracy in small operating spaces.

The "laparoscopic revolution" of the 1980s propelled and encouraged the changes toward less invasive approaches and new techniques, such as modern robot-assisted surgery.

Description of the Robotic System da Vinci

The da Vinci Surgical System is a collections of wristed servant tools called manipulators, which receive digital instructions from an interfaced computer. The manipulators inside the patient's body duplicate the surgeon's hand movements at the console (Figs. 6.1, 6.2 and 6.3). The system consists of three main pieces:

- **The surgeon console** – *where surgeon sits to perform the procedure*
- **The patient cart** – *which holds the instrumentation*
- **The vision cart** – *which house the camera, light source, and other ancillary equipment such as the electrosurgical unit*

The EndoWrist Instruments are available in a wide selection of specialized tip designs. Each instrument has a specific surgical mission such as clamping, suturing, and tissue manipulation. The EndoWrist product line includes:

- *Wide variety of forceps*
- *Needle drivers*
- *Scissors*
- *Monopolar and bipolar electrocautery instruments*
- *Scalpels*
- *Other specific instruments*

Fig. 6.1 da Vinci Robotic System – Instruments and Accessories. (Photograph *courtesy* of Intuitive Surgical, Inc.)

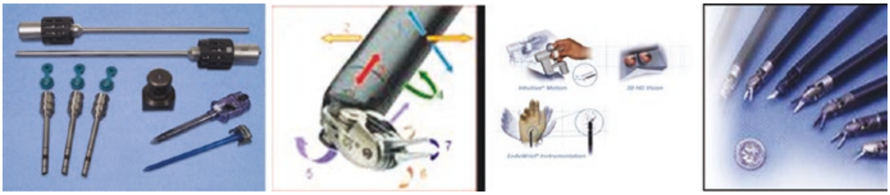

Fig. 6.2 da Vinci Robotic System Si – Instruments and Accessories. (Photograph *courtesy* of Intuitive Surgical, Inc.)

Fig. 6.3 da Vinci Robotic System Xi – Instruments and Accessories. (Photograph *courtesy* of Intuitive Surgical, Inc.)

The da Vinci Surgical System is used in several surgical specialties including urology, gynecology, general surgery, cardiothoracic surgery, pediatric surgery, head and neck surgery, neurosurgery, and breast surgery. Minimally invasive robotic surgery brings important benefits for patients and to the surgical team. The advantages of these systems are many because they overcome many of the obstacles of

Fig. 6.4 Diffusion of Robotic System da Vinci in the World in 2017 (4.149 Robotic System). (Data *courtesy* of Intuitive Surgical, Inc.)

laparoscopic surgery. They increase dexterity, restore proper hand-eye coordination and an ergonomic position, and improve visualization. In addition, these systems make surgeries that were technically difficult or unfeasible previously, now possible (Figs. 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 6.10 and 6.11).

da Vinci *Single-Site*: Instruments and Accessories

da Vinci® *Single-Site*® *Surgery* enables surgeons to operate through a small incision in the patient's umbilicus and is used often for a cholecystectomy or benign hysterectomy.

Single-Site Configuration

Compatible with the da Vinci *Si* and Xi Surgical System (Figs. 6.12 and 6.13)

The five-lumen port provides access for two *Single-Site* Instruments: the 8.5 mm 3DHD endoscope and a 5/10 mm accessory port and insufflation adaptor. The port enables simple and safe entry through a 1.5 cm incision and is designed to be used through curved cannula and to optimize triangulation toward the target anatomy while minimizing external collision of the instruments and camera arms.

Curved architecture separates the instrument arms outside the body wall, maximizing range of motion and minimizing instrument crowding. Instruments and camera cross within the *Single-Site* port and use remote center technology to minimize cannula collisions, arm interferences, and port-site movement. da Vinci System software automatically detects and reassociates the user's hands with the instrument tips to create *Intuitive*® movement through crossed cannula.

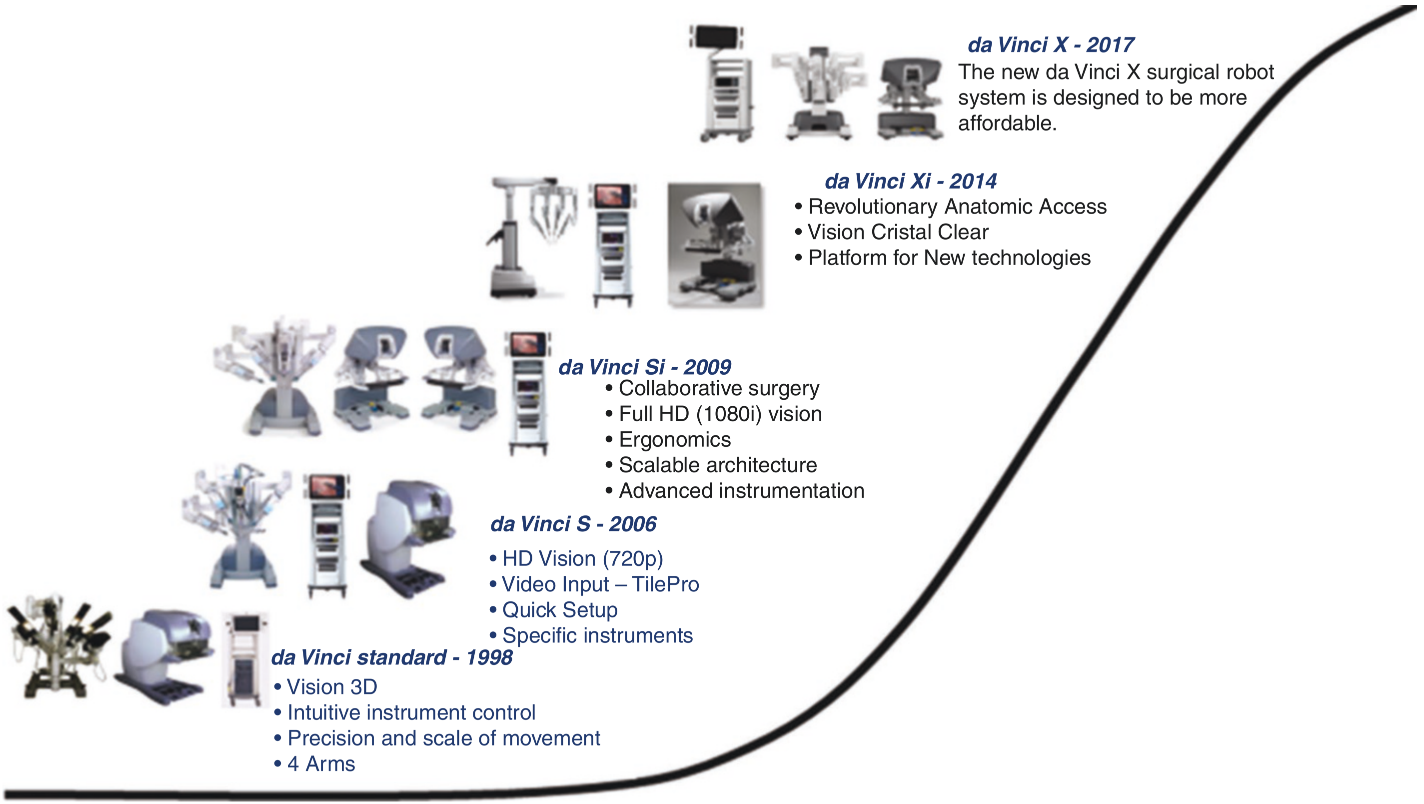

Fig. 6.5 Evolution of da Vinci Robotic Surgery System. (Photograph *courtesy of* ab medica S.p.A.-Italy)

Fig. 6.6 Robotic System da Vinci® S™ 1998. (Photograph *courtesy* of Intuitive Surgical, Inc.)

Fig. 6.7 Robotic System da Vinci® S™ 2006. (Photograph *courtesy* of Intuitive Surgical, Inc.)

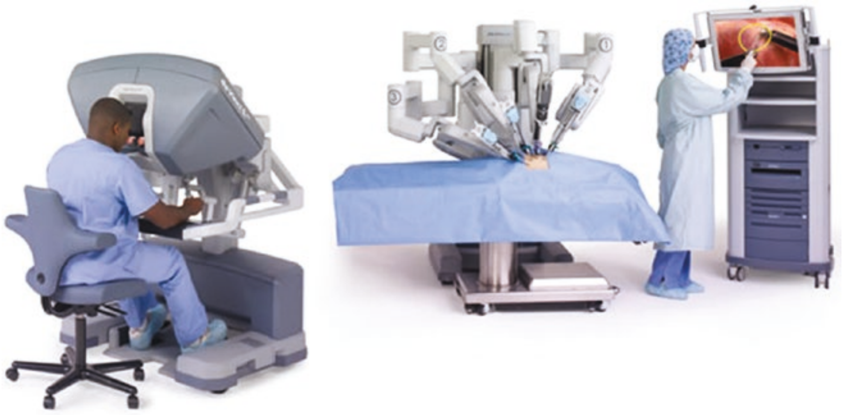

Fig. 6.8 Robotic System da Vinci® S™ 2009. (Photograph *courtesy* of Intuitive Surgical, Inc.)

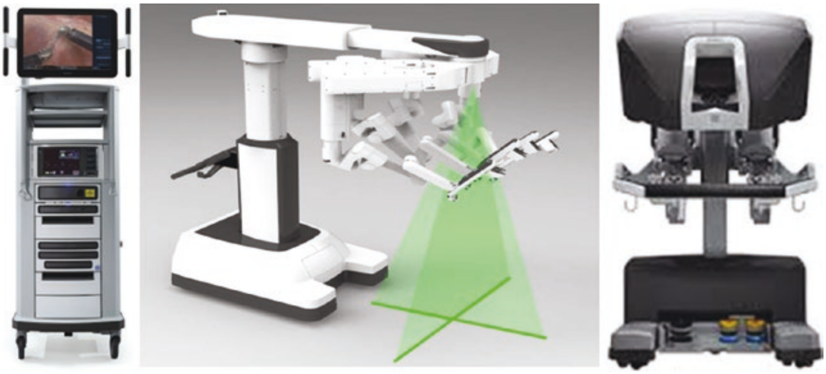

Fig. 6.9 Robotic System da Vinci® Xi™ 2014. (Photograph *courtesy* of Intuitive Surgical, Inc.)

Fig. 6.10 Robotic System da Vinci® X™ 2017. (Photograph *courtesy* of Intuitive Surgical, Inc.)

da Vinci Xi™	da Vinci X™	da Vinci SP™
		

Fig. 6.11 Evolution of Robotic System da Vinci X (*Patient carts*). (Photograph *courtesy* of Intuitive Surgical, Inc.)

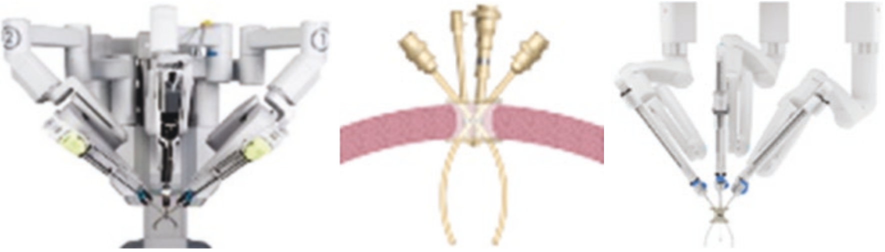

Fig. 6.12 Robotic System da Vinci System Si and Xi Single Site. (Photograph *courtesy* of Intuitive Surgical, Inc.)

Role of the Perioperative Nurse in Robotic Surgery

The various perioperative nursing roles all subsume elements of the behaviors and technical practices that characterize professional nursing. No other area of nursing requires the broad knowledge base, the instant recall of nursing science, the need to be intuitively guided by nursing experience, the diversity of thought and action, the stamina, and the flexibility needed in perioperative nursing endeavors. The perioperative nurse depends on knowledge of surgical anatomy, physiologic alterations and their consequences for the patient, intraoperative risk factors and the means of preventing them, and psychosocial implications of surgery for the patient and his family. This knowledge enables the perioperative nurse to anticipate needs of the patient and surgical team and initiate safe and appropriate nursing intervention rapidly.

The Association of Perioperative Registered Nurses (AORN) has asserted the significance of such safety by affirming that staffing skills mixes must ensure that patients undergoing surgical and invasive procedures have a perioperative nurse as the circulator, and the core activities of perioperative nursing care (assessment, diagnosis, outcome identification, planning, and evaluation; discussed subsequently) are completed by the perioperative nurse (Fig. 6.14).

Fig. 6.13 Sample of single port robotic instruments, Robotic Surgery da Vinci System Si and Xi. (Photograph *courtesy* of Intuitive Surgical, Inc.)

Maryland bipolar forceps

Fenestrated bipolar forceps

Suction irrigation

Perioperative Nursing and Patient Advocacy in Robotic Surgery

Patients undergoing robotic surgery are anesthetized and are powerless to make decisions on their own behalf. During activity of nursing in OR, nurses must not forget patients' perceptions of this new technology. Nurse's duty is to inform, counsel, and comfort the patients about this new technology. A friendly hello from the nurse who performed perioperative preparation would be appropriate to give a patient/s an impression that we are his/her advocate. As their advocate, nurses should give them the opportunity to meet the members of their surgical team and receive all information about surgical procedure. The intraoperative advocate role continues as we position (often in Trendelenburg position) and monitor the patient for the procedure. It is circulating nurse's job to keep the patient safe and free from injury. There should always be nurse focused solely on the patient during highly technology surgical procedure as robot-assisted surgery. To give thorough report to the recovery room nurse is very important for postoperative follow-up.

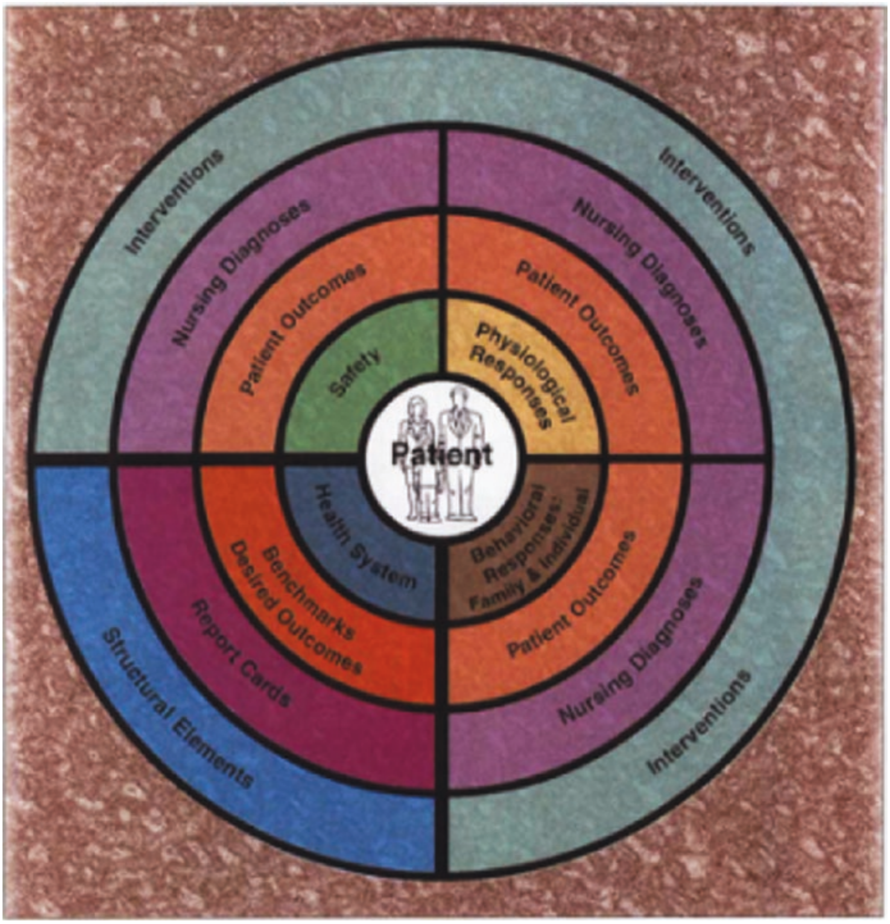

Fig. 6.14 Nursing in OR – JC Rothrock, DA Smith – AORN journal, 2000 – Wiley, Online Library

In conclusion, patient advocacy during robotic surgery is vital for the success of patient's outcomes. Establishing a trusting and positive nurse-patient relationship decreases the patient's fear and apprehension over surgery and this technology.

What Are the Challenges and Opportunities for Nurses?

The role of the robotics nurse specialist is both challenging and exciting because the technology is new and the role is open to interpretation and definition and, because of this, needs a flexible job description. Daily practice shows us the need for continuous education, especially regarding e-nursing skills, creation, and revision of guidelines and specific protocols. Science and technology are advancing at an incredible pace, and a critical analysis of these new developments is the responsibility of the perioperative nurse. Nurses, as members of the robotic surgical team, must demonstrate a very good level of professional knowledge and be an expert in robotic technology. This is demonstrated by playing a key role in data collection, analyzing trends and outcomes, and identifying safety issues. The operating theater nursing staff has an important responsibility to work following best-practice rules. To analyze periodically their roles and skills is an effective instrument to improve everyday practice. The creation and application of guidelines and specific protocols give positive results in daily practice and maintain standards of care.

What Are the Implications for Working as a Multidisciplinary Team?

Robotic technology has increased the need for staff in the operating room. The nurse coordinator, scrub nurse, and circulators involved in a robotics program become as specialized as the doctors doing the actual surgery. When one surgery ends, nurses and surgical technicians are responsible for completing the medical charts, undocking the robot and doing an inventory of the robotic instruments, and then the cleanup and setup for the next case. Everything happens at once, and it is labor intensive. Operating room staff strive to improve efficiency while maintaining the highest quality to benefit the patient, surgeons, and the hospital. This creates much more of a team, with an equal approach within the operating room – which I have found to be not only much more efficient but much friendlier, fun, and, most of all, beneficial to the patient. There is no question that with the expertise of surgeons and good robotic nursing coordinator, scrub nurse circulators, and technicians, the robotic surgery program can be developed. The team approach has helped robotics to be recognized (Figs. 6.15 and 6.16).

What Does Robotic Surgery Mean for Nurse Training?

The training pathway incorporates product training, clinical training, and clinical education for integrated teams of both surgeons and operating theater staff. The primary purpose of training programs is to develop and increase a surgical team's confidence and competence in the use of da Vinci surgical system. The ultimate goal is to develop a self-sufficient team fully capable of performing surgical procedures with minimal product support and instruction. The training programs are designed for surgeons, first assistants, nurses, da Vinci coordinators, residents, and fellows. The da Vinci Skills Simulator contains a variety of exercises and scenarios specifically designed to give users the opportunity to improve their proficiency with the console controls. Simulation is an important part of the learning experience for robotic surgical technology. The exercises range from basic to advance and are designed to be relevant to surgeons and nurses from any surgical specialty (Fig. 6.17).

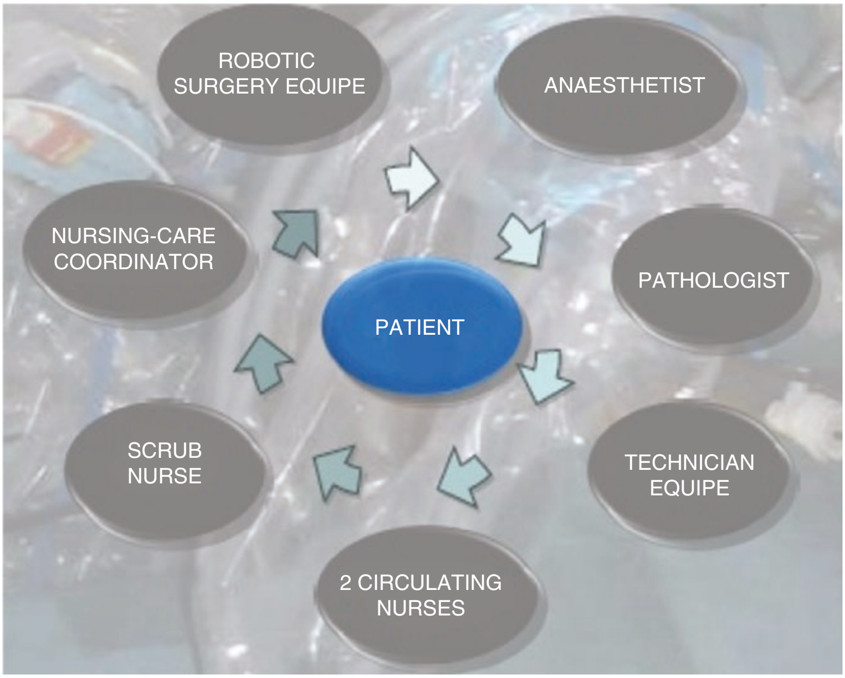

Fig. 6.15 Robotic Surgery – multidisciplinary team work during robotic surgery procedure. (Photograph *D. Lichosik private archive*)

Fig. 6.16 Robotic surgery team – European Institute of Oncology, Milan/Italy. (Photograph *D. Lichosik private archive*)

Fig. 6.17 Nurses training in robot-assisted surgery – learning how to position the patient correctly to avoid neuromuscular injuries. (Photograph *D. Lichosik private archive*)

da Vinci Surgical System Training

The beginning of any robotic program can be challenging as multiple members of the team are learning the technology and their own personal roles on the team. According to the experience of the robotic surgery centers, three to five cases per week during the initiation of the program are necessary to obtain continuity in the learning curve. Very important is to define which robotic procedures need to be performed at the beginning, since the main goal of a robotic team is to standardize the procedure as soon as possible. Different professional figures involved in the robotic program have their own learning curve. Education is clearly an important tool in the development of robotic surgery in the world. “Learning to learn” and “learning to practice” are essential for good clinical practice, especially in a fast-moving area such as robotic surgery (from wide basic knowledge to highly specialized and technological knowledge).

Learning new medical technology requires guided and self-directed training. To that end, *Intuitive Surgical* developed the da Vinci® Technology Training Pathway. The goal is to help teams develop the knowledge and skills needed to use da Vinci System technology safety and efficiently. Designed for integrated groups of surgeons and OR staff, this team-oriented approach was developed because da Vinci training is most successful when the entire team is involved.

The Technology Training Pathway focuses on:

- System knowledge and skill development – develop a working understanding of the da Vinci Surgical System and learn technical skills used in the OR with a da Vinci Surgical System.
- Peer-to-peer education: learn and apply clinical techniques from experienced da Vinci surgeons. Qualified, independent medical professionals conduct surgeon-to-surgeon instruction and mentorship.

The ultimate goal of the da Vinci Technology Training Pathway is to train a surgical team on the da Vinci system technology and provide opportunities to safely integrate the technology into clinical applications. The da Vinci Technology Training Pathway is divided into four phases, with reinforcing activities and supporting tools for both surgeons and OR staff.

Training: da Vinci Skills Simulator

The da Vinci Skills Simulator provides for comprehensive da Vinci Surgical System adoption. When the simulator is integrated with a da Vinci *Xi*, *Si*, or *Si-e* surgeon console, users can engage in the following: surgeons and surgical teams can engage in training with system skills exercises and 3D videos to align training pathways to specific surgical specialties. The *Skills Simulator* exercises ranged from basic to advanced are designed to be relevant to surgeons from any specialty (Fig. 6.18).

Each exercise covers at least one of the following skill categories:

- ***EndoWrist*® Manipulation** – *EndoWrist* instruments are designed to provide surgeons with natural dexterity and a range of motion far greater than even the human hand. These exercises are designed to help users gain familiarity with the movement of these instruments.
- **Camera and Clutching** – The three-dimensional, enhanced high-definition vision of the da Vinci System offers a key clinical advantage in surgery, and these exercises help users improve camera control and learn to use the clutch effectively.

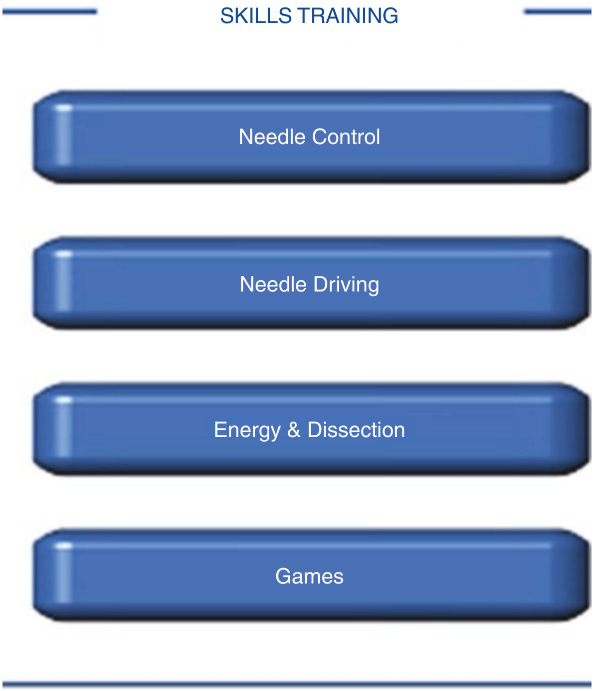

Fig. 6.18 Sample of skills training – Mimic's dV-Trainer™. (Photograph *courtesy* of Intuitive Surgical, Inc.)

- **Fourth Arm Integration** – For more advanced instrument control skills, some exercises include a fourth instrument arm that must be used. This is designed to promote instrument skill and encourages users to think strategically about instrument placement during tasks.
- **System Settings** – The surgeon console features a comprehensive set of controls for user settings. Quiz exercises on the simulator focus on basic setting topics such as icons, ergonomics, and instrument scaling.
- **Needle Control and Driving** – These scenarios are designed to help users develop skill when manipulating needles, including a focus on how to effectively hand off and position needles while practicing with a range of geometries.
- **Energy and Dissection** – The footswitch panel enables users to perform a range of tasks such as swapping between different types of energy instruments. These exercises allow users to gain familiarity with the footswitch panel by letting them practice applying monopolar and bipolar energy while working on dissection tasks (Figs. 6.19 and 6.20).

Fig. 6.19 Training – simulator/MIMIC & ROSS. (Photograph *courtesy* of Intuitive Surgical, Inc.)

Fig. 6.20 Surgical team training – Mimic's dV-Trainer™. Robotic Surgical Simulator. (Photograph *courtesy* of Intuitive Surgical, Inc.)

Creating a robotic surgery program is an ongoing process, not one that is achieved when the first case is completed or a certain number of robots are up and running. Make sure your organization is committed to supporting and developing the program over the long term. Continue to do research is necessary. Development of technology, robotic system improvement, new types of surgery, and more complex cases over time need continuous effort from all staff. Incorporating robotic surgery in surgical activity is exciting, but ultimately only worth the investment in time and money if it ends up making patient care better.

Education is clearly an important tool in the development of robotic surgery in the world. "Learning to learn" and "learning to practice" are essential for good clinical practice, especially in a fast-moving area such as robotic surgery – from wide basic knowledge to highly specialized and technological knowledge.

The Future of Robotic Surgery

The future of robotic surgery is nearly as promising as the human will to invent better ways of accomplishing delicate medical procedures. It is reasonable to assume that the current advantages of robotic surgery systems will be expanded upon in the next generation of medical robotics. Removing human contact during surgery is taking to the next level with robotic surgery systems capable of functioning at greater distances between surgeons control console and the patient side table robotics. This would allow robotic surgery to be conducted with patients in a nearby "clean room," reducing or eliminating the intraoperative infection. It is possible for next-generation medical robotics and robotic surgery to conduct surgical prep work remotely as well.

The bedside assistant is a fundamental member of the robotic team and assumes numerous roles during surgery. By virtue of physical proximity, the assistant acts as the robotic console surgeon's link to the patient. Depending on the type of surgical practice, assistants can be residents, fellows, physician assistants, or nurse practitioners.

Advancements in making robotic surgery systems more capable of replicating the tactile feel and sensation a surgeon experiences during more invasive traditional procedures give the surgeon the best of both worlds. The surgeon can gain the precision and advantages of minimally invasive procedures without losing the sensory information helpful in making judgment calls during robotic surgery.

Until is unknown how robotic surgery would develop and evolve. Robotics does not replace human intelligence, skill, and experience, but there is confidence that it is the surgery of the future.

What Does the Future Look Like for Nurses' Role in Robotic Surgery; What Are the Challenges and the Opportunities?

As more surgeons perform robotic surgery and more patients experience it, operating room nurses see their roles changing as well. A nurse colleague of mine qualified since 1986 says her role traditionally has been a patient advocate offering emotional support, being part of the patient safety team and providing clinical care. Now, technological oversight is a large part of the picture. Before the patient arrives in the OR, nurses make sure the large robotic equipment is set up correctly in the operating room and other instruments and disposable items are ready for the surgical procedure (Figs. 6.21, 6.22 and 6.23).

The patient has to be positioned a certain way depending on what surgery will be performed. Proper patent positioning is essential for safe, successful surgical procedure. The surgical team plays significant role in ensuring uncompromised and physiologically safe patient positioning by understanding the systems affected by positioning and their associated risk. Robot-assisted surgery could be performed on many different anatomic areas; the body may be positioned in multiple, sometimes

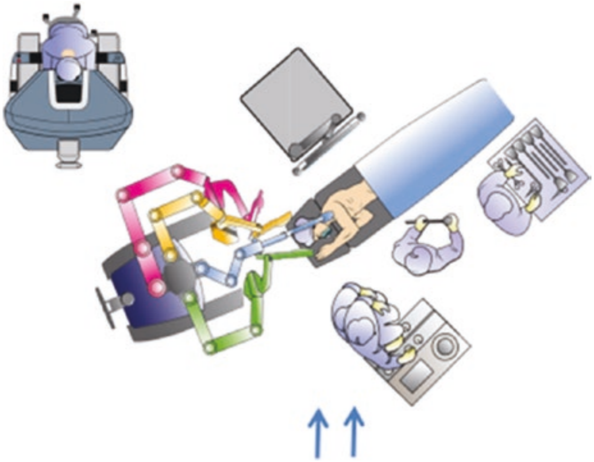

Fig. 6.21 Sample of OR setup for *robot-assisted left lung resection, protocol of European Institute of Oncology, Milan/Italy.* (Photograph *D. Lichosik private archive*)

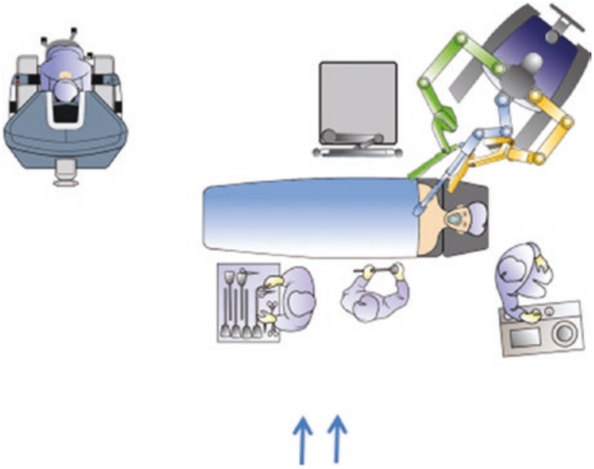

Fig. 6.22 Sample of OR setup for *robot-assisted thymectomy resection (mediastinum left approach), protocol of European Institute of Oncology, Milan/Italy.* (Photograph *D. Lichosik private archive*)

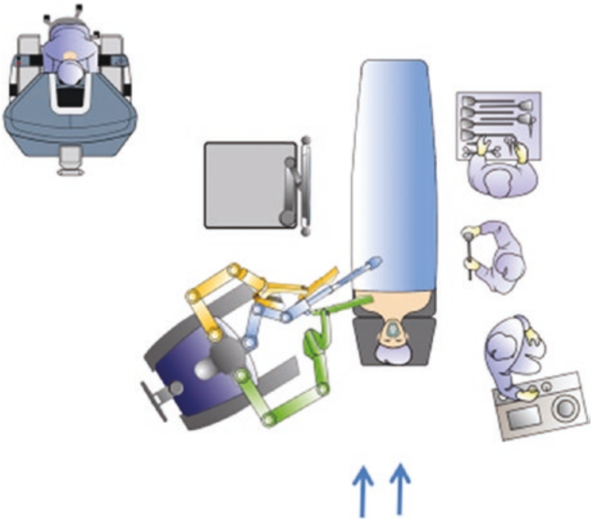

Fig. 6.23 Sample of OR setup for *robot-assisted thymectomy (mediastinum right approach), protocol of European Institute of Oncology, Milan/Italy.* (Photograph *D. Lichosik private archive*)

unnatural, configurations to expose a surgical site. Positioning combined with anesthesia and its physiologic effects can compromise safety of patient undergoing robotic surgery. The goal of surgical positioning includes providing optimal exposure and access to the surgical site, maintaining body alignment, supporting circulatory and respiratory function, protecting neuromuscular and skin integrity, and allowing access to intravenous sites and anesthesia support devices. Accurate patient positioning, careful padding of all pressure points, and appropriate application of anti-skid materials therefore are paramount for preventing neuromuscular injuries. Meeting these goals while maintaining the patient's comfort and safety is the responsibility of every member of the surgical team.

Surgeons use different tools attached to the robot's arms depending on the type of surgery: nurses have to make sure the proper tools are ready to go. Because of the technology, nurses must think of different ways of doing things, to provide the best patient care. During the procedure, the action-taking place in the patient's body is displayed on a high-definition monitor in the operating room. Nurses observe this to anticipate the needs of the surgeon. The reason why many nurses choose to work in the operating theater is that they love anatomy, physiology, and technology. The exciting aspects of robot-assisted surgery are new technology in continuous evolution, the teamwork, and the multidisciplinary surgical practice, especially in the surgical oncology field. Until recently, it was unknown how robotic surgery would develop and evolve. Robotics does not replace human intelligence, skill, and experience, but there is confidence that it is the surgery of the future (Figs. 6.24 and 6.25).

We hope that OR nurses will have the opportunity to be closer to the patient and to express themselves using the technology in the support of patient care.

Integrating Surgical Systems for Autonomy
The Operating Room (personnel) of the Future

Borrowing from the standard practices of other industries

Fig. 6.24 Future robotic surgery operating room (OR). (Photograph *courtesy* from web site of robotic industries, visit 2018)

“Penelope” – robotic scrub nurse

Currently in Clinical Trials

Michael Treat MD, Columbia Univ, NYC. 2003

Fig. 6.25 Future OR nurse – “Penelope” – robotic scrub nurse. (Photograph *courtesy* of Michael Tread MD, Colombia Univ. NYC. 2003)

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Relational Competences

7

Carine Musete

Abstract

Healthcare professionals need to develop relational competences in order to care the patient in an efficient and pertinent manner, a double expertise about themselves and the other. Own consciousness and listening the other are the pillar to adapt the care to the patient's needs.

They are often facing difficulties, which we well call "emotional reaction" or "defense mechanism." It is then crucial that the healthcare professionals understand the outcomes and the emotional process that might influence the relation with the patient, taking into account this underlying notion of fear of death. The intrapersonal intelligence that represents the awakening of consciousness embraces several notions like mental representation, emotions, needs, and responsibility. These notions will foster this work of transformation, which the caregiver will have to go through in order to enter the relational competence.

Keywords

Awakening of consciousness · Needs · Mental representation · Listening the other · Accompanying · Adaptation · Relational competences

Introduction

Today, caring in the cancer patient requires double abilities for the healthcare professional looking toward relevance. On one side, he will have to be aware of his self-awareness and the awareness in the meeting of the other. This double expertise

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C. Musete (✉)
Auto-entrepreneur Consultante en formation, Pontault-Combault, France

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will lead the caregiver to a process of accommodation and adaptation in order to be efficient in his practice.

Severe illness, such as cancer, generates physical and mental suffering and lets the patient face many losses and the idea of death. The caregiver will have to take into account this notion of otherness, the relation to oneself and to others. Catherine Perrotin in her article, InfoKara. 2006;21(1):7–8. https://doi.org/10.3917/inka.061.0007. [2] quotes Catherine Chalier who says that "The suffering of the other defeats the beautiful ordinance of our lives. What is unbearable for the other, what he cannot in any way integrate into his life, weighs a dreadful burden on ours". Indeed, accompanying implies sharing. How can we meet the other without this presence to ourselves?

The most challenging for the caregiver is to allow the other to exist in the care relationship. According to Cécilia Rohrbach Viadas, an anthropologist/nurse, in her research in nursing 2007/3 (No. 90), p. 19–25 [1], "care is a knowledge comprised in human beings. The patients make us discover what is unknown to us, even if we think we are experts in the care". The caregiver does not know he must go to meet the patient in order to adapt his behavior to him in the therapeutic occurrence. This adaptation to the other makes the caregiver develop a real relational intelligence. Relational competence thus becomes a useful or even essential conception for the relation to the other. We will therefore highlight two indicators of the emergence of this skill, the degree of restraint and self-control and the degree of understanding of the other.

To be with the patient, without feeling in danger, and to allow the relationship with the other to exist, it is necessary to understand what echoes for the caregiver in front of the patient. This intrapersonal intelligence, which represents the awakening of consciousness, brings together several notions such as mental representation, emotions, needs, and responsibility. It is important for us to define the awakening of consciousness and then to understand what hinders this experience.

Awakening of Consciousness

> Who is looking outside dreams, who is looking inside is awake. (Carle Gustave Young)

We will start by highlighting what the awakening of consciousness means, where is it located. Claude Hespel in his article "Taming your brain and take control of your life," (January 2017, p. 104) Sapiens, scientific journal (neuroscience-consciousness-conscience), tells us "Today in the West, it is the judgment of the brain which means the physical and legal death from someone. Where does consciousness stand in or out of it? The question remains unanswered, and the convictions on this subject are multiple and controversial. Two extreme beliefs coexist, one making the brain the transmitter owner of consciousness and the other considering it as a simple receiver."

According to Frédéric Lenoir in his preface to Sylvie Dethiollaz and Claude Charles Fourrier's book *Journey to the Limits of Consciousness* [4], it states that the understanding of human consciousness is probably one of the most beautiful scientific adventures to come. Faced with many testimonies from people who claim to have lived where to live unusual phenomena, such as near-death experiences and out-of-body exits, two most common attitudes are credulity and complete rejection. In the near-death experiments, the testimonies are often similar, especially in the case of a cardiorespiratory arrest. The person tells that she sees herself above her body and witnesses her resuscitation. She is able when she returns to her, to restore details of the scene and speeches heard. Facing these phenomena that are developing, more and more scientists are beginning to take an interest in the subject.

Eckhart Tolle in his book *New Earth the Advent of Human Consciousness, Ariane Edition inc, 2005 ISBN:2-89626-007-2,* says "The essential part of awakening is the recognition of your not being aware," of the ego as it thinks, speaks, and acts and recognition of the collective and conditioned mental processes that perpetuate the state of non-awakening. When you recognize what is conscious in you, what makes this recognition possible is actually the emerging consciousness. It is the awakening. It is only by experiencing one thing that one reaches one's knowledge; the accumulation of knowledge does not guarantee knowledge. It is by waking that we truly understand the meaning of the term awakening. "The more the teacher teaches the less the student learns," a story by Confucius. A senior Chinese official traveled far away to ask a Tibetan monk what is the ego and what is the awakening of consciousness? The Tibetan monk replied: "What silly question are you asking me, all this way for that!" The high official got very upset and replied: "That's how you talk to me; do you know who am I and what I am capable of!" The monk replied, "That's the ego." The high official said to him, "Sorry, I apologize for my reaction," and the monk told him, "This is the awakening of consciousness."

As long as we are not aware how this ego, the false self, works, manipulates us, and makes us react in our relationships and in our situations, we will remain prisoners of it despite ourselves. It is therefore important to know how to unmask it in order to allow its dissolution. Indeed the understanding of mental representations is a major asset in the recognition of the functioning of the ego. The awakening of consciousness consists in understanding what we are not, stopping to identify ourselves with our thoughts. I am not what I think but I am the observer behind the thought. "I think so I am," the famous statement of Descartes, who thus associates thought with being, in other words, identity with thought. Jean-Paul Sartre, another famous philosopher, observing intensively the statement of Descartes, realized that the consciousness that says "I am" could not be the consciousness that thinks. When you are aware that you are thinking, this consciousness is not part of the thought.

The Mental Representations

During my lecture "relationship between caregivers and patients after announcement of a cancer diagnose," a problematic was regularly raised by the caregivers: their difficulty with the "aggressiveness" of patients and families.

Often in the pedagogical accompaniment that I was able to carry out with the caregivers on "the caregiver relationship, treated," as part of the post-diagnosis nurse consultation in oncology. A problematic came back regularly for caregivers: their difficulty with the “aggressiveness” of patients and families. Given this fact, I explain to them that there are several possibilities to understand the situation.

At first the caregiver who perceives the behavior of this patient as an aggression answers him: “Do realize you that we are there to treat you and that is how you speak to us.” This reaction may be related to the fact that the caregiver feels aggression on the part of the patient and reacts to this aggression. Reality is nothing but our reality, our perception, a mental construct and not reality.

In a second case, the caregiver perceives real suffering in the patient and the establishment of a defense mechanism. So the only unconscious and unintended way to protect yourself is to say that the aggressive projection is the way the patient expresses he is not feeling well. Here the caregiver is able to tell the patient: “I feel that the situation is complicated for you, do you want to talk about it?” This posture of patient understanding may reflect a caregiver’s acceptance that the patient is at this stage of his or her path in life.

In both cases it is the same patient with the same behavior. Only the caregiver’s perception of the situation changed. I used to illustrate this analysis with a metaphor of the wave. “Imagine you have two children who are overthrown by a wave; one of the kids is scared by the wave, and he drank the cup, and he yells and looks for his mother. The other child bursts out laughing; he is amused by the wave, he asks for more, and he plunges again”. So, it’s the same wave; the problem is not at the level of the wave but how both children really experience the wave. In conclusion, you should consider all situations in your life like a wave. You cannot change people, circumstances, and constraints around you; the only thing you can change is your perception of the situation.

It is neither good nor bad that it is at a given moment the absence of interpretation and the non-judgment allows to feel more serein inside and to welcome the situation. The problem is not outside; it lies in our representation of the situation that impacts on our inner state. This stage represents the first awareness for the caregiver who realizes that what he lives is not outside him. The reading of situations is linked to his knowledge, his education, and his culture, which represents today his world of representation.

In practice analysis sessions, I encourage the caregivers to question the process that is taking place for them in the situations encountered. To highlight the unconscious part that takes control and put them in emotional reaction in spite of themselves. Often they make this remark to me: “I now understand that the patient facing the disease situation puts in place a defense mechanism such as aggressive projection. But I cannot help but react emotionally.” We will try to understand these emotional reactions of the caregiver to allow him to live the meeting with this patient who is suffering. Of course we are naturally unaware of all our thought patterns, and it is by observing our emotions that we can bring them to consciousness.

The mind closes the thoughts but also our emotions and the unconscious processes that operate in spite of ourselves in the lived situations. All these mechanisms, electrical, biological, and organic, can be explained today thanks to the progresses of new technologies. Indeed neuroscience uses brain imaging to understand the different processes that occur in our brain and the behavior associated with it. Philippe Guillemant, a physicist, states in his book *The Physics of Consciousness* [3]: “The environment that we call ‘real’ is illusory.” It is primarily a construction made by our brain. We see the situations we live through the filter of our beliefs. Our thoughts can generate strong emotions that will affect our behavior.

Cell biology also helps to understand the impact of the environment on our internal biology. The way we have learned and the patterns we have received and reproduced are written in our cells. Indeed, epigenetics today speaks of transmission of elements acquired to succeeding generations. Joel de Rosnay in his book *The Symphony of the Living* says [5]: “science explained that we were programmed by our genetic heritage. Now, in the light of recent research, scientists are reviewing their theories”. The new revolution in biology, called epigenetics, shows that our daily behavior to know what we eat, the sports activity that we practice, the relationships we maintain, our resistance to stress, etc. will inhibit or activate some of our genes. We can take back what we live for as the conductor of a symphony and co-author of our life, our health, and our physical and psychic balance.

The caregiver will be confronted in his therapeutic accompaniment with emotions and reactions of the patient such as anger, sadness, mutism, crying, etc. But the one that shakes them most often is the “aggression” of the patient.

The Emotions

> Everyone can get angry. But it is difficult to get angry for good reasons and against who deserves it, at the right time and in the right time. (Aristotle, Nicomachean Ethics)

Daniel Goleman in his work “emotional intelligence” [6], (analyze and control his feelings and emotions and those of others) defines the emotions as those that help us to face situations like danger, painful losses, etc. Emotions are essential for human beings; they are essential for survival and are an integral part of our constitution. For Eckhart Tolle, emotion is the bodily reaction of the mind or the reflection of our mind in the body. An aggressive thought creates in the body an accumulation of energy that can be likened to anger the body is preparing to fight. The thought of being physically and psychologically threatened causes a contraction in the body; it is the physical aspect of what we call fear. Research in neurobiology has shown that a strong emotion can change the biochemistry of our cells. These biochemical changes of the body constitute the physical or material aspect of the emotion. To understand the process that takes place in us, we must observe the emotion. Indeed it is as important to observe the emotions as the thoughts; there can be conflict between these two parts. But often thought will lie because it keeps us in an illusory mental film out of step with reality. The emotion will tell us the truth about our state of mind but especially about our needs of the moment. It is therefore important to ask the question what do I feel? To go toward what is happening to me in this situation? This makes it possible not to identify oneself with the emotion and to refocus on what one feels, on the energy in action inside the body. Usually emotion is the amplified manifestation of a thought form; the energetic charge is often fast and dazzling.

Thanks to new methods that allow us to understand what is happening inside our body and the brain, researchers each time better understand how each type of emotion prepares the body for a different type of reaction. Indeed the Italian neurophysiologist Giacomo Rizzolatti discovered in 1996 particular neurons that he called the "mirror neurons." This discovery shows us that we can no longer believe in our independence from our perceptions. Through our mirror neurons, our emotions enter into vibratory synchronicity with those on the other side. His fear wakes up my anxieties, his anger fuels mine, his sadness is contagious, and his desire excites me and stimulates mine. For Daniel Goleman all emotions are incentives to action. The term emotion is composed of the Latin verb "motere," meaning "to move," and the prefix é, which indicates an outward movement. They also give perceptible signals in the body that a need is satisfied or not.

The Needs Linked to the Emotions

We will now take an interest in the four basic emotions, and for each one of them, we will be able to understand the specific role that they play in our existence. The most important thing is to identify the process in which our emotions are present. We will talk about events or situations most often from which emotions are triggered according to the interpretation of this event that belongs to the domain of the mind, thoughts, and sensory perceptions as a gateway for the visual representation. According to this mental interpretation in most of the time, the emotions flow from it, but there are contexts of survival where the cortex is not solicited; the reptilian and limbic brain manage alone the situation to guarantee the speed of action. Then to these emotions to which are attached, different needs arise behaviors.

Fear is the emotion that is present in the cancer patient on a frequent basis; it is a question of situation where the patient feels "in danger of death." The function of this emotion is protective; it releases the need for protection. The resulting actions are often linked to the mechanisms of defenses, the flight that translates into the patient by the displacement, the attack that is manifested by the aggressive projection, and the inhibition that is translated by the denial.

Sadness is the second emotion that we find in situations of loss; its function is to create transitions we speak of the process of mourning. The need to be comforted and listened to is often linked to this emotion, the action that results from the withdrawal into oneself.

Anger is often present when we encounter an obstacle in our path; for its function it is a question of asserting itself and is linked to a need for reparation and for change. The action that follows is often the attack.

Finally, joy as the fourth emotion manifests itself in situations where the needs are met; for its function to be realized, the action will be generally open to go to the other.

A Notion of Responsibility in Emotions

During my lecture, I often share with the students my personal experience, to make my point more concrete. “When I was younger, I was a rather messy child. When I left home for my studies, I could feel my mother’s concern about my ability to “keep a house clean one day.” When I got married and my mother came to see me, the fact that my son did not tidy up his room, was not a threatening situation for me. But when my mother entered the room of my son, I got angry.” I asked them: “in your opinion what is the problem? Is it the fact that this room is not tidy by my son?” Then I said, “If you had stowed your room, I would not be angry.” Obviously no, my son is not the cause of my problem; he is more of a trigger in the situation I live in, and the cause seems to be my need for recognition of my mother. In fact, today it is my son’s room, which trigger my anger. Tomorrow it might be the kitchen not stowed by my husband or the living room invaded by my daughter’s dolls during the next visit of my mother, that will trigger my anger. The problem will go on as long as I do not face the source, the deep reason which is mine. I use to tell to the students “you’re not responsible for the emotion or reaction of the other; you can be a trigger but in no way the cause of what the other lives”. Everyone is responsible for their own emotions and emotional reactions as they are directly related to an internal need. Although since very young, I was taught to feel guilty and responsible for the emotion of the other. This is a fundamental concept for the caregiver in his relationship with the patient, the notion of responsibility. He is not responsible for the emotion or the reaction of his patient; he can be at a moment a triggering factor but in no way the cause of what he lives. The reaction or emotion of the patient then becomes a lever for his accompaniment.

How to Meet the Patient

Knowing the Other in the Relationship

We will now consider the goal of caregiver support. We mentioned the caregiver helping the patient to become aware of what he is going through, offering a space where the patient can ask his feelings, his questions, and his fears. For that the caregiver will have to go to meet the patient in his world of representation and explore his misunderstandings, his feelings, and his emotions related to the needs, at a “T” moment from his position. The patient enters his choice of destination and not the caregiver. The first question that is asked to the patient before launching the navigation system is the location where he is and where he wants to go. We will use Gardner’s eight types of intelligence to define the different abilities that the caregiver can acquire in his professional practice. We will proceed step by step or process to highlight these skills with regard to multiple intelligences.

The first step is to define the purpose of this support, an essential step for the caregiver who will be guided throughout its accompaniment by it. Indeed, in this context of serious illness, it is essential that the caregiver identifies its place and its role that are part of a complex and dynamic care device. The patient will navigate through troubled and agitated waters (pace of treatments, consultations, medical exams, etc.); he will need benchmarks throughout his journey to guide him to his destination. The caregiver is one of the many benchmarks he will have, to understand his path. We can imagine the patient through a GPS. His life is driven to a destination, and the illness can be regarded as an interference that blurs the directional signals at his GPS receiver. The caregiver is there to help the patient to understand and become aware of the level of interference that can be used to act on it and find a fluid connection to continue its journey. We will define together the GPS that has two parts: the first part, we will call the satellites, represents the reference system of the patient; his beliefs, his values. His whole life is built around these references. When the disease is diagnosed and announced to the patient, he often describes this moment as a shock: “It’s like this the sky fell on my head.” In psychology, we speak of amazement; the patient is stampeded in his identity markers. He is in the fog; he has trouble capturing information. The second part consists of a receiver that has three parts, the antenna that we will name intuition or consciousness, the electrical system thoughts, and finally the battery that represents the autonomy of the patient’s energy and his emotions. Often, to retrieve these localization data, the patient will need to be accompanied at first until he can exercise this new skill unconsciously, living with his illness.

To achieve this goal of alignment to the patient, the caregiver will use the linguistic intelligence to go in the direction of the words used by the patient and her/his representation of the disease, the treatments, his needs, and his feelings.

The Exploration Phase: Understanding Where the Patient Is in His or Her Journey

Communication Tools

The caregiver will use several language variants. He will go through a phase of exploration that it is at the level of the representation of the disease or the feeling of the patient. Using open question is a key element to start from the patient’s perspective: “did you understand what the doctor told you?” The fact of being in this exploratory phase with the patient allows him to redo the film of the different paths through which he has gone through. This exercise of reconstructing thoughts allows him to become aware. With regard to the clarification of the subject and the precision of the meaning, the caregiver will have at his disposal the reformulation and the closed questions. Indeed, the caregiver will have to demonstrate skills in questioning and listening to gain access to the patient’s understanding. In this approach there will be a double expected effect. On one side, the caregiver will be able to access the understanding of the patient on what has been said to him. On the other side, it will make the patient more aware on where he does stand in relation to the disease.

The Phase of Adjustment: To Join the Patient in His Step of Progression

At the very beginning of the implementation of the nursing counseling after announcement of cancer diagnosis in France (cancer plan 2003–2009), some students told me about their difficulty in seeing a patient in consultation, feeling great frustration and guilt for not being able to make the patient verbalize and that he left with his suffering. In view of this experience, I give the caregivers the opportunity to take distance from the situation by having another version of the scenario. I ask them: "In which stage is your patient at the time of your meeting?" Often this meeting was a few moments after the announcement of the diagnosis. This question allows them to take into account a primordial notion, the temporality, the moment "T"; the patient has just received his diagnosis he is under the shock so surely in a psychic incapacity of elaboration. This is not the ability of the caregiver to bring the patient to verbalize, to walk, but the temporality of the patient, who needs time to be able to cash in the shock of the bad news. The caregiver becomes aware of the need for a new skill in his practice, the ability to distance himself from the situations of the patients he will have to accompany. Many establishments in France have subsequently chosen to space the time of the announcement and the nursing counseling from a few days to a few weeks according to the organizations

Attitudes and Postures: Notion of Listening, Empathy, and Detachment

To be comfortable in this exercise of accompaniment, the caregiver will develop postures, to be in the detachment which means the fact of welcoming the patient with his anxieties, his doubts, in what he expresses to be in the active listening to his emotions, his needs. When the patient speaks, it is important for the caregiver to think "when he talk to me what exactly he is telling me" and to focus on what the patient says and not on his interpretation of the speech. The meaning of things for the patient is related to his knowledge, his representations, and his experience. To put away own representation in order to match to the patient's ones requires concentration and psychological availability. The meaning of words is important, but the understanding of the needs of the patient will require a skill that is called the art of detachment, letting go.

With *the logico-mathematical intelligence*, the caregiver will be able to understand the path of the patient and her/his emotions to which her/his needs will be attached.

We speak here about *relational intelligence* more precisely emotional intelligence: allowing the patient to identify his or her emotion, which most of the time in the case of serious illness results in the expression of death anxiety.

Fear is the most met emotion with anger and sadness; the caregiver will help the patient to recognize his emotion, his function, and the need attached to it. To confront oneself with what frightens us makes it possible to apprehend it differently and to be in the process of the reception. So we can reduce the resistance and the suffering. The caregiver's role in this accompaniment is to allow distance from the situation. For this the caregiver has the spatial intelligence, which is reflected in the moment. One of the postures that is essential is *psychic availability*, which refers to the notion of being and the notion of the present moment. The present moment is one of the main ways to access this asset, according to Eckhart Tolle: "Be present as an observer of your mind, that is to say of your thoughts, your emotions and your reactions in various situations. Give at least as much attention to your reactions as the situation or the person who makes you react. Note also the repetitiveness with which your attention is fixed on the past or the future. Do not judge or analyze what you observe. Look at the thought, feel the emotion, watch the reaction. Do not make it a problem. You will then feel something more powerful than any of your subjects of observation: the calm presence that observes from behind the content of the mind, the silent witness."

When the notion of time disappears, the caregiver acquires the capacity to be really there with the patient in a clear posture of accompaniment; indeed the notion of emotional suffering leaves room for empathy and active listening. By seeing what is not allows the emergence of what is truly.

The caregiver is not in the past: the situation of the patient brings her/him back to a personal experience. In this case the caregiver identifies the situation no longer as the anxiety of the patient, but it becomes his own, and the emotional impact according to the caregivers' statements is manifested by fear, and they fell overwhelmed emotionally with a real psychic experience where defense mechanism emerges (often manifested by the false reassurance, the flight ahead, or the rationalization).

The caregiver is neither in the future; the caregiver projects himself through the story of the patient and enters the scenario of what he is afraid to live according to his own representations, the imaginary film that feeds worries and anxieties.

When the caregiver is in the present time, he is then able to become aware of the role and the place he takes in front of the patient when he meets him; he is not "me" but he is "he/she". According to Carl Rogers, this is congruence. This posture is only possible if the carer is clear with who he is, in order to accompany the patient without being in difficulty himself. This skill is acquired through the intrapersonal intelligence that allows the caregiver to do a job on himself. Having self-knowledge, developing self-awareness of situations, the ability of detachment to accept the situation without judgment allows this freedom in action.

Conclusion

To meet the other is the primary goal of the caregiver in his accompaniment. This project of meeting requires for him an awareness of him, his world of representation, to allow the mind to do the work of "disidentification." I propose to the students this notion of visibility of the process facilitated by the model TEB (thoughts, emotions, behaviors). Our thoughts generate emotions according to the meaning that we give to the situation that will produce actions, attitudes, and behaviors. When I change my mind, the process of change is initiated, but we all agree that it is not enough to want to change thoughts so that things change in terms of emotion and behavior that have become habits and unconscious automatisms. This requires a process of identification, change, and transformation. The learning process is a comprehensive process that involves several steps to ensure the transformation and the level of control.

According to A. Maslow, these steps can be summarized as follows:

The first step is “incompetent unconscious”: I do not know that the patient is not the cause of my frustration, my anger, etc. A place of learning such as training is the opportunity for the caregiver to become aware and to have a different perspective on situations.

The second step is “incompetent conscious”: I know that the patient is not the cause of my anger, but I cannot help but react to his behavior.

After the awareness-raising part, there is the experimentation part, confrontation with the new situations. The situation must be confronted several times in order the internal process becomes familiar with another operation. “I know that the patient is in an aggressive projection. Sometimes, I do not react to the situation, other times I react to the situation”.

The third step is “competent conscious”: I know that the patient is not the cause of my anger, I see it in pain, and I welcome the situation because I do not feel in danger, to concentrate on him and not react to the situation. But sometimes when my concentration is down, I still feel a gap between what I do and what I feel. I also welcome this shift. This stage is facilitated by the confrontation with notions, new concepts, like letting go, the acceptance of what is, living the moment “T” with the patient.

Instead of seeing the patient’s reaction as an obstacle, I consider it as an opportunity, a raw material to use in my accompaniment. Repetition brings integration and the installation of the fourth stage “the unconscious competence”: I no longer need to concentrate for action, the unconscious takes over. Then we speak of expertise in the field of relational skills.

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Nursing Diagnosis Specific to Oncology

8

Sultan Kav

Abstract

Nurses, regardless of the areas they work and specialized, are coming under increasing pressure to highlight their contribution into healthcare and patient outcomes. In order to demonstrate nursing contribution to cancer care, visible and quantifiable use of standardized diagnosis, intervention, and outcome terminologies is necessary. Identifying the pattern of core diagnoses, interventions, and outcomes for oncology nurses can direct nursing care in clinical practice and establish future research to target areas of high impact and guide education and evaluation of nurse competencies.

Keywords

Nursing diagnosis · NANDA International · Oncology nursing · Standardized nursing languages

Introduction

Current estimates suggest that the number of people who will be influenced by cancer will increase, which means that more people will require specialized and person-centered care throughout their cancer trajectory [6]. Patients with cancer have to deal with chronic and life-threatening conditions related to the disease and need to manage the effects of multimodal and complex treatment regimens.

S. Kav (✉)
Faculty of Health Sciences, Başkent University, Ankara, Turkey
e-mail: skav@baskent.edu.tr

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Therefore, quality cancer care becomes expected and demanded by the patient and also promised by the healthcare providers [7, 9].

Nurses, regardless of the areas they work and specialized, are coming under increasing pressure to highlight the contribution into the healthcare team and patient outcomes, particularly within the context of rapidly changing healthcare system. The need for meeting efficiency outcomes in the healthcare systems, while assuring the quality of care, has challenged hospitals to implement major organizational changes and has placed nurses under growing pressure to demonstrate their contribution and influence on quality and cost, in terms of health problems they resolve or prevent and health outcomes in patients [19]. In order to demonstrate nursing contribution to cancer care, visible and quantifiable use of standardized diagnosis, intervention, and outcome terminologies is necessary [21, 26].

The standardized nursing languages are a vocabulary that provide to a common communication tool for nurses. The advantages of standardized nursing languages are better communication among nurses and other healthcare professions, increased visibility of nursing interventions, improved patient care, enhanced data collection to evaluate nursing care outcomes, greater adherence to standards of care, and facilitated assessment of nursing competency [26]. The North American Nursing Diagnosis Association International (NANDA-I), one of standardized nursing languages, had translated several languages and is commonly used in nursing practice or education [8, 29].

The primary goals of nursing are to (1) determine client/family responses to human problems, level of wellness, and need for assistance; (2) provide physical care, emotional care, teaching, guidance, and counseling; and (3) implement interventions aimed at prevention and assisting the client to meet his or her own needs and health-related goals. The nursing process, which is a problem-solving approach to the identification and treatment of patients' problems, provides a framework for assisting patients and families to their optimal level of functioning. The nursing process involves five dynamic phases: assessment, diagnosis, planning, implementation, and evaluation [1]. The nursing process guides the actions of nurses in daily professional practice and offers a structure that is concordant with the individual needs of the patient, the family, and the community, representing the main methodological instrument for the systematic performance of the necessary conditions to provide care and documentation in nursing practice [13].

Historical Development of Nursing Diagnosis

The evolution of standardized nursing languages (SNLs) has been occurring for more than four decades [16].

Box 8.1 Standardized Nursing Terminology Sets

- NANDA-I (North American Nursing Diagnosis Association International)
- NIC (Nursing Interventions Classification)
- NOC (Nursing Outcome Classification)
- ICNP (International Classification for Nursing Practice)
- Omaha System
- CCC/HHCC (Clinical Care Classification/Home Health Care Classification)
- PNDS (Perioperative Nursing Data Set)
- NMSD (Nursing Minimum Data Set)
- LOINC (Logical Observation Identifiers Names and Codes)
- SNOMED (Systematized Nomenclature of Medicine) Clinical Terms
- NMMDS (Nursing Management Minimum Data Set)
- ABC (Alternative Billing Concepts) Codes

Work on the classification of nursing diagnoses, beginning in 1973, led to the establishment of NANDA International (formerly, the North American Nursing Diagnosis Association). NANDA is the pioneer and most often implemented nursing diagnoses classification internationally. NIC started in 1987, and NOC followed in 1991. In 2002, North American Nursing Diagnosis Association changed its name to NANDA International (NANDA-I) to reflect the growing involvement of nurses from many overseas countries [16].

ICNP is an international terminology that provides description and comparison for nursing practice and allows for cross-mapping between other terminologies. The classification includes nursing diagnoses, nursing-sensitive patient outcomes, and nursing interventions (https://www.healthit.gov/sites/default/files/snt_final_05302017.pdf) [28].

Other systems were subsequently created; the aim of all of these classification systems is to offer a common standardized language to improve communication among colleagues and codification for research electronic databases. Many initiatives have been developed at the international level to identify a set of items to ensure systematic nursing data collection and documentation: this set of minimum information, called Nursing Minimum Data Set (NMSD), is based on uniform definitions of data divided into assessment, problems, intervention, and outcome categories adopted on a regular basis by the majority of nurses [18]. The first NMDS was established in the USA, followed by Canada, Australia, and more recently Thailand. Among European countries, the Belgian National NMDS, originated in 1998, is widely validated and used as a reference; across Europe the nurse minimum data set has been developed, and examples are also available in France, the Netherlands, Switzerland, Finland, Sweden, Germany, Italy, and Ireland (Butler et al. [3]; Palese et al. [24]; Morris et al. [19]).

Several authors have addressed the use of nursing diagnoses to represent patients' problems in charting the care planning in patient records, to reflect the nurses' judgements on patient' status [21]. Many authors around the world use the NANDA International (NANDA-I) nursing diagnoses to describe what do nurses document in the patient records and also to explain how nurses systematize care planning for different patient populations [17, 20].

A nursing diagnosis contains a definition, defining characteristics, and related or risk factors. NANDA-I (2009) defines a nursing diagnosis as "a clinical judgment concerning a human response to health conditions/life processes, or a vulnerability for that response, by an individual, family, group or community. A nursing diagnosis provides the basis for selection of nursing interventions to achieve outcomes for which the nurse has accountability" (approved at the ninth NANDA Conference; amended in 2009 and 2013) [22]. NANDA-I taxonomy II divided nursing diagnoses in 13 domains (Table 8.1).

Table 8.1 Types of nursing diagnosis

Types	Definition	Explanation and example
Problem-focused nursing diagnosis	A clinical judgment concerning an undesirable human response to health conditions/life processes that exists in an individual, family, group, or community	In order to make a problem-focused diagnosis, the following must be present: defining characteristics (manifestations, signs, and symptoms) that cluster in patterns of related cues or inferences. Related factors (etiological factors) that are related to, contribute to, or antecedent to the diagnostic focus are also required *Example: Chronic Pain related to pathologic processes*
Health promotion nursing diagnosis	A clinical judgment concerning motivation and desire to increase well-being and to actualize human health potential. These responses are expressed by a readiness to enhance specific health behaviors and can be used in any health state. Health promotion responses may exist in an individual, family, group, or community	In order to make a health promotion diagnosis, the following must be present: defining characteristics which begin with the phrase, "Expresses desire to enhance…" *Example*: *Readiness for enhanced Nutrition … expresses willingness to change eating pattern and eat healthier foods'*
Risk nursing diagnosis	A clinical judgment concerning the vulnerability of an individual, family, group, or community for developing an undesirable human response to health conditions/life processes	In order to make a risk-focused diagnosis, the following must be present: supported by risk factors that contribute to increased vulnerability *Example: Risk for infection related to the immunosuppression, malnutrition and invasive procedures*
Syndrome	A clinical judgment concerning a specific cluster of nursing diagnoses that occur together and are best addressed together and through similar interventions	In order to make a syndrome diagnosis, the following must be present: two or more nursing diagnoses must be used as defining characteristics. Related factors may be used if they add clarity to the definition but are not required *Example: Risk for post-trauma syndrome related to traumatic event*

Nurses' interest focus is the human response rather than the disease, because different individuals with the same disease may have different nursing diagnoses. However, some diagnoses are objective and therefore amenable to assessment by observation and measurements, whereas others are more subjective and need a patient-centered approach and/or a conversational style. Clinical reasoning of nurses requires them to identify defining characteristics, because these are observable cues/inferences that cluster as manifestations of a diagnosis, and an assessment that identifies the presence of a number of defining characteristics lends support to the accuracy of the nursing diagnosis [10].

Common Nursing Diagnosis in Oncology

Nursing diagnoses in oncology found in the literature mainly focused on adult patient with a hematological malignancy [27], breast cancer [4, 23], brain tumors [11], adults/elderly patients [12], outpatient chemotherapy [14], and patients with stomach cancer and their family caregivers [2]. Defining characteristics of single nursing diagnosis such as nausea [20] and spiritual distress [5] were studied.

From the analysis of nine studies, this integrative review identified ten of the most common NDs in adults/elderly hospitalized with cancer, namely, anxiety, knowledge deficiency, constipation, self-care deficit for bathing/hygiene, body image disturbance, acute/chronic pain, fear, disturbed sleep pattern, risk of infection, and risk of fluid volume deficiency [12].

Speksnijder et al. [27] have identified 64 relevant nursing diagnoses, formulated by the "NANDA-I classification 2009–2011." Authors reported that the NANDA-I classification 2009–2011 described nursing diagnoses to the adult patient with a hematological malignancy in almost all disease- and treatment-related problems (98%) and therefore concluded that very relevant for hematology-oncology nursing. The most common linkage of NANDA-I, NOC, and NIC (NNN), a set of standardized nursing terminologies used in the study that represents nursing diagnoses, nursing-sensitive patient outcomes, and nursing interventions, prospectively, was Acute Pain—Pain Level—Pain Management. Pain was the dominant concept in the nursing care provided to oncology patients. Risk for infection was the most frequent nursing diagnosis in the adult leukemia and bone transplant unit. In Table 8.2 common nursing diagnosis and core nursing interventions were listed [1, 25, 30].

Table 8.2 Common nursing diagnosis and core nursing interventions specific to oncology

Domain	Class	Nursing diagnosis	Nursing interventions[a]
1. Health promotion	1. Health awareness	Deficient diversional activity	Activity therapy
		Sedentary lifestyle	Recreation therapy
	2. Health management	Readiness for enhanced health management	Financial resource assistance

(continued)

Table 8.2 (continued)

Domain	Class	Nursing diagnosis	Nursing interventions[a]
2. Nutrition	1. Ingestion	Unbalanced nutrition: less than body requirements	Fluid management Nutrition management
	5. Hydration	Risk of deficient fluid volume	Nutritional monitoring
3.Elimination and exchange	1. Urinary function	Impaired urinary elimination	Urinary elimination management
	2. Gastrointestinal function	Constipation	Bowel management
		Risk of constipation	Bowel training
		Diarrhea	Diarrhea management Medication management
4. Activity/rest	1. Sleep/rest	Disturbed sleep pattern	Energy management
	3. Energy balance	Fatigue	Environmental management: Comfort
	4. Cardiovascular/pulmonary responses	Activity intolerance Risk for activity intolerance	Exercise promotion: Strength training
	5. Self-care	Self-care deficit	Self-care assistance
		Impaired home maintenance	Home maintenance assistance
5. Perception/cognition	4. Cognition	Deficient knowledge	Teaching: Disease process
		Readiness for enhanced knowledge	Teaching: Procedure/treatment
	5. Communication	Readiness for enhanced communication	Active listening Preparatory sensory information
6. Self-perception	1. Self-concept	Hopelessness	Hope inspiration
	2. Self-esteem	Situational low self-esteem	Support group
		Risk for situational low self-esteem	Counseling
	3. Body image	Disturbed body image	Emotional support Self-efficacy enhancement Self-esteem enhancement
7. Role relationships	1. Caregiving roles	Caregiver role strain	Caregiver support
		Risk for caregiver role strain	Financial resource management
	2. Family relationships	Interrupted family processes	Home maintenance assistance
	3. Role performance	Impaired social interaction Ineffective role performance	Family involvement promotion

Table 8.2 (continued)

Domain	Class	Nursing diagnosis	Nursing interventions[a]
8. Sexuality	2. Sexual function	Ineffective sexuality pattern	Sexual counseling
			Teaching: Sexuality
9. Coping/ stress tolerance	2. Coping responses	Anxiety	Anticipatory guidance
		Death anxiety	Anxiety reduction
		Powerlessness	Calming technique
		Fear	Coping enhancement
		Grieving	Relaxation therapy
		Impaired resilience	Dying care
10. Life principles	2. Beliefs	Readiness for enhanced spiritual well-being	Active listening
			Spiritual support
	3. Value/belief/ action congruence	Readiness for enhanced religiosity	Crisis intervention
		Spiritual distress	Decision-making support
			Grief work facilitation
			Presence
11. Safety / protection	1. Infection	Risk for infection	Central venous access
	2. Physical injury	Impaired dentition	Chemotherapy management
		Impaired skin integrity	Device management
		Risk for impaired skin integrity	Bleeding precautions
		Impaired tissue integrity	Fever treatment
		Risk for bleeding	Infection control
		Risk for injury	Infection protection
		Impaired oral mucous membrane	Wound care: Nonhealing
		Risk for vascular trauma	Intravenous (IV) insertion
12. Comfort	1. Physical comfort	Impaired comfort	Pain management
		Acute pain	Analgesic administration
		Nausea	Nausea management
		Chronic pain syndrome	Vomiting management
	3. Social comfort	Social isolation	Normalization promotion
			Body image enhancement
13. Growth/ development	1. Growth1.1.	Risk for disproportionate growth	Health screening
			Behavior modification
	2. Development	Risk for delayed development	Developmental enhancement: Adolescent
			Sibling support

[a] The core set of interventions includes those interventions used frequently or predominately

Conclusions

To highlight the unique contribution that nurses make to cancer patient care and effectively manage nursing work, it is essential that information regarding the nursing role be made available to key decision-makers. Therefore, assumptions about the nursing contribution to care must be replaced with empirical evidence of the nursing profession's actual contributions to cancer care [15].

While recognizing the benefits of electronic health records to improve communication, coordination, and quality care, nursing has been challenged to adapt to the impact of technology on the way nurses deliver patient care in each specialty. Identifying the pattern of core diagnoses, interventions, and outcomes for oncology nurses can direct nursing care in clinical practice and provide direction for future research to target areas of high impact and guide education and evaluation of nurse competencies.

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9

Model of Announcing a Diagnosis of Cancer: The French Experience

Carine Musete and Françoise Charnay-Sonnek

Abstract

Announcing a diagnosis of cancer is for a patient like a big stone falling on his head. This disease especially in the past was synonymous with death, devastating side effects, pain, damaged body image, etc. we are less tempted to make such comparison today because today we are likely to live with a cancer disease for years, thank the progress in the medicine and new technologies. Indeed we consider this disease as a chronic disease, and we can live with cancer for a very long time with the exception of certain types of cancer.

Going back decades before, considering the image of cancer and the burden it causes, it made sense that competent authorities couldn't remain indifferent to this situation. All around the world, health organizations led large actions to better face cancer disease and to enhance caring patients with cancer. In Europe, France was one of the first to have established a cancer plan.

Keywords

Cancer plan · Announcing a diagnosis · Supportive care · Holistic approach Multidisciplinary · After cancer

Introduction

Cancer has always been considered as a disease that needs a special attention. Early in the 1970s in the USA, initiatives emerged. The first global cancer plan and call for action was signed by the American president Nixon in 1971, and the National Comprehensive Cancer Control in the USA has been established in 1998 [1].

C. Musete (✉)
Auto-entrepreneur Consultante en formation, Pontault-Combault, France

F. Charnay-Sonnek
Unicancer, Paris, France

F. Charnay-Sonnek, A. E. Murphy (eds.), *Principle of Nursing in Oncology*,
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In 2002 the World Health Organization first published its *National Cancer Control Programmes: Policies and Managerial Guidelines.* Since then, these plans have grown fast, particularly in Europe. By 2003, three European member states had established their own cancer program, Romania, Lithuania, and France. But the other countries didn't stay behind and proceeded in parallel different actions in this direction [2].

The European Union was very supportive by creating the "European Partnership for Action Against Cancer" (EPAAC) [3] in the 2012. "*The European Partnership for Action Against Cancer is a five-year initiative taking place under the umbrella of the European Commission to fill a void in cooperation, collaboration and shared experiences among countries with similar needs and diverse experiences in the field of national cancer control policy*."

It also published in the recent years documents to define services and actions related to cancer control. Most of them are the reference of national cancer plan or national cancer control programs. By 2013 almost all EU countries have adopted some forms of national cancer plan [2].

Hence this book focuses on cancer, and this time of announcing a diagnosis is crucial for the patient; it appears important to address this theme by presenting the French experience because it was one of the first three to have established a cancer plan in Europe. In this chapter we highlight the mainstreams of the different cancer plans which we consider useful for nurses to get a better comprehension of the role they have to play in this regard.

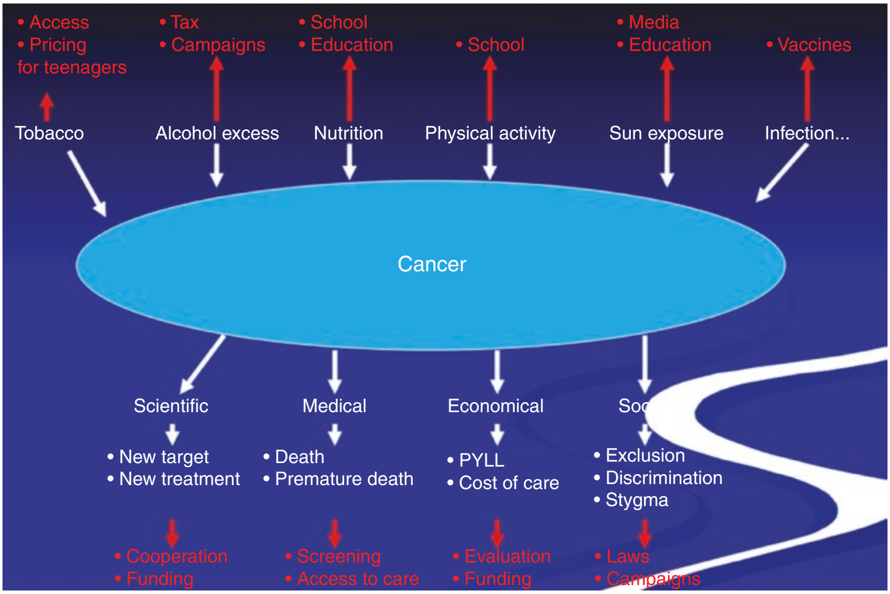
And they have a very important role to play through the whole journey of the patient embracing the posttreatment period. Indeed, after having lived a very protected period in the health-care system, patients often explain to feel quite lonely when returning back home. The reinsertion in social life is not easy for them. At this stage whereby they should be the happiest ones in the world, they might fall in a depression at the dismay of their loves. So, the after cancer period is not worthless and should hold our attention [4]. Nurses can develop their competences in supporting them in coming back in their life before the cancer, even if this life won't be exactly the same as it was. In this chapter we will see the highlights of these different cancer plans starting with the sociological context in 1998.

The Sociological Context

It was a revolution in the French health system in the 1998, when patients and relatives took the floor and expressed themselves publicly during the first general states of the patients with cancer. For the first time, health professionals and representatives of public institutions listened to their testimonies. They evoked a lack of humanity in the care structures, the lack of information, and the lack of coordination between caregivers. They express the need to be accompanied and highlighted the social and legal difficulties they encounter. Following these instances, the French Government in the early 2000s started to think deeply about how to meet those needs. It drove the implementation of the first cancer plan in 2003–2008.

Cancer Plan 2003–2008

Below is a very clear scheme made and presented by Prof David Khayat, M.D., Ph.D., in oncology at the World Cancer Congress around 2003 who with the French president Jacques Chirac drove the implementation of the first cancer plan.



The Holistic Approach

The objectives of a holistic approach are to insure comprehensive support of the person, beyond the technical protocols, through the development of complementary care and palliative care. According to the measures 42 and 43, supportive care options are available to treat symptoms, meet nutritional needs, and provide psychological and social support. They support the development of palliative care as part of the national palliative care program. The care of the sick people is conceived throughout the disease in parallel with the treatment of cancer, in "curative" or "remission" phase.

This concept implies a notion of interdisciplinary. All professionals involved in the cancer care (oncologists, general practitioners, nurses, physiotherapists, etc.) are concerned and work together in close collaboration. Expert's teams are formed to care the patient with complex situation, pain management unit with an assessment and treatment consultation, palliative care unit, psycho-oncology unit, social services, etc.

The Different Sequences of the Announcement Process

Medical consultation: this time is dedicated to the announcement. The purpose of this consultation is to inform the patient about his illness and the therapeutic orientations. It is a time that allows a dialogue with the patient, around the announcement, while respecting the emotions it can arouse. A time to identify the psychological and social conditions of the patient and to present the caregivers likely to be involved in the care. During this medical time, the personalized treatment program is set up. The patient will be informed about the expected benefits and possible side effects and if he wishes the immediate or remote therapeutic risks and the prognostic elements. This will allow the patient to make "informed" decisions about his health.

Nurse consultation: this consultation plays a key role during this time of announcement and in the coordination of the patient journey. It can take place immediately or a few days after the medical consultation. It provides access to a team involved in supportive care (identification and referral to various expertise: occupational therapist, socio-esthetician, psychologist, social worker, etc.). This time of accompaniment must be a time of listening, support, and information for the patient. The nurse makes him reformulate what was said during the medical consultations. He/she approaches the questions of the person (s) who will accompany the patient throughout the care. He/she also identifies psychological and social needs to anticipate care and respond to queries and concerns about therapeutics. Finally, this time foster an articulation between city medicine and hospital medicine around the announcement by associating at a very early stage, all actors likely to care directly or indirectly for the patient during his journey. This coordination involves GP and community nurses in taking decisions, considering the personal and organizational difficulties of the patient. It makes the path between the hospital and the city seamless for the patient.

The Cancer Plan 2009–2013

The Different Axes

Research

Asserting research as the driver of progress in oncology. The report on the progress of the cancer plan on February 4, 2011, shows that there has been a transfer of scientific discoveries for the benefit of patients (there were 157 research projects funded). There were 16 labeled early-stage clinical trial centers. One of the most important action is to trengthen translational research through dedicated funding based on calls for proposals and a policy of multidisciplinary accredited and integrated research sites.

Prevention and Screening

Allowing better consideration of inequalities facing cancer and the implementation of measures aimed at correcting them. The policy of helping people to cess smoking has been strenghtened. Access to nicotine substitutes for pregnant women and people who are entitled to receive full social security cover for medical care has been developed. A funding program created on February 1, 2007 and financed by the social security is used to reimburse the cost of nicotine substitutes and certain drugs used to stop smoking. Given the particular issues involved in stopping smoking during pregnancy, it is proposed to increase the fund to benefit pregnant women.

Care

Reinforcement of the coordination of the care and its extension beyond the hospital for a better implication of the GP. Improve the patient's journey by setting up health posts to coordinate it between the hospital and home. Develop specifications for nursing coordinator missions. Provide 80% of patients with at least one personalized care program (PPS). In May 2011, 885 health facilities met the expected criteria of safety and quality for all types of treatment (chemotherapy, surgery, radiotherapy, etc.). There will also be a desire to develop training that further integrates the social and ethical dimension into care/treatment relationships and to promote the analysis of practices within care teams. University training programmes in three new skills in the oncology field: care coordinators, dosimetrists and anatomo-cytopathology technicians should be developped, as well as a master degree in the coordination of the care pathway for nurses.

Living with and After Cancer

New health and medico-social initiatives to better support people "during and after cancer." Personalized and supporting care after cancer is reinforced with the involvement of the GP.

Generalizing the social evaluation actions within the framework of the announcement system by integrating a social component in the personalized care program, this action implies the nurse coordinator. In order to be able to offer each patient a social consultation during treatment, this consultation is part of the continuity of the social assessment integrated in the announcement system.

Implementing a personalized program after cancer (cMYP) will be adapted to the personal features of the patient. It will include the necessary follow-up and assessment of the risk of relapse and sequelae, the prevention of the risk of second cancer, and the elements related to reintegration in the social life. This action involves offering cancer patients and caregivers psychological support after cancer [5].

Cancer Plan 2014–2019

This plan comforts the last ones. Its main mission is to ensure comprehensive and personalized care, moving from a care pathway, centered on the medical care of cancer, to a path of health taking into account all needs of the cancer patient and his or her loved ones from a physical, psychological, and social point of view. Patients must be able to participate fully in decisions they have to take. They must have appropriate and accessible information at all stages of the journey, including research and clinical trials. All patients who require it must be able to access adequate supportive care. Moreover this plan urges the development of a master degree for nurses specialized in oncology.

Conclusion

The contribution of competent authorities all around the world to support the implementation of adequate measures in order to improve the care of cancer patient is significant. WHO, National Comprehensive Cancer Control Program in the US, EPAAC with the European Commission…etc. The result is convincing. We could observe a real change in France, thanks to the different cancer plans which had been established: process of announcing cancer diagnosis, implementation of the supportive care, coordination of the patient's journey, and improvement of the quality of life after illness.

All initiatives around cancer care taken by different countries might be an example for other diseases.

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Website

Institut National du Cancer: http://www.e-cancer.fr/
Ministère de la santé et de la protection sociale: http://social-sante.gouv.fr
Plan cancer 1 (2003–2007): http://www.e-cancer.fr/Plan-cancer/Les-Plans-cancer-de-2003-a-2013/Le-Plan-cancer-2003-2007
Plan cancer 2 (2009–2013): http://www.e-cancer.fr/Plan-cancer/Les-plans-cancer-de-2003-a-2013/Le-Plan-cancer-2009-2013
Plan cancer 3 (2014–2019): http://www.e-cancer.fr/Plan-cancer-2014-2019-priorites-et-objectifs
Worldcancer congress. https://www.worldcancercongress.org/sites/congress/files/atoms/files/PS47_Khayat-David.pdf

Therapeutic Education

10

Claire Llambrich Molines

> *Among the people who carry out work that directly or indirectly contributes to care provision, the patients themselves are a class of workers who are rarely identified as such. They hold no professional title; the tasks that they accomplish most often go unnoticed, although paradoxically the work is often taken for granted and expected; and of course, the hospital does not pay for it. In fact, the greatest part of this work remains invisible to the professionals […], either because they do not see it being carried out or because it is not defined as work.*
>
> Strauss (1982) [17]

Abstract

Today, people suffering from cancer will live with the disease until the end of their life. Education provision for these people is a necessary complement to care provision. This corresponds to other theoretical models from the sciences of education, psychology and sociology that are distinct from the clinical models of evidence-based nursing and evidence-based medicine. This complementarity offers a holistic approach to sick people, and to familial and social ecosystems, and enables the empowerment of patients who accomplish their patient work, raising awareness of this work and assigning it a social value.

Keywords

Therapeutic patient education (TPE) · Cancer · Teaching · Support · Patient work

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C. L. Molines (✉)
Institut Curie, Paris, France

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Introduction

Contemporary medicine is currently undergoing a transformation. Health professionals who are trained and shaped to cope with situations of acute care know how to cure. Chronic disease by definition cannot be cured. When it is not possible to cure people, how can we care for them? The caregivers are coming up against this new challenge to support patients in taking back control of their decisions, projects and lives that have been momentarily or permanently transformed by cancer. We can see that there are different stages for people with cancer and that even when they are cured they still need support. This experience of the disease inevitably affects everyday life.

The knowledge the patients gain from the experience of the disease often escapes the caregivers. Their subjective experience enables the patients to constitute a sum of knowledge, part of which remains private and out of reach to the care staff.

Who is the expert in this story? The patient as the subject who has experienced the disease or the health professional whose status is legitimized by a society that possesses a piecemeal and subjective medical and health knowledge? Is acculturation possible? Yes, if we consider that evidence-based knowledge of medicine is as important as lay knowledge acquired from the unique experience of the disease in the broad sense. Since the biomedical paradigm is correlated to a task prescribed for the action and being of the patient, the task is necessarily redefined by the patient and realized by incorporating new knowledge enabling an adaption to the psychosocial reality of the disease. Thus, the acculturation of the actors is not only possible but necessary, with a view to providing optimal support for patients suffering from cancer.

Linking evidence-based knowledge, based on “evidence-based medicine (EBM)” or “evidence-based nursing (EBN)” and lay knowledge acquired through the decoding of activities actually undertaken or experienced, enables a considerable enhancement to the thesaurus of the possible solutions in response to a situation of care. Therefore, to better perceive what the cancer is, it seems important to enable patients to use their knowledge, in particular that gained from experience, and to acquire new knowledge, from “EBM or EBN” but also from sociological, anthropological and psychological ways of thinking. TPE makes this possible.

In the first section, we will examine therapeutic patient education and its foundations. Then we will present the example of a therapeutic education programme put in place by a team of nurses in a Parisian anticancer centre. Lastly we will present the changes in the social roles that the implementation of such a mechanism can produce which re-examines the role of each actor, from the patient to the caregiver.

Therapeutic Patient Education, A Springboard Towards Autonomy

Definitions

According to the World Health Organization: “therapeutic patient education must enable the patients to acquire and retain the capacities and skills which help them to live with their disease in an optimal way. Therapeutic education therefore aims to help patients and their families to understand the disease and the treatment, to cooperate with the care staff, and maintain or improve their quality of life" [20]. "The Cancer Patient Education Network" (CPEN), affiliated to the "National Cancer Institute" (NCI), complements this definition by specifying that "patient education permeates all the aspects of the experience of health care and consequently is an essential element in the continuum of care of prevention, detection, diagnosis, treatment, research, life, survival and end of life. Patient education aims to:

- Improve the patients' understanding of their disease.
- Improve the patients' understanding of how to manage several aspects of their disease.
- Improve the patients' self-defence to act independently but in interdependency with their health care providers.
- Increase the patients' motivation to comply with the treatment schedule by means of communication with suppliers.
- Improve the patients' results and prevent or reduce complications.
- Help patients make informed treatment decisions.
- Improve patient use of the medical services by decreasing pointless telephone calls and recourse to the hospital.
- "Increase patient satisfaction with the health service and reduce the risk of professional misconduct" [1].

It appears important to add an additional dimension to these goals. Indeed, when "the patients are no longer the object but the subject of the care provided to them, then the objective is no longer to fight disease but to promote health and the process of prescription gives way to a process of education" [16]. During the course of health promotion, patients should be understood as thinking subjects who act according to their unique perceptions of the world. Thus the tools used in TPE come from psychology, communication and teaching. If people are considered as the author of their lives, then they need to develop emotional and psychosocial skills as a precursor to mobilizing skills that enable decision-making and action.

Techniques and Biases

The Support Relationship

Based on the principles set out by Carl Rogers [15], and on the transformation paradigm described in nursing sciences by Newman, Sime and Corcoran-Perry in 1991 [11], and used by Pepin, Ducharme and Kérouac [13], the practice of TPE is based on mastering the support relationship by mobilizing the technique of active listening [4]. The objective is to provide a serene space for the patients by promoting understanding of their representations of the disease, the treatment and their needs, values, resources, skills [5] and cognitive mechanisms. For this communication technique, the professionals must master the following techniques: listening, non-judgement, reformulation, valourization and questioning through non-inductive open questions. Managing the techniques of the support relationship is indispensable at all levels of intervention in TPE. The caregivers must work on their position and means of communication and respond to their philosophical biases that can be difficult to change. This repositioning requires significant work on oneself.

The effect of this communication technique used in psychology proves to be therapeutic in terms of psychological care which can be used to provide support and help with progression. In addition it can manage shock and anxiety, aid with decision-making and raise awareness of the interior process encouraging empowerment, the feeling of self-efficacy and self-esteem and others. All these levers can be used to develop oneself and to take back the power to act on the situation. The support relationship is a reassuring framework allowing the creation of quality of life and emancipation [19].

Education

One of the founding principles of the educational position is to "think the other person capable" in the manner of Socrates (around 490-399 B.C.) who, using maieutics, postulated that each man already possesses knowledge and that the role of the teacher, who himself knows nothing, is to facilitate the emergence of this knowledge. This philosophical position is not that easy to integrate. Indeed, this is not a case of simply knowing that one should "think the other person capable" but of unconditionally and intuitively "thinking the other person capable …", thus nourishing the trust of others to enable the person to think of him/herself as capable of acting.

Therapeutic patient education essentially relies on five main pedagogical currents: However the last three are mostly the teaching foundations on the TPE.

- Frontal or magistro-centrism teaching: This is the transmissive model of accumulation of knowledge and authority.
- Behaviourism (or behaviourists) described by Watson and Pavlov. This concerns operant conditioning.
- Active or project-based learning, where the reference authors are Freinet, Dewey, Decroly and Oury, is based on learner experimentation.
- Cognitivism is a trend in which the learners mobilize the knowledge that is appropriate for a situation by drawing from their resources and stored knowledge.
- The fathers of the constructivism and socio-constructivism trends are Piaget and Vygotsky, respectively. They postulate that the truth does not exist. The learners construct their reality themselves. Here the information is restructured according to each person's own reality.

In line with these great theories, teaching and learning methods have been developed following different modalities in accordance with the targeted objectives and the representations made by the teachers of the cognitive processes engaged in the learner.

Marcel Lesne [7], in his work compiling the existing educational methods, proposes a classification of three categories that he calls the modes of educational work (MEW): MEW1, MEW2 and MEW3 correspond, respectively, to the transmissive mode, the incentive mode and the appropriation mode. For each of these, Lesne defines the status of the learner and that of the teacher and the social effects in terms of the type of social individual that it constructs. This model is a "tool of clarification of action" [7].

- The transmissive educational mode (type 1) is learning with normative orientation. In this mode, the learners are the *objects* of learning. The teachers possess and transmit their knowledge to the learners. They are recognized as legitimate; they control and sanction. "They accept and exercise the educational authority involved in any act of training" [7]. The educational methods used in this type of work are affirmative methods (teaching the model, demonstrative), interrogative methods, methods known as active, lectures, study of problems and mental training. The principal agents of this type of mechanism are instructors, teachers, lecturers, specialists or holders of a professional power. The social effects of such a mode of education are to prepare individuals for given roles, to close the gap between the individual behaviour and the general requirements of society. More generally, this creates individuals capable of reproducing social models. This MEW is the easiest to use for health professionals.
- The type 2 mode of educational work is an educational mode with personal orientation. The teachers are no longer holders of knowledge. They put the learners in a situation that enables their knowledge to emerge. The learner is *subject*. The individual's creative forces are mobilized by the trainers who establish a dynamic of learning and seek to strengthen the autonomy of the person by encouraging free access to the different sources of knowledge. They explicitly refuse the qualitative power and control that manifests either in the form of self-evaluation or comes from the group. The agents of this mechanism are facilitators capable of creating favourable conditions for learning. This type of education creates individuals who are socially adaptable and capable of reflecting on their actions.
- The type 3 mode of educational work is an educational mode centred on social insertion. In effect, the trainers put the trainees in real conditions. The learners become *agents* in the sense of being able to act. They produce knowledge and anticipate what they have to learn at the same time as acting socially. The learners need a theoretical framework and tools to understand reality. Trainers and trainees share a democratic exercise of power. Sanctions come from reality, from the work. The principal agents of the educational mechanism are the trainers facilitating the relationship between the training and the circumstances of daily life. The learners, as agents, develop the capacity to modify the conditions in which their daily activities are exercised. They are capable of transforming reality.

This approach described by Lesne allows to anticipate the implementation of an educational process with an approach adapted to the targeted objectives. The question being: Should we create individuals who are capable of reproducing a practice (mental or physical) or of reflecting on their practice and transforming it in function to reality? These analyses on the choice of educational method to be used in relation to the social effects that they have on the learners are essential if we concentrate on really achieving the objectives set by the sequences constructed during the production of action of therapeutic education.

Theoretical Foundations

TPE requires a mastery of the help relationship technique, using relevant educational tools with a view to responding to the variability of the mental processes of individuals and ensuring an educational support that is adapted to the particularities of each person. To do so, theoretical models from the social sciences and psychology can be used to support the educational techniques and represent effective practical supports to construct tools and processes that enable learning and personal development.

The NCI website refers to the CPEN who produced the guide: "establishing comprehensive cancer patient education programs: standards of practice". This guide has compiled the international recommendations on therapeutic education since 1993. It references the theories that are useful in TPE and can be used by an educator to better understand the behaviour of individuals as well as that of populations.

	Theory/theory originator(s)/keywords
Individual health behaviour theories/models	Health belief model Source: Hochbaum, G Rosenstock, I & Kegals, S (1950) Perceived threat, perceived susceptibility, perceived severity, benefits and barriers to taking action, cues to action self-efficacy
	Cognitive dissonance theory Sources: Festinger, L (1957); Glanz, L & Rimer, B (1997) Cognition, conflict, consonance, dissonance, motivation
	Theory of reasoned action/planned behaviour Sources: Ajzen, I & Fishbein, M (1969, 1970, 1977, 1980); Behavioural intention, outcome expectancy, evaluation of likelihood of outcome expectancy, subjective norms, normative beliefs, motivation to comply, perceived behavioural control, control beliefs
	Protection motivation theory Sources: Rogers, R (1975); Threat appraisal, coping appraisal, severity vulnerability, self-efficacy, response efficacy
Interpersonal health behaviour theories/models	Social cognitive theory Sources: Bandura, A & Walters, R (1963); Personal factors, behaviour, environmental factors, reciprocal determinism, triadic reciprocality between personal factors, modelling, vicarious learning, self-efficacy
	Theory of interpersonal behaviour Sources: Triandis, H (1977, 1980, 1994, 1995) Cognitive, social, personal factors, habit, intentions, facilitating conditions
	Social support, control, stress and coping Sources: Caplan, G (1974); Cobb, S (1976); House, J (1981); Kahn, R & Antonucci, T (1980) Supportive behaviours, emotional support, appraisal support, informational support instrumental support, social capital

	Theory/theory originator(s)/keywords
	Health locus of control theory Sources: Wallston, B, Wallston, K, Kaplan, G, Maides, S (1976) Expectancy, external locus of control, health externals, health internals, internal locus of control, powerful other, reinforcement
	Elaboration likelihood model Sources: Petty, R (1979) Cacioppo, J (1979) Persuasive communication, central route to persuasion, peripheral route to persuasion, motivation to process, ability to process, nature of cognitive processing, cognitive structure change, central positive attitude change, central negative attitude change, peripheral attitude shift peripheral cue present, attitude, boomerang attitude, persistence, resistance, behavioural prediction
Stage theories/ models	Piaget's child development theory Source: Piaget, J (1950s) Sensorimotor (birth, 2), preoperational (2–7), concrete operations (7–11), formal operations (11–15)
	Precede-proceed model Source: Green, L (1968–early 1980s) Precede: predisposing, reinforcing and enabling causes in education, diagnosis and evaluation Proceed: policy, regulatory and organizational constructs in education and environmental development Phases: social diagnosis, epidemiologic diagnosis, behaviour and environmental diagnosis education and organization diagnosis administrative and policy diagnosis implementation process: evaluation impact, evaluation outcome
	Transtheoretical model/stages of change theory Sources: Prochaska, J & DiClemente, C (1983) Stage, pre-contemplation, contemplation, preparation, action, maintenance
	Diffusion of health promotion innovation theory Source: Rogers, E (1962) Stages of Technological innovation knowledge persuasion decision, implementation, characteristics, relative advantage compatibility, complexity trialability observability, adopter categories, innovators early adopters, early majority, late majority, laggards, roles, opinion leaders, change agents, change aids
	Precaution adoption model Weinstein, N (1988) Work placements: unaware of issue, unengaged by issue, decided to act, decided not to act, decided to act, acting maintenance
Social systems theory	General systems theory von Bertalanffy, L (1950) Interrelatedness and interdependence of all phenomena, physical, biological, psychological, social, cultural
	Social marketing theory Sirgy, M (1984) The five "P's": product, price, place, promotion, positioning

Establishing Comprehensive Cancer Patient Education Programs: Standards of Practice 24 © 1998 Cancer Patient Education Network (CPEN), revised 2013

Example of a Programme: Anticancer Centre Paris

In France, to better understand life paths with cancer as a chronic disease, therapeutic education has been gaining ground in the last decade. The law pertaining to hospital reform and to patients, health and the territories of 21 July 2009 [10] requests that TPE programmes are offered to patients suffering from chronic disease, to ensure a better quality of life by reinforcing their skills but also to encourage compliance with the treatments and reduce readmittance to hospital. This involves the patients being supported by an educational caregiver to learn, make use of and incorporate new knowledge, know-how and clinical knowledge to help them stay alive.

Let us focus on a programme of therapeutic education developed 5 years ago in oncology, at the Institut Curie, Paris, France, to support patients taking oral anticancer drugs at home. The TACTIC programme was designed, created and implemented by a team of nurses. We will focus on the engineering modalities of the project to give an account of the procedural changes in terms of organization before describing the programme and its content, in order to understand the impacts for both patients and professionals.

Project Engineering

The implementation of an action of education requires the willing support of the institution, whatever the motivations (often financial or in the case of France the need for accreditation) and support for the logistical implementation (room, equipment, human resources, training). Prior work with the team on several levels was necessary for the implementation of this programme.

The educational provision occurs during a follow-up consultation for patients taking oral chemotherapy and was created at the initiative of the nurses in 2008. Initially it was decided to train a team of nurses and avoid allocating one single person to the project with a view to making this initiative durable. The team collectively decided to cease conducting the consultation in its previous form. Thus they decided to no longer give raw information but instead change the procedure to enable patients to use their existing knowledge and to obtain new knowledge. We decided to develop a TPE as an integral part of the care as opposed to a more categorized vision that positions education as an annex of the care. This decision required the instigation of training in therapeutic education (certified 40 h training) for the staff participating in the consultations. Participation in the training was on a volunteer basis so as to recruit nurses motivated by this project.

Within the department, regular meetings on the theme of TPE were held at a frequency of one per month to codevelop a common culture around this concept. The whole team was invited to these meetings to ensure that everyone understood and adhered to the values of this new practice, including those who would not be directly providing TPE. Indeed, it is vital to inform all the professionals in the team about the developments and transformations in their department so that they can support and encourage them and so that they recognize the legitimacy of the work accomplished by their peers. To be able to accomplish all this, the doctor head of department and the head nurses supported and accompanied the project, the team and the initiatives which enabled the professionals to feel authorized to develop their practices in consolidating therapeutic education.

In order to develop the TPE, the nurses must change their position, integrate the active listening technique and consider the patients as capable. This paradigm at the level of the team upholds a new value: "it is the patient, even in his/her blindness, who is the guide, as s/he alone is able to indicate the path and give it meaning" [6]. This involves at times reassessing and working on oneself to be able to accept leaving aside one's status of expert and to consider that the patient is producer of a work with an equal status to that of the health professionals. This change may be accomplished through regular coaching of the team members by the programme coordinator. She supports the process of her colleagues and enables them to integrate into the project and to find their place in it. She has a position of leader. The practice requires the nurses to change the paradigm, ascertain their position by integrating themselves into the project and give overall meaning to their actions.

By way of an exploratory phase, a group of patients met to experiment with a photo-language methodology with the aim of forming a focus group on their needs and expectations. Following this, another group of patients tested the programme in real conditions. Their proposals were used to change and readjust the sessions and workshops.

In summary, the ingredients necessary for execution of this TPE programme were the motivation and needs of the actors (professionals and patients), the durability of the project by the creation of a team, training, co-development of meaning, the leadership of a coordinator, institutional support and encouragement from superiors and regular coaching of the team members and of the team in its entirety.

The Programme

It is organized as follows: a shared educational assessment is conducted with the patient at the inclusion stage. "Bespoke" individual sessions and group workshops are offered with respect to the needs of each. The programme is not presented as such to the patient. For the nurses it constitutes a new approach to care provision which unconditionally includes education in the practice. In fact, with the patients the professionals do not use the terms "common educational assessment" or "educational workshops" which we consider as belonging to the hermetic language of the profession (behind the scenes, not necessary in the relationship with the patient). We think that these terms may induce a certain distance through distrust, recalling the rapport maintained in learning in childhood which may prove painful to some people. The use of these words may also distance people "from the heart of the relationship" by creating an overly conceptual rapport to the acts of support. In this way, the therapeutic education becomes an integral part of the care as a position that underpins the overlapping pedagogic and clinical biases.

During the shared educational assessment, the patients undertake an inventory with the caregiver on who they are, what they do, how they represent the disease, the treatments, their projects and how they live on a daily basis (activities, professions, organizations, etc.). This interview is conducted in the nursing consultation room with the patients when they leave the medical consultation with prescriptions of a new treatment to take. The nurse on duty receives the patients who are sent to her by the referring oncologists. At this point, a summary is co-produced with the person to identify the strengths and the weaknesses. The sessions and workshops which follow will be a response to these weaknesses. The sessions are based on the strengths and resources of the patients, enabling them to mobilize new clinical knowledge and work on their emotions, attitudes and feelings (Table 10.1).

Each patient chooses what she/he needs to know among the proposals made by the nurses. Overall the patients who benefit from this programme participate in

Table 10.1 TPE group workshops and individual sessions in the TACTIC programme

Individual sessions	Methods/tools	Skills developed
I know how to take the treatment	Prescription Box of medication Evocation of reality Annual schedule, a fluorescent pen, scissors	Become aware of the chronic nature of the disease, read, understand and interpret the prescription Take the treatment wisely, know the treatment Decide on the start date of administration, decide on where to store the box, divide the daily dose Plan intake over several months at home, swallow the treatment
I can read and interpret the CBC	Their latest complete blood count Fluorescent pen	Know the blood cells, know the function of the blood cells Know the signs of blood cell insufficiency Recognize the prodromes, physically act as a result Anticipate a critical situation, know the standards of the hospital Interpret the CBC with respect to these new norms, make a therapeutic decision Use wisely
I anticipate and I manage the potential side effects	DECLIC ACO game (maps and open questions)	Know the side effects Classify them according to their frequency of occurrence, know the normal clinical signs Recognize the pathological clinical signs, act in accordance with the appearance of these signs Take an appropriate treatment Adapt a treatment (doses, frequency), use wisely

(continued)

Table 10.1 (continued)

Individual sessions	Methods/tools	Skills developed
I can apply dressings alone	Dressing panel Scissors Drawings of cuts	Put the dressings on myself Identify the most suitable dressing depending on my everyday life and on the type of wound Seek help from a relative to explain the treatment Let myself be helped
I understand the physiology	Drawing Animated digital diagrams	Understand a physiological phenomenon, explain the physiological phenomenon
I prepare for the consultation with the doctor	Coaching Risk scale role play	Sound out my expectations of the consultations Prioritize my expectations Imagine the possible responses to each expectation, weigh the risk of each response Decide on the questions to ask, ask them

Group workshops	Methods/tools	Skills developed
I know how to eat when taking oral chemotherapy	FAQ Class of food table menus	Know which foods are compatible and incompatible with oral anticancer drugs Sort foods according to their class, identify my food needs Determine the benefits depending on the types of foods, know about food supplements Put together a menu and complement it if need be
I express my priorities	Short exercises (concepts) Double optical illusions Role play Real-life cases	Compare everyone’s point of view Understand and integrate that we all have a unique vision of the world Identify our mechanisms of action regarding the difference of vision Modify an inward-looking attitude, knows how to say *no* Express oneself humbly in reaction to the situation
I understand the disease and the treatments	Brainstorming Game of decision-making scale treatments, educational drawings	Share his/her representations of the disease and of the treatments Construct a process in a group around these representations Identify the impacts of the disease and of the treatments, understand each treatment Identify his/her place in the care pathway, decide to take his/her treatment Be motivated to act for oneself

four sessions or workshops. These people regularly return to the nursing consultation for a follow-up and can ask to address different themes depending on their needs at the time.

The Effects of the Programme

The assessment of the effects is subject to each person's subjectivity and singularity. Some of the teachings can be assessed in a tangible way, for example, in the case of the evidence-based clinical data to be learnt. However, it is much harder to accurately assess the development of behaviours and patient satisfaction. It could be interesting furthermore to develop an evaluative research protocol to document in a scientific way those effects.

The statements are often in verbatim form simply relating the patients' thoughts. Yet these statements are only discourses on the real and unreal, and there is at times a significant gap between the two. In any event, what we observe on a daily basis in the nursing consultations is that over time people no longer ask the same questions and those previously in the realm of the anxiety such as "the blood results are all in the red, what should I do? is it serious?" are progressively replaced by questions of a procedural and informative nature looking for validation from the professional, such as "my white globules are low, I stopped the chemotherapy". Thus, we observed that the practices change over time and interventions occur earlier and are more wisely judged.

We have also observed that it appears beneficial to have a non-formalized means of "leaving the programme" which seems to be linked to a degree of autonomy acquired by the person, until the appearance of a new need induces him/her come back. If this step is too formalized, this acquired autonomy may be damaged and therefore less beneficial for the individual. TPE is experienced as an opportunity by the patient.

The nurses like to run these workshops and sessions as they come out of them enriched and the co-construction in teams constitutes a meaningful creative investment for their profession.

Furthermore, we have noted that the doctors are often recruited to TPE by the patients. The change of position of the patients in relation to the oncologists provokes a change in their own positions.

In France, the educational actions in hospitals are organized in transversal units of education to promote an educational provision that follows the example of care provision. And the programmes produce very different mechanisms from one department to the next, creating microcultures [8]. This has an effect on the social roles expected of each individual.

Transformation of Social Roles

What the Development of TPE Changes for Professionals

New Modes of Organization of Care

Some nurses remain focused on technical care, while others become more specialized in support and education which are increasingly vast and complex fields open to increasing active channels. According to Pouteau, they "are looking for a new framework of exercise which enables them to mobilize their professional knowledge differently. They endeavour to maintain close links with the care departments, in order to keep up to date with technical developments and avoid giving rise to an overly pronounced differentiation in the roles" [9]. In fact, in the context of professionalization in TPE, it is necessary to support the change in the caregiver's position towards the role and responsibility of an educator.

Towards New Skills

During the design and creation of workshops, the nurses develop and use educational games. Some of these games are suitable for dissemination on a large scale which requires precision and reliability in both form and content. The development of such games requires skills in logic, marketing, game design and legal aspects which broaden the field of action and impact of the professionals. Through these artefacts the nurses develop new skills. Their work is made visible, is formalized and provides them with a degree of recognition.

Gradual Changes in Tasks

When TPE is completely integrated in nursing care to the point where each contact with a patient is an opportunity to enable him/her to grow and to develop for him/herself, it takes nursing practice closer towards advanced practice.

The nurse carries out an individual education session: "interpreting and understanding blood tests (CBC)". So, the patients may establish causal links between the values of the blood test and the intake or not of anticancer medications. They can then call to report that the CBC is too low and that they are suspending the intake of the anticancer drugs. Even telephone consent from the nurse to this decision serves as a validation for stopping the chemotherapy. This also applies to treatment resumption when the values of the complete blood count go back up and for a number of everyday procedures that would otherwise insidiously add to the daily workload of the nurses. Although these "task changes" in fact apply to procedures that should, legally, be performed by a professional and thus fall into the category of illegal practice of medicine, we also perceive that they are often a solution to the organizational constraints. "This phenomenon leads to the emergence of new professions (nurse clinician, advanced practice nurse) based on organizing the work in teams permitting a controlled delegation of tasks and a redistribution of medical time to tasks with higher added value" [14]. A training in TPE and or in advanced practice at master's level represents a means of advancing one's career and decisively increasing the level of responsibility of the nurses, so they receive recognition in their new roles.

Difficulties Encountered in the Change of Role

The resulting questioning of professional territory may feed inter-professional conflicts or at times conflicts with oneself regarding the task that is self-prescribed. We also observe a reluctance to take the risk represented by this change of position or practice. This modifies the points of reference and habits of professional practice and takes the caregiver outside of his/her comfort zone, which is not acceptable for everyone. The analysis carried out by Dominice and Lasserre Moutet [3] shows that "training doctors in TPE" induces a "restructuring of medical thinking". They talk about "sometimes difficult risk-taking" to "assume the status of marginality which can result from such a change of professional perspective" and of the "new representations of what learning means by becoming an educator". According to Veilhan [19], the concept of patient researcher-actor in his/her health pathway may be intelligible, but it is difficult to integrate and appropriate into the core of the educational practice because of the fear of giving up the responsibility of the knowledgeable caregiver.

What the Development of TPE Changes for Patients

Empowerment

The government injunction in response to the increase in cancer patients – to do more with fewer resources – has resulted in a reduction of the time spent in hospital, and this obligation of efficacy requires profound transformations in care provision. An example from Gaspésie (Québec, Canada) is a large territory, a sparse population and a distant reference hospital. These factors have led to a policy to encourage patients to make tutorials on YouTube about common treatments (subcutaneous anticoagulants, etc.) and then circulate these videos by a shared network in connection with the health centres of Gaspésie. The patients involved then refer to this audiovisual resource addressing their concerns, with which they identify almost automatically (e.g., peer learning). The role of the nurses is thus modified; they eventually take on a coaching and supporting role when monitoring the patients who become the author and the actor of their lives. Thus the nurses abandon their role as the expert. This experiment shows that when you allow the patients to develop their potential to learn autonomously, they appropriate this world for themselves and transform it in accordance to their needs. According to Tourette Turgis, "the patients drive TPE forward and produce knowledge: putting the care subject in a situation of knowledge production advances the care" [18]. "Any adult with experience carries unprecedented creativity and must be allowed to reveal this as an actor of change by permanent learning through research" [2]. Thus, being sick becomes in itself an object of research.

A Social Implication

The patients involved in the associations or having participated with the health professionals in the production of the programme or the workshops as a facilitator and creator occupy a position of social mediator and participate in the change of status of the patient. The patients move from being an object of interest to medicine to patients who actively thinks about their place and role and the relevance of their contributions and who are engaged through this pathology to politically represent their peers. This position-taking shifts the boundaries and leads to a step-by-step development of a true social role that undermines [12] definition of the status of the patient as one who cannot work and must obey the doctor. Here the patients become public players and transform society by "producing an asset in the collective and health field" [18]. Tourette Turgis adds that "recognition of the work of the patient becomes indispensable in the light of the chronicization of diseases. 'This expertise of experience' is necessary to improve the system of expertise of care". In this respect we might think that tomorrow the work of the patient will be not only an object of research but also a job, even a profession, with a territory, a customer base, a language, etc.

Conclusion

TPE is a way of caring which, when well anchored in hospital services, can generate a common identity and, thereby, a common, even institutional, project, with benefits such as efficacy at work and a feeling of well-being.

During the implementation of an TPE programme or workshop or even an individual session, the overall vision of the nurses is essential as it reflects the educational foundations enabling learning: non-judgement, complex consideration of the individuals in their singularity, the subjectivity of their actions and choices and the unique causal links no longer pre-established by frames of reference that are not their own.

For Veilhan [19], "the passage from the position of caregiver to that of educator involves taking into account the experience of the patient as a subject possessing intelligence regarding his/her chronic pathology". This means that the professional in oncology should agree to let go and overcome his/her ego. Human beings need to be allowed to change and evolve accompanied by recognition, valourization and the trust of others (patients, peers, superiors, other professionals). TPE enables everyone to learn from the outside world and about themselves. It is indispensable to be able to reorganize one's daily life that has been irrevocably changed by the cancerous disease.

Changing this course of action requires an acceptance of the changes in the social role of the carers and patients. People suffering from cancer in the future may become professionals of their disease so as to add value to the work they accomplish daily to stay alive.

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11

The Advanced Breast Cancer Nurse: A Key Role in the Metastatic Breast Cancer Patient Health Itinerary

Suzanna Winston

Abstract

Hundreds of thousands of women in the world are currently living with metastatic breast cancer. Thanks to the large advances in treatment, it is becoming a chronic disease. These patients express, through questionnaires, their poor quality of life, confusion when faced with the complexity of their healthcare, and a deep feeling of loneliness. The supportive care of these patients in Europe is still largely undeveloped. Within a multidisciplinary team, the advanced breast cancer nurse (ABCN) will play the key role in supportive care from discovery of metastasis, until the patient is transferred to palliative care. The presence of an ABCN should be formalized and funded in all breast cancer facilities. The creation of a healthcare track for metastatic breast cancer patients will facilitate the integration of the nurse into this role and help her to accomplish the mission.

Keywords

Advanced breast cancer · Advanced breast cancer nurse · Clinical role · Supportive care · Quality of life

Introduction

Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death among women worldwide, with an estimated 1.7 million cases and 521,900 deaths in 2012 [17]. The scientific community generally distinguishes early

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S. Winston (✉)
Cliniques Universitaires Saint-Luc, Université Catholique de Louvain, Brussels, Belgium
e-mail: suzanna.winston@uclouvain.be

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breast cancer patients (eBC) from metastatic breast cancer patients (mBC). Despite the absence of precise data, it is considered that 20–30% of eBC patients will develop metastasis [3] and between 5% and 10% of BC patients present already at primary diagnosis with metastasis [4]. It has been estimated that by 2030, the number of deaths will reach 805,116, representing a 43% increase in absolute number of BC deaths [21].

Early breast cancer patients receive a lot of attention, which is absolutely imperative. The number of early breast care nurses (eBCN) is increasing in Europe. They care directly for patients from the primary diagnosis of cancer all the way through the patient's surgery, chemotherapy, radiotherapy, and hormone therapy. Considering the high number of women currently living with mBC, one would think that these supportive care units would be available to them as well. However, paradoxically, the care and follow-up of mBC patients remains largely undeveloped. The activity of the eBCNs does not necessarily transcend to the follow-up of mBC patients. Numerous quality of life (QOL) studies have shown this to be true. It is therefore absolutely essential that our multidisciplinary teams create a structure specifically designed to support these women in their healthcare itinerary: a new oncology nursing role specializing in advanced breast cancer.

Advanced Breast Cancer: A Chronic Disease

Despite the advances in treatment, and even though mBC can be treated temporarily, to this day it does remain incurable. MBC has a median overall survival of 2–3 years and a 5-year survival of 25% [16]. Nevertheless, it is currently considered as a chronic disease. Of course, its prognosis will increase depending upon the immune-histological type present [12] and depending upon the disease's response to the treatments administered [6]. Some women will progress quickly, while others may have up to 10–15 years of survival [11]. Clearly, the chronic nature of the disease significantly alters the continuum of life. On the one hand, it entails multiple treatment lines with their physical and psychological impact on patients, as well as a permanent interference of "medicine" in everyday life. On the other hand, the chronic status of mBC patients significantly impacts medical management. It calls for special attention and management both on a daily and long-term basis.

Advanced Breast Cancer: A Quality of Life Threat

The discovery of metastases highlights a transition in the disease continuum. The impact on the patient's personal life is significant. Reference points are overthrown. New realities must be integrated into their lives: the certainty of no healing, the high probability of death in the short term or midterm, the uncertainty of the effectiveness of treatments, the uncertainty of the duration of treatments, the reality of the chronic state of the disease with the management of its results, and the reality of the personal exhaustion which settles in little by little: physical, psychic, spiritual, and the same exhaustion in their loved ones. It will then be necessary to move toward accepting the cessation of treatment and making decisions related to end-of-life issues.

Numerous QOL studies conducted around the world show a major impact on the quality of life of mBC patients [15]. Starting at the diagnostic until the end-of-life care, the needs related to metastatic disease change according to the stage of the disease [1]. These needs impact all areas of life, bringing on specific cognitive, emotional, relational, psychic, and spiritual concerns, as well as, family and socioeconomic ones, not to mention the purely physical needs related to the disease, its evolution, treatments, and their side effects.

Metastatic breast disease became chronic thanks to the many advances in therapy now available. Yet the QOL of these patients remains problematic. The ever-increasing number of mBC patients worldwide and in Europe calls for action. MBC supportive care must find ways to implement more effective measures. This situation demands specific nursing skills and specific nursing interventions.

The Advanced Breast Cancer Nurse (ABCN): Specific Nursing Competences

Today, in many European countries, eBC patients have access to the services of a breast care nurse (BCN). The BCN cares for the eBC patients from diagnosis until complete remission. Meanwhile, the palliative care teams take care of the mBC patients from the time their treatment is stopped until the end of their lives. However, to this day, a "gap" still remains in the healthcare process of metastatic patients in centers specializing in breast cancer care. This "gap" begins at the discovery of metastasis or locoregional recurrence and continues until the palliative care team takes over care of the patient. Thanks to the many advances in treatment, this gap period tends to extend over several years. These patients are in need of advanced breast cancer nurse (ABCN) special services [18]. The mission of the ABCN is to actively collaborate with the entire medical team in order to fill this gap in the continuum of patients' care. As a result, it contributes to improving the survival rate and the quality of life of the patients. The management of metastatic patients is complex. It varies with each stage of the disease and according to the introduction of different treatment lines. There is a pressing need to spread Europe wide such a nursing function that will update regularly its knowledge so as to keep up with new prospective treatments and offer top-notch follow-up to patients [14]. The third ESO-ESMO International Consensus Guidelines for Advanced Breast Cancer also recommends that these specialized oncology nurses (if possible specialized breast nurses) should be included in the multidisciplinary team concerned with the management of ABC patients [5].

The Advanced Breast Cancer Nurse: Specific Nursing Interventions

Specific nursing interventions will be developed by the ABCN in order to contribute to the improvement of this life-threatening prognosis and the quality of life: supportive care, case management, clinical management, multidisciplinary team membership, communication, and education [18].

Supportive Care

ABCN supportive care manages the care of mBC patients from the discovery of metastasis until the time that treatment is stopped. The ABCN covers this time, however long or short. Yates defines "supportive care" as to identifying multiple physical, psychological, social, sexual, and spiritual needs of clients throughout the continuum of breast cancer care, implementing evidence-based supportive care interventions in a flexible and responsive manner, in the context of a collaborative multidisciplinary approach to care, achieving optimal health outcomes for clients with breast cancer [22]. Supportive care is by far the mBC nurses' primary activity. It underlies every other activity. It is essential because the core of its mission is to care for human beings.

Some basic practices facilitate this mission:

- **Really listen**. Active listening is essential to supportive care. This tool is fundamental in evaluating the patient's information intake, her adherence to the treatment, her autonomy, and the presence of adverse effects and psychological behaviors. Listen actively, and respond knowing that the last questions asked by the patient are often the ones that matter most to them.
- **Connect solutions to needs**. Connecting solutions to needs is the core business of the ABCN supportive care [2]. Needs are changing at every phase of the care continuum. Many initiatives have already been put in place to help patients, both in the medical setting and in the general community, but the actual information is lacking. The ABCN is well-informed about the available help and can therefore provide this information to patients in need.
- **Be aware of family needs**. Include family members in the supportive care as much as possible. Make sure they have access to the psychological and social support they may need [13].
- **Empower patients**. Make them aware of ways they can improve their own quality of life within their cancer experience: it is a recommendation of the International Consensus Guidelines for Advanced Breast Cancer [5].
- **Schedule key appointments**. Schedule appointments in the days following the discovery of the metastatic disease, after each progression of the disease, and following any change in treatment [18]. The study by S. Aranda demonstrated that a face-to-face session and follow-up phone call with a breast care nurse significantly reduce the psychological and emotional needs of those with high initial needs [2].
- **Stick to supportive care**. Be aware that supportive care is not palliative care. The notion of "supportive care" and "palliative care" should never be confused [15].

Palliative care begins when metastatic disease is well advanced and the decision to discontinue treatment has been made. The presence of palliative care nurses in palliative care services is assured. The ABCN, in agreement with the patient, the oncologist, and the attending physician will coordinate the transition period during which the palliative care team will take over management of the patient and her family. This final step will bring to an end the ABCN's duty to the patient.

Case Management Role

The complexity of treatments and the large number of different parties involved require the intervention of the ABCN in the care process. The nurse oversees the coordination of treatments during the entirety of the patient's disease spectrum, in terms of the evolution of the disease, its progress, and changes in the treatment line. She factors in the logistical considerations in order to provide the most comfort for the patient and her family. She ensures that the patient understands her planned appointments. She makes the necessary changes in the patient's care plan based on unforeseen events [18].

Clinical Role

Nonadherence to treatment remains a major obstacle in controlling metastatic disease. Throughout the treatment process, the nurse will assess the patient's compliance. Nonadherence is usually due to forgetfulness (41%) or intolerance to side effects (37%) [7]. The ABCN takes on a coaching role in order to improve treatment compliance. She will regularly assess the presence of side effects, toxicity, pain, and comorbidities. What is the patient's nutritional status? What is her score on the Karnofsky scale? How is her mental state? Are there any recent adverse events in the patient's history? [20]. These elements are to be evaluated regularly during unplanned encounters but also on the basis of scheduled telephone consultations in the case of oral treatments taken at home. The ABCN also holds a key position for the management of PROMs (patient-reported outcome measures) that are often put in place [5]. Lastly, the mBCN oversees the management of the medical need programs. Certain treatments are made available to patients while their marketing authorizations are awaiting finalization. The ABCN will coordinate these programs and monitor drug intake in collaboration with the oncologist. Continuous care, clinical management, health education assimilation, and empowerment are the key parts of the ABCN's clinical role [18].

Multidisciplinary Membership

The ABCN is an active member of the multidisciplinary team: she participates at tumor boards where the cases of the mBC patients are discussed [8]. After these tumor board discussions, she strives to optimize the patient's journey by coordinating the multiple interventions of the different medical specialties concerned. She is present during key consultations, for instance, when the oncologist announces a metastatic disease or the progression of the disease [19].

Throughout the clinical journey, the nurse reaches out to existing resources within the hospital as needed: physiotherapist, psychologist, dietician, sexologist, social assistant, beautician, chaplain, etc. She highly values a good working relationship with the clinical research coordinators. One of her patients might be asked several times throughout her disease process to take part in a clinical research study. She pays close attention to collaboration with the study coordinator. She values his complementarity and the alternation of care depending upon the phase of treatment and the disease progression. Lastly, as the attending physician is informed by the oncologist of the progression of the cancerous disease, the nurse will reach out to him in order to establish the link with the nursing team. “Teamwork is crucial to approach cancer management with unified criteria. Regarding teamwork skills, it was agreed that the ABCN should be capable of proposing, analyzing, consulting and implementing methods that enhance the healthcare process together with the rest of the members of the interdisciplinary team” [18].

Communication and Education

“All ABC patients should be offered comprehensive, culturally sensitive, up-to-date and easy to understand information about their disease and its management” [5]. The ABCN actively contributes to this international recommendation. Several studies have also shown that empathy combined with information reduces psychological distress in BC patients [2]. At each stage of the disease, it is necessary for the ABCN to assess the patient’s understanding of the present situation, to reiterate the information given by the oncologist, to answer questions, and to involve the family in these discussions (with the agreement of the patient).

Patient brochures, websites, and patient association details can all be very useful. It will be the responsibility of the ABCN to regularly monitor these resources for their medical relevance and to ensure they are up to date. These resources, however, do not replace the personalized information provided by the ABCN. One must also be reminded that information on breast cancer generally communicated to the public mainly concerns the eBC. The media and partners encourage eBC patients to position themselves as survivors and winners without taking into account the presence of thousands of women who have no choice to present themselves in that way. This incomplete communication may not only convey false hope, but it is most likely also be a source of isolation. The nurse must help break this feeling of solitude and sense of failure by conveying clear information, offering the chance to hope while at the same time helping them to face the uncertainties of their disease [10]. The presence of multicultural populations in many European countries may require special care: the presence of an interpreter during medical consultations, taking into account personal sensibilities, habits, and customs. The ABCN will strive to optimize these particular communication situations.

The Advanced Breast Cancer Nurse in Europe

The European Cancer Organization (ECCO) which connects and responds to all stakeholders in oncology Europe wide is working to standardize the function of the clinical nurse specialist (CNS). It also recognizes the function of the advanced cancer nurse (ACN), which is considered an expert in at least one aspect of cancer care. ECCO identifies the need for agreement on appropriate levels of education and professional recognition [9].

Conclusion

The increasing number of women living with breast cancer metastases is a true concern. We can hope that they continue to live longer thanks to the current advances in therapy. However, to improve their quality of life in the long term, they need the specialized support of an ABCN. It is expected that multidisciplinary teams, specializing in the treatment of breast cancer, will formally establish the function of an ABCN and put in place a framework that will allow these nurses to accompany mBC patients without exception. In the near future, it would also be useful to evaluate the impact ABCNs' supportive care has on the mBC patients' quality of life.

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Gynecological Cancer

12

Julio C. de la Torre-Montero

Abstract

Gynecological cancer is one of the greatest challenges in treatment, as well as in prevention and early diagnosis, of the set of all diagnosed cancers. At the beginning of the twenty-first century, we have witnessed the arrival of new treatments, new surgical techniques, more precise tools for diagnosis and prognosis, and the great development of antitumoral products, which give patients new perspectives on their prognosis and evolution, including improvement in the patient's quality of life. All of these are important factors in their recovery.

It is important that we know what resources are available: accurate diagnostic tools such as positron emission tomography–computed tomography (PET-CT), effective vaccination programs against the viruses that trigger various types of tumors, and also treatments based on surgery, chemotherapy, monoclonal antibodies, and other tools that enable us to offer patients confidence based on the safety and efficacy of the combination of these treatments.

Cancer prevention—through vaccination campaigns and, above all we can do, education as a key point—is the way to achieve a healthy population, as well as a better quality of life for patients.

Keywords

Gynecological tumors · Cancer treatment · Sexual education · HPV vaccines · Cancer prevention · Oncology nursing

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J. C. de la Torre-Montero (✉)
San Juan de Dios School of Nursing and Physical Therapy, Comillas Pontifical University, Madrid, Spain
e-mail: juliodelatorre@comillas.edu

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Introduction

The paradigm of oncology is undergoing a profound change. This is not the first assertion about it; it is confirmed in every scientific meeting we attend, and social networks and digital information on the internet, as means of communication on the rise, echo this new situation. Oncology nursing—of which we are a part, among a larger number of professionals whom patients encounter in some phases of their illness—is not unconnected to this change. This is a time of precise nursing; to practice this, we need to combine an excellent medical knowledge background with patient expertise, aiming to be able to make ours the sniper's motto "Slow is smooth; smooth is fast" (Sergeant Jack Coughlin, *The Shooter*).

Predictive factors are those associated with response or lack of response to a given treatment, such as the status of cancer antigen (CA) 125. At present, the prognostic and predictive factors validated in routine clinical practice are the tumor size, histological subtype, histological grade, proliferation index, and CA 125 status.

These new hopes are founded on personalization of new therapies and initiatives that work in precise medicine [1], based also on the application of therapeutic targets aimed at the tumor, which are increasingly being identified and marked. Oncology has also opened the way to other disciplines, such as cardiology [2]. Research on the metabolism of these oncological treatments is also making advances in the study of how medicine behaves in the person's body, allowing us to determine its concentrations and evaluate its therapeutic action through pharmacokinetics (how the individual metabolizes the medication) and pharmacodynamics (the effects of the medication). Pharmacogenomics [3] is based on the application of increasingly precise treatments, studying the patient's genetic response to drugs. The emergence of immunotherapy [4] has opened the door to the treatment of tumors with uncertain prognoses and is increasing the survival of many other patients and offering hope to many, who can now feel that their disease is controllable (in an increasing number of cases).

Gynecological cancers are in the group of pathologies that must be taken into account when we talk about the future. Beyond this, oncology nursing is the art of care in the sense of the "little things" that refer to the patient's overall needs.

Anatomical and Physiological Considerations

The gynecological organs are peritoneal, and they are in a highly vascularized localization; thus, the risks of proliferation and metastasis dissemination are higher than those in other types of cancer. These risks apply not only to ovarian cancer (because of the large number of cases that are diagnosed yearly) but also to all cases of gynecological cancer that show high rates of incidence and prevalence. It is for these reasons that we consider gynecological cancer as a cluster of oncology disorders that deserves special high praise for consideration in oncology nursing as a part of a team.

Older women (more than 65 years old) [5] with cervical cancer demonstrate worse survival than younger ones, and it is a fact that they are less likely to receive surgical treatment.

Early detection of cancer is the vital key to success—and even more so in gynecological tumors because of their location and proximity to other anatomical structures of the digestive system and the excretory system.

We can define gynecological cancer as any malignant tumor growth that has its origin in the reproductive organs of women. We can classify these tumors anatomically according to the part of the body in which they appear for the first time. Gynecological cancers originate in the reproductive organs located in the pelvic area, which is located in the subabdominal area.

From top to bottom, we consider the ovaries—a paired organ, oval in shape, and of a variable size between 2 and 3 cm long by 1–2 cm wide, hanging from the mesenteric structures.

The fallopian tubes are also a paired organ and are tube shaped and 5–10 cm long. They are responsible for collecting the mature female reproductive sex cell (ovule) and acting as a bridge between the ovaries and the uterus. They serve a dual purpose by providing the environment where fertilization can take place and by delivering the fertilized/nonfertilized female egg cell into the uterus, which is the central organ in the internal female reproductive system. With a size between 10 and 15 cm, and chalice shaped, the uterus is intended to accommodate embryonic development in the pregnancy process. During the menstrual cycle it undergoes a series of continuous changes, ranging from thickening of the endometrial walls to their detachment. Physiologically, this cycle ranges from 22 to 35 days in length.

The cervix and its union with the vagina is the final continuation of the sexual and reproductive organs. The cervix is elastic and allows menstrual content to pass through to the vagina, which also serves the purpose of receiving the penis during coitus. Together, the cervix and the vagina form the birth canal at the end of pregnancy. Of elastic consistency, the vagina varies in size (from a few centimeters in its basal state to 20 cm during sexual intercourse, reaching its peak size during childbirth) and is located in the pelvis.

A common characteristic of these organs (the vagina and uterus) is their great capacity for change, from their basal state to embryonic and fetal care during pregnancy. These changes are possible thanks to certain characteristics—the thickness of the muscular walls of these organs and their sensitivity to hormonal changes—which are what allow them to carry out pregnancy, in addition to facilitating sexual relations.

The physiology of the gynecological organs faces continuous changes from puberty to menopause. During every cycle, female sex hormones precipitate the conditions that make a new pregnancy possible. If the female ovule and sperm cannot meet in the fallopian tube, fertilization will not happen, allowing the menstrual cycle to continue its course. The first day of the menstrual cycle is the day on which the female stars bleeding, and the cycle ends within an average of 22–35 days.

On day 1 of the menstrual cycle, progesterone and estrogen levels are low. Low levels of these hormones signal the pituitary gland to produce follicle-stimulating hormone (FSH). FSH begins the process of maturing the female follicle sited in the ovary, which will end up with the production of a mature egg cell.

The follicle produces more estrogen to prepare the uterus for pregnancy. During ovulation, close to day 12–14, peak estrogen levels precipitate the release of luteinizing hormone (LH) from the pituitary gland, causing release of the ovule from the follicle. The ruptured follicle releases progesterone and estrogen to prepare the uterus for pregnancy. If the ovule is not fertilized, estrogen and progesterone levels drop and the cycle will be repeated.

Hormonal fluctuations during life are physiologically normal; even if women experience variations over the years, these can be considered normal. The development of cancer sometimes changes the balance and, in terms of caring, we can construct care models allowing a better quality of life and well-being.

Types of Gynecological Cancers and Treatments

Gynecological cancer requires special considerations because of diverse factors—both hormonal factors (especially in premenopausal women) and anatomical factors, as proximity to excretory and digestive systems is an adverse prognostic factor because of the continuity of the anatomical structures.

Each type of gynecological cancer is different and has specific signs and symptoms, as well as different risk factors (all external elements, studied in epigenetics, can increase the probability of cancer), and requires different prevention strategies. All women, then, are at risk of suffering gynecological cancers, and that risk increases with age and hormonal changes, in addition to the influence of the aforementioned risk factors, such as tobacco or alcohol consumption, or exposure to other toxins.

Quality of life is very important in our patients, when we think about their care within a treatment protocol, whether or not it is in the context of research or a clinical trial. The initial diagnosis and follow-up need to consider the level of protein CA 125 as a reliable tumoral marker.

Standard treatment can be briefly summarized as follows: optimal surgery, chemotherapy based on platinum (carboplatin, cisplatin, and oxaliplatin) and taxanes (paclitaxel), anti–vascular endothelial growth factor (anti-VEGF) antibodies, and CA 125 follow-up. Local radiotherapy is indicated after optimal surgery. Best supportive care (palliative care) may be indicated instead of an active clinical trial or when the exclusion criteria for a trial do not allow the patient to participate in it.

We can distinguish between different types of treatments according to both the anatomical structures involved and the stage of the illness.

Ovarian Cancer

Ovarian adenocarcinoma is the most common gynecological cancer and the fifth most common cause of cancer deaths in the world [6].

Adjuvant treatment (except for International Federation of Gynecology and Obstetrics (FIGO) IA grade I), after standard oncology surgery: carboplatin area under the concentration–time curve (AUC 6) plus paclitaxel 175 mg/m^2, 3-hour infusion every 3 weeks for 6 cycles. In selected cases: carboplatin monotherapy (AUC 6), 30- to 60-minute infusion every 3 weeks for 6 cycles.

Advanced Disease

Carboplatin AUC 6, 30- to 60-minute infusion, plus paclitaxel 175 mg/m^2, 3-hour infusion, both administered every 3 weeks for 6 cycles, after primary surgery. Sometimes, 9 cycles are considered (in patients with high levels of tumoral biomarkers).

We consider neoadjuvant chemotherapy and cytoreduction surgery after 3 or 5 cycles of neoadjuvant chemotherapy, especially in stage IIIC (with inadequate surgery, with residual disease measuring >1 cm) and stage IV (with pleural effusion or mediastinal lymph involvement).

Intraperitoneal Treatment

In young women at FIGO stage III with residual disease measuring ≤1 cm after the first surgery, intraperitoneal chemotherapy with cisplatin and paclitaxel is indicated.

Recurrent Disease

If the platinum-free interval is <6 months from the last treatment with platinum/carboplatin, we have the following options:

- Pegylated liposomal doxorubicin 40–50 mg/m^2, 1-hour infusion every 3–4 weeks.
- Topotecan 1.25–1.50 mg/m^2, once daily for 5 days every 21 days.
- Paclitaxel 90 mg/m^2, 1-hour infusion once weekly.
- Rotterdam regimen [7]: carboplatin AUC 4 plus paclitaxel 90 mg/m^2 once weekly for 6 weeks, followed by carboplatin AUC 5 plus paclitaxel 175 mg/m^2 every 3 weeks, for 3–6 cycles.
- Leuven regimen: paclitaxel 90 mg/m^2 plus carboplatin AUC 2.7 on days 1 and 8 every 3 weeks.

If the platinum-free interval is >6 months from the last treatment with platinum/carboplatin, we have the following options:

- Calypso regimen: carboplatin AUC 5 plus pegylated liposomal doxorubicin 35–40 mg/m^2 every 4 weeks for 6 cycles.
- Carboplatin AUC 5 plus paclitaxel 175 mg/m^2 every 3 weeks for 6 cycles.
- Carboplatin AUC 4 plus gemcitabine 1 g/m^2 on days 1 and 8 every 3 weeks for 6 cycles.
- No-platinum alternatives: pegylated liposomal doxorubicin 35–40 mg/m^2 plus trabectedin 1.1 mg/m^2, 3-hour infusion every 3 weeks (OVA-301 study [8]).

Other treatment options:

- Etoposide 50 mg orally once daily after dinner for 21 days every 28 days.
- Hexamethylmelamine 260 mg/m^2 orally for 14 consecutive days every 21–28 days.
- Taxotere: 7–100 mg/m^2, 1-hour infusion every 21 days.
- Oxaliplatin: 130 mg/m^2, 2-hour infusion every 3 weeks for 6 cycles.
- Oxaliplatin 130 mg/m^2 on day 1 plus gemcitabine 1000 mg/m^2 on days 1 and 8 every 3 weeks.
- Pazopanib (category 2B [9]).
- Hormonal therapy: anastrozole (aromatase inhibitor), tamoxifen, megestrol acetate.
- The US Food and Drug Administration (FDA) has approved rucaparib for maintenance treatment of recurrent ovarian, fallopian tube, or primary peritoneal cancer [10].

Low-Frequency Histology in Ovarian Cancer

The histology of about 5–10% of ovarian cancer is classified as being other than adenocarcinoma:

- *Carcinosarcoma*: carboplatin AUC 6 plus paclitaxel 175 mg/m^2, 3-hour infusion every 3 weeks for 6 cycles. At disease relapse: cisplatin 20 mg/m^2/day plus ifosfamide 1.5 g/m^2/day, both on days 1–4.
- *Ovarian carcinoid*: option 1: everolimus (RAD001) 10 mg/day; option 2: streptozotocin 500 mg/m^2/day on days 1–5 every 10 weeks plus fluorouracil 5FU, 5 consecutive days; option 3: cisplatin 75 mg/day every 21 days.
- *Brenner tumor*: cisplatin 75 mg/m^2 every 3 weeks.
- *Germinal tumor*: from conservative surgery alone to surgery plus combinations of bleomycin, etoposide, and cisplatin (known as the BEP scheme).

Endometrial Carcinoma

- From oncology surgery alone (with follow-up) to surgery plus radiotherapy or brachytherapy, plus chemotherapy based on carboplatin plus paclitaxel.
- At disease relapse, megestrol acetate 160 mg/day, carboplatin AUC 5–based chemotherapy, or paclitaxel 175 mg/m^2 plus doxorubicin 45 mg/m^2 plus cisplatin 60 mg/m^2. Alternative treatment option: carboplatin AUC 5 plus pegylated doxorubicin 40 mg/m^2 every 4 weeks.
- Second-line treatment options: carboplatin AUC 5 plus taxotere 75 mg/m^2 plus radiotherapy, or topotecan 4 mg/m^2 once weekly, or paclitaxel 80 mg/m^2 once weekly, or temsirolimus 25 mg total dose once weekly.

Low-Frequency Histology in Uterine Cancer

- *Carcinosarcomas*: surgery, radiotherapy, and platinum-based chemotherapy plus anthracyclines and ifosfamide.
- *Stromal endometrial sarcomas*: radical surgery and hormonal treatment (megestrol acetate, tamoxifen).
- *High-risk sarcomas*: anthracyclines and ifosfamide.
- *Uterine leiomyosarcoma*: from surgery and/or chemotherapy-based treatments.

Cervical Adenocarcinoma and Epidermoids

Human papillomavirus (HPV) has been identified as an etiological factor in large-scale studies of patients with diagnoses of various types of cervical or vulvar squamous cell carcinoma (VSCC).

Treatments range from simple surgery in stage IA1 disease to radical surgery in young patients (in stages IA2, Ib1, or IIA with a tumor measuring <4 cm) plus radiotherapy in stage IB1 with a tumor measuring >3 cm.

In stages IB2, IIA (with a tumor measuring >4 cm), IIB, IIIA, IIIB, or IVA, the treatment is cisplatin 40 mg/m^2 weekly plus concomitant radiotherapy.

In stage IVB, systemic chemotherapy is the first-line treatment, including cisplatin 50 mg/m^2 on day 1 plus topotecan 0.75 mg/m^2 on days 1, 2, and 3 every 21 days for 6 cycles.

Other treatment options:

- Carboplatin AUC 5 plus paclitaxel 175 mg/m^2 every 21 days, or cisplatin 50 mg/m^2 on day 1 plus paclitaxel 175 mg/m^2 on day 1 every 21 days for 6 cycles.
- Cisplatin 80 mg/m^2 on day 1 plus vinorelbine 25 mg/m^2 on days 1 and 8 every 21 days for 6 cycles.
- Cisplatin 50 mg/m^2 plus gemcitabine 1 g/m^2 on days 1 and 8 every 21 days for 6 cycles.

Second-line treatment options:

- Taxotere 75 mg/m^2, 1-hour infusion every 21 days for 6 cycles.
- Irinotecan 125 mg/m^2/week for 4 weeks in a row, followed by a 2-week break.
- Mitomycin C and 5-FU combinations.
- Bevacizumab plus 5-FU.

Vaginal Carcinoma

In cases of either localized disease or advanced disease, the treatment is the same as that used for cervical carcinoma and is based on surgery, chemotherapy, and concomitant radiotherapy.

Vulval Carcinoma

- Stages I and II: surgery, as a unique treatment (free margins of 0.8–1 cm); radical or local.
- Stage III, locally advanced disease: concomitant chemotherapy and radiotherapy, based on platinum treatments; also, erlotinib and pembrolizumab (based on the recommendation in National Comprehensive Cancer Network (NCCN) consensus category 2B).

Prevention

There are several elements that influence gynecological cancer: the hormonal factor, age and its relationship to menopause, hormonal complements associated with menopause and other epigenetic circumstances related to cancer, it could be carcinogenic, looked at from a global perspective, that could trigger a cancer in any location (exposure to a toxin)—in particular, exposure factors that are related to a specific type of diagnosis and where there is a direct causal relationship, such as exposure to papillomavirus and cervical cancer.

Sexually transmitted infections (STIs) are prevalent ingredients for gynecological cancer in the vulva, vagina, and cervix. The different infections that women can suffer in those organs increase the prevalence of cancer in those locations. The correlation is direct, meaning that the increased prevalence of STIs that women may suffer during their active sex lives increases their chances of developing cancer in the vulva, vagina, or cervix. Since the relationship between papillomavirus infection and cervical cancer was demonstrated and vaccines against it have subsequently been developed and implemented, a drastic decrease in the related diagnoses has been seen.

One of the classic cervical cancer prevention pathways is early diagnosis, in the initial phases of tumor cell growth, by the Papanicolaou test [11], which has been used since the 1950s, with a high reliability rate and very low cost, as well as easy access with routine colposcopy. Early prevention in this way is so simple in a sustainable health system; we need to focus not only on our own local health structure but also on a global concept, by thinking about and designing early prevention for less favored sectors of the population and for developing countries.

On the other hand, studies [12] show that there is a relationship between different types of gynecological tumors (ovarian, uterine, and breast tumors) and suggest that preventative work should be oriented in the same direction. With regard to gene expression changes, in patients with BRCA1 and BRCA2 mutations, genetic counseling is of key importance.

Genetic advice applied to prevention, in general, can prevent 5–10% of tumors that can be considered hereditary. Our increasingly comprehensive knowledge of the genes involved in gynecological tumors and their relationship to breast tumors, in what is known as integrative and multiplatform Pan-Gyn analysis, allows creation of prognosis systems that increase the capacity for early screening through decision trees, which can be used in clinical practice [13].

Returning again to the basic questions related to health education, centered on the practice of nursing, we can consider elements that give importance to sexual health from an anthropological perspective, taking into account aspects such as culture and religion, and adapting our work capacities to these issues, basing health programs on the basics of body hygiene, sexual hygiene, infection control, screening for STIs, the life histories of couples and relationships, and active prevention of sexual transmission of diseases with effective barrier methods in risk relationships.

Regarding vaccination, for more than 10 years, effective vaccines have been developed and marketed to combat many strains of human papillomavirus, which cause a large number of diagnoses of cervical cancer, as well as conizations and similar diagnoses in the oral cavity and pharynx, also due to changes and increased relationships with the practice of oral sex.

Currently, there are three effective vaccines (the FDA has approved Gardasil®, Gardasil® 9, and Cervarix® [14]) in the market, aimed against different strains of human papillomavirus. They are effective against new infections; however, they do not protect against existing ones. Vaccination covers prevention of HPV-caused cervical, vulvar, vaginal, and anal cancers; and genital warts.

A vaccination calendar used in Europe and the USA involves a two-dose schedule for boys and girls, initiating vaccination with Gardasil 9® at the ages of 9–14 years. People initiating HPV vaccination at older ages need to be vaccinated in accordance with a 3-dose schedule [15, 16].

With regard to parents, a systematic review and meta-analysis to focus on parents' uptake of HPV vaccination has shown suboptimal levels of vaccination uptake, especially in boys, due to different regulations and economic considerations, although it has been more than 10 years since the initial licensure of an HPV vaccine [17].

We must participate actively in sexual education of girls, boys, and parents, to dispel baseless fears and major worries about vaccination (e.g., "If my children are under protection, they will take risks"). Moreover, it is obvious that vaccination must be made easily accessible in developing countries.

A few final remarks about prevention: it's all about education: avoidance of general risk factors (such as tobacco and toxins) and concrete risk factors (such as unprotected sexual activities); HPV vaccination; and early diagnosis by standardized screening programs, cytology, blood testing, and gynecological management.

Sexuality

One of the most important aspects of gynecological cancer is sexuality and patients' concerns and fears relating to it.

The anatomical localization of gynecological cancer means that from the outset, it may pose complications for pleasurable sexual relations.

The diagnosis and later treatments are factors that influence the sex life of the woman and her partner. As a general rule, this occurs in the diagnosis of any gynecological cancer. Surgery in ovarian and uterine cancer alters the woman's usual hormonal course, which, depending on her age, will suffer certain consequences. Experience says that older women cope better with the diagnosis of gynecological cancer, as well as its consequences for sexual function, when they are asked about this aspect, both directly during the consultation and through specific questionnaires.

With regard to prevention, in a Norwegian study [18] on BRCA1 and BRCA2 testing, women who had undergone risk-reducing salpingo-oophorectomy reported better sexual functioning if they received more care from their partner and were current users of systemic hormone replacement therapy. There was no association between hormone levels and sexual pleasure in these patients.

We can consider the use of estrogen and nonhormonal gel or lubricants [19] to facilitate sexual relations for our patients: nonhormonal lubricants may be particularly useful in cases of a hormone-sensitive cancer diagnosis. Sexual relations do not always have to be centered on coitus, and we need to teach people about this. Also, we must never forget that it is important for us to encourage each patient to express herself and ask for professional help; to listen to every problem; and to identify potential health issues and develop techniques and skills to prevent and solve them.

Health Education: Quality of Life

Globally, gynecological cancer is one of the most prevalent types of cancer in the world, in both developed countries and developing countries. Sexual education, as part of health education, is a very important issue to address, appropriately considering cultural and religious aspects [20–22].

In terms of care, we need to address the specific case of every women, at any age, and in any physical and psychological situation. This can be helped by quality-of-life (QOL) questionnaires, such as FACT-G (Functional Assessment of Cancer Therapy—General) [23, 24], which assesses physical, sociofamilial, emotional, and functional well-being and cancer-related treatment symptoms, including fatigue, nausea, and pain. There are also others, such as the EORTC (European Organisation for Research and Treatment of Cancer) cancer QLQ (QoL questionnaire) and its specific module (QLQ CX-24 [25]) for cervical cancer, which is the second most common gynecological cancer and the fourth most common malignancy in women.

The standard EORTC QLQ-C30 questionnaire [26] assesses general cancer QOL. It has been translated into, and validated in, over 100 languages, and is an easy tool to use. We have academic free modules available for endometrial cancer (EORTC QLQ-EN24), and ovarian cancer (EORTC QLQ-OV28). If there is interest in asking about information that patients have received from professionals, we have the EORTC QLQ-INFO25 questionnaire available.

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13 The Patient Journey in Prostate Cancer: Key Points for Nurses

Christine Remacle

Abstract

The optimal care pathway for patients with prostate cancer (PCa) should be multidisciplinary and multi-professional. Nurses from a variety of disciplines (e.g. medical oncology, urology, radiation oncology) should be implicated in educating patients and guiding patient care across the broad spectrum of available treatments.

For this purpose, nurses involved in managing PCa patients should be educated about the different treatments and their possible adverse events. Most PCa are slow-growing indolent tumours that will be best managed by active surveillance. Nurses play an important role in reassuring and empowering the patient in that process. Localised disease is best treated by surgery and/or radiotherapy, each offering a different philosophical approach. Nurses play a central role in guiding the patient in the difficult decision of the treatment choice. They will be the guardian of a shared decision-making and protect the principle of equipoise by involving patients in the treatment choices. Advanced PCa, at its various stages of progression, is most often treated by hormonal therapy. Hormone therapy does not eradicate PCa but rather switches it to a more chronic state. This means that the patients will be treated for an extended period of time. Hormone therapy may profoundly affect various emotional and physical aspects of the patients and severely impacts its well-being. Countermeasures are known but rarely explained to patients. Nurses are ideally positioned to provide treatment information, education and self-management recommendations regarding side effects and symptom management. According to these numerous treatments, all nurses will be there to provide emotional and psychological support regarding patient's coping process which will improve adherence in his treatment plan.

C. Remacle (✉)
King Albert II Institute for Cancerology and Haematology, Cliniques Universitaires Saint-Luc, Brussels, Belgium
e-mail: christine.remacle@uclouvain.be

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Prostate cancer · Prevention · Risk factor · Treatments · Side effects · Education Adherence

Introduction

Epidemiology and Risk Factors

PCa is the most frequent cancer in men. A recent systematic analysis of the Global Burden of Disease Study has estimated that there were 1.6 million incident cases worldwide and 366,000 deaths in 2015 [1]. Prostate-specific antigen (PSA) testing has resulted in a pandemic rise of PCa diagnosis with a clear shift towards men being diagnosed with earlier disease. Epidemiological studies have linked PCa risk to family history, age, ethnicity, insulin-like growth factors, lifestyle, diet and environmental and occupational exposures [2]. More studies are needed to fully understand these risk factors and implement effective preventive methods [2]. Genetic abnormalities predisposing to PCa have been identified [3]. Hereditary risk exists if the brother or father is diagnosed with PCa before the age of 65. Germline mutations in DNA repair genes, similar to breast and ovarian cancers, have been recently identified and should now be detected routinely [4]. This means that performing a complete anamnesis of the patients' family cancer history is critical, and this is not only for PCa but also for other cancers as well.

Pathophysiology and Staging

Most of the time, PCa evolution is very slow, explaining why active surveillance is used more often than for any other cancers. Unfortunately, there are aggressive PCa that will evolve locally, spread through lymphatic vessels and bone, develop metastases and cause the death of the patient if not treated appropriately.

PCa are classified by *risk categories*. The adjudication to a category is based on the PSA value; the extension of the cancer, defined by the TNM staging; and the aggressiveness of the cancer, defined by the Gleason score.

The TNM Classification

The standardised method for describing the tumour extension is the TNM classification of the UICC [5]. The T stage describes the local invasion of the primary tumour through the prostatic capsule, the seminal vesicles, the bladder and the rectal wall. The N stage describes the extent of the spread into local, regional and distant lymph nodes. The obturator and hypogastric ganglia are the first affected. The M stage describes the distant extension, or metastases, that develop most frequently in the bones of the axial skeleton (column, pelvis), femurs and ribs and in the lung or liver.

The T stage is defined by digital rectal examination or by multiparametric MRI.

The N and M stages are conventionally defined by a contrast-enhanced CT or the thorax, abdomen and pelvis and by a ^{99m}Tc bone scintigraphy. These techniques have limited diagnostic accuracy and tend to be replaced by whole-body imaging modalities such as PET/CT with prostate-specific tracers (^{11}C-Choline or ^{69}GA-PSMA) or whole-body MRI [6].

The Gleason Scoring System

A precise anatomopathological examination is required to evaluate the aggressiveness of the cancer. The Gleason score quantifies the architectural anarchy of the cancer glands, assigning a primary and secondary grade to cells based on their appearance relative to normal prostate tissue [7]. The Gleason grade ranges from 1, well differentiated, to 5, poorly differentiated. The Gleason score ranges from 2 to 10, taking the sum of the two grades which represent the two glandular "pattern" most frequently met. In practice the lowest score is now assigned a 6, although it is on a scale of 2–10. This leads to a logical yet incorrect assumption on the part of patients that their cancer is in the middle of the scale, compounding the fear of their cancer diagnosis with the belief that the cancer is serious, thus leading to an expectation that treatment is necessary. To address the above deficiencies, a new 5 Grade Group system has been developed. These ISUP Grade Groups now range from 1 (Gleason score ≤ 6) to 5 [7].

Prostate Cancer Risk Grouping

In order to assign patients to the various treatments, patients are stratified by risk groups based on the extension, the Gleason score (GS) and the PSA value [8].

- *Low-risk localised PCa* are those with a PSA ≤10 ng/ml, a GS <7 (ISUP grade I) and TNM cT1-2a.
- *Intermediate-risk localised PCa* are those with a PSA 10–20 ng/mL, or GS 7 (ISUP grade 2/3) or cT2b.
- *High-risk localised PCa* are those with a PSA > 20 ng/mL or GS > 7 (ISUP grade 4/5) or cT2c
- *Very high-risk localised PCa* (or locally advanced) are those with any PSA, any GS cT3-4 or cN+ and any ISUP grade.
- *Metastatic PCa* are those with positive lymph nodes beyond the pelvis, skeletal or visceral metastases.

Comorbidity, Age and Treatment Choices

Evaluation of health status and life expectancy is important in clinical decision-making on screening, diagnosis and treatment of PCa since it is very common in older men. In localised disease, a minimum of 10 years of life expectancy is considered mandatory for any local treatment. However, it is more important that older men are not denied effective treatment simply because of age. Resolution of impairments in frail men allows a similar urological approach as in fit patients.

Table 13.1 G8 screening tool

Items	Possible responses	Score
Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties?	Severe decrease in food intake	0
	Moderate decrease in food intake	1
	No decrease in food intake	2
Weight loss during the last 3 months?	Weight loss >3 kg	0
	Does not know	1
	Weight loss between 1 and 3 kg	2
	No weight loss	3
Mobility	Bed or chair bound	0
	Able to get out of bed/chair but does not go out	1
	Goes out	2
Neuropsychological problems?	Severe dementia or depression	0
	Mild dementia	1
	No psychological problems	2
BMI (weight in kg)/(height in m^2)?	BMI < 19	0
	BMI 19 to <21	1
	BMI 21 to <23	2
	BMI $\geq$ 23	3
Takes more than three prescription drugs per day?	Yes	0
	No	1
In comparison with other people of the same age, how does the patient consider his/her health status?	Not as good	0
	Does not know	1
	As good	2
	Better	3
Age	>85	0
	80–85	1
	<80	2

Health Status Screening

The International SIOG PCa Working Group recommends that treatment for senior adults should be based on a systematic evaluation of health status using the G8 screening tool (Table 13.1) [9]. Healthy patients with a G8 score > 14 should receive the same treatment as younger patients. Patients with a G8 score $\leq$ 14 should undergo a full geriatric evaluation assessing comorbidity, nutritional status and cognitive and physical functions, to determine if the impairment is reversible. Frail patients with reversible impairment should receive the same treatment as younger patients after resolution of their geriatric problems. Disabled patients with irreversible impairment should receive adapted treatment. Patients who are too ill should receive only palliative treatment.

Comorbidity

Comorbidity is a major predictor of non-cancer-specific death in localised PCa treated with RP and is more important than age [10]. Ten years after not receiving active treatment for PCa, most men with a high comorbidity score had died from competing causes, irrespective of age or tumour aggressiveness. Measures for comorbidity include Cumulative Illness Score Rating Scale-Geriatrics (CISR-G) [11] and Charlson Comorbidity Index (CCI) [12].

Nutritional Status

Malnutrition can be estimated from body weight during the previous 3 months (good nutritional status <5% weight loss; risk of malnutrition, 5–10% weight loss; severe malnutrition, >10% weight loss).

Cognitive Function

Cognitive impairment can be measured using the mini-COG (mini-cog.com), assessing the patient's ability to make an informed decision, and is deemed increasingly important in health status assessment.

Physical Function

Measures for overall physical functioning include Karnofsky score and ECOG scores. Measures for dependence in daily activities include activities of daily living (ADL; basic activities) and instrumental activities of daily living (IADL; activities requiring higher cognition and judgement).

Local Treatments of Prostate Cancer

There are several treatments available. They will be decided based on the risk group, the age and comorbidities of the patients and its personal preferences.

Active Surveillance

Active surveillance should be offered to men with low-risk localised PCa [13, 14]. The risk of death from these cancers is very low <5% and not influenced by an initial treatment. Regular PSA and DRE with annual or biannual biopsies are enough, eventually completed by MRI. The quality of the initial diagnosis is critical. The biopsy ideally should have been done properly and complemented with an MRI of the prostate. MRI-targeted prostate biopsies reduced the risk of missing aggressive cancer [15]. The main benefit of active surveillance is to avoid the side effects of the treatment [16]. Active surveillance has to be differentiated from watchful waiting that consist of simply following patients in poor condition or with severe comorbidities and delaying treatment upon emergence of symptoms.

Education for regular exercise and dietary measures in daily life should be advocated. Nurses play a central role, together with the psycho-oncologist, in helping patients to cope with the diagnoses of cancer. It is not easy at first for a man, and often more for its caregiver, to understand that a cancer will be simply followed and monitored. This specific monitoring requires special support. The nurse is optimally positioned to understand the patient-specific needs and refer him to colleagues with specific competences (i.e., psychologists for specific psychological support, physiotherapists for exercise medicine, dietitian for specific diet advice).

Radical Prostatectomy (RP)

RP consists in the total excision of the prostate, the seminal vesicles and the pelvic lymph nodes in case of high-risk localised disease. RP can be performed via an incision in the lower abdomen, via laparoscopic approach or via robotic-assisted laparoscopic route.

The main side effects of RP are infertility, urinary stress incontinence and erectile dysfunction [16]. Incontinence is common after the intervention and improves in the first few months. Severe incontinence affects 5–10% of operated patients [17]. Moderate incontinence affects 15–30% of the patients, especially men over 65 years of age. Erectile dysfunction affects 20–80% of the patients [17]. This depends strongly on the quality of the erections before the surgery and the possibility of preserving the neurovascular bundles of the prostate. It may take several years to see a return of erections [16]. Orgasm can be preserved without erection.

Radiation Therapy

Ionising radiation destroys cancer cells. As such, radiation therapy is one of the most common treatments of cancer. In external beam radiation therapy (EBRT), the radiation is produced by an external source or particle accelerator. They reach the cancer cells but also some healthy cells that have the capacity to renew themselves. The delivered dose varies between 66 and 80 Grays. This dose is delivered in regular fractions to improve the effectiveness of the treatment and to preserve the surrounding healthy tissues. In low-dose rate (LDR) or high-dose rate (HDR) brachytherapy, the radioactive seeds are directly implanted in the prostate so that radiation is delivered locally. LDR seeds are implanted permanently.

Early side effects appear after within a few weeks, resulting from an irritation of the neighbouring organs: the canal of the urethra and the bladder (frequent urge to urinate, difficulty urinating, burning while urinating), the rectum and the anus (more frequent and sometimes more painful desire to go to stool), with tenesmus (false needs), anal burns [17]. Rectal bleeding is possible, and the appearance or aggravation of haemorrhoids is common. Late urinary side effects occur in 10–15% of patients (frequent urination and difficulty urinating, more rarely incontinence and haematuria). Late gastrointestinal side effects result in blood in the stool mainly in case of constipation. Blood in the stools is not so common and should trigger a proctoscopy to exclude another pathology. Erectile dysfunction occurs in 50–60% of patients gradually after a few months or even a few years.

Recently, the indications of radiotherapy have been extended also to patients with “oligometastatic” cancer, that is, those with limited metastatic deposits. Stereotaxic radiotherapy of the metastases offers the perspective of delaying systemic treatment [18].

High-Intensity Focused Ultrasound Treatment (HIFU)

HIFU aims to destroy the tumour by microwave. Ultrasound emitted by an endorectal probe will selectively burn the areas of the prostate that will become necrotic. The association of a resection of the prostate is frequent. This treatment is being evaluated. However, it can be proposed to patients for whom the other options of radical treatment are not possible.

Long-term side effects are frequent urination, sometimes leakage, urinary tract infection, small bleeding and urine removal of tissues destroyed by ultrasound. Long-term side effects are seen in <10% of the cases of urinary stress incontinence and in 8% of the cases a narrowing of the urethra and the appearance of an erectile dysfunction.

How to Choose Between Local Treatments?

The treatment plan should be discussed in a multidisciplinary setting with all the different specialties involved in treating prostate cancer: urologists, radiation oncologists, medical oncologists, pathologists, etc. The treatment plan should be structured on two questions. Is a treatment required and, if yes, what are the treatment options? The first question is especially important for patients with low-risk localised disease and those with multiples comorbidities. In case active surveillance or watchful waiting is recommended, specific support should be provided.

When radical treatment is advocated, the patients will have to choose between surgery, radiotherapy and a more investigational strategy such as focal therapy. For each treatment, there are different modalities. Hormone therapy will be recommended in most cases radiotherapy will be offered to the patient.

Unfortunately, studies comparing these modalities are scarce. Therefore, it is difficult to give clear information to the patient, and it must be assumed that the effectiveness of the different treatment is similar. In addition, there is a clear risk that physicians will recommend their own preferred strategy. In that context, the main role of the nurse is to consolidate that the dialogue around the different options remain patient-centred and not physician centred.

The recently published ProtecT trial provides some insights of the different side effect profiles between radiotherapy and surgery but only for low- and intermediate-risk localised PCa [16]. But there are several good retrospective series highlighting the same facts [17, 19]. In a nutshell, RP is associated with a greater decrease in sexual function and urinary incontinence than either EBRT after 3 years. There are usually no meaningful differences in either bowel or hormonal function beyond 12 months or in in other domains of health-related quality-of-life (HR-QoL) measures. In high-risk localised PCa that tend to require more multimodality treatments, however, the difference in side effects and HR-QoL vanishes over time.

An exhaustive knowledge of these data is essential to support the patient in the process of choosing the treatment that fits his cancer stage and his life expectations and own philosophy. The patient who is worried about keeping his prostate and fears the cancer may remain will most likely choose RP. The patient who is anxious about developing side effects, especially ED, will tend to opt for radiation therapy. It is therefore very important to listen to the patient and make him well aware that he will have a life after the treatment. During the after treatment, he will have to face and to live with the side effects of the treatment.

Hormone Therapy of Prostate Cancer

PCa cells' survival is conditioned by the presence of male hormones or androgens. The testosterone, produced mainly by the testes, is the main androgen. The adrenal glands produce other hormones that also contribute to prostate survival. Hormone therapy can be conducted either by suppressing the production of testosterone by the testis, i.e., androgen deprivation therapy (ADT), and by the PCa cells themselves, or by directly interfering with the androgen receptor itself.

Indications of Hormone Therapy

Hormone therapy can be used alone or in combination with other treatments.

Hormone therapy is used in combination with radiation therapy for up to 6 months in intermediate-risk localised PCa and for 6–36 months in high-risk localised PCa. Most patients will recover a normal testosterone thereafter but for the elderly patients.

After RP, hormone therapy is used exclusively for patients with positive lymph nodes.

Hormone therapy by ADT has been the uncontested treatment for locally advanced and metastatic PCa. Based on a series of important studies demonstrating a benefit in overall survival (OS), ADT is nowadays combined with 6 cycles of docetaxel chemotherapy or abiraterone [20].

Unfortunately, most of the advanced cancer will progress on ADT and transform into castration-resistant prostate cancer (CRPC). The molecular determinants of CRPC progression are better understood today and have led to the development of second-line hormone therapies that will be discussed hereunder.

Androgen Deprivation Therapy (ADT)

Suppression of the production of testosterone can be achieved by surgical removal of the testis (surgical castration or orchiectomy) or by inhibition of the effect of the gonadotrophin-releasing hormone (GnRH) that is stimulating the production of the luteinizing hormone (LH) in the pituitary gland.

GnRH analogues are often preferred to surgical castration for psychological reasons and because surgical castration is not reversible. GnRH agonists come in the form of GnRH agonists or antagonists.

GnRH agonists block the effect of GnRH in the pituitary gland, resulting in a decrease in the production of LH and follicle-stimulating hormone (FSH) and therefore testosterone. Leuprolide, goserelin, triptorelin and histrelin are the most prescribed GnRH agonist [21]. They are administered in monthly, trimonthly, six-monthly or even yearly depot. GnRH agonists induce a transient increase of testosterone (surge) during the first injection that may stimulate the growth of the cancer and aggravate urinary or skeletal symptoms. Therefore it is recommended to prescribe an antiandrogen for 4–6 weeks with the first injection. The reversibility of LHRH agonists is a considerable advantage that allows intermittent ADT. The testosterone rarely recovers, however, if the treatment lasted for more than 1–2 years and if the patient is over 65 years old.

GnRH antagonists are a newer class of drug that directly block the production of LH and FSH. They act quickly, with >90% of patients being castrated within 3 days [22]. Only degarelix is commercially available, as a monthly depot injection. It is not necessary to combine them with an antiandrogen. They are thus indicated in patients with a high-disease burden. Initial data indicate that they may also decrease the incidence of cardiovascular events [23].

Side Effects of ADT

The side effects of ADT are related to the suppression of testosterone that, beyond its role on PCa cells, exerts ubiquitous functions in the male body [24–26]. These side effects, to some extent, are very similar to the symptoms of menopause in women.

Mood Changes

The patient may complain of fatigue, discomfort, weariness, lack of vitality and lack of interest in activities that previously attracted him. These psychological disturbances can lead to depression if health professionals do not pay attention to it and do not sensitise the patient and his family to the first symptoms of distress and depression.

Fatigue

Fatigue is the most common side effect of cancer and of a variety of treatments. Fatigue results from multiple causes; it can be cancer related and/or treatment related. According to a systematic review, cancer patients may benefit from exercise therapy [24]. Exercises improve the physical functioning and psychological well-being of prostate cancer patients during and after treatment. There is strong and consistent evidence that physical activity reduces the risk of most major cancer sites and that between 9% and 19% of cancer cases could be attributed to lack of sufficient physical activity in Europe. Ideally, exercise programmes should be tailored to each patient's physical condition and should be supervised by a physiotherapist.

Sexual Dysfunction (SD)

An important decrease of sexual desire and impotence is common. Erectile dysfunction is observed to varying degrees. However, if the patient had normal sexual function before treatment, it is still possible to maintain erections. The implementation of a multimodal therapy can give positive results. Aucoin and Wassersug have suggested that given the right cultural setting and individual motivation, ADT may enhance rather than hinder both social and sexual performances [27].

Hot Flushes

Hot flushes are one of the most common and most bothersome side effects of ADT. Hot flushes are described as sudden and uncomfortable heat sensations in the face, neck and back, lasting from seconds up to an hour. The Moyad scale can be used to assess the importance of hot flushes, evaluating them from mild to very severe [28]. Hormonal agents such as megestrol acetate, medroxyprogesterone acetate, cyproterone acetate and low-dose diethylstilbestrol are very popular to treat bothersome hot flushes. Selective serotonin reuptake inhibitors (i.e., venlafaxine or citalopram), alpha-adrenergic inhibitors (i.e., clonidine) and GABA analogue gabapentin can be prescribed as alternatives to hormonal agents, although their efficacy is usually lower. Patients should be informed to avoid triggering situations such as cold temperature from air conditioning and the intake of alcohol or spicy food. Plant extracts, especially sage extracts, can also be recommended.

Anaemia

Haemoglobin level will drop by 10% in at least 90% of patients on ADT. Anaemia may worsen fatigue [29]. Bone marrow extensive invasion frequently occurs in mCRCP patients. In those patients, anaemia may be aggravated. Haemoglobin levels should be closely monitored in patients treated with ADT. Transfusion and in severe case recombinant human erythropoietin may be required.

Sarcopenia

Sarcopenia (loss of skeletal muscle mass), associated with increased fat gain, is also an androgen-induced consequence. It can lead to sarcopenic obesity deleterious to the patient. He will complain of a faster feeling of fatigue and difficulty in performing certain exercises that were previously easy to perform [30].

Metabolic and Cardiovascular Disorders

The relationship between ADT and an increased risk of cardiovascular disease (CVD) is intensively disputed since large epidemiological survey and prospective trials provide controversial results. In addition, two different aggravating factors coexist: an acute effect of testosterone, FSH, or GnRH flare on atherosclerotic disease and long-term consequences of metabolic changes. The first may be a class effect of GnRH agonists, not seen with GNRH antagonists; the second probably linked to any mechanisms of testosterone suppression.

Acute cardiotoxicity of ADT may be seen in patients with a previous history of cardiovascular events (CVE) [31]. Even a short-term course of ADT may significantly increase the risk of presenting a new CVE. This acute toxicity is pharmacology dependent, since it is less frequent with GnRH antagonists, which don't produce an initial flare of testosterone, FSL and LH [32].

Chronic cardio toxicity of ADT can result from changes in the patient's body mass and composition [33]. Suppression of testosterone causes a situation known as sarcopenic obesity, combining muscular atrophy and an increase in fatty tissue. By creating an imbalance between lean and fatty mass, sarcopenic obesity induces many of the phenotypic features of the metabolic syndrome, such as increased subcutaneous fat, increased total and high-density lipoprotein (HDL) cholesterol and increased adiponectin levels. The main cause of these metabolic changes is an increased peripheral resistance to insulin, leading to type 2 diabetes. These metabolic changes may be facilitated by reduced physical activity resulting from fatigue and depression. These changes may also increase the risk of cardiovascular disease [34].

Monitoring and prevention of cardiovascular events. Physicians should carefully monitor the metabolic and cardiovascular parameters of patients treated with ADT, including blood pressure, serum lipid level, haemoglobin and fasting serum glucose levels. Physicians should encourage patients to adopt a healthier lifestyle, including an appropriate low-fat diet and regular physical exercise. Resistance training is a form of strength training in which each effort is performed against a specific opposing force generated by resistance. Resistance exercise is used to develop the strength and size of skeletal muscles. Properly performed, resistance training can provide significant functional benefits and improvement in overall health and well-being [35].

ADT-Induced Bone Loss

The association between surgical castration and accelerated bone loss, and the fact that administration of oestrogens does not prevent this, was first described more than 15 years ago [36]. Prospective studies measuring bone loss associated with ADT have been performed for more than 10 years and have consistently observed a significant deterioration of bone mineral density (BMD) over time. Substantial bone loss begins very early in the course of treatment with ADT. Several epidemiologic studies have confirmed that CTIBL increases the risk of fragility fractures, which in turn may decrease survival. Several risk factors for fragility fractures have been identified, the most important being the duration of ADT. In Alibhai's survey, independent predictors of fragility and any fracture were increasing age, prior bone thinning medications, chronic kidney disease, prior dementia, prior fragility fractures and prior osteoporosis diagnosis or treatment [37].

Prevention and Treatment of CTIBL in ADT-Treated Patients

Patients should be encouraged to make specific lifestyle changes: cessation of smoking, moderate alcohol and caffeine consumption and regular weight-bearing exercises [38]. Patients should also be encouraged to consume a healthy diet of foods and beverages containing calcium (dairy) and vitamin D (fatty fish). The recommended daily intake of calcium should be 1200–1500 mg, and serum levels of hydroxyvitamin D should be maintained at ≥30 ng/mL. If required, supplementation with cholecalciferol at doses of 800–2000 IU/day should be given. Physical exercise is also a very important part of preventing bone loss. Resistance exercise is particularly favourable for maintaining or improving bone mass and architecture while also being safe for older people [39].

Osteoporosis is a disease that needs to be treated appropriately. The last posted version of the National Comprehensive Cancer Network (NCCN) guideline on prostate cancer advises pharmacologic treatment for men when the 10-year probability of hip fracture is ≥3% or major osteoporosis-related fracture is ≥20% [40]. The NCCN guidelines recommend assessing fracture risk using the FRAX algorithm (www.shef.ac.uk/FRAX/index.htm) by considering CTIBL as "secondary osteoporosis."

Pamidronate (60 mg IV every 12 weeks), zoledronic acid (4 mg IV every 12 weeks or annually) and alendronate (70 mg orally weekly) have been studied for the prevention of CTIBL in prostate cancer in a randomised controlled trial [41]. All the trials have shown a significant improvement in lumbar BMD, but none have demonstrated a reduction in the risk of fracture. The RANKL inhibitor denosumab (60 mg sc. every 6 months) is the only agent that has been shown to decrease the incidence of new vertebral fractures and is thus indicated in that setting.

Checklist for monitoring patients receiving ADT

Before initiating treatment:

Inform the patient about the occurrence of hot flushes, and provide lifestyle recommendations to avoid excessive triggering
Inform the patient and his partner about libido, mood and cognitive changes
Encourage maintaining and even increasing social activities and networking, possibly referring to patient support groups
Inform in due time the patient's general practitioner, cardiologist and endocrinologist about initiation of ADT. Advise the patient to schedule a follow-up visit with these specialists within 6 months
Provide dietetic counselling and recommend resistance exercise. This will be done optimally by referring the patient to a dietitian and physical therapist or by administering a specifically designed coaching programme
Search for risk factors of bone loss, and perform an immediate DXA scan, if they are present

During treatment:

In addition to PSA and testosterone measurements and imaging studies that are required for oncologic follow-up, it is recommended to measure the weight and abdominal perimeter (or preferably body fatty tissue content by impedance technique), blood pressure and dose haemoglobin, fasting cholesterol (total and HDL), triglycerides and glucose levels. In case of abnormalities, refer the patient to a specialist
Advise a DXA scan after 1–2 years of ADT

Suppressors of Intracellular Steroidogenesis Synthesis

Abiraterone acetate inhibits CYP17A, a key enzyme that mediates androgen synthesis in the testes and adrenal glands and also suppresses cortisol synthesis [42]. CYP17A is activated in men receiving ADT and is responsible of ADT escape or castration resistance (CRPC). Until very recently castration resistance was consistently a lethal stage of the disease. Abiraterone acetate increases overall survival of CRPC patients. Together with enzalutamide, this is the standard of care management of the early CRPC patients [4]. Recently it has been shown also to benefit patients with newly diagnosed high-risk metastatic prostate cancer in combination with ADT [43, 44].

Abiraterone induces an elevation of corticosterone that may lead to fluid retention, hypokalaemia and hypertension. To prevent these side effects, abiraterone must be combined with corticosteroids such as prednisolone, prednisone or dexamethasone. Actually, the standard dose of corticosteroid use in mCRPC is 5 mg bid of prednisolone and prednisone. At that dose, Grade 1–4 fluid retention or oedema was seen in 28% of the patients, hypokalaemia in 17%, hypertension in 22% and ALT and AST increase in 12 and 11%. For each of these side effects, Grade 3–4 rate was ≤5% [45].

Close monitoring of patients receiving abiraterone is recommended by the European Medicines Agency (EMA) [46]. The decision of administering abiraterone should be carefully weighed in patients with comorbidities such as a history of cardiovascular disease or with medical conditions that might be compromised by fluid retention, increases in blood pressure and hypokalaemia and in patients taking CYP2D6 substrates with a narrow therapeutic index. Before initiating this treatment, hypokalaemia and arterial hypertension have to be corrected. A monthly monitoring of blood pressure, serum potassium and symptoms of fluid retention is recommended. Prior starting treatment, ALT, AST and bilirubin levels must be measured and then every 2 weeks for the first 3 months of treatment and monthly thereafter.

Antiandrogens

Antiandrogens were initially developed to block the residual secretion of testosterone by the adrenal glands. They directly inhibit the effect of testosterone on the intracellular receptor in prostate cells without inducing a decrease in testosterone in the blood.

First Generations of Nonsteroidal (NSAA) and Steroidal (SAA) Antiandrogens

NSAA and SAA are primarily prescribed in a short-term association with GnRH agonists to prevent the flare. Historically, they have also been combined for longer duration with GnRH agonists in a strategy called maximal androgen blockade. The clinical benefit of administering NSAA beyond 6–8 weeks is, however, low compared to side effects [47].

In locally advanced but non-metastatic cancers, bicalutamide can also be prescribed alone at the dose of 150 mg per day. Several trials have suggested a similar benefit to GnRH agonists but with a more favourable side effect profile [26].

Side effects of NSAA include gynaecomastia (sometimes painful swelling of the breasts) and digestive disorders. These are usually moderate and often disappear when treatment is stopped.

Enzalutamide, Apalutamide and Darolutamide

These three drugs are newer generations of AR receptor antagonists, designed to overcome castration resistance in PCa cells containing AR amplification or overexpression [48]. Enzalutamide is the only one being actually commercially available. It is generally very well tolerated, adapted to long-term administration and can be given before or after chemotherapy. This AR receptor has demonstrated significant efficacy in men with metastatic CRPC [49, 50]. The most common Grade 1–4 side effects were fatigue (36%), back pain (27%), constipation (22%) and hypertension (13%). Enzalutamide is a strong inducer of CYP 3A4 and a moderate inducer of CYP2C9 and CYP2C19. These combinations should be avoided if possible. Conversely, concomitant use of strong CYP2C8 inhibitors can increase the plasma exposure to enzalutamide.

Enzalutamide belongs to a class of antiandrogens that can lead to a risk of seizures. Patients with a history of seizures or with other risk factors for seizures were not eligible for the AFFIRM and the PREVAIL trial. Fatigue is the most badly advertised side effect of enzalutamide. The unadjusted percentages of men reporting fatigue for all grades were slightly higher in enzalutamide arms (range 28–38% vs. range 20–29%) of the pooled analyses for double-blind, randomised, placebo- or bicalutamide-controlled trials of enzalutamide for mCRPC [51]. Grade 3 fatigue AEs were reported by <10% of men and in similar proportions in both arms (1–6% vs. 1–7%). Younger men (<75 years) experienced less fatigue vs. older men (20–35% vs. 21–42%), regardless of treatment. Patients, however, have to be counselled that fatigue is a reported adverse event.

According to the European public assessment report (EPAR), no specific monitoring is recommended for patients on enzalutamide. The EMA advises additional INR monitoring in case of co-administration with warfarin (CYP2C9 substrate) [52].

The decision of administering enzalutamide should be carefully weighted in patients with a history of seizures, with predisposing factors for seizures, using concomitant medications that may lower the seizure threshold, or patients using CYP3A4, CYP2C9 and CYP2C19 substrates with a narrow therapeutic index [52].

Special Interventions for Nurses Along the Prostate Cancer Care Pathway

The cancer patient has to deal with treatment-related events that impact on his quality of life as well as with difficulties depending on his personality (i.e. his representations, beliefs, motivation, anxiety). The BMQ questionnaire is a good tool for quickly identifying abnormal beliefs about treatment [53].

In order to pay particular attention to patient's motivation, ask yourself the following questions: is the patient motivated to change his behaviour? What is the importance of this motivation? What kind of motivations does the patient have? Are his motivations relevant? Anxiety is often linked to uncertainty, lack of information, waiting for results, poor understanding of disease, treatment and side effects or problems and concerns with the family and/or the care team. In order to understand who these patients are and where they stand in their coping process, it is important to take into account the difficulties they have to face. This is where the nurse comes in.

To be sure that the patient perceives where he stands in his coping process, the following questions should be asked at each new treatment proposition. Tell me what is going on with you. Tell me what's the physician treatment adaptation. Why this new treatment proposal now? These questions will likely generate the opportunity for the nurse to re-explain the disease and/or the treatment and/or the treatment plan, if needed, respecting the rhythm of the coping process of the patient. Nurse should avoid informing the patient before he has told what he knows about his disease and his treatment plan.

The nurse is the best positioned to support the patient in his coping process along the path of his treatment plan. The ultimate goal is that the patient is becoming an empowered partner that understands his disease and its treatment and actively participates to it. That is why education is so essential. In in the end, this will improve compliance and adherence to the treatment.

One of the most challenging aspects of managing PCa patients is PSA. For many patients PSA is not only the prostate-specific antigen but rather a "patient stress amplifier". PCa patients perceive their disease through their PSA. If it decreases, even by a glimpse, the patients will feel better. Whenever it increases a little bit, the patients will consider its cancer is progressing. One of the caricatural consequences of this is that usually when you ask the patient, "how are you?", he answers, "I will let you know when I know my PSA". Educating the patient about the real value of PSA monitoring and especially his poor prognostic value is a key element in helping the patient to cope with his disease. That education is crucial for any phase of the disease in which active monitoring is the best option or when monitoring patients receiving drug with no or little effect on PSA such as RA223, denosumab, or zoledronic acid. M Keswick Jencks appropriately quotes on this topic that "Above all what matters is not to lose the joy of living in the fear of dying". In the case of PCa patients' case, we could almost say "Above all what matters is not to lose the joy of living in the fear of the PSA level" .

Regarding the Importance of a Multidisciplinary and Most Professional Team

The entry in the patient's journey happens at the time of diagnosis. The following important step of the treatment pathway can be summarised as this. Treatment proposition can be summarised in four steps.

Step 1 It is important that any new diagnosis and any new treatment are discussed in a multidisciplinary team meeting (MDT), with all the different medical specialities being present. The goal of that meeting is to discuss the most appropriate treatment, options, according to the latest guidelines and research. In our institution, that meeting is organised by the Coordinating Nurse (CN). The MDT panel then assigns a physician in charge of the debriefing consultation. The referring physician announces the diagnosis or disease progression and presents the treatment plan.

Step 2 The patient is then seen by the CN, right or soon after. The objective of that second announce is to evaluate what the patient understood from the consultation with the physician. Patients are often so stressed by the diagnosis of cancer that they lose most details of the discussion. The CN is there to repeat or complete the diagnosis and treatment plans when needed. Sometimes it consists in simply summarising and simplifying what has been explained and coordinating the different appointments needed for the treatment. The CN will educate and give advices about the treatment, side effects and pathways. Additional phone calls can be also planned. The CN should use a check list with tips to evaluate side effects and to give advices if needed. The CN will also evaluate how the patient is handling all of this new information and detects any frailty that could interfere with the treatment. Listening to the patients is what helps CN the most to determine what the patients might need when they sometimes don't realise it themselves.

Step 3 One of the key functions of the CN is the referral to specific colleagues for more specialised support. It is important to tailor the process to each individual patient. It doesn't have to be immediate; the nurse will always try to seek the optimal time to offer additional support. For example, the CN will never force a patient to see a psycho-oncologist but rather proposes it if distress is detected. The patient can still refuse, and the proposal can be rediscussed at later nurse consultation if still needed.

Step 4 The patient does not live in the hospital; it is very important to establish a link between the patient's environment and the clinic. In most countries, the general practitioner (GP) is that preferred link. He needs an in-depth information about the diagnosis, the treatments and its side effects because the patient will often go to him for advice when unsure of what to make of his current situation. This is also helpful later on this process because GPs have more proximity. Throughout these steps, CN hope to help the patient adapt/cope with his new situation and empower him to take part of the process. He will be an actor in his treatment.

Conclusions

Scientific evidence, professional experience and the testimony of patients have already confirmed the benefit of the patient's active role in the management of prostate cancer. The patient will face many stressful events throughout his journey, and he will have to be supported along the way. A tailored information, adapted to his own level, and a deep understanding of what is happening will be instrumental to involve and empower the patient. The nurse plays a critical role in giving the patient the ability to identify his needs, to help him solve practical, or more philosophical, problems and to control his own life while keeping a positive attitude. Motivating him to talk about his disease, move and exercise and eat better is helpful not only to manage the side effects of treatments but to keep the disease under control. Finally, there is little doubt that it is contributing to maintaining and improving his quality of life.

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Bladder Cancer and Renal Cancer

14

Bente Thoft Jensen and Susanne Vahr Lauridsen

Abstract

This chapter aims to summarize the current evidence base on pre- and postoperative nursing interventions in surgical uro-oncological care focusing on the core cancer continuum of care from diagnose to entering the survivorship phase. Enhanced recovery after surgery (ERAS) is a multimodal approach aiming to enhance physical, nutritional, and psychological recovery in anticipation of surgery, mitigate the burden of disease, facilitate the return of patient health status to baseline values, and decrease postoperative morbidity. This chapter will describe the significant role of evidence-based nursing care in bladder and renal cancer surgery within an ERAS context.

Keywords

Muscle invasive bladder cancer · Renal cancer · Radical cystectomy · Nephrectomy Prehabilitation · Rehabilitation · Enhanced recovery pathways · Cancer care Survivorship

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B. T. Jensen (✉)
Department of Clinical Medicine, Aarhus University & Chair of Bladder Cancer SIG-Group, European Association of Urology Nurses, Aarhus, Denmark
e-mail: benjense@skejby.rm.dk

S. V. Lauridsen
Department of Urology, Copenhagen University Hospital & Chair of the European Association of Urology Nurses, Copenhagen, Denmark

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Bladder Cancer

Bladder cancer is the second most common urologic malignancy and the 6th most common cancer. The majority (93%) of the tumors are classified as urothelial cell carcinoma (UCC), which may be non-muscle invasive (NMIBC) or muscle invasive bladder cancer (MIBC) (Fig. 14.1). The majority of tumors (Ta and T1) and carcinoma in situ (CIS) are flat and noninvasive, but high-grade types can progress to MIBC. NMIBC is treated with transurethral resection of the bladder (TUR-B) often followed by intravesical instillations of chemotherapy or immunotherapy. Intravesical immunotherapy using *Bacillus* Calmette-Guerin (BCG) is the most common treatment for NMIBC usually administrated by the urology nurse [1].

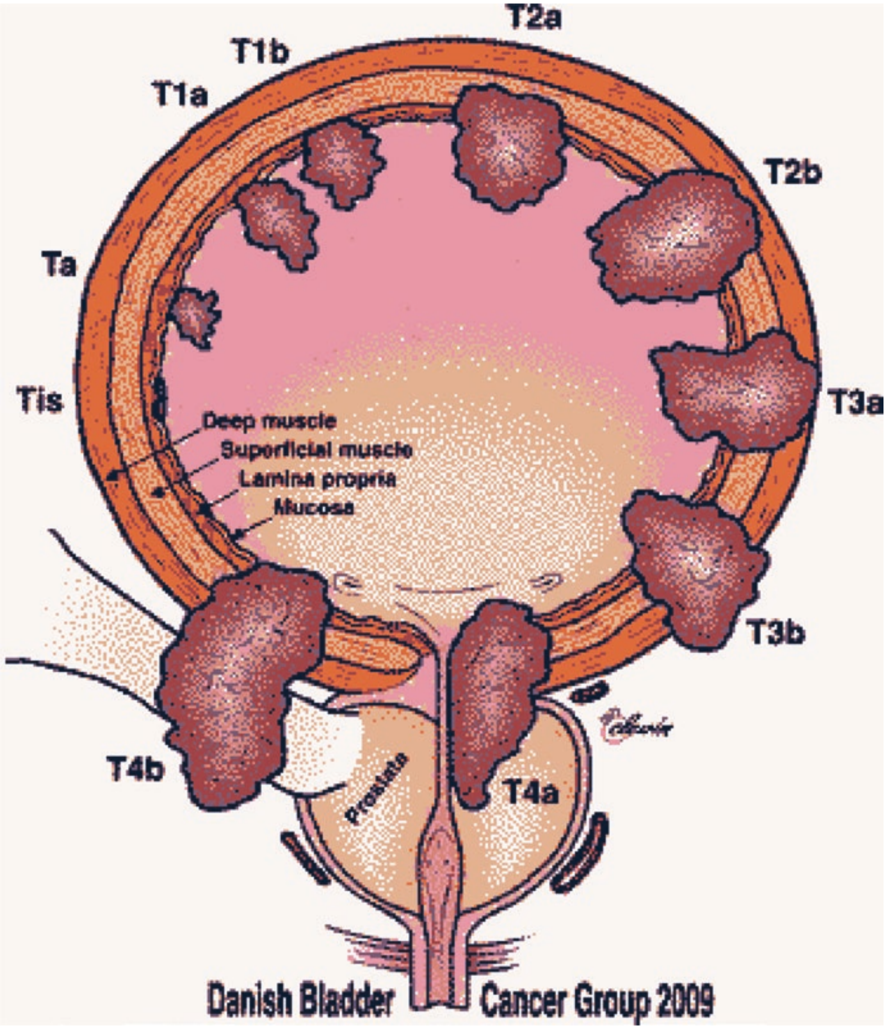

Fig. 14.1 Classification of bladder tumors. (Courtesy of DA-BLA-CA ref. Jørgen B. Jensen)

Radical cystectomy (RC) remains the first-line treatment when diagnosed with MIBC, T2-T4aN0M0, or high-grade NMIBC. Radiation therapy is an alternative approach in, e.g., frail patients not considered candidates for surgery or may be a specific preference from the patient based on informed and shared decision although the survival rate is inferior to RC [2]. RC is one of the most complex procedures in major abdominal oncology surgery and includes removal of the bladder together with prostate and seminal vesicles in men and anterior vaginal wall, uterus, and adnexa in women plus extended lymph node dissection (LND) and subsequently establishment of a urinary diversion [3]. The urinary diversion is mandatory and can be performed as a continent or incontinent diversion. Ileal conduit is the most common incontinent diversion (uro-stoma), whereas the continent diversion (neobladder) is a more complex procedure and depends on the tumor margins and more rarely a continent cutaneous reservoir (Indiana pouch).

At time for surgery, MIBC patients are generally characterized by a mean age around the seventh decade and with a high burden of comorbidity according to the Charlson comorbidity index (CCI) score yielding 33% has a CCI on 3–4 and 31.2% scorer ≥5. There is a 4:1 predominance in men over women. Moreover, approximately 27% are at severe nutritional risk, and approximately 80% are former smokers, whereas 30% are current smokers. Across Europe, approximately 30–40% have undergone neoadjuvant chemotherapy. In total, the MIBC patients are considered a “frail” population, and RC is followed by a high risk of perioperative morbidity. Even high-volume centers report more than 60% of the patients experience at least one complication within the first 3 months postoperatively [4]. Apart from smoking which is attributed to more than 50% of the cases, occupational exposures such as aniline dyes, aromatic amines, and polycyclic aromatic hydrocarbons are associated with high risk of developing bladder cancer (used, e.g., by painters, rubber industry workers, and hairdressers).

Renal Cancer

Renal cell carcinoma (RCC) is the third most common genitourinary tumor, the 7th most common cancer, and one of the most vascular cancers [1]. RCC and urothelial cell carcinoma of the renal pelvis and ureter are different cancers and have different treatments [1]. RCC is not a single malignant neoplasm, but a group of several different tumor subtypes, each with a unique genetic profile; the most common histological pattern is clear cell. RCC is often diagnosed incidentally at the time of radiographic imaging for other complaints.

For localized RCC, surgery is the only curative treatment with high-quality evidence. According to oncological and quality-of-life outcomes, localized tumors are best managed by partial nephrectomy (PN) rather than radical nephrectomy (RN), if technically feasible irrespective of the surgical approach [5]. There is a 1.5:1 predominance in men over women, with peak incidence occurring between sixth and seventh decade of age. According to CCI, the comorbid burden is modest compared to MIBC patients reminding CCI does not encompass hypertension, lung disease, and coronary artery disease in the absence of myocardial infarction. In a large population-based study, only 25% had a CCI score above 1, and more than 51% had no comorbidities [6]. However, postoperative mortality is 2%, and complications are reported in up to 11% in 90 days postoperatively [5, 7]. Regarding lifestyle factors 48% are former smokers, whereas 11% are current smokers, approximately 40% of RCC patients are classified as obese, and about 34% suffers from hypertension [5, 8]. Alcohol is not reported to be an independent risk factor, and moderate consumptions seem to have a protective effect [5]. Having a first-degree relative with kidney cancer is also associated with an increased risk of RCC. A number of other factors have been suggested as being associated with higher or lower risk of RCC, but have not been confirmed. These include specific dietary habits and occupational exposure to specific carcinogens, but the literature is inconclusive.

This chapter focuses on the surgical pathways in RC, PN, and RN.

The Surgical Challenge

Surgery causes a cascade of reactions including release of stress hormones and inflammatory mediators such as cytokines, responsible for the systemic inflammatory response syndrome (SIRS) [9]. SIRS causes catabolism of glycogen, fat, and protein, and the consequences of protein catabolism is the loss of muscle tissue, which is a short- or long-term burden for functional recovery. Surgery remains a cornerstone of oncology treatment, and minimally invasive approaches including robot-assisted procedures have improved safety and patient outcomes. However, despite these advances, resections of the bladder and the kidney have mortality rates of 2–3%, and high postoperative morbidity persists even for lower-risk procedures like nephrectomy.

Enhanced Recovery After Surgery Programs in Urology

Enhanced recovery after surgery (ERAS) programs are based on a multimodal approach usually involving multi-professional healthcare teams including nurses, nurse leaders/nurse coordinators, dieticians, physiotherapist, oncologists, anesthesiologists, and surgeons. The ultimate goal is to reduce SIRS and minimize postoperative organ dysfunction and postoperative morbidity and enhance rehabilitation leading to improved patient outcome and secondly to reduce healthcare costs [10]. The success of ERAS protocols (ERPs) began more than 25 years ago in Denmark within the field of colorectal surgery led by Professor Henrik Kehlet. He challenged old conservative doctrines across perioperative care by letting patients drink clear fluids until 2 hours before surgery and eliminating most bowel preparation before surgery and post-surgery, avoiding drainage/tubes or removing immediately after surgery and having patients drinking and eating as soon as possible after surgery as well as early progressive mobilization by sitting and walking the same day or the day after surgery.

Although the evidence of the ERAS concept has mainly been gained and documented in colorectal surgery, ERAS has successfully improved recovery across surgical specialties, and the concept is internationally recognized as standard of care although interpreted different and lacks full implementation. Especially the urology community has been criticized for reluctant implementation. Enhanced recovery after surgery protocols (ERPs) are continuously refined with respect to surgical procedure since Wilmore and Kehlet described the core evidence-based components in 2008 [11]. The Society of ERAS has procedure-specific ERPs and implementation tools (www.erassociety.org). Today healthcare providers across the world (despite the nature of healthcare services) have transferred the ERAS concept besides colorectal surgeries to several other specialties such as gynecology and head and neck surgery and urology and is now expanding its role into prehabilitation interventions in major cancer surgery and thereby another emerging role of nursing care [12, 13].

In the recent RC-ERP from 2013 by Cerantola, there is a list and an overview of the level of evidence of any of the 22 components included in the guideline [14]. The basic recommendations such as preoperative preparations, reducing SIRS, pain management, early postoperative oral intake, and immediate postoperative progressive mobilization are in general and applicable to both PN and RN pathways.

Nursing Within the Context of ERAS

The genesis of ERAS based on the question "why is the patient still in hospital today?" given the following answer will clearly address the patients' individual recovery problems [12]. The question clearly indicates that the nursing profession has a pivotal role and a significant opportunity to impact the core surgical cancer care continuum from diagnosis to survivorship (Figs. 14.2 and 14.3).

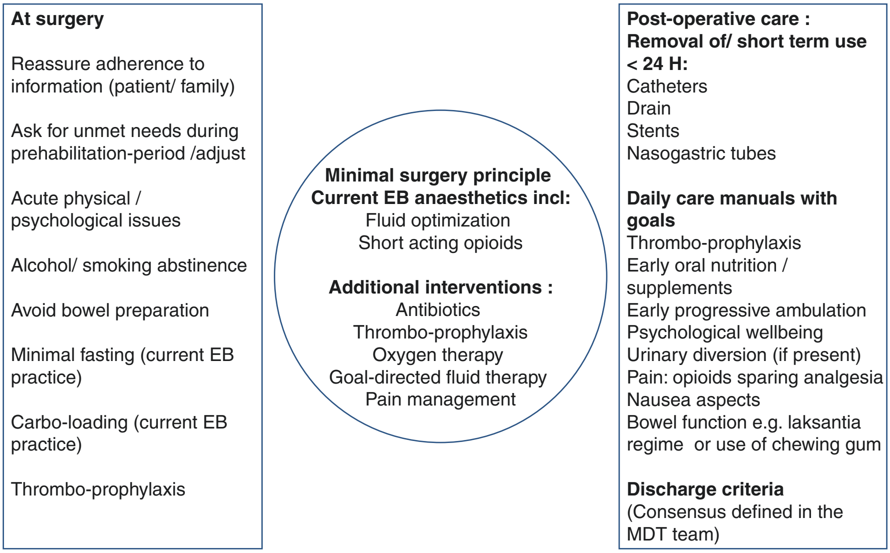

Fig. 14.2 Overview of basic perioperative ERAS components in urology

Through early patient screening, patient involvement, pre- and postoperative habilitation assessments, and documentation of patient status, the nurse can provide evidence-based interventions designed to improve physical and psychological health and contribute to the efforts of reducing the likelihood of patients developing future chronic impairments (Table 14.1).

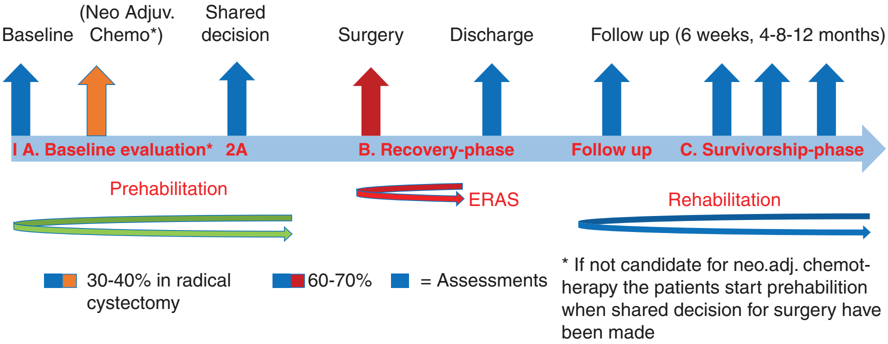

Fig. 14.3 The multi-professional cancer care continuum – urology surgery

Table 14.1 Overview of nursing interventions in prehabilitation

	Assessment and *suggestions* for tools	Multimodal team
Home-based physical exercise Program including element of resistance and endurance training or physical training at the hospital institution	Baseline functional capacity Power rig measuring leg power or 6-min walking test Monitor daily achievements in the personal logbook	Physiotherapist or the specialized nurse instructs the patient/family to the exercise program Adjust mutual expectations to the exercise program Apart from the exercise program, every patient is encouraged to do physical activity with moderate intensity for 30 min every day (walk, swimming, dancing, cycling) Instruct the patient to call the team in case of questions or problems Inform the patient/family that exercising is safe within the given framework
Nutritional intervention	Baseline nutritional screening Nutritional risk score (NRS) [15] Subjective global assessment Nutritional status Handgrip strength Bio-impedance Monitor protein/energy intake in a personal logbook for at least 1 week before surgery	Dietician and/or specialized nurse instructs and advices the patient in oral intake of protein/energy/oral supplements and how to document the daily intake before surgery The team motivates and encourages the patient by: Emphasizing the goal of prehabilitation Explaining the synergistic association between physical exercises, nutritional intake, sedentary lifestyle, and recovery

Table 14.1 (continued)

	Assessment and *suggestions* for tools	Multimodal team
Smoking and alcohol	Assess baseline information of the daily use of tobacco and alcohol consumptions Use Fagerstrom score in the case of replacement therapy	The specialized nurse informs the patients of the possibility of professional counselling and replacement therapy if necessary
Stoma education	Ask the patience of any experience/knowledge regarding living with a stoma Show a pixie of pictures of a "real stoma" at different stage postoperatively Hand out best educational material/information material Show different stoma material/solutions. Use the Urostomy Educational Scale (UES) to measure progress in self-efficacy pre- and postoperatively	The stoma nurse informs and instructs the patient/family of basic skills necessary to change a stoma appliance The patient performs a total change of appliance under guidance using the educational "stoma-kit" The stoma nurse encourages the patient to practice at home using a "stoma-kit" developed for practice
Sexual health	The sexual counselor (specialized nurse) approach the patient (and partner), e.g., using the "PLISSIT model" as a framework for the consultation Inform the patient of scheduled postoperative consultations General tool measures current sexual function, needs, and well-being	The sexual counselor informs the patient (and possibly partner) of the changes in bodily function after surgery and the possible impact on sexual function Moreover, it is emphasized that sexual health aspects are an integrated aspect of the recovery program
Psychological	BCNAS-32 – unmet supportive care needs assessment HADS (Hospital Anxiety and Depression Scale) score Health-related quality of life (EORTC- QLQ-C30 + EORTC BLS 24)	The surgeon and specialized nurse informs carefully the patient and family regarding the surgery and well-known reactions in relation to being diagnosed with cancer The nurse acknowledges that level of possible anxiety is individual and emphasizes our engagement in supportive care needs in any way along the pathway

Organization

In any ERAS pathway, anchor-based leadership and consensus on treatment and care pathways are key factors and a necessity for successful implementation, medical performance, clinical outcome, and patient satisfaction. In multimodal pathways it is essential to define the responsibilities of all healthcare professionals involved and requires commitment and team approach driven by the hospital, departments, and nurse leaders. Nursing standard of care pathways and algorithm must be clearly described in ERPs for pre- and postoperative interventions including everyday goals, nursing documentation aspects, patient-education material pre- and postoperatively, and tools for shared decision. The growing evidence of prehabilitation interventions has high-volume cancer centers (e.g. the Netherlands and Denmark) in Europe initiated multi-model prehabilitation academies which systematically involve, educate, and inform the patients and families when scheduled for surgery.

On the ERAS website, tools are provided to facilitate and support the implementation process. Moreover, manuals including evidence-based elements to include in the ERAS program are available as well as programs to support documentation of assessments and achievements. Of note, ERAS is not a "one-size-fits-all" program beyond the surgery itself but rather spans specific individualized assessments and interventions that are likely to improve or maintain health status along the cancer care continuum.

Nursing Interventions

Prehabilitation

Prehabilitation is defined "as the process of enhancing an individual's functional capacity before scheduled surgery." The aim is to withstand the tolerance for the upcoming physical challenge and the surgical metabolic stress response caused by tissue trauma, periodically starvation reduced physical activity and anxiety, which in total contribute to a rapid decline in functional capacity [16, 17]. Poor preoperative performance has been shown to increase risk of mortality and prolong recovery suggesting that the preoperative period may be the most favorable time to optimize the overall condition and proactively involve the patients in own recovery [18–20]. Although significant advances in diagnostic procedures, surgical technique (mini-laparotomy and robot-assisted RC), anesthesia, and perioperative care, the continuously high burden of postoperative morbidity and long-term impairments indicates that the urological patients remain candidates for further optimization beyond the surgical procedure. ERAS has until recently primarily focused on perioperative period. However, the "unutilized window" of time from diagnosis to surgery has gained increasing attention in the effort to enhance recovery and reduce postoperative impairments.

Currently, prehabilitation in major surgical cancer is considered as an integrated part of the core cancer continuum of care [21] (Fig. 14.3) and can be seen as an extension of the original ERAS concept. The prehabilitation concept includes physical and psychological assessments that accommodate a baseline functional capacity, identify impairments, and provide interventions to support physical and psychological health aiming to reduce the incidence and severity of per- and postoperative impairments [21, 22]. The scope of prehabilitation is yet expanding from the original single physical interventions to multi-professional complex programs including both double and triple modalities (see below). The evidence base on prehabilitation and the impact on recovery and health-related quality of life (HRQoL) has until recent years mainly been accomplished in orthopedic and cardiovascular and colorectal surgery contrary to the relatively few procedure-specific clinical studies in uro-oncology cancer surgery [23–27]. However, prehabilitation is moving forward and slowly being recognized by national health boards as a key player in both MIBC and RCC pathways (www.sst.dk). The multimodal team offers a platform of different competencies, which works synergistically and includes all key factors in prehabilitation of the patient (Table 14.1).

The Role of Physical Prehabilitation Intervention

Poor preoperative fitness and physical status are well-known risk factors for serious postoperative complications and prolonged disability. Neoadjuvant oncologic therapies may be associated with additional degradations of physical fitness before surgery. Again, prehabilitation is not a "one-size-fits-all" program before surgery but rather involves specific individualized assessments and interventions that are likely to improve outcomes for each patient.

This expanding scope of prehabilitation is likely due to the acknowledgment that non-exercise interventions may be beneficial as well as that prescribing exercise as a single modality shortly before surgery may actually be detrimental to some patients who lack physiologic reserves. For example, frail elderly patients known to be at high risk for postoperative complications often present with decreased muscle mass and low protein reserves, and they may not tolerate an increase in exercise before surgery *without* protein supplementation. Although there is a rising movement in Europe and Canada acknowledging the potential unutilized resources and benefits prehabilitation may add to optimize the recovery in cancer surgery, much remains to be implemented and further studied. Currently there is no dose/response evidence-based recommendation regarding duration and intensity adjusted to the individual cancer patient. Thus, recommendations of the level of activity and exercises are derived from general sports medicine although encouraging high evidence in the field supports the ongoing efforts of prehabilitation in cancer surgery. Currently, patients are recommended to be physically active (aerobic element) with moderate intensity for 30 minutes every day combined with exercises to empower muscle strength and endurance targeting the major muscle groups involved in mobilization, in and out of bed, chair-raise performance, stair climbing, and gait speed.

The functional capacity of patients encompasses aerobic endurance capacity and muscular strength and can be considered a central element in the preparation of patients for surgery [28, 29]. Three studies in MIBC patients preparing for RC have shown that a short-term-home-based exercise program consisting of simplistic exercises is feasible and effective and can increase physical capacity and cardiopulmonary fitness. Thus there is an increased ability for early mobilization which again may improve postoperative outcome [23, 25, 27]. A RCT study introducing a short-term home-based exercise-based prehabilitation program of a 2-week period showed a patient adherence of 66% fulfilling ≥75% of the standardized exercise program [25]. All patients in the study received oral supplements according to guidelines [9]. The physical program consisted of exercises to empower muscle strength and endurance targeting the major muscle groups involved in mobilization, in and out of bed, chair-raise performance, stair climbing, and gait speed. Muscle capacity was expressed as muscle power (W/kg) in the lower extremities which correlates with the ability to perform physical activities [30, 31]. The program significantly improved leg extension power of 18% in the intervention group compared to standard (no intervention). Postoperatively, an everyday progressing physical program followed up the prehabilitation program (look postoperative care). LOS or complications were not reduced, whereas time to independently perform activities of daily living was significantly improved as well as HRQoL after 4 months in domains relevant to recovery [32]. The same level of adherence of 65% was shown in another study implementing a prehabilitation program consisting of both a nutritional and a physical component over a 2-week period. In this study all patients were *instructed by the clinical nurse specialist to a standardized exercise program* composed by the comprehensive cancer center survivorship program for all types of cancer patients awaiting or undergoing treatment [33]. Highly specialized physiotherapists from the survivorship clinic educated the specialized nurses allocated to the program. The program consisted of both endurance and resistance training. Capacity was measured using the 6-minute walking test [34]. A significant mean increase of 10.6% in functional capacity was measured from baseline to 6-week follow-up. Moreover, bone mass was also significantly improved from baseline [23]. Another pilot study reports promising results regarding the impact of cardiopulmonary fitness on postoperative complications although not significant [27]. All three studies document that a home-based short-term physical prehabilitation is feasible and effective.

The nurse role: The specialized nurse can under supervision by the physiotherapy team assess baseline status and instruct the patients to a basic standardized exercise program when referred to surgery (RC, PN, RN). The nurse will after the instruction handle out a personal manual where the patient can log everyday achievements including contact details in case of problems and or need of reassurance (Table 14.1 and Fig. 14.4).

The Role of Nutritional Intervention

The indication for nutritional therapy in the prehabilitation phase is prevention and treatment of catabolism and possible malnutrition before urological surgery (RC, PN, RN). The intention is essentially maintenance of nutritional status

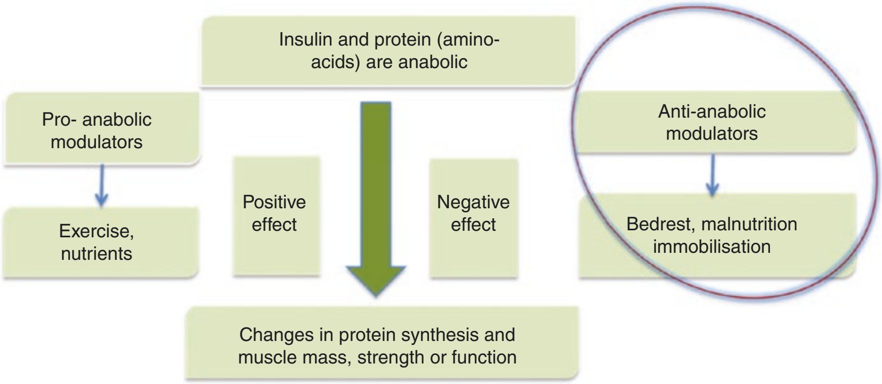

Fig. 14.4 The synergistic association between physical activity and nutrients

aiming to reduce the risk of postoperative complications and mortality [9]. In clinical practice the goal is to identify patients at risk and provide sufficient support for protein intake to achieve anabolism and energy to maintain body composition [9, 21, 35]. Nutrition interventions may be indicated even in patients without clear disease-related malnutrition if it is anticipated that the patient will be unable to eat or cannot maintain oral intake for a relative long period postoperatively [9, 36]. The amount of dietary protein or supplemental protein needed depends on the disease severity and the patient's actual nutritional status [9, 19, 37]. Limited evidence supports preoperative nutritional interventions although evidence suggests that the outcome is improved if malnourished individuals are adequately fed for at least 7–10 days before surgery [38]. In the case of severely malnourished patients who cannot be adequately fed orally or enterally, preoperative enteral treatment is indicated, and surgery may be postponed although seldom because of the oncological risk.

The nurse role: All patients undergo nutritional screening when referred for surgery performed by the nursing staff using the local recommended screening tool, and in some centers handgrip strength or bio-impedance measurements are standard baseline assessments (Table 14.1). All patients referred for RC are as per default considered at moderate risk due to the upcoming surgical challenge and will routinely be offered oral protein supplements three times a day in at least 1 week before surgery. The nurse or dietician (if available) informs by pixies or other material the patients and their families on how to eat and cook smart based on their current eating habits. All patients are educated and informed of the impact and the "wicked" association between physical activity, nutrition, and sedentary lifestyle on postoperative recovery. Moreover, the importance of eating 1 hour after being physically active and before bedtime ensures maximal absorption. Finally, the patients are encouraged to monitor total energy and protein intake in the personal logbook using the nutritional module. In case of the screening reveals the patient is at high risk or challenged by any comorbid condition, the dietician and the surgeon will advise further.

The Role of Smoking and Alcohol

High alcohol consumption and daily smoking reduce the immune capacity leading to an increased risk of infection and impaired wound healing [39, 40]. In addition risky drinking increases the endocrine stress response to surgery, leading to deterioration of existing conditions which thus increases the risk of postoperative morbidity [41]. The effect of smoking and risky alcohol drinking on outcomes after radical cystectomy remains debated [42]. Most observational studies show that the risk of readmission for an infectious complication, recurrence, and cancer-related death after radical cystectomy are associated with continued smoking, whereas others have questioned this [43–48]. In surgery daily smokers and people drinking above 2 units (24 g ethanol) a day are at increased risk of developing wound complications, general infections, and pulmonary complications [41, 49]. Intensive smoking and alcohol cessation intervention 6–8 weeks before elective surgery reduces the incidence of postoperative complications with approximately 50% [50, 51], but cancer surgery like RC often takes place within 2 weeks. The hypothesis is that interventions within this timeframe may improve recovery (pathophysiological mechanisms, such as tissue perfusion and oxygen delivery, ciliary, and immune function) and reduce SIRS, arrhythmias, and bleeding time [39, 41, 49]. Until now no RCTs have evaluated the effect of smoking or alcohol cessation interventions on complications and HRQoL in RC or any specific urologic procedure. An ongoing multicenter study expects to present results in 2019 [52]. Despite the fact that more studies show that patients were satisfied by being offered support in hospital to quit smoking prior to surgery and that the majority were motivated by the possible health gain following, the belief that smoking relieves stress serves as a major barrier for smokers to quit and for healthcare professionals to recommend quitting [53, 54]. A systematic review shows that smoking cessation is associated with reduced depression, anxiety, and stress and abstainers improve positive mood and quality of life compared with smokers who continue to smoke [55]. The risk of alcohol drinking in relation to surgery is now reflected in the American Society of Anesthesiologists (ASA) physical status classification system score (https://www.asahq.org/resources/clinical-information/asa-physical-status-classification-system), meaning that it is important to identify patients drinking more than 2 units of alcohol per day.

The nurse role: Addressing smoking cessation will help all patients. Nurses should use the validated instrument “The 5 A’s” [56]. The nurse should *assess* smoking habits – ask if they smoke and *assess* nicotine dependency – use Fagerström score, *advice* to stop smoking, *assist* to stop smoking by counseling, or *arrange* referral to quit lines/clinics. During hospitalization the nurse should provide the patient with nicotine replacement therapy according to the Fagerström score. The nurse should assess the alcohol drinking pattern of the patient and support patients who drink more than 2 units per day to stop drinking as soon as possible in relation to surgery. If the patient is drinking more than 5 units per day, the patient should be offered supportive medical treatment against development of withdrawal symptoms.

The Role of Preoperative Stoma Education

Urostomy care requires manual skills and emotional adaption in order to secure self-efficacy [57], and there is mounting evidence that stoma care ability is the most important variable predicting positive adjustment to life with a stoma and increase the perception of HRQoL [58–61]. Survivors have described significant unmet needs such as lack of early stoma education and patient involvement [62, 63]. Positive impact of preoperative stoma marking on clinical- and patient-reported outcome (PRO) has been reported [64, 65]. Consensus for good clinical practice have until recently been based on expert knowledge suggesting preoperative stoma care education may be beneficial [66, 67]. In a recent RCT, a significant effect on self-care skills was seen after integrating stoma education into the prehabilitation program. The intervention consisted of 1.5-hour hands-on-training stepwise introducing skills necessary to independently change a stoma appliance. Stoma-kit was handed out for home-based training, and progress was measured using the quantitative Urostomy Education Scale. The significant level of self-care skills was maintained throughout the study period of 1 year postoperatively [68–70].

The nurse role: all nurses at the department can perform standardized uro-stoma care. However, in most departments highly educated stoma nurses introduce the patient to the future life living with a uro-stoma and educates the patient and family. As an integrated part of the prehabilitation program, the stoma nurse explains the procedure of how the stoma will be created, shows pictures or videos of patients with a stoma at different stage postoperatively, introduces stoma material, and performs a basic change of a stoma appliance together with the patient. The stoma nurse takes the patient through each step in the procedure by using a stoma mock-up. The patients are encouraged to perform a full change of appliance at least twice during the prehabilitation period using the stoma-kit. The nurse can measure progress in self-efficacy by using the validated Urostomy Education Scale from baseline throughout the follow-up period, and the patient can notice the developments.

The Role of Sexual Health

RC is commonly associated with treatment-related sexual dysfunction and varies from mild to severe impact on the individual in both genders. However, common concerns are seen in all types of cancer requiring major surgery in the pelvic floor like PN and RN [71, 72]. Sexual health is related to anatomic, physiologic, medical, psychological, and interpersonal components [73, 74]. Female sexual dysfunction are reported to surpass that of male dysfunction, and less attention has been paid to identify and treat sexual problems of females; moreover, there is a lack of treatment options compared to that for comparable conditions of the male [73]. Although poorly identified, impaired sexual function has been recognized as the primary source of self-assessed distress among patients undergoing RC [75]. A review examining unmet needs in MIBC patients preparing for RC found only 6 patients of the 30 patients surveyed reported efforts to educate them on the possibility of sexual dysfunction following treatment [63, 76]. The patients requested preoperative supportive information focusing on future sexual function in relation to treatment modalities, involvement of partners, and the ability to have sexual intercourse and orgasm.

The nurse role: a nurse educated in the field of sexuality is a necessity when approaching the patient (or partner). Information of future sexual health and what can be expected is clearly an unmet need requested by the patients. The importance of talking about sexual health may not be so obvious for the clinical staff compared to the oncological risk. There is, however, a need for articulating the aspect before surgery and assuring that we continuously will be aware of their sexual health. Sex may still be a relatively high taboo for healthcare staff, patient, and the partner. Thus it is pivotal to provide specialized competencies, stepwise move forward, and indicate that we will take the lead in this conversation and/or consultations unless the patient has other preferences.

Psychological Well-Being and Shared Decision-Making

Although the literature is sparse, new evidence in colorectal surgery (ERAS program) points toward psychological well-being is a pivotal aspect in the prehabilitation phase due to the association with short- and long-term impairments [77]. Two recent qualitative studies have explored MIBC patients' experience preparing for surgery: First, a 6-week smoking and alcohol cessation intervention was well received, and it was perceived as an integral part of preparing for surgery [54]. Second, a patient-centered approach using the shared care decision model is important with respect to gender preferences for surgery, understanding treatment options, risks, family aspects, and own involvement in care [78, 79]. Nurses have for years known some patients have a high level of anxiety before surgery. However, recently anxiety has been reported by patients as an unmet need in major cancer pathways and now recognized as important factor in preparations for surgery. There is no clear recommendations in the field, although recent research have introduced new approaches to work with the patients/families and provide strategies to reduce the level of anxiety and not only react upon symptoms postoperatively.

The nurse role: the multimodal team is aware that anxiety in the prehabilitation phase may have major implications for being motived for optimization and preparations for surgery. It is however important to confront the patient and explain we recognize and understand the situation. On the other hand, it is likewise important to explain that other patients have shared the same experience but reported that they somehow were manageable when involve in own care. Clearly more evidence is needed in this underreported field.

Recovery and Rehabilitation

Currently, the most common outcome measure used to measure the success of an ERP is the hospital length of stay (LOS). Although it was an outcome of interest when ERAS was launched, it is in fact only a surrogate marker of recovery and may be a too elastic parameter without clearly defined discharge criteria. Importantly, LOS does not necessarily reflect the true recovery of a patient who has to convalesce at home. It is important to focus our efforts during the postoperative period beyond the LOS and readmission rate, by understanding the factors that influence return to normal daily living after discharge from the hospital. Moreover, LOS is not a goal in itself. The implementation of ERAS in the past decade has evidently cut down LOS from weeks to only a few days in many surgical pathways including RC, PN, and RN. The question "why is the patient still in the hospital today?" remains interesting and clearly addresses the actual condition of the day and still support a goal-directed postoperative care program to prevent further complications or impairments. The ultimate goal is to minimize postoperative organ dysfunction and enhance rehabilitation.

Within an ERAS context, the postoperative period or recovery phase has quite a few endeavors which must be carefully administrated by the nurse. In clinical practice the nurse usually act as the anchor of the multimodal care team (bladder or kidney). Therefore, it is a prerequisite the nursing staff are aware of recent evidence of care. The nurse will accordantly to ERP`S plan todays activities in cooperation with the patient and support and encourage the patients to fulfill everyday goals in the best possible way. Moreover, she will often be positioned as the coordinator between the collaborators such as physiotherapist, surgeons, dieticians, and case managers. Every key player carefully documents today's achievements in a personal patient-log together with the patient or if not available in the medical record.

In Fig. 14.2, the well-known and most important postoperative focus areas for ERP are listed. There are of course local differences although most elements in the ERPs should be considered and possible to accomplish despite local differences and challenges. The areas that need to be addressed are several: nasogastric tubes, catheters, drains, stents, early oral nutrition, stoma care, enhanced progressive mobilization, smoking cessation, etc. It can be argued that a properly informed patient with no pain, nausea, or vomiting and without drains and tubes, as well as free from postoperative complications, should be willing to eat and ambulate. However, a patient with any of these issues will or may not necessarily be able to eat and/or ambulate. Therefore, early mobilization, early oral intake, and bowel function should be considered and monitored as outcome measures similar to LOS and being key components of ERP. When all discharge criteria are accomplished, the patient is ready to be discharged and start-up the rehabilitation program with or without support from primary care. At discharge all key players have updated the actual status of the patient, and suggestions for rehabilitation activities are individually addressed such as exercise recommendation to further improve functional and nutritional status and continued smoking cessation. The ability to independently change a stoma appliance is not a discharge criterion, and most patients may have a follow-up visit in a stoma clinic 5 weeks postoperatively. All patients have follow-up appointments according to national guidelines. At any consultation, all aspects included in prehabilitation program and problems during admission are addressed. In order to enhance rehabilitation, the multimodal team is an integrated part of the cancer follow-up program and the rehabilitation program, and besides the oncological state, the team will assess and address any unmet needs or impairments the patient may report.

Survivorship

Because of the demographic development and the eldering population, an increasing number of patients will be diagnosed with a cancer. Improved treatment of cancer has changed the view on cancer from a deadly disease to a chronic disease for the majority of patients. Concurrently, the patients are discharged as soon as possible because of lack of capacity in many countries. In total, we may live longer due to early diagnosis and treatment, and many patients may have long-term impairments. Often there is a gap between the rehabilitation periods and when entering the survivorship period (no matter how a survivor is defined). Sequela after oncological cancer treatment is well known but surgical patients may have add-on due to removal of organs and permanently loss of bodily functions and difficulty to adapt. Fortunately, there is a growing interest to establish cancer sequelae clinic focusing on organ-related functional impairment following pelvic cancer treatment. In acknowledgment of the patient-reported long-term impairments and the impact on HRQoL, several cancer centers are committed to focus on developing survivorship programs. Nurses will again take a leading role in delivering evidence-based care and proactively initiate and develop a research environment providing new evidence for survivorship care. The objectives of survivorship clinics are to improve clinical- and patient-reported outcome, empower patients in taking control of their illness by using new technologies and methods to inform them, develop self-management skills to support needs, and prevent long-term problems. In addition health professional's competencies in managing long-term effects of cancer treatment with the use of clinical tools to support and inform health services. Within the aforementioned objectives, an outstanding possibility has arisen combining academic and clinical nursing skills and hopefully provides a strong interdisciplinary approach to health science and applied nursing research in practicing uro-oncological nursing care.

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Management of Pleural Burden in Metastatic Lung Cancer and Malignant Pleural Mesothelioma

15

Maria Parsonage

Abstract

The burden of malignant pleural disease continues to rise, and the discovery of a malignant pleural effusion is a common problem in patients with lung cancer and malignant pleural mesothelioma. Symptomatic pleural involvement can present clinicians with a number of diagnostic and therapeutic challenges. Radiologically apparent pleural involvement requires thorough investigation and its discovery commonly represents metastatic disease across many tumour types. Histopathological pleural molecular subtyping has dramatically increased the availability of novel targeted therapies in advanced thoracic malignancy, and modern pleural intervention strategies can offer patients timely evidence-based fluid management. The impact of modern pleural research has reshaped the way in which patients are managed, shifting from what was historically a more surgical and radiological domain to the more medically focused approach. Developing pleural teams are in an excellent position to influence change in the current economically challenging environment by providing this group of patients with advanced disease, rapid management in an ambulatory setting. The use of validated prognostication tools and image-guided symptom control strategies help us to offer our patients more individualised pleural management. The chapter aims to summarise the available data around the pathophysiological mechanisms of pleural fluid production whilst considering methods of investigation, tumour staging and prognostication through to patient focused, therapeutic intervention strategies.

Keywords

Pleural disease · Malignant pleural effusion · Tumour staging · Lung cancer Malignant pleural mesothelioma · Prognostication · Pleural aspiration · Intercostal chest drain · Thoracoscopy · Indwelling pleural catheter

M. Parsonage (✉)
Respiratory Medicine, Wirral University NHS Hospital Trust, Wirral, UK
e-mail: maria.parsonage@nhs.net

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Burden of Disease

Cancer is the leading cause of death globally accounting for around 8.8 million deaths annually. The World Health Organisation suggest that with lung cancer accounting more than 1.69 million deaths annually worldwide, it remains one the most frequent causes of cancer-related mortality, and is arguably the most deadly [36]. In men, around 85–90% of the cases of lung cancer are found to be attributable to tobacco smoking, and there remains a year-on-year global increase [36]. The majority of patients with lung cancer will present at stages III and IV with an overall survival of just 9.5–16.8%, respectively [13]. Regardless of gender, lung cancer remains a leading cause of mortality worldwide (WHO 2018 [36]; National Lung Cancer [22]; Torre et al. [31]).

Despite this, one of the greatest advances in modern lung cancer management over the last decade is the concept of personalised medicine, whereby therapeutic intervention is based upon specific histologic and genetic tumour characteristics [32]. In terms of cell types, non-small cell lung cancer (NSCLC) is the commonest type of lung cancer with an overall diagnostic incidence of 85% in all lung cancer cases. The two most common histopathologic large cell subtypes are that of adenocarcinoma and squamous cell carcinoma. Historically, little attention was paid to subtype distinction in those smaller tissues samples, and no therapeutic implications existed within the NSCLC classification. The situation changed dramatically with the discovery of the novel effective inhibitor targets, epidermal growth factor (EGFR) mutations and anaplastic lymphoma kinase (ALK) rearrangements in patients with advanced lung adenocarcinoma [32]. Histopathological molecular testing is now a prerequisite in those tumours classified as adenocarcinoma or when an adenocarcinoma cannot be excluded. These advances in the understanding of such specific molecular pathways and genomic subtyping using immunohistochemistry have allowed clinicians offer a much more focused approach with genetically targeted immunological anticancer therapies [36].

Neuroendocrine tumours are found in up to 20% of lung cancer with its histological subtypes including large cell neuroendocrine carcinoma (LCNEC) and small cell lung cancer (SCLC). The tumours are high-grade and largely peripheral, are commonly associated with cigarette smoking and have a much higher incidence in men once again. SCLC is distinguishable from NSCLC due to its rapid doubling time, high growth fraction and the early development of distant metastases [8]. NICE recommend assessment by a thoracic oncologist within one week following a decision to treat SCLC [21]. Although SCLC is known to be highly responsive to chemotherapy and radiotherapy, it is particularly aggressive with the majority of patients seeing a relapse with this broadly resistant disease, often at just a few months from the initial therapy.

In terms of occupationally related deaths, it is estimated that globally there are 2.3 million each year, with asbestos exposure contributing to the largest proportion of deaths [28]. Malignant pleural mesothelioma is a rare but fatal form of thoracic cancer meaning that a thorough occupational history and para-exposure history should be sought in those patients presenting with a suspected pleural malignancies with a causal link to asbestos exposure. High-risk occupations include dock and shipyard workers, electricians, plumbers and launderers [35]. The true global burden of disease from mesothelioma remains unclear; however, Delgermaa et al. [7] suggest crude and age-adjusted mortality rates for all mesothelioma deaths of 6.2 and 4.9 per million population, respectively, with a mean age at death of 70 years. The associated risk factors for a malignant pleural mesothelioma include a male prevalence and occupational exposure, and rarely, in familial cases, it is linked to the mutation of the breast cancer (BAP1) gene [35].

The NICE 2015 clinical guideline recommends a referral for an urgent chest radiograph to exclude mesothelioma in those aged over 40, who present with *unexplained* symptoms of cough, fatigue, breathlessness, chest pain and anorexia, when they may have never smoked or have evidence of prior asbestos exposure [20]. Pleural malignancy when discovered is typically unilateral, with bilateral involvement accounting for just 3% of cases, and a differentiation between a malignant pleural mesothelioma and metastatic pleural malignancy remains challenging [35]. The more recently published British Thoracic Society Mesothelioma [35] guidelines also advocate a more targeted approach in terms of diagnostic immunohistochemistry from both pleural biopsy and pleural cytology specimens. It is recommended that those who are diagnosed with lung cancer and mesothelioma have a care plan based on a holistic needs assessment at diagnosis and other key stages of care [19].

Pathophysiology and Pleural Burden

The pleura is a delicate membrane of mesothelial cells covering the lung and inner surface of the chest cavity, creating a *pleural space* or cavity that usually contains around 0.1–0.2 mL/Kg of fluid bilaterally. The pleural cavity is enclosed between the *parietal* mesothelium which is located on the inner surface of the thorax, the diaphragm and the mediastinal tissues and the *visceral* mesothelium present on the lung surfaces, and both membranes are joined at the level of the hilae. The pleural space and the physiological composition of the serous pleural fluid allows an almost frictionless apposition of the mesothelia throughout respiration, thus limiting any damage to opposing sliding surfaces (Negrini in Astoul [23]). The pleural fluid provides the essential lubrication which enables a synchronous lung and chest wall movement of which has been thought to facilitate adequate ventilation. Interestingly however, human studies do not appear to show any long lasting ventilatory effects following surgical removal in pleurectomy or following a chemical pleurodesis of this complex structure, thus raising the question of its physiological relevance [14].

In health, fluid enters the pleural space through the capillary network following which it is efficiently removed via the lymphatics of the parietal pleura. The normal volume of pleural fluid in an adult is around 17mls/day for a 70 kg person with a total pleural drainage of up to 1–2 L/day. The pleural lymphatics system has a large absorption capacity with a rate of reabsorption at 20 times the rate of production [17]. A pleural effusion quite simply describes an excess volume of fluid within the pleural cavity between the parietal and visceral pleura. Excessive fluid accumulation occurs when there are pathophysiological processes involving inflammation and impaired lymphatic drainage causing an imbalance between fluid production and fluid absorption [2]. An accumulation of pleural fluid can give rise to a restriction in forced vital capacity resulting in a ventilation defect; however, this commonly depends upon the amount of fluid, the rate of development and the underlying aetiology of disease.

It is well known that a number of both pulmonary and systemic causes can give rise to the pathological accumulation of pleural fluid. The diagnostic differentiation of pleural transudates and exudates following thoracentesis remains the single most important step in determining the aetiology of a pleural effusion [14]. A pleural fluid exudate is determined by a pleural protein of >30 g/L, and subsequent evaluation of the pleural pH, glucose, lactate dehydrogenase (LDH) red cell counts and gram staining and cytological analysis are required to further identify the underlying cause.

These are complex pathophysiological processes, and there can be an overlap within identification, for example, 25% of heart failure-related effusions may be exudative, especially when a patient is taking diuretics whereby a small number of transudative effusions may be proven malignant [14]. Light's criteria can help further determine a transudate from an exudate. The three determinants that can be used are (a) pleural protein/serum protein ratio of >0.5 (b) pleural LDH/serum LDH ratio >0.6 or (c) pleural LDH >two thirds the upper limit of the laboratory reference range of serum LDH [12].

A radiologically apparent pleural effusion can be found in up to 0.3% of the population per annum [16]. A confirmed exudative pleural effusion following thoracentesis suggests disease from within the parietal pleura, and this can be due to a variety of inflammatory conditions with pneumonia being the most common. Patients with a symptomatic pleural effusion often present through an emergency route, commonly requiring both urgent diagnostic and therapeutic intervention of common symptoms that may be suspicious for malignancy. Unilateral pleural effusions or persistent bilateral effusions will almost always require additional evaluation to exclude an underlying malignancy in those fit enough for further investigation. The discovery of a malignant pleural effusion represents advanced metastatic disease and is seen in around 7–23% of patients with lung cancer, significantly affecting tumour staging and overall prognosis [16].

The precise pathophysiological mechanisms of pleural fluid formation and absorption will often depend upon the underlying aetiology [27]; however, radiologically apparent pleural effusions, pleural thickening or nodularity is concerning for malignancy, and such discovery will almost always require thorough investigation. A malignant pleural effusion is simply defined as an excess accumulation of exudative pleural fluid with the discovery of malignant cells [26]. Modern guidance and diagnostic pathways can help guide timing and urgency within the investigation of a pleural effusion, with the primary aim of establishing an underlying definitive diagnosis and excluding malignant disease [2] (Fig. 15.1).

It is well described that lung cancer commonly affects the pleura in a number of ways, and whilst most confirmed pleural effusions in this setting are proven to be malignant, a nodular malignant extension to the pleural may not always produce a

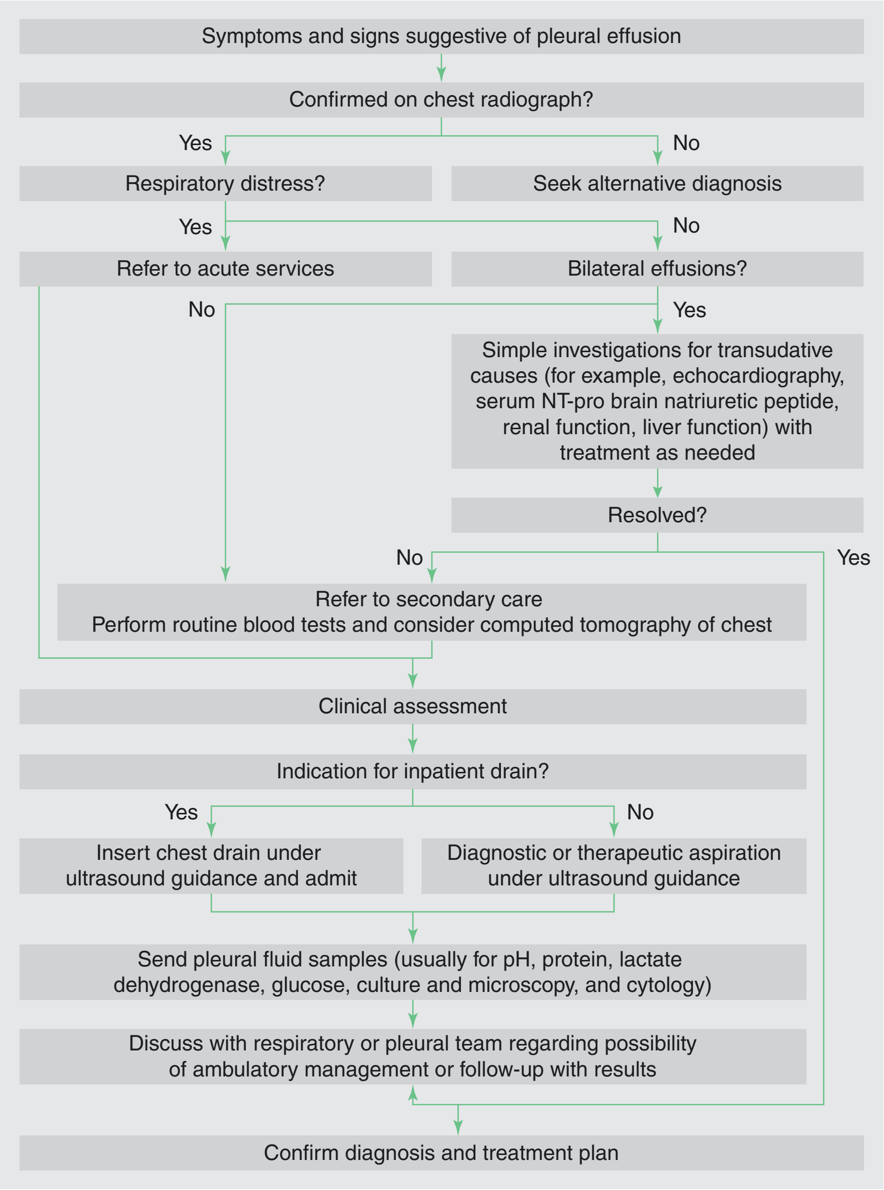


Fig. 15.1 Suggested algorithm for the early investigation of suspected pleural effusion [2]. (Permission granted by BMJ Publishing Group)

radiographically apparent effusion on chest imaging [16]. The goal of any initial evaluation in a suspected pleural malignancy is to obtain sufficient clinical and radiological information in order to inform suitable diagnostic tissue biopsy sampling, tumour staging and targeted treatment [30]. Pleural cytology has a mean sensitivity of 60%; however, yield depends upon the underlying tumour, sample preparation and pathologist experience [26]. Tumour cells tend to metastasise through the ipsilateral visceral pleura via the pulmonary vessels, and secondary dissemination of the parietal pleura occurs by seeding along adhesions in the pleural fluid [26].

Up to 70% of exudative pleural effusions will have malignancy confirmed with histological analysis [38]. Lung cancer, breast cancer and lymphoma are the commonest causes of malignant pleural effusion. It has been estimated that as many as 100,000 patients per year who have been diagnosed with lung cancer will go on to develop a pleural effusion with associated poor quality of life, affecting morbidity and mortality [16]. Malignant pleural mesothelioma is the most common type of primary pleural malignancy associated with a malignant pleural effusion [26]. The incidence of all-cause pleural malignancy continues to rise despite tumour type due to an ageing population with greater comorbidity [14]. There remains a steady increase in the number of confirmed lung cancer and malignant pleural mesothelioma cases, with presentation at stage IV remaining our biggest challenge [22].

Tumour Staging

The majority of malignant pleural effusion is caused by metastatic disease, and most commonly associated with lung cancer in men [26]. Modern lung cancer strategies continue to improve, and accurate tumour staging remains an essential element of such lung cancer management and prognostication. The globally validated TNM system considers anatomical spread of cancer by factors of tumour size and invasion, extent of lymphatic spread and presence of metastatic disease, and it informs multidisciplinary strategies for both clinical and surgical staging investigations and appropriate treatment strategies [37].

The International Association for the Study of Lung Cancer (IASLC) staging and prognostic factors committee examined data from 94,708 cases of lung cancer from around 16 countries around the globe. After exclusions, 70,967 cases of NSCLC and 6189 cases of SCLC were analysed to inform the eighth edition of the TNM classification for lung cancer. Updated descriptors and categories led to the migration of certain TNM subsets based upon survival analysis [9]. In terms of malignant pleural mesothelioma, data from 1987 patients across 29 centres was analysed. This comprised of 509 cases with only clinical staging information, 836 cases with only pathological staging information and 642 cases with both clinical and pathological information available [35] (Fig. 15.2).

Imaging

It is essential to confirm the aetiology of a pleural effusion in order to provide the most clinically appropriate and timely treatment. The role of imaging is firmly established in the workup of a suspected malignant pleural effusion [26]. It is known that malignant infiltration of the pleura is common across a number of different

Primary tumour (T)	**Lung cancer**	**Primary tumour (T)**	**Mesothelioma**
Tx	Primary tumour cannot be assessed or tumour proven by presence of malignant cells in sputum or bronchial washings but not visualised by imaging or bronchoscopy	Tx	Primary tumour cannot be assessed
T0	No evidence of primary tumour	T0	No evidence of primary tumour
Tis	Carcinoma in situ		
T1			
T1a (mi)	**Minimally invasive carcinoma**	T1	Tumour limited to the ipsilateral parietal pleura with or without diaphragmatic pleural involvement
T1a	**Tumour ≤1 cm in greatest dimensions**		
T1b	**Tumour >1 cm but ≤2 cm in greatest dimensions**	T1a	No involvement of visceral pleura
T1c	**Tumour >2 cm but ≤3 cm in greatest dimensions**	T1b	Tumour involvingvisceral pleura
T2	Tumour >3 cm but ≤**5 cm** or tumour with any of the following features: - **Involves main bronchus regardless of distance from the carina but without involvement of the carina** - Invades visceral pleura - **Associated with atelectasis or obstructive pneumonitis that extends to the hilar region, involving part or all of the lung**	T2	Tumourinvolving each of the ipsilateral pleural surfaces (parietal, diaphragmatic and visceral pleura) with at least 1 of the following: - Involvement of the diaphragmatic muscle - Involvement of tumour from the visceral pleura into the underlying pulmonary parenchyma
T2a	Tumour >3 cm but ≤4 cm in **greatest dimension**		
T2b	Tumour >4 cm but ≤5 cm in **greatest dimension**		
T3	Tumour >5 cm but ≤7 cm in **greatest dimension** or associated with separate tumour nodule(s) in the same lobe as the primary tumour or directly invades any of the following structures: chest wall (including the parietal pleura and superior sulcus tumours), phrenic nerve, parietal pericardium	T3	Locally advanced but potentially respectable tumour; tumour involving all of the ipsilateral pleural surfaces (parietal, mediastinal, diaphragmatic, and visceral pleura) with at least 1 of the following: - Involvement of the endothoracic fascia - Extension into the mediastinal fat - Solitary, completely respectable focus of tumour extending into the soft tissue of the chest wall - Nontransmural involvement of the pericardium

Fig. 15.2 Combined TNM staging from (**a**) the eighth edition of TNM classification for lung cancer (Goldstraw et al. [9]) and (**b**) eighth edition AJCC/UICC staging for malignant pleural mesothelioma [35]. (Produced with permission from Elsevier and Thorax respectively)

T4	**Tumour >7 cm in greatest dimension** or associated with separate tumour nodule(s) in a different ipsilateral lobe than that of the primary tumour or invades any of the following structures: **diaphragm**, mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, oesophagus, vertebral body, and carina	T4	Locally advanced, technically unresectable tumour; tumour involving all of the ipsilateral pleural surfaces (parietal, mediastinal, diaphragmatic, and visceral pleura) with at least 1 of the following: - Diffuse extension or multifocal masses of tumour in the chest wall, with or without associated rib destruction - Direct diaphragmatic extension of the tumour to the peritoneum - Direct extension of the tumour to the contralateral pleura - Direct extension of the tumour to a mediastinal organ - Direct extension of the tumour into the spine - Tumour extending through to the internal surface of the pericardium with or without a pericardial effusion or tumour involving the myocardium
Lymph node involvement (N)	**Lung cancer**	**Lymph node involvement (N)**	**Mesothelioma**
Nx	Regional lymph nodes cannot be assessed	Nx	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis	N0	No regional lymph node metastasis
N1	Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension	N1	Metastases in the ipsilateral bronchopulmonary, hilar or mediastinal (including the internal mammary, peridiaphragmatic, pericardial fat pad or intercostal lymph nodes) lymph nodes
N2	Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)	N2	Metastases in the contralateral mediastinal, ipsilateral or contralateral supraclavicular lymph nodes
N3	Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)	-	-
Distant metastases (M)	**Lung cancer**	**Distant metastases (M)**	**Mesothelioma**
M0	No distant metastasis	M0	No distant metastasis
M1 Mla **M1b** **M1c** ***NB: Changes to the seventh edition are in bold.***	Distant metastasis present Separate tumour nodule(s) in a contralateral lobe; tumour with pleural or pericardial nodule(s) or malignant pleural or pericardial effusion **Single extra thoracic metastasis** **Multiple extra thoracic metastases in one or more organs**	M1	Distant metastasis present

Fig. 15.2 (continued)

tumour types; however, pleural burden in the setting of lung cancer remains the highest incidence and often indicates an overall poor prognosis. Confirming malignant pleural disease in any setting can be challenging for practitioners and requires appropriate clinical examination, targeted chest radiographic techniques and timely referral. Pleural disease burden represents a significant challenge to both patients and healthcare resources in such a demanding economic environment.

Various imaging modalities are available to help guide diagnosis and optimise ongoing management strategies in pleural burden. Whilst there are several available imaging techniques, a posterior-anterior chest radiograph (CXR) remains the primary imaging method in an initial survey, often providing early indicators within initial tumour staging [33]. Pleural effusions may be radiologically apparent as blunting of the costophrenic recess on a chest radiograph with as little as 200mls of fluid and pleural deposits or thickening may be seen. Up to 15% of patients with lung cancer will have a demonstrable pleural effusion on chest radiograph at diagnosis [16]. Further diagnostic evaluation of the pleura will require the application of other imaging modalities such as thoracic ultrasound, computed tomographic (CT) scans of the thorax and abdomen, magnetic resonance imaging (MRI) and F-18-fluorodeoxyglucose positron emission tomography (FDG-PET) in order to detect thickened pleura or the malignant invasion of underlying structures.

Contrast-enhanced CT scanning is the current gold standard imaging modality for the pleura when seeking a diagnosis in a newly discovered pleural effusion; it may not only reveal a primary tumour, pleural thickening or nodularity but also may identify potential biopsy targets [2]. However, CT is not perfect, and data suggests that this modality will not demonstrate definitive evidence of malignancy in up to one in three patients with a pleural malignancy. Therefore, careful follow-up and assessment of suitability for further invasive diagnostic investigation depending upon performance status may be indicated if malignant radiological characteristics are not identifiable [26].

As in all areas of medicine, improving safety within invasive thoracic investigations is essential. The National Patient Safety Agency [11] undertook a review of 12 deaths and 15 cases of serious harm following pleural intervention. Common themes were identified around level of experience, supervision, site of intervention, anatomical anomalies and inadequate imaging. The report suggested that trainees should consider certain variables for pleural intervention including timing, training and familiarity of equipment, and it *strongly advised* the use of thoracic ultrasound for pleural intervention. The NPSA reports recommendation was mirrored by the British Thoracic Society pleural guidelines, whose evidence concur that ultrasound guidance will both increase the likelihood of success and reduce the risk of organ puncture in pleural intervention [10].

Much data exists suggesting thoracic ultrasound is a highly specific and sensitive tool used within imaging of the pleura. Thoracic ultrasound provides pleural teams with an instantly available imaging modality of increased sensitivity when quantifying and detecting pleural fluid in comparison to that of a plain chest radiograph alone. The discovery of pleural or diaphragmatic thickening and nodularity on thoracic ultrasound is highly specific for malignancy and can inform timely investigation into suspected malignancy [26]. The use of thoracic ultrasound is now commonplace in modern pleural management, and its diagnostic role in pleural burden extends beyond the identification of safe aspiration of fluid [10]. Ultrasound is not only more sensitive in detecting pleural fluid to help guide pleural drainage techniques and pleural-based masses, pleural thickening or nodularity is also easily visualised to improve reliability within the acquisition of targeted pleural biopsies [16]. Thoracic ultrasound guidance is well known to improve the rate of successful pleural intervention and reduce the risk of complications, with a sensitivity and specificity of 76.6% and 60.3% when compared to clinical judgement versus ultrasound, respectively [10].

Thoracic imaging modalities in pleural malignancy may confirm the presence of a non-expandable or trapped lung, suggesting an inability of the lung to expand normally within the pleural space [3]. Such radiological diagnoses of pleural burden combined with the subsequent discovery of malignant cells within the parietal pleura and pleural fluid reflect disseminated disease and poor performance status. Overwhelming symptomatic dyspnoea is described as the commonest symptom in this setting, reflecting a reduced compliance of the chest wall, depression of the ipsilateral diaphragm, mediastinal shift leading to a reduction in lung volume and impaired ventilation [27] (Fig. 15.3).

Patients with such extensive pleural burden often present in a debilitated state with a myriad of disabling symptoms including cough, chest discomfort, poor appetite, weakness and lethargy. Abnormal thoracic imaging can require a number of diagnostic and therapeutic strategies using invasive techniques such as thoracentesis, intercostal chest drain insertion, thoracoscopy and targeted pleural biopsy depending upon performance status and overall prognosis [18].

Prognostication

Many factors are used to predict overall survival in malignant pleural disease burden with the decision to offer pleural intervention depending upon the patients wishes, presence of symptoms and mean survival rate. Prognostication in malignant pleural disease depends upon a number of variables, and an individualised approach to predicting survival should be taken. Appropriate patient selection is vital, and it is essential that any pleural procedures are carried out in the patients' best interest and not just because of technical possibility [3]. Treatment options are often determined by symptoms, performance status, tumour type and its response to systemic therapy and the degree of expansile lung [27].

It is known that a malignant pleural effusion represents advanced metastatic disease, and data suggests a median survival of 3–12 months, dependent upon a number of individual factors, with the shortest recognised survival time commonly observed in those malignant effusions secondary to lung cancer [4, 15, 27]. Research suggests that a massive pleural effusion is associated with a worse prognosis, independent of age or histological tumour type, and survival time is worse in all stages of lung cancer [38].

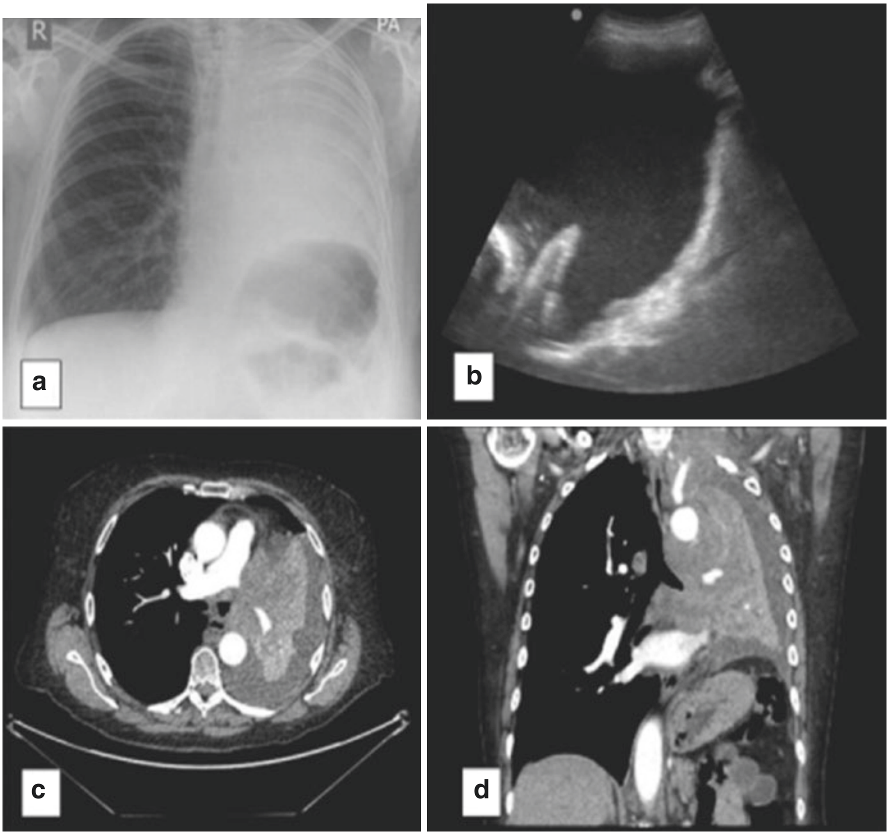


Fig. 15.3 (**a**) Chest radiograph showing complete whiteout of the left hemithorax. The central location of the trachea concurs with the presence of underlying lung collapse and pleural effusion. (**b**) Thoracic ultrasound showing an echogenic pleural effusion, diaphragmatic inversion and nodularity. Transverse (**c**) and coronal (**d**) computed tomography images confirming complete left lung collapse and an associated pleural effusion. (Produced with permission from Wilczynska and Davies [34])

A large number of mainly retrospective studies have examined factors determining prognosis. Analysis of demographics, pathological tumour type, symptoms, performance status and markers of inflammation have been examined in an attempt to determine accurate prognosis when guiding management [35]. The retrospective data consistently demonstrated that performance status was an independent predictor of survival in malignant pleural disease allowing appropriate selection for palliative management; however, there was a need for wider research [38]. Chest wall pain and weight loss have also been examined as prognostic variables in malignant pleural mesothelioma, and both were independently associated with poorer overall survival and the recent mesothelioma guidelines recommending the use of prognostic scores at diagnosis [35].

Clive et al. [4] provided the largest series of prospective prognostication data to inform their LENT predictive tool. Data were obtained from 221 patients from the UK, the Netherlands and Australian cohorts, and survival analysis was examined. The data found a wide range of median survival, with a 74-day median survival in the lung cancer group when compared with 339 days in the malignant pleural mesothelioma group. A clinical risk score was created to help predict survival and guide management in those with a malignant pleural effusion. The LENT score examined four key variables inclusive of pleural fluid lactate dehydrogenase (LDH), eastern cooperative oncology group (ECOG) performance status, serum neutrophil to lymphocyte ratio (NLR), and histological tumour type. The combined LENT prognostication score risk stratified patients into low-, medium- and high-risk groups with a median (IQR) survival of 319, 130 and 44 days, respectively. Again, those with lung cancer commonly fell into the highest-risk category, and systemic inflammation was an important risk factor. A higher LENT score was found to be associated with a worse overall prognosis, and combined scoring was found to be statistically superior to that of performance status alone [4].

Validated prognostic scores are easy to calculate and can often help inform clinicians when considering suitability for pleural intervention. Pleural drainage may not offer an overall survival benefit; however, any subsequent interventions should be aimed at relieving disabling respiratory symptoms and improving quality of life. Therapeutic pleural drainage can rapidly improve performance status thus having a positive effect upon quality of life in patients with advanced malignancy. It is well reported that symptomatic malignant pleural effusion represents an advanced metastatic disease, and given the continued rise in new cancer diagnoses, the pleural burden for the patient often remains high [4]. In terms of prognostication, when expected survival is short, a less-invasive and palliative-focused end of life approach is preferred [38].

Pleural Management Strategies

Modern oncological treatments are more advanced, and accurate prognostication at presentation may help individualise treatment strategies [4]. Pleural disease is recognised as an important subspecialty within respiratory medicine, and more recently there has been a paradigm shift from the traditional surgical approach to a more medically and patient focused perspective. Historically, patients with malignant pleural disease were often managed conservatively, whereas more recently patients presenting with a suspected pleural malignancy are now “genotyped, phenotyped and treated on an ambulatory basis” [26].

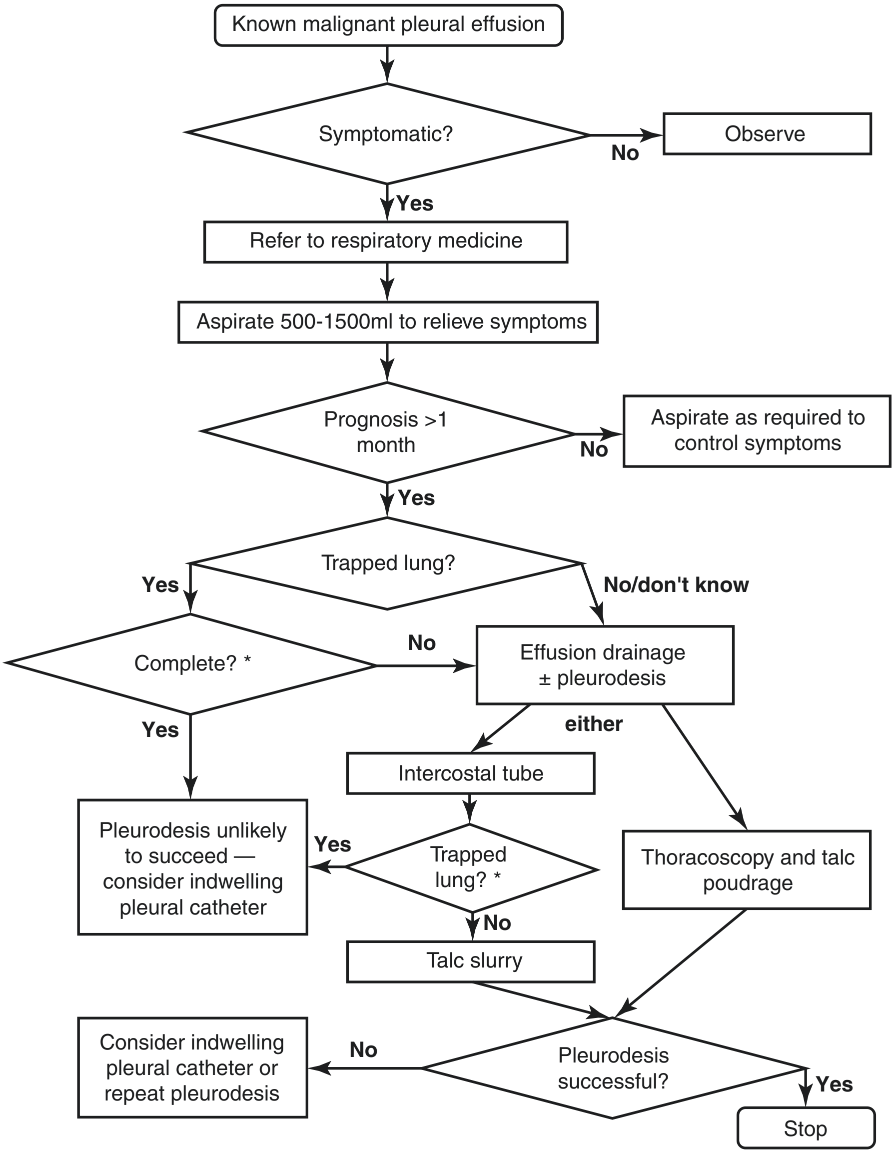
Specialist pleural teams are in a position to offer patients who have traditionally needed extended admissions, more timely pleural intervention in an ambulatory setting. Not only does this approach demonstrate improved patient safety, it also has positive effects upon waiting times, admission duration and overall bed day costs. Hospital pleural teams are truly multidisciplinary usually with a lead respiratory consultant with an interest in pleural disease management at its core. A clinical nurse specialist is essential for holistic needs assessments and advance care planning, research and, more recently, many have developed practical skills within thoracic ultrasound and autonomous pleural intervention. A successful pleural service depends upon the support of a wide array of specialist services across oncology, radiology, pathology, nursing, clerical and surgical teams. Pleural teams are in an excellent position to streamline care and enhance a patient-focused pathway, and such specialist review not only informs early diagnoses and prognosis but also provides rapid therapeutic intervention whilst strengthening practical training across specialities [1]. Enhancing pleural disease pathways however remains dependent upon the availability of pleural facilities available within individual organisations [3].

Guidelines suggest that a malignant pleural effusion is best managed through complete pleural drainage and instillation of a sclerosant to promote pleurodesis to prevent reaccumulation or by the insertion of a more permanent device to enable repeated community drainage [27]. The Clive et al. [5] Cochrane meta-analysis examined 62 studies involving 3248 patients to try to determine the optimal management for adults with a malignant pleural effusion in terms of pleurodesis success [5]. They examined administration of a pleurodesis agent using a chest tube or thoracoscopy and indwelling pleural catheters. The outcome suggested that talc poudrage following medical thoracoscopy appeared to be the most effective method of preventing fluid reaccumulation; however, patient-centred outcomes including side effects, quality of life and patient satisfaction were inconsistently reported calling for wider research in this area [5] (Fig. 15.4).

Patient presentation and the subsequent urgency of intervention for a pleural effusion will always depend upon the magnitude of pleural burden, the rate of fluid accumulation and the patients underlying respiratory reserve [2]. The majority of patients with malignant pleural disease, especially in those with a massive pleural effusion, will be symptomatic, and modern guidance advocates timely and definitive management strategies over repeated thoracentesis [24]. Patients should always be offered an initial therapeutic procedure to assess both symptomatic improvement and rate of fluid reaccumulation before considering patient-focused definitive management [26]. If the patient does not gain relief from pleural drainage, then further invasive management is rarely indicated, and a more supportive, palliative care-based approach should be taken. Any informed treatment decisions should always be patient-centred and recommendations should be based upon performance status, burden of symptoms and expected survival times using evidence-based prognostication [3, 4, 27, 35].

Observation

All patients presenting with a unilateral pleural effusion should have timely and appropriate investigations to exclude malignancy, and pleural investigations for bilateral pleural effusion may be considered if there are atypical features or a failure to respond to initial therapy [10]. Standard blood tests can be helpful to assess for the presence of co-existing infection or blood loss, and they also help evaluate cardiac, renal and hepatic function in order to inform differential diagnoses [2]. Observation is rarely indicated in the setting of confirmed malignancy as most



* There is no evidence as to what proportion of unapposed pleura prevents pleurodesis. We suggest that <50% pleural apposition is unlikely to lead to successful pleurodesis

Fig. 15.4 Management algorithm for malignant pleural effusion [27]. (Produced with permission from BMJ Publishing Group Ltd. & British Thoracic Society) patients with a radiologically apparent pleural effusion will have presented with significant symptoms of breathlessness and cough, with a number experiencing disabling chest pain due to disseminated pleural malignancy. Howevere, there are a small proportion of patients in whom pleural disease is found incidentally upon routine chest imaging, and they may describe minimal symptoms. In those with a confirmed malignant pleural effusion, observation may be recommended if a patient is asymptomatic and the tumour type is known; however, most patients should be offered early follow-up and be made aware of the available treatment options for definitive pleural intervention as most will become symptomatic over time [27].

Thoracentesis

Thoracentesis or pleural aspiartion is defined as a minimally invasive, sterile procedure, whereby a needle or catheter is inserted through the subcutaneous tissues of the thorax, over the superior surface of the rib, avoiding the intercostal neurovascular bundle, through the parietal pleura and into the pleural cavity in order to obtain a pleural fluid sample. This is usually the first-line enquiry when investigating an unexplained unilateral pleural effusion or persistent bilateral pleural effusion. In those patients presenting with larger pleural effusions in the setting of a known malignancy, both a diagnostic and therapeutic approach is also required, not only to confirm if the histological cell type is related to a known malignancy or if a synchronous primary exists. The risks of thoracentesis include bleeding, infection, pneumothorax and visceral injury, but these risks are reduced with an experienced operator or an appropriately supervised trainee. With re-expansion pulmonary oedema after the removal of larger volumes of fluid, however, the risk is low [26]. The safety of pleural intervention will be further enhanced through the use of point-of-care thoracic ultrasound, leading to a greater chance of success within both diagnostic aspiration and therapeutic drainage of larger volumes [2]. The primary aims of thoracentesis in this setting are to both secure a pathological tissue diagnosis and alleviate any disabling symptoms that a pleural effusion may cause.

The sensitivity of a cytological yield following thoracentesis in a suspected malignant pleural effusion often depends upon the underlying malignancy but in diagnostic terms, pleural sampling may give rise to an overall initial diagnostic sensitivity in up to 60% of cases [27]. Histopathological analysis of pleural fluid in lung adenocarcinoma may have a 78% yield, whereas confirmation of mesothelioma and squamous cell carcinoma represents 27% and 25%, respectively [25]. Conversely, there are also a small number of patients with lung cancer in whom microscopic pleural analysis actually excludes a metastatic pleural malignancy, in which case it is recommended that the pleural effusion is excluded as an M1a staging descriptor [9]. The diagnosis of a malignant pleural mesothelioma from cytological pleural fluid testing is known to be highly variable, ranging from 16% to 73%, with immunohistochemistry from a pleural biopsy shown to give a more consistent yield in the mesothelial subtypes of epithelioid, sarcomatoid and biphasic mesothelioma. Although lung cancer is reported to be associated with short median survival times, non-epithelioid histology in the setting of malignant pleural mesothelioma is also associated with a significantly shorter overall survival [35].

Histological confirmation in all-cause malignancy within the pleura or pleural fluid represents advanced disease and presents practitioners with complex management challenges around early symptom control, prognostication and choice, in terms of suitability for definitive pleural management. This patient group have a high burden of disease with a worse prognosis and minimal life expectancy with a deteriorating performance status. Repeated therapeutic thoracentesis is only usually recommended for those with chemotherapy-sensitive tumours such as SCLC and lymphoma to enable early treatment or in those obviously at the end of life [26]. A more definitive approach is usually preferred in all tumour types to enhance longer-term symptomatic relief and reduce the risk of pleural adhesions that may complicate thoracoscopic poudrage or indwelling pleural catheter insertion at a later date.

Intercostal Chest Drain

Small-bore Seldinger tube drains are traditionally used in the drainage of malignant pleural effusions allowing subsequent insertion of sterile-graded talc as a sclerosant to aid pleurodesis. Chest drains for pleural effusions are inserted using point-of-care thoracic ultrasound, and larger effusions should be drained in a controlled manner in order to reduce the risk of re-expansion pulmonary oedema. The insertion of talc slurry into a chest drain is thought to cause an acute inflammatory response through the local activation of the coagulation cascade and fibrin deposition [27]. Successful pleurodesis is defined as fusion of the parietal to visceral pleural with resulting obliteration of the pleural space [26]. The most important requirement that informs the potential effectiveness of pleurodesis is a radiologically confirmed apposition of the parietal and visceral pleura. Incomplete expansion may be caused by pleural thickening in a non-expandable or *trapped* lung, and proximal large airway obstruction from tumour or persistent air leaks are known to be associated with pleurodesis failure [27]. Intercostal chest drains play an important part in the management of pleural effusions; however, they are usually associated with prolonged hospital stays of between 4 and 7 days for talc pleurodesis [26] and a greater risk of complications including unintentional displacement, persistent air leaks, and interpleural infection. Although more modern pleural intervention has largely replaced the standard use of Seldinger drains, they still play a part in those decompensated patients presenting an emergency with a massive pleural effusion requiring urgent pleural intervention.

Thoracoscopy

Thoracoscopy either under sedation or general anaesthesia is the investigation of choice for the diagnosis of a suspected malignant exudative pleural effusion in those with inconclusive pleural cytology [10]. It is also useful for complete pleural drainage and talc poudrage in those with a better performance status and a confirmed malignant pleural effusion, and it is associated with a more successful chance of pleurodesis in around 80–90% of patients [10, 27]. The ultrasound-guided procedure involves the introduction of an induced pneumothorax followed by complete drainage of pleural fluid, acquisition of fluoroscopic pleural biopsies and, finally, directly visualised talc poudrage in the majority of patients. An overnight admission is usually required in order to reinflate the induced pneumothorax; however, larger centres have demonstrated shorter stays with the use of portable suction devices.

The more invasive, surgical video-assisted thoracoscopy that is performed under general anaesthesia and requires single lung ventilation. It remains appropriate in a subset of patients with benefits demonstrated in those with smaller pleural effusions containing more septations and adhesions [29]. The overall advantage, however, is that the surgeons are in a better position to proceed with other thoracic surgical options at the time of procedure if deemed appropriate [10]. The alternative approach of local anaesthetic thoracoscopy performed by respiratory physicians under sedation, when compared to surgical video-assisted thoracoscopy, is an increasingly available alternative offering a similar diagnostic sensitivity of 92.6% in comparison to 95%, respectively [2, 10]. Thoracoscopy is a safe and well-tolerated procedure in carefully selected patients, it has a low perioperative mortality rate of <0.5% [27], and major complications such as empyema, haemorrhage and pneumonia are rare [10].

Indwelling Pleural Catheter

Traditionally, patients presenting with a suspected pleural effusion would be admitted to a secondary care facility for a battery of diagnostic investigations and extended therapeutic intervention; however, changes in attitudes and technology now facilitate an ambulatory care model in this setting [2].

Fenestrated indwelling silicone pleural catheters are now commonplace in the developed world, and although traditionally only recommended for those with an underlying non-expandable or trapped lung, or failed pleurodesis, there has been a shift towards their first-line use as an alternative to pleurodesis following the TIME-2 trial [3, 6]. Patients may wish to minimise the time spent in hospital by choosing an indwelling pleural catheter over attempted pleurodesis given median predicted survival times of just 44 days (Clive et al. [4]). Indwelling pleural catheters were reported to improve breathlessness when compared to talc slurry pleurodesis, despite lower pleurodesis success rates (Clive et al. [5]; Fig. 15.5).

Tunnelled catheters are inserted as a day case using point-of-care ultrasound guidance, allowing community drainage with the cost-effective devices [16]. Complications following insertion are rare but may include pain, pneumothorax and infection due to tunnelling, with many centres advising prophylactic antimicrobials immediately following insertion. Smaller-scale studies suggest that tunnelled catheters are safe in chemotherapy [2]. Patients or family members can be trained using

Fig. 15.5 (**a**) Patient in position whose skin has been marked for ultrasound-guided insertion of indwelling pleural catheter. (**b**) Indwelling pleural catheter in situ

drainage bottles that are attached to the one-way valve, and community nurses and palliative care teams are in a valuable position to offer ongoing support.

The most commonly reported symptom when established tunnelled catheters is pain during drainage. However, this can be easily managed by administrating pre drainange opiate analgesia and ensuring controlled pleural drainage. Spontaneous pleurodesis will occur in between 50% and 70% of cases, and this can be measured by radiological confirmation and the absence of pleural fluid following which the catheter may be removed (Mishra et al. [16]). Indwelling pleural catheters are highly suitable for use in patients with symptomatic malignant pleural disease, lung entrapment, poorer performance statuses and higher LENT prognostic scores.

Conclusion

In summary, classifying the underlying aetiology of pleural burden is vital to inform tumour staging, prognostication and therapeutic intervention strategies. Despite novel advances within histopathologic subtyping and therapeutics, many patients develop with advanced and incurable lung cancer requiring a palliative approach. Patients are more commonly presenting with stage III and IV disease at an older age and with multiple pre-existing comorbidities [13]. The majority of patients with malignant pleural disease will be symptomatic, and modern guidance advocates timely and definitive pleural strategies. Patients with disseminated pleural disease in suspected or confirmed thoracic malignancies will often have disabling symptoms requiring early specialist therapeutic intervention. Despite whichever pleural management approach is chosen, a supportive holistic assessment is always recommended to explore the patient's wishes, and support them with their ability to cope both physically and psychologically with intervention and the timing of recovery [3, 15, 19].

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Gastric Cancer

16

Helena Sofia Azevedo de Oliveira Magalhães

Abstract

The treatment of patients with gastric cancer requires a multidisciplinary clinical perspective in which the nurse plays a very important role. Caring for the gastric cancer patient poses enormous challenges to the nurse, requires constant scientific updating and evidence-based practice, as well as a strong patient/family involvement, making him/his family an active participant throughout the process.

Keywords

Gastric cancer · Treatment · Nurse role

Survival

According to Allemani et al. [1], for most cancers, 5-year survival rates remain among the highest in the world in the USA and Canada, in Australia and New Zealand, and in Finland, Iceland, Norway, and Sweden.

For gastrointestinal cancers, the highest levels of 5-year survival rates are seen in Southeast Asia: in South Korea for cancers of the stomach (68.9%), colon (71.8%), and rectum (71.1%); in Japan for esophageal cancer (36.0%); and in Taiwan for liver cancer (27.9%).

Despite this cancer survival rate increase in the world, there are still large asymmetries that can probably be attributed to some degrees of inequality in access to diagnostic and treatment services.

H. S. A. de Oliveira Magalhães (✉)
Day Hospital of Hemato-Oncology, Portuguese Oncology Institute, Lisbon, Portugal
e-mail: hmagalhaes@ipolisboa.min-saude.pt

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Globally, for stomach cancer, survival rates remain low, despite the big investments that have been made at diagnosis and treatment levels.

Risk Factors

Stomach cancers are related to several risk factors, such as environmental ones and lifestyles, namely, *H. Pylori* bacterium gastric infection, diets high in salt, smoking, high alcohol consumption, low vegetable consumption and high consumption of preserved foods, overweight and obesity, sedentary lifestyle, and some genetic predispositions.

Therapeutic Modalities

Most stomach cancers are diagnosed only at an advanced stage as, initially, patients do not have specific symptomatology.

The symptoms may include weight loss, early satiety, dysphagia, dyspepsia, vomiting, and iron deficiency anemia.

The diagnosis and staging are fundamental to implement the most appropriate treatment. The decision about what treatment to apply is made by a multidisciplinary team.

The treatment is different depending on the stage of the tumor and the conditions of the patient. According to Smyth et al. [6]:

Surgery resection is potentially curative, at early stages, although many patients suffer a relapse after surgery. Therefore, the use of combined treatments is increasingly recommended.

Perioperative (before and after surgery) **chemotherapy** with a platinum/fluoropyrimidine combination is recommended for patients with resectable gastric cancer. Clinical trials have demonstrated an increase in patient survival when compared to surgery alone.

Adjuvant chemotherapy to patients undergoing surgery without prior administration of chemotherapy, postoperative chemoradiotherapy, or adjuvant chemotherapy is recommended.

Chemotherapy is also used to treat people at **advanced stages**. In this case, the intention is only palliative.

Nurse Role

The Nursing Consultation aims to teach and advise on the proposed treatments, reconciling them with the patient's needs assessment and consequent nursing diagnoses.The main objectives of the Nursing Consultation are the clarification of doubts related to the therapeutic proposal presented and practical aspects associated with each treatment – including location, duration and periodicity, some possible side effects, and guidance on the contacts and/or resources to be used.

Most patients undergo chemotherapy on an outpatient basis, without the need for hospitalization.

The advantages of the outpatient clinic are the reduction of infections associated with healthcare, reduction of hospital costs, and especially the possibility of the patient maintaining his social and family standards with greater independence and quality of life.

Patient-centered care entails sharing responsibility for self-care and therapy follow-up, along with the tools and support they need to carry out that responsibility and ensure that transitions between care providers, departments, and institutions are respected, coordinated, and efficient (Cooley et al. [4]).

The nurse has the very fundamental role of empowering the patient to make him manage and control his symptoms and promote his own participation in the care.

Nurses, because of their proximity, play a key role in teaching and monitoring the patient.

Different forms of chemotherapy administration, with more comfort for the patient and the same safety levels, have been used, namely, the possibility of the patient doing chemotherapy through disposable elastomeric infusion pumps, oral chemotherapy, or subcutaneous chemotherapy.

The disposable elastomeric infusion pumps allow the accurate continuous infusion of chemotherapy, do not require a battery, promote the autonomous mobility of the patient, and reduce the risk of infections associated with healthcare (Siqueira et al. [5]).

It is essential for the nurse to explain to the patient how the device works, the side effects of the drug, and all the warning signs that should lead him to contact the care team.

The device requires some care, namely, the elastomeric infusion pumps should be protected inside a plastic bag during showers; the wire should always be close to the body, without being twisted; and the air bleed filter and the infuser end should both be kept dry, making sure that the clamp belonging to the needle does not interrupt the flow. It should be checked daily if the elastomeric membrane is getting loose. It's also important to check for accidental leaks and being careful to not misadjust the infuser of the needle extension.

Oral chemotherapy has been in increasing use because it has advantages for the patient, such as reducing travels to the hospital, reducing the number of punctures needed and promoting greater independence. Due to specific care and associated toxicities levels regarding the use of this therapies, it requires some patient education, and that the nursing team do some signal monitoring and check patient symptoms carefully. It is very important that nurses follow up the patients with oral antineoplastic therapies in order to promote adherence to therapy and self-care. Educating the patient and promoting adherence to therapeutics are key nursing interventions (Torcato [7]).

Some patients still devalue oral chemotherapy a bit, referring to fears that it is not as effective or omitting some shots.

The success of oral chemotherapy depends on the patient a lot – co-responsibility – it's important to make sure that the right dose of the drugs is taken at the right time. Any questions or doubts should always be presented to the cancer care team (American Cancer Society [2]).

Although the patient is usually engaged in its recovery process, the impact of the diagnosis causes a variety of feelings, perceived as doubts and uncertainty and making most patients feel their life and comfort are threatened. There is a lot of new information that is not always possible for them to assimilate. Finding support on a person of reference is very important, and it also has the function of helping the patient in the fulfillment of the treatments and in his life activities. The caregiver will be the link between the nurse and the patient and should always be informed of the likely potential effects of all the used medication as well as the strategies to be implemented to minimize them. The caregivers should be told to contact the healthcare team whenever they have questions about any symptoms or side effects that may bother the patient so they can help manage them.

Often patients, due to their fragility, seek and consume natural products such as antioxidant supplements, medicinal plants, and infusions aimed at protecting the immune system, hoping to combat the disease or minimize some effects of the treatments. However, some of these products may interfere with cancer treatments, altering their effectiveness and causing serious damage to the patient (Campos [3]).

Regarding surgery, and after clarifying with the health team exactly what type of surgery will be performed, along with its risks and how the recovery will be done, one of the key aspects that causes greater anxiety to both patients and their families is food. It is very important to clarify some aspects related to food because the doubts about the types of diet that should be followed are surely among those that cause greater distress to the patient and the caregiver.

Some of the surgery consequences will be a lesser ability to regulate the passage of food to the intestine, causing dumping syndrome; decrease or absence of hydrochloric acid and digestive enzymes; some difficulty in digestion and proper absorption of food; B12 vitamin, iron, folic acid, calcium, and vitamin D deficiencies; and symptoms such as diarrhea, anorexia, early satiety, vomiting, nausea, malabsorption, hypoglycemia/hyperglycemia (characterized by tremors, palpitations, tachycardia sweats, and pallor), lack of appetite, weight loss, indigestion, and sometimes reflux.

All these consequences can be minimized through nutritional intervention and compliance with nutritional recommendations. The nurse, in conjunction with the nutritionist, should inform and advise patients on nutritional recommendations in order to provide good general health and prevent secondary complications.

Initial recommendations are to have smaller, more frequent meals – 6–8 daily. Patients should only eat small amounts of food the first times, increasing the amounts according to their tolerance. They should eat slowly, chewing food really well. After meals, they should get some rest for a few minutes, sitting or lying down.

Going from a liquid to a paste-like diet should also be done according to their tolerance. Patients can slowly move to a low-fat soft diet composed primarily of mashed food, in the form of puree, smoothies, and mashed vegetables. Their diet should be mostly liquid, and food must have an easily digestible consistency – soups with mashed meat or fish and mashed rice or pasta, milkshakes, yogurts, lactose-free or soy milk, and natural unsweetened fruit juices. After some time, patients can start eating foods with different consistencies, but their tolerance should always be assessed.

Initially, patients should ingest liquids 30 minutes before or after the meals; over time, small amounts of liquids can be taken during the meal (patients should not drink more than 100–200 ml each time). The intake of very sweet products is to be avoided, as should be the intake of any juices with added sugars. Natural fruit juices without any added sugar should be preferred. Vegetables should be gradually included in the diet, depending on patient's tolerance. Consumption of high-fat foods should only be made very moderately; the intake of cow's milk should be also avoided, and patients should opt for yogurts or soy milk or lactose-free milk. A good source of protein should be included at each meal, but the consumption of mainly insoluble fibers should be very moderate initially. At a posterior phase, the consumption of soluble fibers (peeled fruit, banana, rice) can be increased. Salt consumption should always be moderate too.

These recommendations are for the postoperative period, and the patient should be instructed to gradually introduce other foods of his liking, according to tolerance.

Diet guidance should always be individualized, considering tolerance, and adapted to each patient.

Conclusion

Treatment of the patient with gastric cancer strongly implies a multidisciplinary approach that involves the patient as an active element throughout the process and the use of scientific criteria and practices based on evidence.

There should be a constant concern not only about the patient's response to treatments but especially with his quality of life, during and after treatments. Both the caregivers and the nursing team must always have present what should be best for the patient.

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Pancreatic Cancer

17

Chulja J. Pek

Abstract

Epidemiology

Pancreatic cancer has a very poor prognosis, and its therapy is an interdisciplinary challenge. At the time of diagnosis, tumors are usually not eligible for resection, and chemotherapy results in terms of cure are disappointing.

Diagnostics

The abdominal CT scan is currently the golden standard for the radiological diagnosis of pancreatic cancer.

Treatment

Surgery is currently the only available treatment for pancreatic cancer with a chance of curing the patient. Neoadjuvant treatment is a promising novel strategy but is currently only being performed within a clinical trial setting.

Palliative Care

Palliative and/or supportive care is aimed at treating the multiple morbidity occurring in patients with pancreatic cancer. In many cases, palliative care is the only treatment option due to the late stage of diagnosis. A case manager which is accessible to the patient, family, general practitioner, and other professionals involved and who is familiar with the diagnosis and treatment from beginning to end offers trust, clarity, and continuity.

Keywords

Pancreatic cancer · Obstructive jaundice · Poor prognosis · Whipple procedure · Oncology nurse · Quality of life · Multidisciplinary approach

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C. J. Pek (✉)
HPB Surgery, Erasmus University Hospital, Rotterdam, The Netherlands
e-mail: c.pek@erasmusmc.nl

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Epidemiology

Pancreatic cancer has a very poor prognosis with a long-term survival rate of 1–5% [1], and its therapy is an interdisciplinary challenge [2].

Complete local resection combined with adjuvant chemotherapy for six months is currently the only curative treatment. Unfortunately, the overall survival with this treatment is only 15–20 months. Pancreatic carcinoma represents the fourth leading cause of cancer-related mortality in the western world with more than 100,000 deaths in Europe and the USA per year [3]. The majority of pancreatic cancers (85%) are adenocarcinoma of ductal origin. It is more common in men (men/woman 1,5:1) [4] between the age of 60 and 70 years. Pancreatic cancer can be divided in three stages: resectable (15%), locally advanced (35%), and metastatic disease (50%). Most pancreatic cancers occur in the head of the pancreas (60–70%). A minority is found in the body (5–10%) and tail (10–15%) [5]. At the time of diagnosis, a pancreatic head carcinoma is usually smaller than 3 cm, but in spite of their limited tumor size, the majority of pancreatic head cancers (85%) are not eligible for resection at the time of diagnosis. This is due to advanced local tumor extension or the presence of distant metastasis mostly due to liver metastasis or para-aortic lymphadenopathy [5]. Tumors of the pancreatic body and tail are usually much larger at the time of diagnosis, because they present late with nonspecific symptoms. These tumors are usually not eligible for resection. Tumors originating in the distal common bile duct or ampulla may also grow into the pancreatic head, and together with pancreatic head carcinoma, these tumors are often grouped together under the name periampullary tumors.

Cause

The causes of pancreatic cancer are not clearly identifiable, but research shows that pancreatitis, smoking, alcohol abuse, obesity, type 2 diabetes, gallstones and/or cholecystectomy and pancreatic cysts can increase the risk of developing pancreatic cancer. High risks are smoking, *Helicobacter pylori* infection, non-blood group, and obesity. Medium risks are type 1 diabetes, alcohol abuse, and chronic pancreatitis. Low risks are allergy, cholecystectomy, hepatitis-b infection, and family history [6].

Patients with hereditary pancreatitis have a high risk of developing pancreatic cancer. Other inherited genetic disorders cause about 10% of all forms of pancreatic cancer [4]. For example, 15–20% of the patients with hereditary melanoma have a high risk of developing pancreatic cancer, while Von Hippel-Lindau is considered a low risk.

Symptoms

If the pancreatic cancer is located in the head of the pancreas, the first symptom is usually obstructive painless jaundice. However, the very first symptoms may also consist of general and nonspecific complaints, such as overall malaise, fatigue, tension within the upper abdomen, pain in the epigastric region, steatorrhea, diarrhea, and debilitated blood sugar levels (hyperglycemia). Obstructive jaundice is jaundice resulting from an obstruction of the bile duct by a benign or malignant lesion (tumor). A pancreatic head tumor can obstruct the final part of the bile duct because the distal bile duct is anatomically situated in the head of the pancreas.

The symptoms of obstructive jaundice are very disabling and have a major impact on the quality of life. The yellowness is caused by high levels of serum bilirubin, and this is sometimes associated, when precipitating in the skin, with pruritus all over the body. High levels of bilirubin also cause a reactive gastritis accompanied by nausea, loss of appetite, and vomiting. Additional symptoms include acholic feces, dark-colored urine (like Coca-Cola), unintentional weight loss, fatigue, depression, and sleep disturbance [7].

Nursing Perspective

The symptoms in patients with pancreatic cancer are often complex, multifactorial, and challenging to manage [7]. The most common nursing problems with their causes and symptoms are summarized in the nursing diagnosis at the onset of the disease, in accordance with the methodology of the PES structure (North American Nursing Diagnoses Association, NANDA-1), in Table 17.1. The Nursing Intervention Classification [8] and the Nursing Outcome Classification [9] may be helpful to plan the nursing activities. Nursing activities are aimed at reducing the patient's burden, observing the course of the symptoms' progression and reporting any relevant changes. Supportive care should start at the time of the diagnosis. The wide spectrum of symptoms and the complexity of its management requires a multidisciplinary approach, in which the goals consist of both symptom relief and improving the quality of life [10].

Diagnostics

In case of jaundice, the first diagnostic step is performing an abdominal ultrasound. This test rules out bile stones as the cause for the jaundice. The treatment for bile stones is completely different from treating pancreatic tumors. If bile stones are ruled out and there is a suspicion of pancreatic or periampullary cancer because a

Table 17.1 Nursing diagnosis at onset of pancreatic cancer

Problem	Etiology	Symptoms
Fever	Cholangitis	Sweating
Dehydration	Fever, vomiting, diarrhea	Overall malaise, thirst
Loss of appetite	Biliary gastritis	Vomiting, pain, nausea
Thirst, nycturia	Hyperglycemia	Dry mouth, dry skin
Exocrine insufficiency	Diarrhea, steatorrhea	Fatty, sticky stool
Pruritis	Hyperbilirubinemia	Scratches, skin defects
Loss of weight	Malignancy	Gastrointestinal disorders
Gloom, fatigue	Depression	Insomnia
Pain	Tumor growth	Abdominal pain, backache

distal bile duct obstruction is present, the next step is performing a CT scan. It is recommended to perform a CT scan of the abdomen before any endoscopic interventions take place, because once the biliary tree has been manipulated, this might obscure the visualization of (small) tumors [11].

Laboratory

The laboratory findings for pancreatic cancer are usually nonspecific. However, in combination with imaging, high levels of tumor markers CEA and CA 19-9 (without dilated bile ducts) may contribute to an increased suspicion of pancreatic cancer [12]. Increased CA 19-9 serum levels are found in patients with pancreatic cancer but also with hepatocellular, ovarian, bronchial, colon, and gastric cancer as well as cholestatic disease, chronic pancreatitis, and other inflammatory diseases. Therefore, the sensitivity and specificity vary substantially but can be useful in the staging of the diagnosis of pancreatic cancer. Elevated CEA serum levels are also found in gastrointestinal cancers, such as colorectal and pancreatic cancers and in benign diseases such as peptic ulcer, pancreatitis, biliary obstruction, inflammatory bowel disease, and also among cigarette smokers [13].

Abdominal Computed Tomography (CT)

The abdominal CT scan is the golden standard for the radiological diagnosis of pancreatic cancer [14]. CT scanning should be performed before endoscopic retrograde cholangiopancreatography and the insertion of an endoprosthesis since artifacts and post-ERCP pancreatitis may hamper the diagnostic accuracy of the CT. A pancreatic carcinoma is a hypovascular tumor; it presents itself as a hypodense mass on the CT scan. The mass is usually ill-defined. In 10–15% of all cases, the tumor is isodense and as a result possibly difficult to detect. Tumors smaller than 2 cm may also be difficult to detect on a CT scan due to their small size. In these cases, indirect signs may be helpful to diagnose a pancreatic tumor, such as the presence of the double duct sign, atrophy of the pancreatic tail, or fullness of the pancreatic head (loss of the lobular appearance of the pancreatic parenchyma).

Magnetic resonance imaging of the pancreas (MRCP) is also a very sensitive tool for detecting a mass but offers no significant additional staging information; hence CT scanning remains the recommended test [14].

Endoscopic Ultrasound (EUS)

The EUS involves the insertion of a probe into the mouth and down into the stomach and duodenum. The tip of the tube has an ultrasound probe that transmits sound waves. These sound waves are recaptured by the probe and converted into images. EUS-guided fine needle aspiration (FNA) is safe and effective, especially for pancreatic head masses; however tumors in the body or tail of the pancreas should be conducted with caution for risk of seeding tumor cells [15]. EUS-guided

FNA has sensitivity and specificity similar to that of CT-guided FNA cytology (FNAC). EUS allows for very detailed imaging of the pancreas, as well as for performing a pancreatic biopsy at the time of the examination such as FNA or fine needle biopsy (FNB).

EUS has some risks of complications. The main complication related to this procedure is pancreatitis, ranging from 0.5% to 2% and rarely followed by abdominal pain, fever, infection, bleeding, and perforation (less than 1%). Complications caused by the sedation, which is used during the procedure, are mostly comprised of cardiac or pulmonary complications. Despite high sensitivity, specificity is rather limited, especially in the differential diagnosis of inflammatory processes [16].

Endoscopic Retrograde Cholangiopancreatography (ERCP)

This procedure is performed by a gastroenterologist using a thin and flexible scope. A wire with a chip at the tip of the scope transmits digital video images to a TV screen. The scope is inserted through the mouth, throat, esophagus, and stomach into the duodenum. Once the papilla of Vater is identified, a plastic cannula is passed through the endoscope into the bile duct or the pancreatic duct. After the procedure, the patient should remain in observation in the recovery area for 1–2 hours until the medication given has worn off.

Many patients in whom a pancreatic head tumor is detected by means of ultrasound still undergo an ERCP. Although ERCP has a high sensitivity for detecting pancreatic head tumors, it is nowadays no longer indicated as the diagnosis can usually be made using non-invasive tests. In addition to being invasive, ERCP offers no useful tumor staging information. It is doubtful whether preoperative bile duct drainage by ERCP is beneficial for the patient. Preoperative biliary drainage may potentially even increase the risk for postoperative infectious complications [17]. Nevertheless, some patients may benefit from preoperative relief of jaundice in case of untreatable pruritus, acute cholangitis, or renal dysfunction resulting from obstructive jaundice. Patients for whom the surgical procedure is delayed due to neoadjuvant therapy or logistical issues, the need of nutritional support and preoperative biliary stenting is also required. For preoperative biliary drainage, the use of self-expandable metal stents (SEMS) is preferred to plastic stents since SEMS are associated with significantly lower complication rates and stent dysfunction [18].

The most common complication to occur is post-ERCP pancreatitis as a result of the contrast agent that is added into the pancreatic duct and subsequently causes irritation of the pancreas. Other serious risks are perforation, anaphylactic shock, bleeding, or depressed breathing, but these complications are very rare. In case these complications should occur, the patient will need to be hospitalized for a few days.

Percutaneous Transhepatic Biliary Drainage (PTBD)

During this procedure a fine needle is inserted under image guidance into an intrahepatic bile duct. A guidewire is inserted through the needle into the biliary system. A plastic biliary catheter is placed over the guidewire into the biliary system, and then the guidewire is withdrawn. The catheter is secured at the skin insertion site. The percutaneous drainage is performed as a preoperative procedure for resectable malignancies, prior to neoadjuvant chemotherapy, or as a palliative technique. Indications for percutaneous management of malignant biliary obstruction include high biliary obstructions, failed endoscopic drainage, postoperative cases with biliary obstruction, recurrent malignancies, and multiple segmental strictures. PTBD has no absolute contraindications, but it is a very invasive procedure, so its necessity should be carefully considered before performing this procedure. Relative contraindications are hemorrhagic disorders, allergy to iodinated contrast agents, and ascites. The technical success rate ranges between 70% and 95%. The procedure is performed by a radiologist specialized in interventional radiology.

The potential risks of PTBD are cholangitis, bile leakage, catheter dislodgment, and infection of the skin insertion site. Rare complications include hemophilia, sepsis, pneumothorax, and biliothorax.

With this high-risk intervention in particular, nursing observations and activities will be crucial for its success rate and for lowering the re-intervention rate [19]. Patients with resectable pancreatic cancer that undergo PTBD have lower survival rates [18]. EUS-guided biliary drainage is a preferred alternative to PTBD if the endoscopist has advanced expertise. Presently, mastery of EUS-guided biliary drainage is in need of a better training system and use of the appropriate model, so that practitioners can obtain exposure and expertise [20].

Nursing Perspective

Nursing aspects during the diagnostic process are shown in Table 17.2. In addition, the nurse has an important role in guiding the patient's physical burden but also in

Table 17.2 Nursing activities during diagnostics

		Preparation				During study		Care after diagnostic study	
	Lab	Medication	IV	NBM[a]	Antibiotic prophylaxis	Pain management	Lab TBR[b], TLC[c], CRP[d]	Vital signs	Iodine reaction
CT scan	RF[e]	metformin	Yes	No	No	No	No	No	Yes
EUS	CGG[f]	OAC[g]	Yes	Yes	No	ANES[h]	No	Yes	No
ERCP	CGG[f]	OAC[g]	Yes	Yes	Yes (fever)	ANES[h]	Yes	Yes	No
PTC	CGG[f]	OAC[g]	Yes	Yes	Yes	ANES[h]	Yes	Yes	No

[a] *NBM* nil by mouth
[b] *TBR* total bilirubin
[c] *TLC* total leucocyte count
[d] *CRP* C-reactive protein
[e] *RF* renal function
[f] *CGG* coagulation
[g] *OAC* anticoagulants
[h] *ANES* anesthesia

managing the psychosocial aspects during this period with much uncertainty and fear of potential outcomes now a possibly fatal disease has been diagnosed.

Treatment

Surgery is currently the only treatment available for pancreatic cancer with a chance of curing the patient. Today, standard resections can be performed with mortality rates below 5% in specialized high-volume centers. The morbidity of this treatment can be up to 50%, and unfortunately, the five-year survival after curative resection is only 10% [2].

Resectable

Pancreatic cancer can be divided in three stages: resectable (15%), locally advanced (35%), and metastatic disease (50%). Resectable tumors >two cm are categorized as borderline resectable and classified in the resectable treatment strategy. In case of no vascular involvement and distance metastasis, the tumor is radiologically resectable and upfront surgical resection is indicated. If the tumor burden includes major vessel involvement, the tumor is staged as locally advanced. In this case, there is no indication for surgery. Neoadjuvant treatment is a promising novel strategy but is currently only being performed within a clinical trial setting. Distance metastasis makes sure that we are dealing with metastatic stage of the disease.

Upfront Surgery for Resectable Tumors

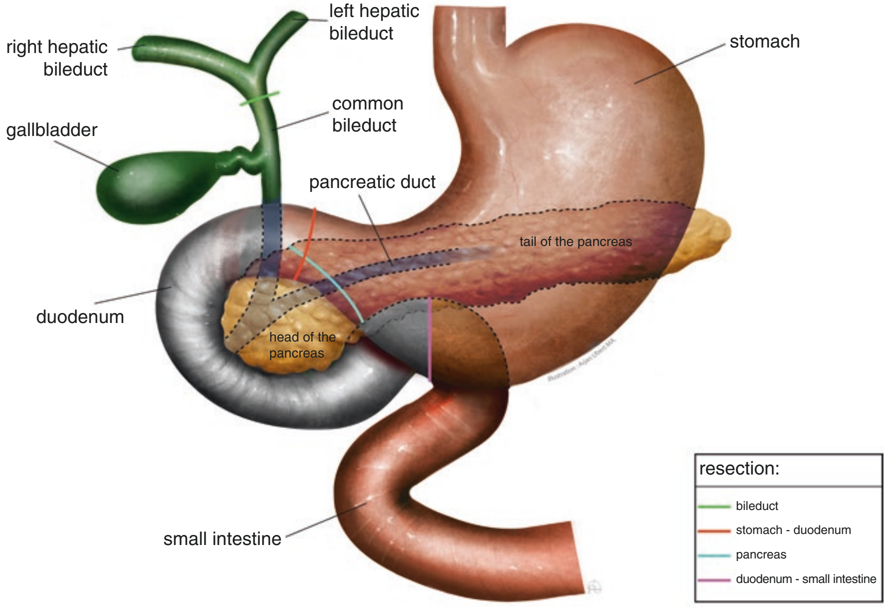
When a (borderline) resectable tumor is diagnosed in the head of the pancreas, the current standard treatment is upfront surgery. Routine preoperative biliary drainage increases the rate of complications [17], early surgery is indicated if the bilirubin level is <250.

The surgical procedure is known as the Whipple operation or pancreatoduodenectomy, named after Allen Oldfather Whipple, a professor of surgery from New York (1881–1963), who performed the first Whipple procedure in 1940 (Fig. 17.1).

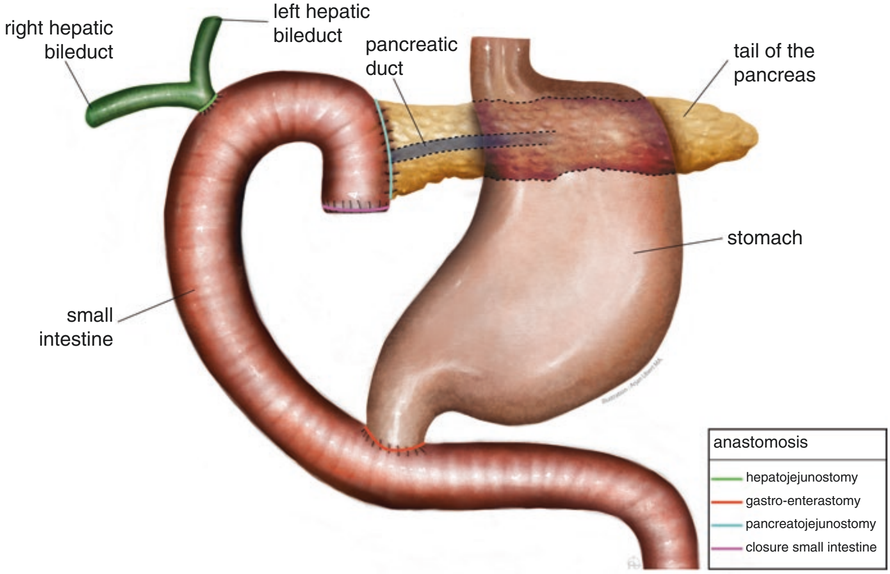
With this operation the pancreatic head, the distal bile duct, the duodenum, and the gallbladder are removed. Thereafter, three anastomoses are made, namely, the gastrojejunostomy (connection between the stomach and intestine), hepaticojejunostomy (connection between the bile duct and intestine), and a pancreaticojejunostomy (connection between the pancreas and intestine).

Neoadjuvant Treatment

The main purpose of neoadjuvant treatment is threefold: (1) improve probability of radical resection, (2) selection of patients with rapid disease progression who would thus undergo unnecessary surgery and (3) early treatment of occult



Before Whipple (pancreatoduodenectomy)



After Whipple (pancreatoduodenectomy)

Fig. 17.1 Whipple procedure (pancreatoduodenectomy) metastasis [21]. Neoadjuvant therapy is becoming an increasingly valuable upfront therapy for (borderline) resectable disease, but the optimal regiment is not yet known. Multiple clinical trials are currently evaluating several treatment strategies [22].

Nurse's Role and Perioperative Care

The nurse can make the difference for the patient and his/her family in such matters as accessibility for questions, worries, or changes that are occurring in the course of the disease. Additionally, preoperative education to patient and family is valuable, considering that pancreatic cancer patients have a wide range of questions. Moreover, it is important to carefully dose the information provision to avoid overloading the patient [23].

Besides taking care of patient education, an experienced specialized nurse is capable of assessing whether patients are also operable in addition to being resectable, especially elderly patients should be carefully selected [24].

The ward nurse plays a very important role in the successful recovery of a patient after surgery, wherein knowledge of the normal course of recovery is essential to observe and recognize complications in a timely manner. The nurse observes the patient 24 hours a day and may warn the physician for any adverse changes in recovery. A combined medical and nursing clinical pathway could be helpful to guarantee the progress in recovery and emphasize the most important issues that have to be paid attention to. This pathway could also serve as a uniform guideline for young and newly graduated nurses and doctors. Table 17.3 shows an overview of the symptoms, incidence, and treatment of the most frequent postoperative complications after a

Table 17.3 Postoperative complications

Complication	Abdominal abscess	Delayed gastric emptying (DGE)	Pancreatic leakage	Wound infection
Incidence	30%	25%	20%	15%
Definition	Infected fluid collection	Nausea and/or vomiting without mechanical obstruction	Amylase drain >3x serum level day 3 postoperative	Wound opened by removing sutures due to pus or redness
Signs and symptoms	Agitation, fever, abdominal pain, DGE	Nausea, vomiting, burping, hiccups, tachycardia, aspiration	Pain, sepsis, bleeding, DGE	Rubor, dolor, calor, edema tachycardia, fever, septic matter
Risk factors	Leakage Gastrojejunostomy Hepaticojejunostomy, pancreatojejunostomy	Leakage anastomoses, diabetes, malnutrition	High BMI, soft tissue pancreas, normal pancreatic duct	Duration operation, diabetes high BMI, smoking, preoperative biliary stent
High-risk moment	Day 5–14 postoperative	Day 3–14 postoperative	Day 3–14 postoperative	Day 3–14 postoperative

(continued)

Table 17.3 (continued)

Complication	Abdominal abscess	Delayed gastric emptying (DGE)	Pancreatic leakage	Wound infection
Physical exam	Vital signs, abdominal examination, aspect drain fluid	Hyperthympania in epigastrio	Vital signs, aspect drain fluid	Vital signs
Additional exam	Lab: Hb, CRP, leukocyte, creatinine, INR CT scan	Lab: Na, K, creatinine, CRP, leukocyte consider CT scan to exclude abscess	Lab: determine amylase drain fluid consider CT scan	Consider culture in case of persistent infection or suspicious *Pseudomonas*
Treatment	Drain in situ, electrolyte supplementation abscess drainage, treat sepsis (antibiotics, consider ICU), stomach tube (ico vomiting)	Stomach tube, electrolyte supplementation prokinetics, antiemetics stomach tube (ico vomiting)	Drain in situ, electrolyte supplementation drainage abscess, treat sepsis (antibiotics, consider ICU), stomach tube (ico vomiting)	Open wound and rinse wound if fascia partial dehiscence consider abdominal strap (comfort), if complete dehiscence consider relaparotomy
Nursing implications	Observe drain fluid humidity content	Humidity content	Observe drain fluid humidity content	Observations wound (bulging intestines)

pancreatoduodenectomy. This overview is a valuable and clinically relevant contribution to specialized clinical care and can be helpful for nurses within daily clinical practice to help them recognize and interpret observed signs and symptoms.

Pancreatic exocrine insufficiency is diagnosed in approximately half of all patients scheduled to undergo resection. For this reason, it is of great importance to observe for exocrine insufficiency symptoms such as steatorrhea, loose stool, a lot of feces, and weight loss in the long term. The majority of patients develop severe exocrine pancreatic insufficiency after pancreatoduodenectomy [25].

The role of the ward nurse is also of great importance at the moment of hospital discharge, on the one hand to assess whether the patient has adequately recuperated from the surgery and on the other hand to ensure a good transition from hospital to home. This will firstly result in more patient self-confidence and secondly may prevent possible readmissions.

Adjuvant Treatment

Adjuvant chemotherapy after surgery aims to limit the chance of recurrence, but the results of this type of treatment are very limited, and the risk of systemic local recurrence or distant metastasis is as high as 77%. Based on the results of the ESPAC-3 study [26], the worldwide chemotherapy standard for adjuvant treatment is gemcitabine. Survival after surgical resection without adjuvant therapy is approximately 20 months [27]. The outcomes of the ESPAC-4 trial were published in March 2017 [28], which resulted in replacement of the standard gemcitabine adjuvant therapy by gemcitabine and capecitabine combination therapy. In recent years, new chemotherapeutic protocols have brought about marked improvement in palliative care, but further trials are needed to improve the outcome of surgical treatment with curative intent [29].

Follow-Up

The purpose of the clinical follow-up of pancreatic cancer is a check for a recurrence of the tumor. Recurrence of the cancer probably occurs because of remaining undetected microscopic malignant cells. These cells may increase in number until they show up on imaging as a new tumor. In case of recurrence, no curative treatment is available. Some specialists do not burden the patient with further standard visits to the hospital and invite the patient to consult only in case of problems.

If the patient visits the outpatient clinic on regular basis, this will give an opportunity to monitor both the recovery after surgery and the emotional changes and also provides the opportunity to conduct research by allied health professionals in order to improve the quality of life and the professional support.

Non-resectable

Non-resectable pancreatic cancer is tumor with vascular invasion and/or distant metastasis. It comprises the tumors of which literature shows that surgery is not going to be useful. In fact, the patient is exposed to severe risks without a chance of being cured.

Locally Advanced Pancreatic Cancer (LAPC)

In terms of incidence, locally advanced pancreatic cancer is the largest group of pancreatic cancers. Typical for this stage of the tumor is vascular involvement. However, there is no worldwide consensus about this definition. Literature shows that extensive vascular reconstruction does not lead to survival benefit. Conventionally, LAPC is treated like metastatic disease with systemic induction chemotherapy.

Chemotherapy regiment for LAPC has existed since 2011 and consists of FOLFIRINOX [30], but recently published data from a RCT show promising results with nab-paclitaxel- gemcitabine versus gemcitabine alone [31]. Worldwide, considerable research is done into which medication will offer most benefits. Unfortunately, no drug has been found in recent decades that can cure this form of cancer.

Metastasis

The median survival for metastatic pancreatic cancer is 3–6 months [32].

In case of metastatic disease, the treatment focuses on palliating symptoms and on releiving complaints. FOLFIRNIOX is currently the standard chemotherapy treatment for palliative treatment with the intent to inhibit tumor growth and thereby postponing complaints caused by the tumor growth for as long as possible. Second-line treatment of pancreatic cancer is not robust [33] and should be carefully considered in terms of risks and benefits for the patient [31].

Palliative care

Palliative and/or supportive care is aimed at treating the multiple morbidity occurring in patients with pancreatic cancer. In many cases, palliative care is the only treatment option [10]. Considering that almost 80% of all patients diagnosed with pancreatic cancer are unresectable and that their symptoms are very stressful, a high quality of palliative care is essential [34].

Supportive care aims at reducing hospital admissions, preserving quality of life by means of optimal symptom management for biliary and duodenal obstruction, ascites management, malnutrition, pain treatment, and psychosocial support.

Jejunal obstruction

Complaints as fatigue, loss of appetite, nausea, vomiting and unintended weight loss are caused by jejunal obstruction and/or biliary obstruction. These symptoms typically manifest themselves in the early diagnosis of pancreatic cancer but also in recurrent cancer after surgery.

As a result of the tumor progression of pancreatic cancer, the mass may grow into the duodenum and thus cause obstruction of the intestine. Placing a stent is generally associated with more favorable short-term results, whereas surgical gastrojejunostomy may be a better treatment option for patients with a more prolonged survival [35].

When a patient suffers from an obstruction of the intestine due to recurrence after Whipple surgery, the same considerations may be made regarding the abovementioned interventions.

Biliary obstruction

Around 90% of all patients with pancreatic cancer will have jaundice during some stage of their illness [36].

Reduced bile duct disturbance due to a tumor or recurrence can be treated by placing a metal stent in the bile duct. Placement of this stent initially occurs by means of an endoscopy. The endoscopic route is safer than percutaneous insertion [31]. However, tumor growth or a former operation may obstruct the endoscopic route. A second choice may then be to drain the bile duct by placing a percutaneous drain (PTBD) and a metal stent.

Ascites

The absence of literature concerning the natural process hinders the choice for therapeutic options.

Malignant ascites in patients with pancreatic cancer develops mostly at the time of liver metastasis and peritonitis carcinomatosis. Ascites can cause complaints to varying degrees. The number and the severity of the complaints depend in particular on the amount of ascites. A large amount of ascites can have a negative impact on the quality of life. Ascites fluid is usually bright yellow. The fluid can be cloudy (indicating a high protein content) and/or contain a bloody aspect. The most widely used method is a relieving ascites puncture (paracentesis). This allows a temporary relief of the symptoms, such as dyspnea and praline belly for usually 1–2 weeks in 93% of the cases [37]. Repeated puncture is often necessary, and there has to be a balance between the effect and the duration of the punctures on the one hand and the burden of the punctures on the other hand. If they are not too stressful, there is no reason to be reluctant to perform regular punctures. In case of liver cirrhosis, medicinal treatment is preferred. If there is need for more than one puncture per 1–2 weeks and life expectancy is no longer than a few weeks, a permanent catheter can also be used. This catheter is inserted by a hospital physician, with optional ultrasound guidance. A permanent catheter can be in situ for a few days or even indefinitely. The main complications of a catheter are skin infections at the insertion site, bacterial peritonitis, sepsis, clogging of the catheter (due to cloudy or bloody ascites), and leakage at the insertion site.

The value of diuretics in the treatment of malignant ascites is very limited and is not indicated in malignant ascites due to a peritonitis carcinomatosis.

Malnutrition

Malnutrition is highly prevalent in patients with pancreatic cancer, which can be explained by the presence of anorexia, early satiety, depression, anxiety, nausea, vomiting, postprandial abdominal pain, diarrhea, and cancer cachexia [10]. An assessment of the nutritional status is best performed by a healthcare professional. Malnutrition should be treated in a multidisciplinary setting and a high-volume center. The professional needs to be not only an expert in nutrition but also in pancreatic insufficiency and in enzyme supplement therapy [38]. Due to the high prevalence of malnutrition, early nutritional intervention is crucial, by which enteral nutrition is preferred over parenteral nutrition [39].

Pain

Pancreatic cancer may cause pain, usually in the stage when the tumor burden is expanding. Pain is a complicated complaint and can be provoked by nerve pressure from the tumor. The pain sensation travels through the nervous tracts to the brain. Besides the physical, emotional, and social sides of pain, everyone experiences pain in a different way. Pain is observed in almost all patients with advanced pancreatic cancer, so managing the pain must be done aggressively by following the guidelines on pain treatment [40].

Radiotherapy and coeliac plexus block can lead to pain control. It frequently allows for a decrease in the total amount of systemic drugs and thus their side effects and should be performed in patients with a well-preserved performance status. The input of a pain specialist is often requested [31]. There are some misunderstandings about cancer pain within the patient population. For example, many patients wait too long to start using pain medication. Patients are afraid that at the moment the pain increases, the dosage cannot be adjusted anymore or they are afraid of getting addicted to the medication. However, proper pain medication makes it possible to undertake and enjoy activities that are still feasible and thus contributes to a better quality of life.

Psychosocial aspects

Pancreatic cancer patients and depressive symptoms are common psychological disturbances. Depression significantly lowers the quality of life in pancreatic cancer patients [41].

Nursing perspective

The nursing care and observation for both physical and psychological strain and changes in their life are essential for the patient and the family after the diagnosis of pancreatic cancer. A case manager which is accessible to the patient, family, general practitioner, and other professionals involved and who is familiar with the diagnosis and treatment from beginning to end offers trust, clarity, and continuity. A professional who has the authority to indicate and prescribe medication would be the most recommended professional to function as a case manager. In countries where the legislation is adapted for nurses trained in advanced nursing practice, the nurse practitioner could fulfill this role eminently.

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Evidence-Based Nursing of Patients with Hematologic Malignancies

18

Patrick Crombez

Abstract

Actual insides in the pathogenesis of hematologic malignancies have contributed to significant advances in the diagnosis and evolving treatment options for these diseases. This evolution warrants expanded and specialized knowledge and skills development for nurses to provide expert care to these patients. Understanding these new approaches needs, beyond basic training in hematology, a continuing education program for nurses as well as the development of critical thinking when reading scientific literature to provide evidence-based nursing interventions.

Expert and highly complex practice includes comprehensive assessment with validated tools, early recognition of a complication, prompt action, and care management (preventive and curative) in collaboration with the patient and other healthcare providers. Supportive care to improve the quality of life of our patients extends beyond symptom management and includes social, psychological, and spiritual care.

Nurses in hematology should also take the leadership in the development of new models of care such as nurse-led consultation, outpatient care, patient self-management, and survivorship care provision for the increasing number of hematology cancer survivors.

New and more general challenges to be faced by the hematology nurse are the occurrence of antimicrobial resistance, adherence to oral treatment, and effective and equal care to all patients in a context of multiculturality.

This chapter will highlight these recent advances and, there were possible, describe the evidence-based nursing interventions to assure high-quality physical and psychosocial care for hematologic patients.

P. Crombez (✉)
Department of Hematology and Hematopoietic Stem Cell Transplantation, Jules Bordet Institute, Brussels, Belgium
e-mail: patrick.crombez@bordet.be

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Evidence-based nursing interventions · Specialized knowledge and skills · Comprehensive assessment · Validated tools · Early recognition · Leadership · New models of care · Patient self-management · Innovative models of hematology survivorship care plans

Introduction

Actual insides in the pathogenesis of hematologic malignancies have contributed to significant advances in the diagnosis and treatment of these diseases.

This chapter will highlight these recent advances and, there were possible, describe the evidence-based nursing interventions to assure high-quality physical and psychosocial care for hematologic patients.

As the domain of caring for patients with hematologic malignancies is very broad and extensive, it is not possible in one chapter to be totally all-inclusive.

A brief overview of the most common hematologic malignancies will be followed by a focus on new treatment strategies, independently from the diseases. The aim is to highlight current and future therapeutic strategies other than classical chemotherapy and their nursing-related issues. Some major and specific complications, associated with hematologic malignancies and their treatment, and evidence-based nursing interventions will be described. More common complications in oncology such as nausea, vomiting, hair loss, disseminated intravascular coagulation, venous thromboembolism, etc. will not be discussed in this chapter.

I hope this will help nurses to achieve the final aim which is to obtain the integration of personal, social, and professional life for these patients without residual disease or uncontrolled complications.

Short Overview of Major Hematologic Malignancies

Acute Leukemia

Acute myeloid (AML) and lymphoid (ALL) leukemia are both a heterogeneous group of diseases characterized by uncontrolled proliferation of neoplastic myeloid, respective lymphoid, cells interrupting normal hematopoiesis. Acute leukemias progress rapidly and are fatal for some weeks if left untreated.

Acute leukemia is mostly diagnosed “par hazard” during a routine blood control or during evaluation of symptoms demonstrating circulating blasts or cytopenia.

In this case a bone marrow aspiration and/or biopsy will be taken to explore.

The presence of blasts in the bone marrow and their *morphologic*, *cytogenetic*, *immunophenotypic* examination need to be completed by the exploration of specific mutations as well as by *karyotyping* as by a more refined *molecular study* of specific gene mutations. Recently, researchers [1] found that a more extensive analysis of gene mutation is paramount to guide *prognostic risk stratification* and therapeutic decisions.

Acute leukemia with complex karyotypes and translocations such as t(6;11), t(4;11), and other abnormalities of 3q and del (5q) is associated with poor outcome. AML presenting with t(8;21), t(15;17), or inv(16) have favorable outcome. Cytogenetic abnormality t(9;22), known as Ph chromosome, in adult ALL is associated with poor prognosis but occurs in less than 5% of children with ALL.

In general, one may conclude that AML has a better prognosis in adults while ALL has a better prognosis in children, but detailed exploration of prognostic factors is required.

Different *classification* systems exist for AML such as the FAB and the WHO classification and for ALL such as the WHO classification. More in-depth information is beyond the scope of this chapter as it can be find in specific textbooks. It is important for nurses to keep in mind that these classification systems can change according to new and more accurate diagnostic technology and intracellular molecular discoveries.

More important for nurses are the *clinical features* of acute leukemia and the symptoms observed in acute leukemia. These are the consequences of bone marrow suppression by leukemic cells resulting in neutropenia, thrombocytopenia, and anemia. Constitutional signs such as weight loss, anorexia, fatigue, weakness, and fever and signs of bleeding such as epistaxis are common in these patients, and some of them need prompt recognition and management (cf. 3). Patients also may present symptoms due to leukemic infiltration of organs, such as gingival hypertrophy and perirectal abscesses. Headache, papilledema from increased intracranial pressure, and visual disturbances may indicate central nervous system (CNS) involvement which is rather common in ALL. Lumbar puncture should be performed in all patients with ALL to evaluate CNS involvement. Bleeding in patients with AML can result from thrombocytopenia or disseminated intravascular coagulopathy (DIC) or a combination of both. DIC is seen in about 80% of patients with acute promyelocytic leukemia. Hyperleukocytosis is a well-known condition in patients with ALL and include a white blood cell (WBC) count higher than 100.000/mcl leading to symptoms of spontaneous tumor lysis syndrome, an oncologic emergency that can be potentially fatal and needs to be treated promptly either by chemotherapy or leukapheresis.

Treatment of AML and ALL differs in terms of duration, but in both cases the goal is to achieve complete remission (CR). In AML an induction chemotherapy is initiated, based on anthracyclines (daunorubicin) combined with cytarabine, with the aim to obtain a CR which means less than 5% of blasts in the bone marrow, the absence of blasts containing Auer rods, and no extramedullary disease. Cytogenetic CR and molecular CR are obtained if respectively undetectable abnormal karyotype and lower or undetectable molecular abnormalities like FLT3. Patients who achieve a CR after initial induction chemotherapy receive a consolidation chemotherapy based on high-dose cytarabine. Allogeneic hematopoietic cell transplantation (HCT) is considered in high-risk patients depending upon cytogenetic and molecular profile, age and performance status, predicted treatment-related mortality, and availability of a donor. The aim of the consolidation therapy is to “consolidate” the status of CR.

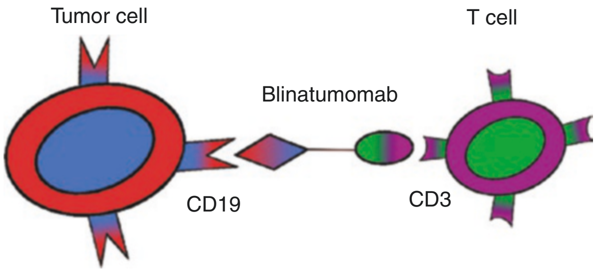

Fig. 18.1 Mechanism of action for blinatumomab as bispecific T-cell engager (BiTE). One arm of blinatumomab binds to CD3, and the other binds to CD19. This engages the unstimulated T-cells which destroy the CD19+ cells. (© Wu et al. 2015 from: Blinatumomab: a bispecific T-cell engager (BiTE) antibody against CD19/CD3 for refractory acute lymphoid leukemia. Journal of Hematology & Oncology, 2015, Volume 8, Number 1, Jingjing Wu, Jiaping Fu, Mingzhi Zhang and Delong Liu, Fig. 18.2)

Adult ALL is nowadays treated based on highly effective pediatric regimens. These schemes are more complex and consist of multiple phases including induction, consolidation, maintenance, and intensification treatments. Each phase is based on a combination of systemic chemotherapy with synergistic agents that mainly target lymphoid leukemic cells like cyclophosphamide, methotrexate, cytarabine, vincristine, an anthracycline, L-asparaginase, and steroids.

Monoclonal antibody rituximab may be added to chemotherapy if leukemic cells express CD20 as well as a tyrosine kinase inhibitor (TKI) in case of Ph + ALL. Prevention or treatment of CNS involvement will be done through IT chemotherapy of cytarabine, methotrexate, and steroids at low doses. The first two products are also given intravenously at high doses as they cross the blood-brain barrier and may be sufficient as CNS prevention but not in case of treatment of CNS involvement because therapeutic concentrations are not maintained in the cerebrospinal fluid.

Blinatumomab is an effective new immunotherapy agent to induce remissions in refractory B-cell ALL in adults. CD19 is a surface antigen expressed in B-cell development and in more than 95% of B-precursor ALL blasts, making it a promising target for immunotherapy. Blinatumomab simultaneously binds CD3-positive cytotoxic T-cells and CD19-positive B-cells, causing the T-cells to induce lysis of the normal and malignant B-cells (Fig. 18.1, Turner et al.[2]).

It is obvious that the toxicity profile of the treatment of both AML and ALL is different which means also a different approach for nurses (cf. point 4).

Chronic Leukemia

As it is the case for acute leukemia, one can distinguish myeloid (CML) and lymphoid chronic leukemia (CLL).

CML is characterized in more than 90% of cases by a translocation t(9;22), named *Philadelphia chromosome* (Ph), resulting in a fusion gene BCR-ABL. Patients with Ph-negative CML have a less good response to therapy with TKIs and so also a decreased survival.

Note that the presence of Ph chromosome has an inverse outcome compared to the case of adult ALL were Ph + patients have a poor outcome.

Although CML can occur in *three phases* (chronic, accelerated, or blast phase), the majority of patients are diagnosed in chronic phase without symptoms. Symptomatic patients may suffer from general signs such as weight loss, fatigue, night sweats, or splenomegaly. Hyperleukocytosis and above 100,000 white blood cells/mcl may also be present and may be accompanied with hyperviscosity which may induce visual changes like blurring, diplopia, and even loss of vision. Confusion and disorientation may also be observed.

In the accelerated phase, patients may also present dyspnea and fever. The phase is characterized by the presence of 10–19% of blasts, mostly from myeloid origin, in the peripheral blood or bone marrow.

In case of blast crisis with 20% or more blasts, CML is transforming in AML (rarely ALL) with similar signs and symptoms.

The *treatment* of CML has changed totally since more than a decade now. There where allogeneic HCT was the only curative option, the introduction of TKIs, which inhibit BCR-ABL tyrosine kinase causing death of leukemic cells, gives patients effective therapy with less toxicity. Imatinib is commonly used as first treatment option, but if patients cannot tolerate or are resistant to imatinib, they may benefit from second-generation TKIs such as dasatinib or nilotinib.

These treatments are given orally, and patients are followed in an outpatient setting. Patient education by nurses is paramount especially regarding the understanding of the importance of adherence to TKIs therapy and regarding prevention and management of side effects as fluid retention including pleural and pericardial effusion, diarrhea, nausea and vomiting, abdominal pain, headache, and rash.

As TKIs are known to have a lot of drug interactions, nurses should review patient's concomitant medication to avoid increased or decreased concentrations of TKIs.

CLL or chronic lymphocytic leukemia is a chronic monoclonal B-cell lymphoproliferative disease resulting in an accumulation of functionally incompetent lymphocytes. Most patients are elderly with currently a median age of 70 years which means that in the future, due to extended life expectance, the number of patients with CLL will increase.

The most common *chromosomal abnormalities* are deletion 13q, deletion 11q, deletion 17p, deletion 6q, and trisomy 12. The first mentioned is the most frequent cytogenetic abnormality that occurs in half of all cases and had better outcomes if it is the only detected abnormality. Deletion of 17p is associated with a more aggressive clinical evolution, poor response to treatment, and shorter overall survival (OS).

CLL often (70%) is accompanied by hypogammaglobulinemia and puts these patients at high risk for opportunistic infections including pneumocystis, viral reactivation such as CMV, and encapsulated bacterial infections.

Patients with more advanced CLL may suffer from B symptoms such as recurrent unexplained fever, drenching night sweats, unexplained weight loss, and excessive fatigue. Nurses should educate patients regarding the early recognition and reporting of these symptoms.

Patients with CLL not always require *treatment* at the time of diagnosis which mean that asymptomatic early-stage disease should be left untreated ("wait and see" attitude) until symptomatic progression appears.

If treatment is needed, many options are available, and various novel agents under investigation show promises for the treatment of CLL.

Although alkylating agents (chlorambucil, cyclophosphamide) were the standard for treatment of CLL, combination immunochemotherapy is used with high CR rates. One well-known example is FCR, a combination of fludarabine, cyclophosphamide, and rituximab (a monoclonal antibody, anti-CD20). New combinations with bendamustine, an agent with alkylating and antimetabolite properties, and rituximab or new monoclonal antibodies such as alemtuzumab (anti-CD52) and ofatumumab (anti-CD20) are even effective in refractory CLL.

All these treatments are given in the outpatient setting, and therefore patient education regarding disease- and treatment-related side effects is paramount as patients must manage them themselves.

Bendamustine hydrochloride is a novel bifunctional mechlorethamine derivate for the treatment of patients with chronic lymphocytic leukemia and acts primarily as an alkylating agent. The administration of bendamustine consists of IV infusion for 30 min [3].

Lymphoma

The complexity and various types of this very heterogeneous group of diseases need, to be comprehensive, an exhaustive description what should take too much space in this chapter. Therefore, I will consciously restrict to essential information without going in detail of every type of lymphoma.

Mainly, one may distinguish *non-Hodgkin lymphoma and Hodgkin* disease (HK). The latter is a malignant lymphoma with large abnormal lymphoid cells, named Reed-Sternberg cells, which are B-cells. HK represent approximately 10% of lymphomas and occurs more frequently in adolescents and young adults.

Non-Hodgkin lymphoma (NHL) covers a variety of different diseases as well as in the B-cell lineage as in the T-cell lineage.

B-cell neoplasms or B-cell NHL occurs mainly in older patients with a median age of 66 years at diagnosis and covers a huge range of diseases.

Several risk factors for developing B-cell NHL are described such as viruses (EBV, HIV, Hepatitis B and C virus, and HHV-8), autoimmune disorders, and long-term use of immunosuppressive agents, all of them linked with a dysregulation of the immune system.

Classification of B-cell NHL based on clinical, histologic, and molecular insights on the disease has led to changes of classification systems over time. REAL and WHO classification systems are well-known and used in clinical practice. In 2008 the WHO classification, based upon REAL classification principles, was updated and will still evolve in the future [4].

Grading B-cell NHL is important for treatment decision and prognostic reasons. One may distinguish three groups: low grade (long doubling times), intermediate grade, and high grade (very short doubling times). Low-grade disease is chronic but not curable, while intermediate- and high-grade diseases are clinically more aggressive but potentially curable.

Staging is used to define the extent and the location of disease and ranges from I to IV according to the Ann Arbor system. PET scan imaging is becoming essential for pretreatment staging and for therapeutic monitoring.

The International Prognostic Index (IPI) for B-cell lymphoma has now been revised as a consequence of new genetic information and new treatment options. The IPI remains predictive, but it identifies only two risk groups. Redistribution of the IPI factors into a revised IPI (R-IPI) for diffuse large B-cell lymphoma (DLBCL) provides a more clinically useful prediction of outcome. The R-IPI identifies three distinct prognostic groups with a very good (4-year progression-free survival [PFS] 94%, overall survival [OS] 94%), good (4-year PFS 80%, OS 79%), and poor (4-year PFS 53%, OS 55%) outcome [5].

Clinical features are strongly associated with the extent of the lymphoma and can go from painless lymphadenopathy to organ damage, spinal cord compression, and a variety of generalized signs and symptoms including B symptoms (cf. supra).

Treatment of B-cell NHL is mainly based on a combination of chemotherapy with monoclonal antibodies. Chemotherapeutic regimens like CHOP containing anthracycline and cyclophosphamide are classically used, but the addition of rituximab to CHOP-like regimens has significantly improved survival in CD20 expressing B-cell NHL such as follicular lymphoma and diffuse large B-cell lymphoma. However, Fc receptor polymorphisms and CD20 downregulation following repeated rituximab exposure is an ongoing challenge and highlights the need for advancement in alternative treatments. Therefore, other anti-CD20 monoclonal antibodies (MoAbs) are under study such as ofatumumab, a fully humanized second-generation type I CD20 antibody, and obinutuzumab, a humanized type II anti-CD20 antibody [6]. Radiolabeled MoAbs, such as ibritumomab tiuxetan, is a novel way of targeting lymphoma cells taking advantage of its inherent radiosensitivity.

Treatment with selinexor reduces proto-oncogene proteins and shows synergetic activity with dexamethasone in patients with follicular B-cell non-Hodgkin lymphoma. It is an oral drug and can be combined with chemotherapy, proteasome inhibitors, and other agents with minimal increased toxicities [7].

Copanlisib has been shown to induce tumor cell death by apoptosis and inhibition of proliferation of primary malignant B-cell lines and is given in a 1-hour IV infusion.

CAR T-cell therapy is a treatment option where patient's T-cells are changed in the laboratory, so they will attack cancer cells. Blood from a vein in the patient's arm flows through an apheresis machine, which removes the white blood cells, including the T-cells. Then the gene for a special receptor that binds to a certain protein on the patient's cancer cells is added in the laboratory and then given to the patient by infusion. The special receptor is called a chimeric antigen receptor (CAR) (National Cancer Institute).

Radiation therapy is considered in some cases and may be combined with chemical treatment. Autologous (aHCT) and allogeneic HCT are also to be taken into account, especially in young patients with poor prognosis for both B-cell NHL and T-cell NHL.

T-cell neoplasms or T-cell NHL covers a wide range of diseases involving T-cells and NK-cells and represent only 15% of NHL. More than two thirds are peripheral T-cell lymphoma (PTCL); the term “peripheral” refers to the fact that the disease arises from mature T lymphocytes or NK-cells from the peripheral zone of the thymus [8].

PTCL is a rare and heterogeneous group of disorders associated with a very poor prognosis.

Cutaneous T-cell lymphomas (CTCLs) are characterized by an infiltration of the skin by neoplastic T-cells and are mostly recognized as mycosis fungoides (MF 50% of all cutaneous lymphomas and mostly indolent) and Sézary syndrome (SS less than % and aggressive). T-cell NHL can be present as nodal disease, but extranodal and leukemic or disseminated forms may occur.

Staging for MF and SS is important for determining prognosis and treatment.

Morphologic analysis and *immunophenotyping* as well as *molecular profiling* for *genetic translocation* and analysis of *T-cell receptor* (TCR) *gene rearrangements* are used to differentiate the subtypes of PTCL. Clinical parameters such as patient age and the location of involvement are also taken in account for diagnosis.

PET scan is used to assess organ involvement and to guide the choice of site for biopsy.

Prognostic Index for PTCL is like IPI for B-cell lymphoma and is refining over time. The introduction of more effective treatments in PTCL, including new drugs, allogeneic stem cell transplantation, and biological response modifiers, improves the outcome and changes the variables predicting response and survival [9].

The Ann Arbor staging classification is used for staging PTCL.

As consequence of the absence of optimal *treatment* for PTCL, the NCCN [10] recommends a clinical trial as the preferred initial option. If this is not possible, the treatment of T-NHL is based on the combination chemotherapy as for B-NHL such as CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) or CHOP with etoposide (CHOEP). In case of high or intermediate-high IPI score or stage III–IV disease, these regimens are alternated with high-dose methotrexate and cytarabine or ICE (ifosfamide, carboplatin, and etoposide).

In refractory PTCL, one may consider treatment with approved brentuximab (anti-CD30) or romidepsin, a histone deacetylase inhibitor (HDAC), or a HDAC under investigation such as belinostat. Alemtuzumab (anti-CD52) in combination with CHOP and zanolimumab (anti-CD4) are also under investigation [11].

If the disease is responding to therapy, one may consider autologous or allogeneic HCT with myeloablative or reduced-intensity conditioning (RIC) as consolidation [10].

Bortezomib, a proteasome inhibitor, has been well tolerated and active as a single agent [12] or in combination with gemcitabine plus doxorubicin [13] in relapsed or refractory CTCL patients.

Multiple Myeloma

B lymphocytes mature into immunoglobulin-producing plasma cells (IgG, IgA, IgM, IgE, and IgD), which are responsible for humoral immunity. Each immunoglobulin has a particular role and function in the immune response. In multiple myeloma (MM), a plasma cell neoplasm, an abnormal overproduction of one of these immunoglobulins occurs (M protein) with secondary organ effects including renal, bone, bone marrow, neurologic, and immune dysfunction.

Among the differential diagnoses of MM are monoclonal gammopathy of unknown significance (MGUS) and smoldering multiple myeloma (SMM) [14]. MGUS is an asymptomatic premalignant condition that precedes myeloma and does not require immediate treatment. SMM is a more advanced premalignant and asymptomatic precursor to MM with distinct clinical findings and a greater risk of progression to MM.

The major criterion in the *diagnosis* of MM, still considered incurable, is the presence of a monoclonal spike (M-spike) on electrophoresis of blood serum or urine. To complete the "classic triad" in the diagnosis of MM, more than 30% plasma cell proliferation in the bone marrow and osteolytic lesions must be added to the presence of a M-spike. The importance of cytogenetic profiles such as aneuploidy, translocations, and deletions to accurately stage MM in patients is still under investigation.

Criteria for the diagnosis and response to treatment include *clinical signs and symptoms* due to myeloma-related organ dysfunction.

Treatment is indicated when a patient has active MM with evidence of end-organ damage as defined by the CRAB criteria (Calcium elevation greater than 10.5 mg/l, Renal dysfunction with serum creatinine greater than 2 mg/dl, Anemia with hemoglobin less than 10 g/dl, and Bone lesions).

Chemotherapy regimens such as VAD (vincristine, adriamycin, and dexamethasone) or oral melphalan and prednisone have been the gold standard in the past. Since improved genomic understanding of MM development, chromosomal changes, and the bone marrow microenvironment, the expected life span changes from 7 to 60 months. The first group of novel agents to treat MM was drugs with immunomodulatory and antiangiogenic properties such as thalidomide, lenalidomide, and pomalidomide. Ongoing studies will define further how and when the agents can be used in the treatment of MM.

Cancerous cells depend on proteins regulated by the proteasome for proliferation, metastasis, and survival. Proteasome inhibitors, such as bortezomib and carfilzomib, are another new class of anti-myeloma drug.

However, patients with MM refractory to both immunomodulatory drugs (IMiDs) and proteasome inhibitors have a very poor prognosis leading to a need for newer drugs with innovative mechanisms of action and requiring further investigation in randomized controlled trials. Monoclonal antibodies (MoAbs) have multiple mechanisms of action and seem to be most effective when given in combination with other agents. Key MoAbs in clinical trials include elotuzumab, dacetuzumab, siltuximab, daratumumab, bevacizumab, and denosumab. Other drugs under investigation in MM are oral histone deacetylase (HDAC) such as vorinostat and panobinostat, mTOR inhibitors such as temsirolimus and everolimus, and Akt inhibitors such as afuresertib and perifosine. Akt protein kinase B is an enzyme that plays a crucial role in glucose metabolism, cell survival, and transcription [15].

Since the emergence of novel drugs for the treatment of MM average survival for individuals with MM has increased, nevertheless most patients relapse. Unfortunately, MM eventually becomes refractory to treatment, and novel agents with sophisticated mechanisms are needed based on the understanding of the underlying biology and pathways of myeloma cells. Genetic expression and protein signaling pathways are promising areas of research.

The role of autologous (aHCT) (tandem) and allogeneic HCT with myeloablative or reduced-intensity conditioning (RIC) is still to be clarified, but guidelines exist to determine which patients can benefit from a HCT [16, 17].

Specific and Major Complications in Hematologic Malignancy and Treatment: Evidence-Based Nursing Interventions

This subsection provides an overview of major, new, hematologic specific, or life-threatening complications. When applicable, evidence-based nursing interventions are described. Prompt recognition and management of hematologic emergencies, as well as supportive care, are paramount for nurses caring for patients with a hematologic malignancy who require often complex care. The aim is to reduce morbidity and mortality and to optimize quality of life in this population.

New treatment options in hematology lead to new complications, so nurses need continuing education programs to stay up-to-date with in-depth knowledge and to assure high-quality care to patients throughout the whole disease trajectory.

Since the last decade there has been a clear shift in the treatment of hematologic malignancies from chemotherapy to combination therapy, adding targeted therapy, both biologic and molecular. Biologic-targeted therapy is sometimes also given alone.

Targeted biotherapy is directed toward a specific target on the cancer cell, reducing damage to normal cells. These groups of agents include MoAbs, immunomodulatory agents, immune checkpoint inhibitors, and miscellaneous agents such as HDAC inhibitors. According to which group of agents is used, one may observe less or more specific toxicities.

In the following some specific complications due to new hematologic treatments will be discussed.

Infusion Reactions and Cytokine Release Syndrome

MoAbs may be totally mouse protein (suffix momab), chimeric mouse, and human (suffix ximab), mostly human with a small part mouse (suffix zumab), or entirely human (suffix umab). The development of humanized monoclonal antibodies has reduced the occurrence of human antimouse antibodies in patients; nevertheless human antihuman antibodies may be developed, and infusion reactions can still occur. Until now, the relationship between infusion reactions and the development of human antimouse antibodies or human antihuman antibodies has not been documented [18].

One must keep in mind that infusion reactions associated with the use of monoclonal antibodies are not the only one as the risk for infusion reactions is also associated with other oncologic agents such as L-asparaginase used in ALL. Infusion reactions are either allergic reactions to foreign proteins (i.e., IgE-mediated allergic responses) and classed as type 1 hypersensitivity responses or are non-IgE-mediated reactions. Nonallergic infusion reactions are complex, resulting from cytokine release, and are associated with monoclonal antibodies that react with circulating blood cells.

Most monoclonal antibodies have the potential to cause the cytokine release syndrome.

Although the incidence of reactions varies among MoAbs, most reactions occur during the first infusion as the tumor burden is highest. Most infusion reactions related to monoclonal antibodies are mild (grade 1 or 2). The National Cancer Institute (Table 18.1) has classified infusion reactions caused by cytokine release into *severity grades* to standardize the reporting of the side effects. Prompt and

Table 18.1 NCCN Common Terminology Criteria for Adverse Events (CTCAE), version 4.03 distinguishing between infusion-related reactions and CRS

Grade					
	1	2	3	4	5
Hypersensitivity (allergic reaction)	Transient flushing or rash; drug fever <38 °C	Rash; flushing; urticaria; dyspnea; drug fever ≥38 °C	Symptomatic bronchospasm, with or without urticaria; parenteral medication(s) indicated; allergy-related edema/angioedema; hypotension	Anaphylaxis	Death
Acute infusion reaction (cytokine release syndrome)	Mild reaction; infusion interruption not indicated; intervention not indicated	Requires therapy or infusion interruption but responds promptly to symptomatic treatment (e.g., antihistamines, NSAIDs, narcotics, IV fluids); prophylactic medication indicated for ≥24 hours	Prolonged (i.e., not rapidly responsive to symptomatic medication and/or brief interruption of infusion); recurrence of symptoms following initial improvement; hospitalization indicated for other clinical sequelae (e.g., renal impairment, pulmonary infiltrates)	Life-threatening; pressor or ventilatory support indicated	Death

accurate documentation of the infusion event is very important to assist the clinician in deciding if restarting the treatment is feasible and safe. Initial *signs and symptoms* of cytokine release reactions and anaphylactic reactions often are identical. A quicker onset of symptoms increases the severity of the reaction.

Symptoms of CRS typically occur within 30–120 min after infusion has been initiated and can manifest even later in the case of CAR T-cell therapies. (https://www.cancer.gov/publications/dictionaries/cancer-terms/def/car-t-cell-therapy).

The most common signs are rigors/chills, fever, rash, pruritus, local or diffuse erythema, dyspnea, bronchospasm, tachypnea, and hypoxemia. In rare cases, patients may have acute respiratory distress syndrome accompanied by chest pain, palpitations, hypotension, tachycardia, arrhythmia, and in extreme cases cardiac arrest.

Evidence-Based Nursing Interventions

As *preventive* measures, an in-depth understanding of the treatments that nurses are administering and the infusion risks of each agent is imperative, including comprehension of what type of infusion reaction is most likely associated with the drug. A *clinical anamnesis*, particularly including any previous allergic reactions, is a very useful risk assessment tool for oncology nurses. Premedication (e.g., antipyretics, antihistamines, steroids) is recommended prior to a monoclonal antibody as prophylaxis for cytokine release syndrome, especially for the first infusion. If some premedication is taken orally, oncology nurses should ensure that the patient has really taken them before each infusion. A stepwise manner of infusion or fractionated dosing is recommended for the first infusion. Baseline assessments including vital signs should be documented prior to the infusion. During infusions, oncology nurses must continue to assess the patient's vital signs frequently and pay attention for any signs or symptoms of an infusion reaction. The first hour is the most likely for infusion reactions to occur, but vigilance is necessary throughout the entire infusion as a reaction could occur at any time. Any delay in recognition of the signs can compromise the patient's outcome.

Patients and family members must be well educated about the potential for an infusion reaction and be assured that most infusion reactions are caused by cytokine release, are mild, and are easily manageable. Nevertheless, patients must also understand the need to report reactions immediately.

Patients also must be aware about the possibility for a delayed reaction following discharge from the infusion and must know what needs to be promptly reported to the healthcare provider. Even a mild reaction may rapidly progress to a life-threatening respiratory or cardiovascular situation.

The *management* of an infusion reaction or CRS starts with the early recognition of signs or symptoms and prompts action by firstly stopping the infusion but keeping the IV line open. Vital signs should be obtained, and the patient should be placed into a recumbent position with elevation of the lower extremities if hypotensive. Airway, breathing, and circulation should be assessed immediately. In case of bronchospasms and airway obstruction, oxygen therapy should be initiated. Corticosteroid administration may be considered, and bronchodilators are given for bronchospasm. Vital signs assessment should be done every 2–5 min until the patient is stable. More intensive treatment such as the administration of dopamine and fluid replacement is rather seldom. In a second period nurses should observe for cutaneous manifestations with or without pruritus which occurs mostly in anaphylactic incidents [19].

Whether an infusion reaction is a true anaphylactic reaction or a cytokine release reaction may be difficult to distinguish, but the timing may be useful as anaphylactic reactions occur mostly immediately (first few minutes) after the start of infusion, whereas a CRS occurs mostly within 30–120 min of the beginning of the infusion. Anyway, the nurse's attitude is the same, which means effective symptom management based on patient's symptoms and status.

Once symptoms are totally resolved, the infusion may be restarted at 50% of the infusion rate with a close follow-up of the tolerance [20].

Documentation should include [21]:

- Preinfusion assessment (i.e., the drugs administered, doses, number of previous
- infusions of the agent, and infusion rates)
- Symptoms at onset and course of progression
- The timing of symptom onset
- Intervention, timing, and patient response
- Time of symptom resolution
- Discharge instructions or transfer to emergency services

Peripheral Neuropathy

Advances in onco-hematologic therapy include several new, highly active agents such as thalidomide and bortezomib that have potentially dose-limiting neurologic effects. These effects are present particularly in the peripheral nervous system (PNS), which is more sensitive than the central nervous system (CNS) to neurotoxic effects of chemotherapy. Autonomic fibers are also affected.

The *pathogenesis* of chemotherapy-induced peripheral neuropathy (CIPN) is not totally understood and may vary depending on agents administered. Chemotherapy drugs are believed to first damage sensory axons and start symmetrical beginning in the distal end of the longest axons (i.e., the toes of both feet) from the toes to the feet to the ankles and then to the lower legs. CIPN in the upper extremities occurs later and moves from the fingertips to the hands and so on. However, some patients notice CIPN in their hands first. Axons can regenerate if the offending agent is removed but is not completely reversible.

The mechanisms of neuronal repair are not well clarified but may involve circulating nerve growth factor (NGF) which is reduced after neurotoxic chemotherapy (cisplatin, vincristine). Most drugs that may induce PNP used in hematologic patients are vinca alkaloids, platinum analogs, proteasome inhibitors, and immunomodulatory drugs.

Risk factors are treatment related such as the chemotherapy agent involved, the total cumulative dose, and previous and concomitant administration of other neurotoxic chemotherapy drugs.

Patient-specific risk factors may include preexisting sensory neuropathy due to alcoholism or diabetes and exposure to certain toxins or metals [22]. One must not forget that some hematologic diseases can be accompanied by neurotoxicity, which is the case in multiple myeloma.

The impaired function and *symptoms* depend on the type of nerves affected, which can be motor, sensory, or autonomic nerve fibers [23]. Vinca alkaloids, especially vincristine, are neurotoxic to the sensory and autonomic peripheral nervous system. Other vinca alkaloids are less likely to cause CIPN. Most frequent signs include pain and paresthesia of the feet and hands, distal hyperesthesia, and loss of deep tendon reflexes, while autonomic manifestations are mostly limited to constipation and ileus. Proteasome inhibitors and immunomodulatory drugs are mostly toxic to the sensory peripheral nerves (Fig. 18.2).

CIPN is a common adverse effect that affects patient quality of life and adherence to cancer treatment.

Although there are many methods to *assess and grade* CIPN, a standardized method has not been established but should include resultant levels of functional impairment that patients experience in activities of daily living (ADLs) by using a combination of subjective and objective measures. To date, no consensus exists on the most appropriate patient self-report scale for use in oncology practice. So, there is still a need to identify valid and reliable assessment tools that measure or assess CIPN in adult patients receiving chemotherapy. The total neuropathy score (TNS) could be considered for use with a broader oncology population because this scale has been tested in more than one tumor type and take into account objective and subjective measures. Reduced versions of the TNS were

Fig. 18.2 Characteristics of CIPN. (Source: Clinical Journal of Oncology Nursing, Dec 2007, Vol. 11(6), 901–913, 13p, Chart found on p902; Note based on information from Visovsky et al. [23])

Sensory symptoms
Paresthesia
Hyperesthesia
Hypoesthesia
Dysesthesia
Pain
Numbness and tingling
Hyporeflexia or areflexia
Diminished or absent proprioception
Diminished or absent vibratory sensation
Diminished or absent cutaneous sensation
Diminished or absent sense of discrimination between sharp and dull

Motor symptoms
Weakness
Gait disturbance
Balance disturbance
Difficulty with fine motor skills (e.g., buttoning clothing, writing)

Autonomic symptoms
Constipation
Urinary retention
Sexual dysfunction
Blood pressure alterations

developed because the original instrument was time-consuming. The TNSc is a clinical version of the TNS scale and evaluates only clinical signs and symptoms of CIPN [24].

A more practical tool to assess signs and symptoms of peripheral neuropathy is the neurotoxicity assessment tool (Fig. 18.3, Tariman et al. [25]).

The *treatment* of PNP is based on patient's symptomatology and actual knowledge of the efficacity of treatment. A great deal of practical clinical knowledge has been gained with oxaliplatin but is applicable to patients receiving other neurotoxic agents. No data support prophylactic use of any of the medications. Agents with neuroprotective potential include calcium/magnesium (Ca++/Mg++), glutathione, vitamin E, and other agents, as well as NGFs [29]. Several drugs, such as gabapentin, pregabalin, tricyclic antidepressants, and topical lidocaine patch 5% to the affected area are tested to treat PNP, but none demonstrated significant efficacy. For the present, treatment of CIPN relies on reducing or discontinuing the offending agent when CIPN develops and treating the symptoms of neuropathic pain. Agents used to decrease dysesthetic pain and allodynia that may accompany CIPN include anticonvulsants, tricyclic antidepressants, opioids, and topical agents, which incorporate knowledge about the pathogenesis of painful neuropathy. The American Society of Clinical Oncology (ASCO) convened a multidisciplinary expert panel to review the literature and to provide guidance on the effectiveness of prevention and treatment options for

Fig. 18.3 Neurotoxicity assessment tool. (Source: Clinical Journal of Oncology Nursing, 2008, Vol 12(3), 29–3, 8p, chart found on p31; Note Based on information from Calhoun et al. [26]; Cella [27]; Cella et al. [28])

Instructions for patients

By circling one number per line, please indicate how true each statement has been for you during the past seven days using the following scale.

0 = not at all
1 = a little bit
2 = somewhat
3 = quite a bit
4 = very much

I have numbness or tingling in my hands.	0	1	2	3	4
I have numbness or tingling in my feet.	0	1	2	3	4
I feel discomfort in my hands.	0	1	2	3	4
I feel discomfort in my feet.	0	1	2	3	4
I have joint pain or muscle cramps.	0	1	2	3	4
I feel weak all over.	0	1	2	3	4
I have trouble hearing.	0	1	2	3	4
I get a ringing or buzzing in my ears.	0	1	2	3	4
I have trouble buttoning buttons.	0	1	2	3	4
I have trouble feeling the shape of small objects when they are in my hand.	0	1	2	3	4
I have trouble walking.	0	1	2	3	4

Instructions for healthcare professionals

This assessment tool is provided to help you evaluate peripheral neuropathy in patients receiving chemotherapy. Healthcare professionals may find discussion of patients' responses helpful in determining the grade of neuropathy as defined by the National Cancer Institute Common Terminology Criteria for Adverse Events (http://ctep.cancer.gov); however, no direct correlation exists between assessment scores and toxicity grades.

CIPN in adult cancer patients. The only drug demonstrating efficacy from a randomized, double-blind, placebo-controlled trial is duloxetine [30, 31]).

Evidence-Based Nursing Interventions

To date there are no evidence-based nursing interventions that can be recommended or that are likely to be effective for nursing practice.

At baseline, patients should receive education about the symptoms of peripheral neuropathy and the importance of reporting symptoms. Nurses play a critical role in caring for patients at risk for CIPN, including baseline and ongoing assessment during and after treatment, patient teaching the signs and symptoms of peripheral neuropathy, safe chemotherapy administration, symptom management, and timely consultation of other interdisciplinary team members.

Topical analgesic agents such as baclofen/amitriptyline/ketamine gel and lidocaine cream might be helpful for painful CIPN [32]. Results with capsaicin, the only agent well studied for painful neuropathy, have been mixed and may range from significant pain reduction and improved ability to perform activity of daily living (ADLs) to worsening pain and intolerable burning after application.

Late effects of CIPN may continue to produce a significant burden of suffering for cancer survivors.

Hematopoietic Cell Transplantation (HCT)-Related Complications

In this subsection, thrombocytopenia, neutropenia, and febrile neutropenia will be discussed although these complications are not specifically related to HCT and are equally frequent and challenging for oncology nurses caring for patients with acute leukemia.

Specific transplant-related complications that will be described are oral mucositis, hemorrhagic cystitis, sinusoidal obstruction syndrome, engraftment syndrome, and graft-versus-host disease.

Thrombocytopenia

Thrombocytopenia is defined by the National Cancer Institute [33] as a condition in which there is a lower-than-normal number of circulating platelets in the blood and is the primary cause of bleeding in patients with hematologic malignancy. Thrombocytopenia can be further subdivided into mild, moderate, and severe subgroups as per NCI [34] CTCAE criteria. Although platelet count is an indicator of the potential risk of bleeding, the correlation is imprecise and varies based on the underlying condition and other clinical factors which means that the number of platelets considered “safe” lacks well-defined evidence, and there is no established threshold above which platelets should be maintained to avoid bleeding. The risk of bleeding generally increases only when platelets fall below 20×10^9/L.

Symptoms associated with thrombocytopenia include minor signs such as ecchymosis or petechiae or more overt signs such as epistaxis, hemoptysis, hematuria, hematemesis, melena, vaginal bleeding, or oozing from vascular access lines.

Hemorrhage may also occur as a life-threatening event, such as major cerebral or gastrointestinal bleeding.

Treatment of thrombocytopenia should not only take in account patient's number of platelets but also his clinical condition. Local treatment measures such as hemostatic cotton can be used in case of epistaxis.

The transfusion of platelets plays an important role in the prevention and management of bleeding. The risk of bleeding greatly increases in patients when the platelet count is less than 10 × 10^9/L. The decision whether to transfuse platelets or not if less than 10 × 10^9/L, as a prophylactic attitude, is common in clinical practice but contradicted in the literature. Platelet transfusions may be given when the platelet count falls below a prespecified platelet count (e.g., 10 × 10^9/L) to prevent bleeding, or they may be given to treat bleeding (such as a prolonged nosebleed). The routine use of platelet transfusions to prevent bleeding in these patients has not previously been supported by high-quality evidence. A Cochrane review found low- to moderate-grade evidence that a therapeutic-only platelet transfusion policy is associated with increased risk of bleeding when compared with a prophylactic platelet transfusion policy in hematology patients who are thrombocytopenic due to myelosuppressive chemotherapy or HCT [35]. Prophylactic platelet transfusion is recommended if patients with a platelet count less than 50 × 10^9/L require procedures such as placement of central catheter or a bone marrow aspiration. The question about prophylactic versus therapeutic platelet transfusion is important as poly-transfused patients may develop an inappropriately poor response due to antiplatelet Abs against platelet antigens (PLA) or HLA antigens, known as alloimmunization. This occurs when Abs are formed against foreign antigens on donor platelets or against HLA antigens on contaminant WBCs present in transfused blood products. The use of leukoreduced blood products has significantly reduced the incidence of alloimmunization which still varies between 20% and 85% in patients with hematologic malignancies who have prolonged thrombocytopenia and require multiple platelet transfusions.

Other strategies to reduce the risk of alloimmunization and refractoriness are the use of crossmatched platelets and the use of HLA-matched platelets.

Evidence-Based Nursing Interventions

A key intervention in the prevention and management of bleeding in patients with cancer is the judicious use of prophylactic and therapeutic platelet transfusions because of the well-established association between bleeding and thrombocytopenia. A strong evidence base exists to guide the use of platelet transfusions, and oncology nurses should be knowledgeable of the recommended guidelines for platelet transfusions, including threshold platelet levels. The clinical condition of the patient should be taken into account because patients with fever and bacteremia or sepsis consume more platelets and an expected drop down of platelets can occur.

Nurses should be knowledgeable of the recommendations for the use of the cytoprotective agent mercaptoethanesulfonate sodium (mesna) to prevent ifosfamide- or cyclophosphamide-associated hemorrhagic cystitis. The total daily dose of mesna is 100% of the ifosfamide/cyclophosphamide dose. Mesna and forced saline diuresis are recommended for cyclophosphamide administration in the stem cell transplantation setting.

Hormonal agents are very effective in preventing normal menstrual bleeding in such patient populations and are considered an effective clinical practice, particularly in the hematopoietic stem cell transplantation population. Oncology nurses have a pivotal role in the prevention and management of bleeding, as well as in the education directed at self-care and prevention of injury for patients expected to experience thrombocytopenia.

Neutropenia and Febrile Neutropenia (FN)

Neutropenia is defined as a reduction in circulating neutrophils, usually an absolute neutrophil count (ANC) <1500 cells/microL, and severe neutropenia is usually defined as an ANC <500 cells/microL or an ANC that is expected to decrease to <500 cells/microL over the next 48 h. The risk of serious infection increases as the absolute neutrophil count (ANC) falls to the severely neutropenic range (<500/μL = grade 4 according to NCCN) and is higher in those with a prolonged duration of neutropenia (>7 days). The duration and severity of neutropenia directly correlate with the total incidence of all infections and of those infections that are life-threatening [36].

Infection has been reported as the leading cause of non-relapse mortality among allogeneic HCT recipients [37]. In addition to the myelosuppressive effects of the conditioning regimen, immunosuppressive therapy for graft-versus-host disease prevention, previous infections, underlying malignancies, and malnutrition places transplantation recipients at a higher risk for developing neutropenic complications. The type of infections that may occur corresponds to the specific immunologic deficiency that accompanies each phase of the transplantation process. During the pre-engraftment phase (first 30 days post-HCT), bacterial infections predominate, along with fungal infections for patients with prolonged neutropenia. In the mid-recovery phase (30–100 days post-HCT), viral and fungal infections are more commonly observed. During late recovery phase (more than 100 days post-HCT), the risk for developing invasive fungal infections in addition to viral and bacterial infections is higher in patients with chronic graft-versus-host disease due to the maintenance of immunosuppressive drugs [38].

Risk models to predict outcomes for patients who develop FN enable healthcare providers to identify patients who likely would have an uncomplicated recovery and those most likely to suffer major complications. The Multinational Association of Supportive Care in Cancer (MASCC) developed a predictive model for patient evaluation at the time of presentation with FN in which the outcome measure was either uncomplicated recovery (avoid hospitalization and be treated with an oral anti-infective regimen) or development of serious complications requiring IV antibiotics [39]. In patients with hematologic malignancies, this model may be applied for patients with lymphoma or multiple myeloma but not in the case of acute leukemia or in the HCT setting as these patients are in a myeloablative status and per definition at high risk.

Signs and symptoms of febrile neutropenia are depending on the site of infection and on the causal pathogen, but mostly neutropenic patients present only fever as the first sign of infection. The most likely source is endogen, especially translocation of bacteria from the gastrointestinal tract into the blood.

Preventive and therapeutic interventions mainly involve the administration of empiric antibiotics, growth factors, and in some rare cases with for life-threatening infections the administration of granulocyte transfusion. The usefulness of colony-stimulating factors in transplant patients is still not clear, and the use depends on the transplant center as some hematologists prefer not to administer G-CSF due to an immunocompromised effect in the transplant setting.

There is also some debate regarding the use of antibiotics in febrile neutropenia; the empiric use is a universally accepted standard; however, choosing the type of antibiotic varies across institutions due to the development of antimicrobial resistance. Therefore, local epidemiology of bacterial infections at the transplant unit should guide decisions.

Evidence-Based Nursing Interventions

Interventions for prevention of infection according to their level of evidence are developed by the American Oncology Nursing Society (ONS) and include nonpharmacologic interventions such as environmental and lifestyle modifications (neutropenic precautions) and pharmacologic interventions with the use of antibiotics and colony-stimulating growth factors [40]. For transplant patients, the following interventions are *recommended for practice*: antibiotic, antifungal, and antiviral prophylaxis in at-risk patients; CSFs, including biosimilars in at-risk patients; hand hygiene (with alcohol sanitizer); contact precautions for resistant organisms; influenza, pneumococcal, and meningococcal vaccination; adherence to general infection control recommendations; catheter care bundle for prevention of CLABSI (Central Line-Associated Bloodstream Infections); environmental interventions; and chlorhexidine skin preparation. *Effectiveness is not established* for antimicrobial-coated central venous catheters, disinfecting IV catheter caps, granulocyte transfusions, protective isolation, staff training, and urokinase IV catheter flush. *Effectiveness is unlikely* for restriction of fresh fruits and vegetables and frequent IV tubing component changes (based on information from Oncology Nursing Society [41]).

In case of febrile neutropenia, it is well-established that the first hour of the first febrile episode is crucial (golden hour) to start IV antibiotics. Any delay in administration of antibiotics beyond the golden hour may conduct the patient in a life-threatening situation. It is crucial for nurses to take prompt action by documenting a potential infection, to stabilize the hemodynamic parameters of the patient, and to start rapidly the administration of antibiotics.

Oral Mucositis

Mucositis is an inflammatory process that can involve the mucosal epithelial cells from the mouth to the rectum. Oral mucositis is a distressing toxic effect and one of the major side effects of the myeloablative conditioning used to prepare patients for

HCT. About 70–99% of patients receiving myeloablative conditioning for HCT experience severe oral mucositis, generally when their neutrophil counts fall below 500 cells/μL [42]. One needs to differentiate mucositis involving the oral cavity and the remainder of the gastrointestinal tract that require use of a scope-type device for close examination. As a result, oral cavity mucositis has been the focus of most of the studies reported to date.

Once believed to involve a linear process, mucositis is now understood as a complex process involving many different factors, including cytotoxicity of treatments, the inflammatory process, cellular apoptosis, cytokines, and microorganisms in the oral cavity. Sonis [43] developed a proposed theoretical model to facilitate understanding of the complex process involving five successive phases: initiation, message generation, signaling and amplification, ulceration, and healing (Fig. 18.4).

When the inflammation progresses to a breakdown in the protective mucosal barrier, the microorganisms normally present in the oral cavity and throughout the gastrointestinal tract can enter the bloodstream and cause potentially life-threatening infections such as bacteremia and sepsis that require prompt strategic intervention. In addition to the risk of infections, mucositis causes pain, restricts oral intake, and contributes to malnutrition, interruption of treatment, and increased hospitalizations.

Risk factors that predispose an individual to oral mucositis may be divided into local and systemic; however, these factors are not isolated from one another. Local risk factors include oral hygiene status, salivary flow rates, defective and sharp restorations, and the presence of prostheses. Saliva has several mucoprotective effects, including lubrication of tissues, prevention of trauma and irritation, and protection against microorganisms. Systemic risk factors include age, nutritional status, the staging and diagnosis of cancer, treatment regimen, use of medication, degree of granulocytopenia during treatment, and a patient‘s genetic predisposition.

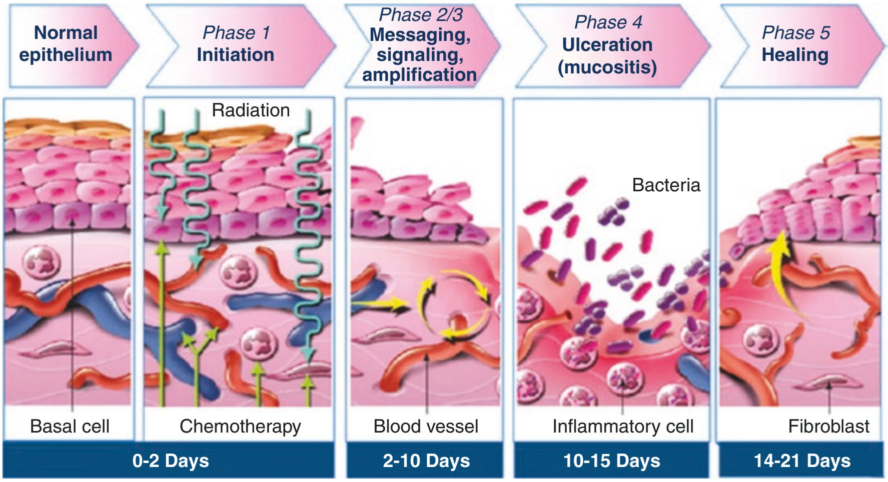

Fig. 18.4 The five phases of development of mucositis from Hyloris pharmaceuticals. (Adapted from Sonis, J Support Oncol 2004;2(Suppl 3):3–8)

Evidence-Based Nursing Interventions

Oral mucositis is one of the best examples in oncology of nursing-sensitive patient outcomes, where preventive and management nursing interventions may reduce the incidence, the severity, and pain related to oral mucositis.

The work by Oncology Nursing Society (ONS) Putting Evidence Into Practice (PEP®) mucositis team attests to the commitment of oncology nurses to make a difference in patient outcomes through evidence-based practice [44].

The evidence-based practice starts with a baseline and a systematic daily assessment of the oral cavity by using a validated and practical tool such as the WHO grading scale which considers objective clinical findings, subjective feeling of pain, and the need for parenteral nutrition. The WHO scale ranges from 0 to 4 (Table 18.2).

Mucositis interventions *recommended for practice* are oral care protocols to provide consistent frequent oral hygiene, prophylactic mouth rinses, and routine assessment for early detection; sodium bicarbonate mouth rinses; cryotherapy or the topical application of cold with ice water, ice cubes, ice chips, or ice lollipops during chemotherapy infusion with agents with a short half-life; low-level laser therapy that showed significant high effect sizes for reducing prevalence, severity, pain, and duration of mucositis; and palifermin. *Likely to be effective* are benzydamine rinses which lower severity and pain of mucositis and prophylactic chlorhexidine mouth rinses.

Effectiveness is not established for all other products such as allopurinol mouthwash, amifostine IV, calcium phosphate mouth rinse, glutamine, honey, etc. Evidence for these interventions is limited because of inconsistent research results, small studies, and study designs.

Not recommended for practice are the use of chlorhexidine (nonprophylactic) which did not improve existing mucositis and the use of sucralfate.

Hemorrhagic Cystitis

Hemorrhagic cystitis (HC) is a troublesome and potentially life-threatening complication of HCT. HC can appear within a few hours after chemotherapy or after weeks or months. Early-onset HC (EOHC, within 48 hours after receiving chemotherapy) is usually associated with the conditioning regimen, while late-onset HC (LOHC within 21 days or later posttransplantation) is associated with viral infection such as polyoma BK virus, adenovirus, and cytomegalovirus (CMV).

Patients with hemorrhagic cystitis often experience poor quality of life, severe pain and discomfort, and prolonged hospitalizations. Despite numerous advances in stem cell transplantation methods, hemorrhagic cystitis is difficult to control, and treatment options are few without any evidence-based strategy.

Table 18.2 WHO scale for oral mucositis

WHO scale for oral mucositis				
Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
No oral mucositis	Erythema and soreness	Ulcers, able to eat solids	Ulcers, requiring liquid diet	Ulcers, oral alimentation not possible

EOHC is usually associated with the conditioning regimen, particularly cyclophosphamide (CY), widely used in the HCT setting. Acrolein, a urinary metabolite of CY and ifosfamide, is thought to be responsible for the urothelial toxicity.

Evidence-Based Nursing Interventions for EOHC

Hyperhydration associated with diuresis alkalinization and mesna represents the current gold standard for preventing EOHC in HCT regimens containing CY [45]. However, preventive urethral catheterization and continuous bladder irrigation (CBI) showed conflicting data, and routine use is not supported. Nursing practice should consider the benefits and harms of preventive catheterization and CBI in patients who received HCT conditioning including high-dose CY [46]. CY must be given in the morning to ensure the possibility for the patient to empty his bladder and to not retain acrolein. The administration of mesna must respect the correct timing with a first infusion 15 min before CY followed by an infusion every 4 h until 24–48 after the last dose of CY. The preferred route is IV as patients often suffer from nausea and vomiting during high-dose CY.

Further systematic review is warranted, and additional prospective multicenter studies with larger samples are needed to explore the balance between benefits and harms for these invasive measures.

LOHC associated with BK virus is characterized by painful hematuria secondary to inflammation and breakdown of epithelial cells of the bladder mucosa.

BK virus is found in most patients after stem cell transplantation, and most immunocompetent adults are BK virus seropositive. The reactivation of BK is clinically linked with hemorrhagic cystitis in stem cell transplantation recipients. Higher-severity grades indicate increased mortality risk. Bladder irrigation or even cystectomy may be necessary to treat prolonged, high-grade hemorrhagic cystitis. Many alloimmune processes, such as acute GVHD, occur after allogenic transplantation and are believed to possibly contribute to development of BK viruria and hemorrhagic cystitis [47]. Damage caused to the uroepithelial cells may provide an environment that supports BK virus replication and reactivation. In addition, patients experiencing acute GVHD also are prescribed immunosuppressive agents which decreases host immunity and enhances BK virus reactivation or replication.

Evidence-Based Nursing Interventions for LOHC

There are no specific evidence-based nursing interventions for LOHC. Open questions that need to be investigated are if a baseline detection of BK viruria and identifying patients at risk could be useful and if hyperhydration in case of microscopic hematuria could prevent worsening of HC.

A retrospective study by Miller et al. [48] showed significant difference in the cumulative incidence of severe BK virus-induced HC in the group receiving ciprofloxacin with 1 of 44 patients developing HC, compared with 11 of 48 patients without prophylaxis.

Unfortunately, very little effective or standardized treatment exists for BK virus-associated hemorrhagic cystitis. Cidofovir inhibits BK virus replication in vitro and in vivo [49] and may be administered either IV or through bladder instillation.

Table 18.3 Hematuria grading [49]

Grade	Hematuria findings
I	Microscopic
II	Macroscopic
III	Macroscopic with cloths
IV	Requiring instrumentation for clot evacuation Leading to urinary retention Requiring surgical intervention May also include elevated creatinine levels and renal impairment

Based on information from Droller et al. [49]

However, cidofovir is not used prophylactically because of its nephrotoxic and myelotoxic properties. Close surveillance of renal function and daily or fractionated diuresis are crucial.

Additional reported treatments for severe hemorrhagic cystitis include intramuscular vidarabine, hyperbaric oxygen, amifostine, factor VIII bladder irrigation or instillation, and intravesicular instillation of E-aminocaproic acid, alum, formalin, silver nitrate, sodium hyaluronate, prostaglandins, GM-CSF, and fibrin glue. In cases of bladder irrigation, keeping the fluids for irrigation at ambient temperature may alleviate discomfort. There is still need for more research-based evidence without conflicting results, but hyperbaric oxygen and intravesicular fibrin glue seem promising and relatively well supported by patients. If obstruction occurs, cystoscopy can be performed. Selective embolization of bladder arteries and catheterization of both ureters to rest the bladder are actions that can be taken in severe cases. Cystectomy remains the last resort if all other treatment attempts fail. Knowledge of treatments for HC and their side effects are paramount for oncology nurses to assure prompt action if necessary and quality care.

Complications of the irrigation can be prevented or minimized by close monitoring and recording of fluid balance. It is also important to maintain patient comfort by adequate pain management and general nursing interventions such as comfortable positioning and assistance with personal hygiene. The need for information and psychological support should be assured for both patient and family.

For both EOHC and LOHC, it is very important to assess daily or twice a day HC with a validated and easy to use tool such as the scale from Droller (Table 18.3).

Sinusoidal Obstruction Syndrome/Veno-Occlusive Disease

Sinusoidal obstruction syndrome (SOS), formerly called veno-occlusive disease (VOD), is a potentially life-threatening consequence of high-dose chemotherapy used during the conditioning pre-HCT and is of vascular endothelial origin. SOS occurs during the time frame beginning immediately after chemoradiotherapy and up to 30 days after transplant, although later instances have been reported. When drugs used in hematopoietic stem cell transplant conditioning regimens are metabolized in the liver, hepatocytes produce toxic metabolites. These metabolites trigger the activation, damage, and inflammation of the endothelial cells lining the sinusoids (small capillary-like blood vessels in the liver). The activated sinusoidal endothelial cells release inflammatory cytokines and chemokines which break down the extracellular matrix

Table 18.4 New EBMT criteria for SOS/VOD diagnosis in adults from Mohty et al. [50]

Classical SOS/VOD	Late-onset SOS/VOD
In the first 21 days after HSCT	>21 days after HSCT
Bilirubin ⩾2 mg/dL and two of the following criteria must be present: Painful hepatomegaly Weight gain >5% Ascites	Classical VOD/SOS beyond day 21 OR Histologically proven SOS/VOD OR Two or more of the following criteria must be present: Bilirubin ⩾2 mg/dL (or 34 μmol/L) Painful hepatomegaly Weight gain >5% Ascites AND Hemodynamical or/and ultrasound evidence of SOS/VOD

that supports the structure of the sinusoids. This allows the deposit of debris, and endothelial cells can dissect off and embolize. The damage leads to an increase in the expression of tissue factor (TF) and plasminogen activator inhibitor-1 (PAI- 1). This coagulopathy causes an increase in clot formation and a decrease in the breakdown of clots. The deposition of fibrin and the clot formation will contribute to the narrowing of the sinusoids and may ultimately lead to hepatic sinusoidal obstruction.

There are several diagnostic criteria developed for SOS. The most recent diagnostic criteria proposed by EBMT [50] are for classical SOS with onset within the first 3 weeks after HSCT, but if SOS develops after day +21, elevated serum bilirubin level is not always seen, which leads to a modified version of the criteria which can be used for diagnosis of late SOS [50] (Table 18.4).

Symptoms of SOS are weight gain, fluid retention and symptoms related to fluid retention (pleural effusion, pulmonary infiltrate, hypoxia), overt edema and ascites, hepatomegaly and jaundice, and abdominal discomfort and pain.

No proven medical *prophylaxis* exists, but sodium heparin, prostaglandin E1, ursodeoxycholic acid, and low molecular weight heparin have been given, without proof of effectiveness.

Defibrotide is approved for *treatment* of severe SOS, but supportive treatment according to symptomatology remains the most frequent attitude in clinical practice. Defibrotide protects the endothelial cells, reduces inflammation, and restores thrombo-fibrinolytic balance.

The recommended dose is 6.25 mg/kg body weight administered as a 2-h, IV infusion every 6 h (to a total dose of 25 mg/kg/day). Recommendation for treatment duration is at least 3 weeks but should continue until the symptoms and signs of severe VOD resolve.

Evidence-Based Nursing Interventions

There are no specific evidence-based nursing interventions, but it is obvious that nurses are indispensable in this daily monitoring, not just to weigh patients (threshold of >5% for weight gain) daily combined with a meticulous fluid balance but also to being alert to more unspecific symptoms such as abdominal discomfort and pain. For successful identification, diagnosis and treatment of SOS nurses should receive specific education on SOS/VOD to understand the importance of their role. Performing abdominal girth measurement needs to use a marked line for placement of the measuring tape and to choose one position (i.e., sitting/standing/lying) for the patient, to be used consequently. Findings should be precisely documented, and any changes promptly reported.

Engraftment Syndrome (ES)

ES is known as a capillary leak syndrome or cytokine release syndrome and is more frequent after auto-HCT although it is also described in allo-HCT as well, especially when reduced intensity conditioning (RIC) is given prior to transplantation.

The most prevalent *symptoms* are noninfectious fever, rash, and pulmonary edema with an onset of symptoms from 7 days before to 7 days after engraftment.

Other diagnoses such as infection, drug rash, diarrhea associated with infection or medication, and intravenous-related fluid overload should be excluded. Broad-spectrum antibiotics should be started until infection is ruled out. If cultures are negative and symptoms remain after 48–72 h of antibiotic treatment, corticosteroid *treatment* can be initiated. Methylprednisolone in doses of 1–3 mg/kg/day IV are recommended until symptoms begin to disappear. Response to treatment is usually seen within 2–3 days. Corticosteroids could then be switched to oral administration and should be slowly tapered. Supportive care with IV fluids, electrolyte supplements, and oxygen therapy may be necessary depending on the symptoms.

Evidence-Based Nursing Interventions

There are no specific evidence-based nursing interventions, but monitoring of fever and obtaining cultures from blood, urine, stools or other suspected sites of infection must be standard attitude. Perform skin assessment at least daily and note any rashes. If a rash is detected, patient's medication chart needs to be reviewed for detection of possible drug rash.

Patient education about signs and symptoms of ES and explaining what it is and why it occurs, as well as side effects of corticosteroids such as diabetes, are important.

Graft-Versus-Host Disease (GvHD)

Acute and chronic graft-versus-host disease (GvHD) is still a major cause of morbidity and mortality in patients who undergo allogeneic HCT and affects approximately 30–40% of recipients. GvHD happens because the donated cells are not identical to the cells of the patient (the host) with donor T-cells attacking host's organs.

Acute GvHD (aGvHD) is a reaction of donor immune cells against three main host tissues, namely, the skin, liver, and gastrointestinal tract [51]. Chronic GvHD (cGvHD) is a syndrome of variable clinical features mimicking autoimmune diseases. Manifestations of chronic GvHD may be restricted to a single organ or may be widespread, with a major impact on quality of life for survivors.

Donor T-cells play a central role in mediating GvHD following interactions with activated host and donor antigen-presenting cells (APC). A complex network of cytokines, chemokines, cellular receptors, and immune cell subsets then modulate T-cell/APC interactions that result in the initiation and maintenance of GvHD. The three-phase process for aGvHD includes initial tissue damage from the conditioning therapy, activation of host APC, and activation and proliferation of donor T-cells.

Signs and symptoms of aGvHD depends on the target organ.

Skin

Acute GvHD causes a rash which is usually flat and red and often occurs on the hands, feet, and around the ears and upper chest, at first. This can spread over the whole body. It is often itchy and sore and can feel like sunburn. A biopsy may be taken but is not always conclusive.

Gastrointestinal

Signs and symptoms include weight loss, stomach discomfort and pain, nausea, vomiting, and diarrhea. The diarrhea can be profuse with several liters a day with or without secretions and from ulceration of the mucosa.

Biopsy in this group of patients is more informative.

Liver

Jaundice from hyperbilirubinemia is the most important sign of liver GvHD with a cholestatic pattern of elevated conjugated bilirubin, alkaline phosphatase, and gamma-glutamyl transpeptidase. It may be accompanied by pruritus. It is often difficult to perform biopsy due to the increased risk of bleeding as these patients are often still profound thrombocytopenic.

However, it is well documented that some level of aGvHD is beneficial. It has been found that relapse rates post allograft were lowest in patients with aGvHD versus those without.

Classification of aGvHD based on Glucksberg-Seattle criteria is shown on Table 18.5.

Prophylaxis of GvHD at most centers is based on calcineurin inhibitors (CNIs) such as cyclosporine-A along with short-course methotrexate (MTX). Despite standard prophylaxis, approximately 40% of patients receiving HLA-matched HCT will develop GvHD requiring high-dose corticosteroids. Other drugs for prevention are mycophenolate mofetil (MMF), mainly used in reduced-intensity transplant conditioning regimens, tacrolimus, sirolimus, and antithymocyte globulin (ATG). Today cyclophosphamide is also often given in the posttransplant period.

Treatment of aGvHD starts only from grade II or more with as standard systemic high-dose corticosteroids at 2 mg/kg body weight. Other therapeutic options include extracorporeal photopheresis, infliximab, etanercept, mesenchymal stem cells, and other immunosuppressive under investigation.

Management of cGvHD is even more complex and will not be discussed here. Chronic GvHD commonly occurs in patients who previously had aGvHD. However, single organs alone may be affected; cGvHD nearly always affects multiple sites

Table 18.5 Classification of aGvHD based on Glucksberg-Seattle criteria

Stage	Skin/maculopapular rash BSA	Liver bilirubin (mg/dl)	Gut (ml diarrhea/day)
0	No rash	<34 umol/L	<500 ml/day
1	<25% of body surface area	34–50 umol/L	>500–999 ml/day or persistent nausea with histological evidence stomach/duodenum
2	25–50% of body surface area	51–102 umol/L	1000–1500 ml/day
3	>50% of body surface area	103–255 umol/L	>1500 ml/day
4	Generalized erythroderma with bullous formation and desquamation	>255 umol/L	Severe abdominal pain with or without ileus

Grade	Skin	Liver	Gut
I	Stage 1–2	–	–
II	Stage 3	Stage 1	Stage 1
III	–	Stage 2–3	Stage 2–3
IV	Stage 4	Stage 4	Stage 4

with the eyes, mouth, skin, GI tract, and liver mostly involved. In the past it was considered that if patients developed signs and symptoms of GvHD after day 100, they had cGvHD, even if clinically the patient appeared to have acute manifestations. Today acute and chronic GvHD are distinguished by clinical features rather than time from transplant. The clinical score describes how affected the patients are by their inability to perform activities of daily living. The evaluation covers the involvement of individual organs and sites [52].

Evidence-Based Nursing Interventions

There are no specific evidence-based nursing interventions, but a lot of care can be given to relieve the patient from frequently troublesome symptoms of aGvHD as well as to provide topical care.

Skin Care

The aim is to maintain the integrity of the skin. Regular application of emollients, organic coconut oil or other natural lipids (e.g. olive oil), topical antipruritic agents, and topical immunomodulators (e.g. steroid/tacrolimus cream) and use of high SPF sunscreen are suggested. In case of grade IV cutaneous aGvHD and bullous formation with desquamation, one may apply irrigation with sterile water and an antibacterial cream (e.g., Flamazine) and protect the area from the air to minimize pain and risk of infection.

Gastrointestinal

Patients who develop diarrhea will have stool samples sent to exclude any infectious cause such as clostridium or CMV.

Quantification is paramount as the volume of diarrhea determines the grade of intestinal aGvHD and the decision to start corticoids or not.

There is still no consensus about the way of administration of nutrition in case of intestinal aGvHD, either by enteral feeding with a feeding tube or with a gastrostomy (rather for long-term) or by intravenous total parenteral nutrition. The question that one should ask is whether enteral nutrition will permit adequate uptake of nutrients in case of severe intestinal aGvHD. Nevertheless, an adequate nutrition plan must be decided to ensure the nutritional status of the patient.

In case of upper GI disturbance, with nausea and vomiting, one needs to advice on small and frequent meals as well as supplements. Patients who develop grade IV GI aGvHD may benefit from the use of Flexi-Seal fecal collection devices.

Liver

The main nursing interventions are supportive care according to the symptomatology.

As the physical as well as the psychological impact of aGvHD is huge, nurses need to explain what is happening and give information about therapeutic decisions and assure the patient.

Conclusion

The evolving treatment options of hematologic malignancies warrant expanded and specialized knowledge and skills development for nurses to provide expert care to these patients. New drugs with other mechanisms of action and new side effects must be faced in the context of outpatient setting. Understanding these new approaches needs, beyond basic training in hematology, a continuing education program for nurses as well as the development of critical thinking when reading scientific literature to provide evidence-based nursing interventions.

In the setting of increasing ambulatory care and the era of patient- and family-centered care, patient participation, and shared decision-making, patient education based on the patient's needs is paramount and only possible when nurses are themselves well documented with sufficient knowledge.

Expert and highly complex practice includes comprehensive assessment with validated tools, early recognition of a complication, prompt action, and care management (preventive and curative) in collaboration with the patient and other healthcare members. Supportive care to improve the quality of life of our patients extends beyond symptom management and includes social, psychological, and spiritual care.

Above clinical management of patients with hematologic malignancies, nurses in hematology should take the leadership in the development of new models of care such as nurse-led consultation, outpatient care, patient self-management, and survivorship care provision for the increasing number of hematology cancer survivors. To provide quality survivorship care, innovative models of hematology survivorship care plans are required which address long-term physical and psychosocial well-being.

New and more general challenges to be faced by the hematology nurse are the occurrence of antimicrobial resistance, adherence to oral treatment, and effective and equal care to all patients in a context of multiculturality.

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Advanced Nursing Practice: The Way to Go? – How to Progress in Your Speciality

19

Maya Zumstein-Shaha

Abstract

Healthcare systems around the world struggle with increasing numbers of elderly persons and persons with chronic diseases, penury of well-qualified healthcare professionals, and rising cost. Changes in healthcare also affect children. However, this group will not be discussed in this chapter. One of the responses offered as countermeasure to some aspects of this crisis is new roles for healthcare professionals. In nursing, advanced nursing practice is one such role that currently draws much attention. In this chapter, advanced nursing practice will be introduced, its relevance for oncology nursing will be explored, and recommendations will be offered. Additionally, a brief overview of the state of development in select countries, namely, the United States, Canada, the United Kingdom, Switzerland, Germany, and Austria, will be presented.

Keywords
Progress of praxis · Progress of scientific disciplines · Oncology nursing · Advanced nursing practice · Comparison

Introduction

Around the world, healthcare systems are facing three major challenges. Firstly, we are living longer than before with an average age expectancy of 71.5 years for men and women worldwide. In Europe, life expectancy is given at 76.8 years as opposed to

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M. Zumstein-Shaha (✉)
Division of Nursing, Department of Health, Bern University of Applied Sciences,
Bern, Switzerland
e-mail: maya.zumsteinshaha@bfh.ch

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60.0 years in the African region WHO [80, 81]. With increasing age, individuals are more likely to develop one or more chronic diseases such as cardiovascular health problems or cancer. Due to the advances in medicine and related disciplines, individuals suffering from chronic diseases or who are multimorbid continue with their health problem [1, 2, 12]. Nevertheless, healthcare systems are increasingly fragmented, which presents a huge challenge to individuals [44]. Navigating through these healthcare systems requires detailed knowledge and understanding, which is sometimes lacking. In addition, individuals require energy to successfully manage the healthcare system adequately. Energy may be a short commodity due to the health problem. A highly fragmented healthcare system also threatens the flow of communication and continuity of care. Therefore, individuals suffering from chronic diseases need to be able to manage highly challenging situations due to their chronic disease and require specialized support and care services to manage daily life. For this purpose, healthcare professionals need specific education as well as structural and organizational conditions that allow for such services [54–56].

Secondly, healthcare systems are confronted with a severe shortage of well-educated and well-qualified professionals. In the United States, the shortage of physicians working full time in 2025 is predicted to be between 124,000 and 160,000. At the same time, there are specific challenges associated with the new generation of physicians. The number of women choosing to become physicians is increasing. With it, there is a demand that work as a physician may also account for family life. In addition, physicians of the newer generation prefer part-time work possibilities [47]. Among the nursing workforce, the numbers appear even more dramatic. It is estimated that over one million nurses are lacking to either account for the current workforce retiring or to fill vacancies. This large number of nursing shortage is predicted to vary greatly, though, depending on the economic situation. It is observed that in economic crises, the nursing shortage is decreasing significantly, whereas it is growing again in economically stable situations. Thirdly, healthcare systems are forced to manage cost more effectively than ever. Nevertheless, healthcare systems are expected to provide adequate, safe, and ethical care to individuals who need it. Measures to reduce costs have been only marginally successful to this date and have largely supported the fragmentation of the healthcare system [46, 47]. Hence, it is imperative to find new ways of managing these challenges. One way of responding to this situation is the development of new models of care that include a reorganization of the demands, population needs, and related tasks including a reconsideration of the work domains of the various healthcare professionals. For example, nursing professionals cannot employ all their skills or knowledge as their full potential is not exploited. Interprofessional work and education constitute important aspects of this endeavor, which will promote mastering the current challenges. Hence, new and innovative education models need to be developed and implemented to help prepare the future healthcare professionals for their work [46–49].

Background

Noncommunicable diseases remain the most frequent cause for disease and death around the world, WHO [80, 81]. This group of diseases is expected to double until 2050 [59]. Cardiovascular health problems are the most frequent cause of death worldwide followed by cancer with about 8.8 million deaths. There are approximately 14 million new cases of cancer worldwide per annum. Over the forthcoming two decades, the incidence of cancer is expected to rise by 70%. About 30% of the cancer cases are related to unhealthy lifestyle including obesity, sedentary lifestyle, alcohol consumption, or tobacco use. In addition, specific infections – i.e., hepatitis or human papilloma virus – account for about 25% of the cancer incidences in underdeveloped regions of the world, WHO [80, 81]. Top cancer in terms of incidence is lung cancer followed by breast and colorectal cancer all over the world. In terms of death, lung cancer still constitutes the most frequent cause followed by stomach and colorectal cancer worldwide [32].

Cancer is perceived to proceed across several stages from screening through diagnosis to end of life. These stages are not linear. Patients may go through some of the stages several times or never. Generally, the following stages are identified: the preventive stage, the diagnostic stage, the treatment stage, the survivorship, the stage of disease progression, the end-of-life stage, and the grieving stage [6] (Fig. 19.1).

As lifestyle factors such as healthy nutrition, active life, and moderate to no consumption of alcohol or tobacco are considered contributing to the incidence of cancer, prevention focuses on advocating measures to improve our lifestyles. National health departments regularly launch campaigns to improve knowledge and to sensitize the population for elements of healthy living (for examples see https://www.cdc.gov/healthcommunication/campaigns/index.html or https://www.bag.admin.ch/bag/en/home/themen/mensch-gesundheit.html). Another important element of cancer prevention is screening campaigns, for example, for early detection of breast cancer or colorectal cancer. Although population-based screenings on national level are discussed controversially, there are indications that screening may contribute to better health outcomes [28]. Due to the growing progress in genomics, there are possibilities of detecting potentially carcinogenetic setups and predispositions. Based on this information, preventive measure may be undertaken such as more intensive and individualized cancer screening programs [5].

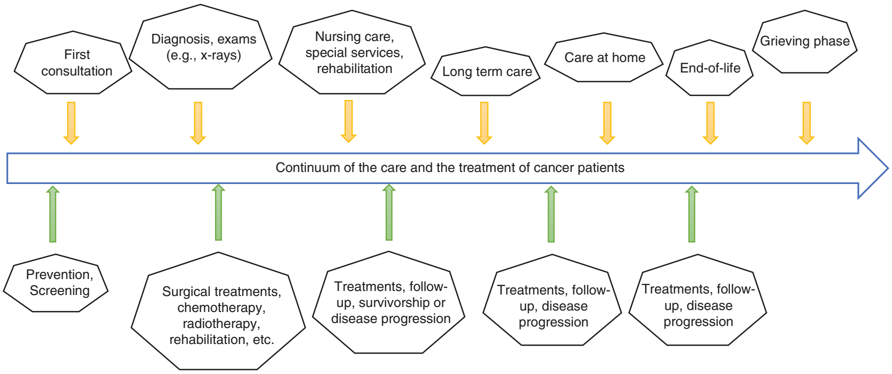

Fig. 19.1 Cancer care continuum

A health problem or symptoms such as pain provoke individuals to consult with healthcare professionals. In some cases, previous genetic counselling has provided some information on hereditary disposition. Hence, individuals consult with a healthcare provider. To identify the health problem, diagnostics are initiated (e.g., see www.nccn.org). Various exams, consultations, and discussions with healthcare professionals happen at this stage to determine the diagnosis [67]. Depending on the severity of the health problem or the symptoms, individuals are seen at outpatient departments, with specific exam appointments at the hospital. It is recommended to consult the interprofessional team at a tumor board before deciding on therapeutic treatment recommendations [29, 50].

The diagnostic phase not only entails undergoing sometimes invasive exams but is perceived to be anxiety-inducing. Individuals experience high levels of distress and uncertainty. Individuals are confronted with life's finitude, and they defer to the health professionals for guidance and support [52, 83]. At the diagnostic phase, healthcare professionals must break the bad news to individuals about the cancer. For healthcare professionals, breaking bad news constitutes a highly challenging situation. It is essential that the healthcare professionals possess high-quality communication skills and that there is sufficient room and time for this endeavor. For the individuals being diagnosed with cancer, receiving this information is difficult. It has been demonstrated that individuals may not fully understand the disease, the impact of the disease on their lives, or the consequences of the treatments of this disease for them [72].

Treatments start after the individuals agree to the plan. Several different treatment possibilities exist comprising surgical interventions to remove the cancer, neoadjuvant and adjuvant radiation therapy and chemotherapy, targeted therapy, and immunotherapies. There are specific treatments including stem cell transplantation, hyperthermia, photodynamic therapy, blood transfusion, and donation as well as lasers (see https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types.html). Depending on the latest evidence, and the cancer, these therapies are combined. Although the cancer is being treated, individuals may continue to experience symptoms such as pain. In addition, the treatments often entail side effects such as dehydration or nausea. Therefore, individuals undergoing cancer treatment must be well prepared to manage these situations at home. Nevertheless, crises may occur such as severe nausea that necessitates immediate healthcare support and therefore emergency department consultations. The individuals with cancer are required to have an adequate support system such as families around them for help in such situations [76]. Disease symptoms, treatment-related side effects, and the burden of comorbidities often lead to hospital and emergency department consultation in cancer patients [4].

At this stage, individuals experience moderate anxiety and uncertainty and are sometimes bothered by the confrontation with life's finitude [52, 83]. However, it has been demonstrated that many needs of these individuals remain unknown or unassessed and therefore unmet. Individuals with lower levels of education or income, women or younger individuals, survivors, children of individuals with cancer, or family members of individuals with cancer and impaired health can experience more unmet needs [3, 16].

During the treatments and afterward, individuals with cancer must undergo monitoring exams at regular intervals. These monitoring visits are considered highly stressful for the individuals. The focus during these consultations is renewed or continued cancer growth, disease progression, or recurrence as well as long-lasting side effects [83]. In some cases, the individuals require rehabilitation or additional care services [68]. Should the monitoring visit indicate a recurrence of cancer or disease progression, healthcare professionals need to talk about the prognosis of the disease. Discussions about prognosis constitute a highly demanding situation for both the individual with cancer and the healthcare professionals. Therefore, it is very important that the healthcare professional may have sufficient skills to manage this situation. It is also recommended that healthcare professionals reflect on the type of information that needs to be communicated and the way of this communication [20]. There are indications that specific interventions for the individuals with cancer and their families may contribute to better quality of life [16].

Sometimes, individuals with cancer require prolonged care beyond the treatments. Similarly, some individuals require specific services by specialized healthcare professionals such as specialized care at home or at the outpatients' department.

At some stage, cure is no longer a viable option, and the cancer cannot be treated with complete remission as an outcome. It is possible that the individuals with cancer continue to live life, but the disease burden with symptoms such as pain generally increases. At this palliative stage, individuals with cancer may need to be cared for by the interprofessional team that includes palliative medical and nursing care specialists. It is recommended to include these specialists as early in the cancer continuum as possible [74, 75, 79]. Integration of palliative care at an early stage in this continuum can lead to more accurate disease perception. Thus, decision-making at the end of life may be positively influenced. It is possible to provide general care at an institution or at home with support by a specialized palliative care team. Specialized support by an interprofessional palliative care team is essential in complex and unstable disease situations and can be provided within institutions, at outpatient departments as well as at home.

For families it is recommended to provide support beyond the demise of the individual with cancer. Such support may contribute to an improved grieving process, avoid the development of pathologic grief, or provide support to all persons concerned, particularly if children are involved. The support may be provided within institutions, at outpatient departments as well as at home.

Nursing Care Activities Within the Cancer Continuum

Within the cancer continuum, many different healthcare providers are implicated. Without claim for exhaustiveness, these healthcare providers include physicians of various disciplines, nurses of various disciplines, technicians, pharmacists, physiotherapists, nutrition experts, and social worker. Besides the support of these other healthcare professionals, individuals with cancer may need tailored nursing care from specialists such as advanced practice nurses, enterostomal therapists, or case managers in addition to general nursing care within the care continuum.

Nurses in oncology care work in the roles of providing direct patient care, educating patients, families, and other healthcare professionals, being a leader and researcher [13]. Oncology care involves healthcare delivery, education, and counselling aiming at health promotion and prevention, contributing to early detection, and promoting "optimal individual and family functioning throughout the disease continuum" (Brant et al. [13], p. 9). It is expected that oncology nurses can identify and respond to individuals' reactions to a cancer diagnosis and subsequent treatments. Such work is provided in many different contexts – inpatients' and outpatients' departments, rehabilitation settings, etc. – to individuals with cancer. The care context needs to provide adequate conditions for nurses to being able to perform this work [13] (Table 19.1).

It is indicated that general nursing education may not suffice to provide comprehensive oncology care. The oncology nurse is expected to provide care coordination and collaborate closely with other healthcare professionals to provide high-quality care to individuals with cancer and their families. In the United States, the Oncology Nursing Society indicates that additional education is required,

Table 19.1 Overview of select nursing care activities across the cancer continuum

Stage	Activities
Overall	Provide case management to support patients during the disease trajectory and manage interfaces at different locations between different healthcare professionals Provide information about the cancer registries Manage patient research enrollment and participation Participate in tumor boards and represent nursing care Provide additional information to patients and families if necessary Support patients and families in ethical decision-making Contribute or elaborate evidence-based standards, guidelines, or related basic documentation Ensure high-quality nursing care and high patient safety Contribute to improved professional practice and interprofessional collaboration [11, 13]
Prevention	Provide information and/or education about preventive measures (such as genetic counselling, healthy living) and/or lifestyle changes (e.g., smoke stop, active lifestyle) Engage in public relations on healthy living, about cancer [13]
Diagnostics	Provide counselling to individuals with a risk of hereditary cancer as part of genetic counselling which includes diagnostic testing, predictive and pre-symptomatic genetic tests, carrier testing, and pharmacogenomic testing Provide education on effective coping strategies for dealing with stress and anxiety [23] Support individuals and families during the process of genetic counselling Provide education on diagnostics, testing, hereditary components, symptoms, symptom management, medication adherence, etc. Provide psychosocial support through, e.g., active and nondirectional listening, ensuring open communication channels between healthcare professionals, individuals, and families, transmitting important information to specialists, and integrating family members [13]

(continued)

Table 19.1 (continued)

Stage	Activities
Treatments	Conduct specific, oncological, and comprehensive assessments of the individual in collaboration with other healthcare professionals to determine, e.g., current health condition, functional status, pain, fatigue, cognitive impairments, neuropathies, spiritual and psychosocial health, family situation, knowledge about the disease, treatments, symptoms, etc. Possess professional, evidence-based knowledge about the treatments and their side effects, prophylaxes of mucositis, hair loss, etc. Provide education on treatments, their side effects, symptoms such as nausea and fatigue, prophylaxes, pain management, medication management, etc. Engage in prevention by promoting lifestyle changes such as smoke stop, foster skin care, etc. Provide counselling and support for self-management at home and living with cancer including identifying reference persons Assess symptoms, evaluate tailored interventions, determine further preventive or therapeutic interventions, and provide information, education, counselling, and support to patients [13] Assess wounds, determine an action plan, execute tailored interventions, and provide information, education, counselling, and support to patients Provide psychosocial support and care with regular and systematic screening of distress, depression, and/or anxiety, including addressing existential issues, provide information, education, counselling, and support to patients Promote compliance by explaining medication and provide information, education, counselling, and support to patients Provide support and counselling for patients in ethical decision-making and include families Identify reference persons for follow-up and provide education to patients and families about risks and managing emergency situations, etc. [13]
Survivorship	Organize and support interprofessional care, e.g., in the form of outpatients' consultation services [13]
Disease progression	Provide comprehensive symptom management Promote psychosocial support to alleviate psychosocial burden Organize and integrate palliative care early in the cancer care continuum Promote advance care planning and address existential issues Promote advanced directives by providing explanation, information, and counselling Provide support and counselling for patients for ethical decision-making and include families Promote research participation Foster network and social support development including the establishment of an emergency plan [13]
End of life	Provide palliative care to alleviate symptoms and symptom burden Provide psychosocial care and promote and support dignity at the end of life Promote psychosocial support to alleviate psychosocial burden Provide support and counselling for patients for ethical decision-making and include families [13]
Grieving	Provide support and counselling to families [13]

Legend: This table draws on a work paper that was developed as part of the nursing concept for the establishment of the comprehensive cancer center of the Insel Group AG, Bern, Switzerland [43]. However, this list is not at all comprehensive, nor is it structured along the different levels of education of nurses which includes cancer-specific knowledge and skills. Several certifications are available to promote expertise in cancer care [13]. The competency profile of the oncology nurse generalist has been determined [33]. In addition, there are evidence-based standards that provide guidance for chemotherapy treatments [60]. Besides direct patient care, oncology nurses are expected to engage in lifelong learning, to extend their own knowledge base continually in order to constantly improve care delivery [13].

In Europe, the European Oncology Nursing Society (EONS) also recommends additional education to nurses working in oncology care. For this purpose, the EONS has established a cancer nursing curriculum that can be adapted to the specificities of each European country. The curriculum can be put in practice and delivered by local oncology societies in each country (see: http://www.cancernurse.eu/education/eons_cancer_nursing_curriculum.html). For this curriculum, EONS has drawn on the recommendations of the Institute of Medicine report about the future of nursing [30, 48, 49]. It is recognized that, currently, nurses may not be able to work "to the full extent of their education and training" (EONS [30], p. 13). In addition, it is maintained that additional expertise is required for nurses working in oncology care that extends beyond basic nursing care as obtained via general basic nursing education. Oncology nurses are expected to "create a therapeutic environment" for individuals with cancer and their families to thrive and to provide person-centered care (EONS [30], p. 13). Besides, oncology nurses need to acknowledge their own limitations and be accountable for their practice [30].

Oncology care may require specific knowledge on cancer and cancer-specific therapies that goes beyond basic nursing education. Therefore, tailored further education is needed that may lead to additional certification. Particularly, nurses administering chemotherapies are expected to advance their knowledge. Certified education exists to promote administration of chemotherapy, thereby improving the quality of care.

Broad and in-depth knowledge and experience in cancer care are equally important. Nurses with such extensive experience often need further support to identify the most adequate further education to move forward in cancer care. For this purpose, a frame of reference combining the concept of advanced nursing practice by Hamric et al. [38] and the theory "From novice to expert" by Benner [8] may yield additional insight.

By using the concept of advanced nursing practice as a starting point, it is possible to conceive nursing as comprising other important elements than patient care, namely, counselling or coaching and evidence-based practice. The levels of competence by Benner [8] may help identify corresponding competencies per level in regard to the seven areas of nursing proposed by Hamric et al. [38]. Although the concept by Hamric et al. [38] and the model by Benner [8] are formulated more generally, this model here may be adapted to cancer nursing. With this model, nurses, managers, educators, and researchers are able to determine the competences on each level and to provide tailored support or education for nurses to move onward in their professional career. Bird and Kirshbaum [9] propose the combination of these two models. It is stated that Hamric et al. [38] have consulted the model by

Benner [8] to account for the transitioning into the role of an advanced practice nurse and to highlight the importance of self-reflection for career-relevant advancement. The educational recommendations formulated by the Oncology Nursing Society of the United States, the European Oncology Nursing Society, or respective oncology nursing societies in each country also allow for the development of tailored education to achieve high-quality oncology nursing care. With the increasing demands of healthcare systems, specific as well as extended knowledge will be necessary to achieve high-quality care. Hence, advanced practice in nursing constitutes an important element in oncology nursing [13].

Advanced Nursing Practice in Oncology

The term "advanced nursing practice" refers to the concept elaborated by Hamric et al. [38]. The concept of "advanced nursing practice" comprises at least four roles in the United States, namely, nurse practitioner (NP), clinical nurse specialist (CNS), certified nurse-midwife (CNM), and certified registered nurse anesthetist (CRNA). The conceptual definition is given as: "Advanced practice nursing is the patient-focused application of an expanded range of competencies to improve health outcomes for patients and population in a specialized clinical area of the larger discipline of nursing" (Hamric et al. [38], p. 71). The regulatory definition provided by Hamric et al. ([38], p. 70), maintains that "a nurse who has completed an accredited graduate-level education program preparing her or him for the role of certified nurse practitioner, certified registered nurse anesthetist, certified nurse-midwife, or clinical nurse specialist; has passed a national certification examination that measures the APRN role and population competencies; maintains continued competence as evidenced by recertification; and is licensed to practice as an APRN."

Advanced practice nursing requires from nurses to have a graduate-level education, i.e., a master's or doctorate in nursing. The clinical practice provided by advanced practice nurses should encompass the following six aspects:

1. Nurses are expected to employ a holistic view of patients and families within their daily environment and in healthcare.
2. It is necessary to develop a therapeutic relationship with patients and families and work collaboratively with them.
3. The clinical performance is on expert level.
4. Nurses use reflective practice.
5. Advanced practice nurses include evidence-based knowledge to guide practice.
6. These nurses are able to draw on and employ several methods that are tailored to patients' and families' needs to manage health and illness (Hamric et al. [38], p. 76).

As is demonstrated in the Fig. 19.2, nurses in advanced practice have additional competencies in the domains of guidance and coaching, consultation, evidence-based practice, leadership, collaboration, and ethical decision-making. Time is

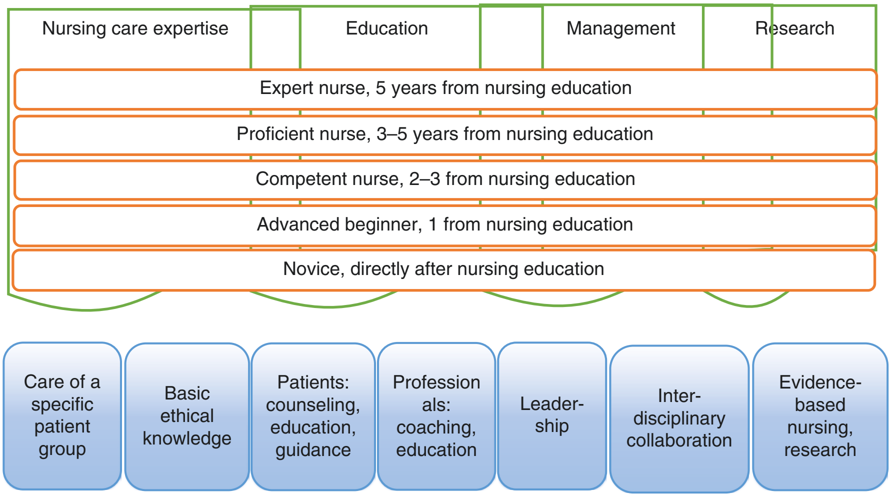

Fig. 19.2 Model combining the concept of advanced nursing practice [38] with the theory "From novice to expert" [8]. (Legend: In this schematic, the concept of advanced nursing practice [39] is combined with the theory "From novice to expert" [8]. With the help of the concept advanced nursing practice [39], nursing is delineated. In addition, the four domains of nursing practice, management, education, and research are identified. The theory by Benner [8] is used here as a career model and builds on concept of advanced nursing practice [39]. Each level of competence cannot only be reached with education but also includes practice experience and capacities of self-reflection [8]. The latter capacities help nurses to critically appreciate their work and learning, to draw conclusions, and to continue learning as a result)

essential to fully develop all these competencies after completing graduate education (Hamric et al. [38], p. 77).

Internationally, advanced nursing practice is described as practice provided by a "registered nurse who has acquired the expert knowledge base, complex decision-making skills and clinical competencies for expanded practice, the characteristics of which are shaped by the context and/or country in which s/he is credentialed to practice. A master's degree is recommended for entry level" (International Council of Nurses [45], p. 6; Pulcini et al. [62], p. 32).

Advanced nursing practice can be offered in a variety of medical domains. However, the field of activities, i.e., the scope of practice, is dependent on the national regulations of the role. Generally, advanced nursing practice comprises comprehensive history taking and evaluation of the health condition; diagnosing including conducting diagnostic exams or writing referrals to physicians and specialists; prescribing medication, treatments, and plans of care or referrals; deciding on hospital admission and discharge; providing patient education and health promotion; engaging in case management and interprofessional collaboration; evaluating services; and conducting research [62]. Generally, advanced practice nurses are perceived to constitute one response to the many challenges that current healthcare systems face. Advanced practice nurses are considered adequate support for patients with chronic diseases and multimorbidity [15, 38, 77].

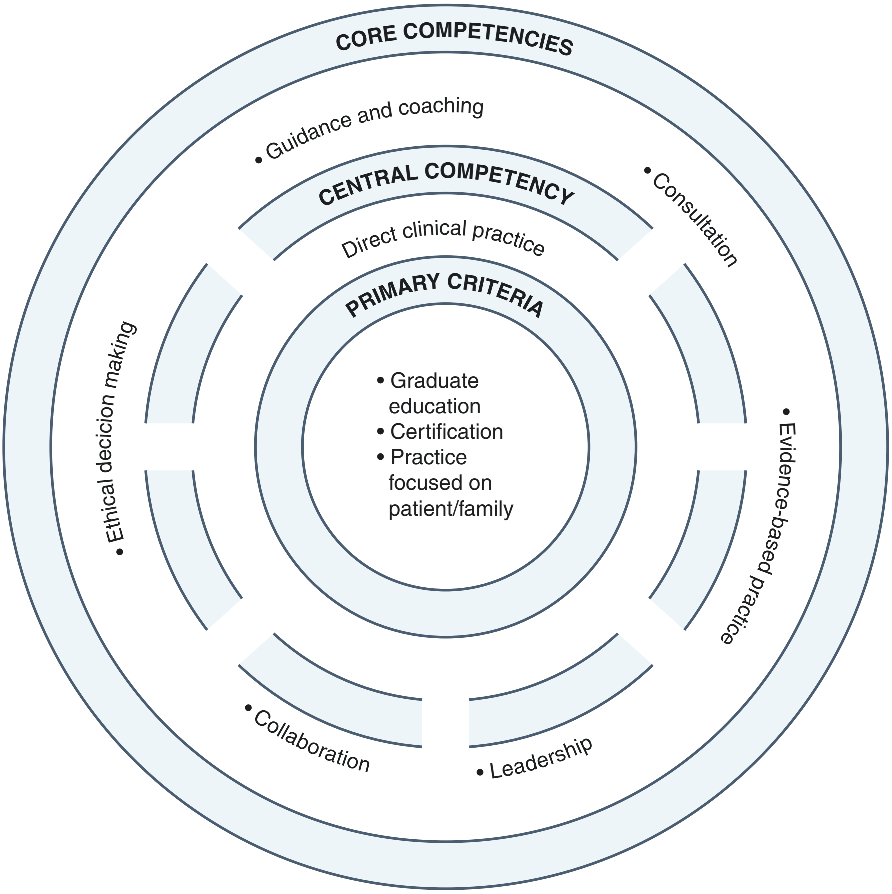

Fig. 19.3 Core competencies of advanced practice nursing. (Legend: This figure has been developed by Hamric et al. ([38], p. 77) to illustrate the extent of advanced practice nursing. This figure is reproduced by kind agreement from Hamric et al. [38])

Advanced practice nurses possess their own area of expertise, in which they may work quite on their own, i.e., autonomously. Therefore, advanced nursing practice not only requires nurses to have more education and competencies; practice needs to account for this. For nurses to be able to work in advanced practice, they need to have some sort of autonomous practice. In addition, they need to be knowledgeable about "legal issues, regulations and credentialing, understand and contribute to health policy considerations, strengthen organizational structures and cultures to support advanced practice nursing, enable outcome evaluation and performance improvement, understand financial issues and costs, and be knowledgeable about marketing issues and contracting considerations" (Hamric et al. [38], pp. 80–81). To illustrate all these additional competencies, Hamric et al. [38] have developed Figs. 19.3 and 19.4.

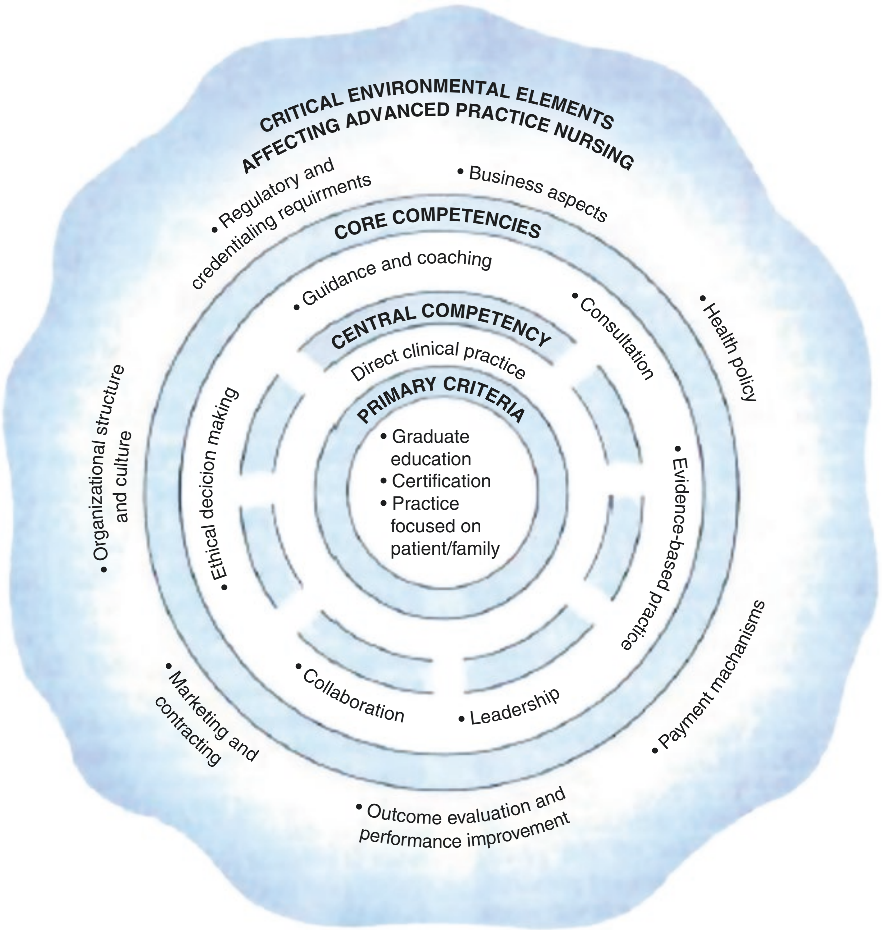

Fig. 19.4 Critical elements in advanced nursing practice. (Legend: This figure has been developed by Hamric et al. ([38], p. 80), to illustrate the additional aspects of advanced practice nursing. This figure is reproduced by kind agreement from Hamric et al. [38])

Advanced practice nurses must fulfill many expectations. They are asked to implement evidence-based knowledge, conduct comprehensive clinical assessments of patients, and provide tailored support to patients for them to better manage daily life [21]. Advanced practice nurses should be able to provide adequate information and to support families. These nurses in their advanced practice are expected to support other healthcare professionals – within nursing and from other disciplines – in applying evidence-based knowledge. Therefore, advanced practice nurses promote collaboration in the interprofessional team. Professional leadership and promotion of innovations for nursing practice are equally expected in the performances of advanced practice nurses.

In practice, advanced practice nurses usually care for one specific patient group. Thus, these nurses develop an in-depth knowledge of this patient group that will promote the conceptualizations of new studies and research. Advanced practice nurses can initiate these studies and, thus, contribute to enlarging the knowledge base. Due to the inclusion of finances and costs, advanced practice nurses are aware of these issues of patient situations and closely collaborate with social services. These nurses guide patients and their families through the healthcare system. Ethical decision-making is promoted.

Finally, advanced practice nurses demonstrate critical reflective thinking and analytical and research skills. In addition, they develop and maintain interprofessional relationships beyond the institution, and they become involved in politics to promote the well-being of patients and their families or the needs of a specific patient group as well as advanced nursing practice [38].

It has been demonstrated that advanced practice nurses improve patient outcomes directly. Due to their case management and coordination activities, a smaller number of healthcare professionals are involved, and, therefore, continuity of care is ensured. Similarly, a smaller number of healthcare professionals involved in care contribute to reduced loss of information and a lower number of sources of error. Advanced practice nurses employ a person- and family-centered approach and become reference person. They support patients and families throughout the disease trajectory [38, 41, 71, 77].

Advanced nursing practice has evolved due to severe shortages for many reasons among the medical professionals, i.e., physicians, to respond to needs of specific populations or to provide adequate triage services and ensure low-level access to care. Since 1965, advanced nursing practice has been regulated in the United States on national and state level. In the United Kingdom, the crowing of general practices and the growing number of patients all over have contributed to the implementation of advanced nursing practice [62].

The Oncology Nursing Society of the United States has taken up the new role and inherent possibilities of advanced nursing practice [13]. The oncology advanced practice nurse (Oncology APRN) is defined as "as expert competency and leadership in the provision of care to individuals with an actual or potential diagnosis of cancer" (Brant et al. [13], p. 12). For oncology advanced nursing practice, it is necessary to have a master's degree in nursing and additional knowledge on oncology care that goes beyond basic nursing education. Hence, the Oncology Nursing Society in conjunction with the Oncology Nursing Credentialing Corporation offers specific education and credentials for oncology nurses who want to move into the advance nursing practice role. Oncology advanced practice nurses are able to determine cancer-related health issues, provide an adequate diagnosis, and propose a tailored response to the health problem. It is stated that oncology advanced practice nurses possess thorough knowledge on nursing and other theories that allow for providing comprehensive care to individuals with cancer. In addition, oncology advanced practice nurses are expected to engage in or conduct research to enlarge the body of knowledge. Oncology advanced practice nurses are expected to provide care to the individual including the family. For oncology advanced practice nurses, the credentialing is provided by the Oncology Nursing Society of the United States and the Oncology Nursing Credentialing Corporation. Licensure is provided by each state of the United States (Brant et al. [13], p. 14) (Table 19.2).

Advanced nursing practice in oncology includes a broad spectrum of activities and is perceived to promote improved communication within the interdisciplinary team, speed up referral and other transitioning processes, and help patients and their families orientate themselves within the healthcare system [11, 42, 51]. Nurses in

Table 19.2 Overview of advanced practice nurses (APN) in oncology care of select countries

Country	Denomination	Regulation	APN in oncology (examples)
United States	The term "advanced nursing practice" (ANP) includes four roles: Advanced practice registered nurse (APRN) Certified nurse-midwife (CNM) Certified registered nurse anesthetist (CRNA) Clinical nurse specialist (CNS) [38]	Credentialing for Oncology APRN through Oncology Nursing Credentialing Corporation (ONCC) and Oncology Nursing Society (ONS). Licensure by states [13]	Advanced practice registered nurse (APRN) for survivorship care [22] Advanced practice registered nurse (APRN) in the cancer setting [10, 11] Clinical nurse specialists in oncology care [7]
Canada	The term "advanced nursing practice" (ANP) includes two roles with subdimensions: Clinical nurse specialist (CNS) CNS/NP blended role Nurse practitioner (NP) Primary health care nurse practitioner Acute care nurse practitioner [25]	Credentialing by Canadian Nurses' bodies and states of educational programs of advanced nursing practice. Licensure by states [18, 57] Certification for oncology advanced nursing practice by the Canadian Association of Nurses in Oncology [17]	Oncology advanced practice nurses work exist, e.g., in breast cancer care, hematological cancer care, and palliative care [14, 53]
United Kingdom	The term "advanced nursing practice" (ANP) includes two roles: Clinical nurse specialist (CNS) Nurse practitioner (NP) (Secretary of State for Health 2007) [64]	Credentialing by the Royal College of Nursing Council for Healthcare Regulatory Excellence (CHRE)	Lung cancer clinical nurse specialist [51, 58] Acute oncology clinical nurse specialist [78] A variety of clinical nurse specialists and nurse practitioners in oncology, i.e., chemotherapy, etc. [31]

(continued)

Table 19.2 (continued)

Country	Denomination	Regulation	APN in oncology (examples)
Switzerland	The term “advanced nursing practice” (ANP) includes two roles: Clinical nurse specialist (CNS) Nurse practitioner (NP) [63]	Credentialing and licensure is currently being developed. In the canton of Vaud, a specific regulation for advanced nursing practice has been passed (Canton of Vaud) 19	Oncology advanced practice nurses based on the model by Hamric et al. [38] are getting established all over Switzerland French part of Switzerland: advanced practice lung cancer nurse (APLCN) [65, 66] German part of Switzerland: breast cancer care nurse [70, 73]
Germany	The term “advanced nursing practice” (ANP) includes several roles: Advanced practice nurse in palliative care Breast care nurse Advanced practice nurse for vulnerable individuals (Deutscher Berufsverband für Pflegeberufe e.V. – Bundesverband [24])	Legal bases and regulations exist; however, there is no state-wide credentialing (Deutscher Berufsverband für Pflegeberufe e.V. – Bundesverband [24])	In the domain of breast cancer care, nurses with additional certification exist [34]. These nurses offer specific services grounded in the concept of advanced nursing practice developed by Hamric et al. [38]
Austria	The term “advanced nursing practice” (ANP) includes two roles: Clinical nurse specialist (CNS) Nurse practitioner (NP) (German Association of the Nursing Profession (DBfK), Austrian Association of Health Care and Nursing (ÖGKV), & Swiss Association of Nurses (SBK) [35])	Legal bases acknowledging the nurses’ scope of practice and independent practice exist [37]. Several educational programs exist; however, credentialing has yet to be developed [36]	It appears that advanced nursing practice needs to be established [36, 69]

Legend: For descriptions of advanced nursing practice roles in other countries, it is recommended to consult Hamric et al. [38], Heale and Rieck Buckley [40], Parker and Hill [61], Pulcini et al. [62], and Zug et al. [82]

advanced practice roles are working in various settings, i.e., inpatients, outpatients, in the community, etc. However, the label of “advanced practice nurse” is not protected, and, therefore, many different terms exist. Depending on the respective context, the scope of practice and competencies varies. It is noted that nurses in advanced practice are essential for well-functioning and high-performing healthcare systems. These nurses are growing into fixtures in healthcare systems. Patients rely on them for facilitated healthcare system access and for support to better manage daily disease-related demands [27].

Conclusion

Cancer presents many different challenges not only to the person concerned or his/her respective family but also to the healthcare professionals involved. It has been highlighted that within the cancer care continuum, various activities may occur that require respective specific training and education. The model presented above (Fig. 19.2) may provide some support to conceive the various roles within the cancer care continuum and to determine the levels of competencies that nurses may require. It is indicated that oncology nurses are expected to increase their knowledge base not only through experience but also by obtaining further certified education. Although certification will promote the quality of the education provided, and enhance the recognition of the scope of practice of the nurses, additional and tailored education is necessary to support nurses with broad and in-depth experience in cancer care.

In addition, advanced nursing practice will become – before long – a fixture in the healthcare systems. Various essential activities are associated with this role, namely, taking care of patients across the whole cancer care continuum, independent of the setting and beyond hospital. Advanced practice nurses can work as part of a team or on their own [9]. However, further research is needed as currently nurses in advanced practice roles are not able to work to the full extent of their capacities or roles [26].

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Children with Cancer: Communication, an Essential Component of Care

20

Faith Gibson

Abstract

There is no doubt among experts that improved communication will help children and young people better understand, prepare for, and cope with their illness, the procedures they may undergo, discharge from hospital, return to school, any relapses that may occur, and in some cases, their last weeks of life. There is also evidence to suggest that children and young people should be involved in decisions that affect them when they are able to do so and that most would like to be active participants in their health care, or at least have the choice to participate. Nurses are well situated to share information and be a conduit for the translation of complex information. Essential for success is the need to understand the needs and preferences of parents/carers, children and young people, and the tailoring of information requires appreciation of these triadic encounters and the roles that each member takes, as well as how these roles change over time. We have a research programme, dedicated to improving communication in children's cancer care, to ensure timely access to high quality information for parents and their children. It is this programme of research that I will draw upon as the basis for this chapter, using evidence from our own research as well as published work to offer insights and practical suggestions for approaching and managing complex interactions.

Keywords

Children · Young people · Parents/carers · Communication strategies

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F. Gibson (✉)
Centre for Outcomes and Experience Research in Children's Health, Illness and Disability (ORCHID), Great Ormond Street Hospital for Children NHS Foundation Trust, Faculty of Health and Medical Sciences, University of Surrey, London, UK
e-mail: faith.gibson@gosh.nhs.uk; f.gibson@surrey.ac.uk

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Introduction

Though cure is not guaranteed, chances of survival have improved dramatically for children diagnosed with cancer [1, 2]. Questions about how to communicate effectively have now focused on supporting children with a life-long chronic illness [3]. It is reported 'for virtually all parents, becoming a parent of a child with cancer marks a striking, biographical shift' (Young et al. [4], p. 1837). A major part of this shift involves parents taking on information-sharing roles during their child's treatment, most predominantly executive-like roles, managing what and how their children are told about their cancer diagnosis [5]. Three factors described as contributing to restricted parents' communication with their child include information overload and emotional turmoil, lack of knowledge and skills for disclosing the diagnosis and assumptions about burdening the child when discussing cancer [6]. There is a clear dissonance between parents' desires to be informed in order to make decisions about care and treatment and the steep learning curve and new language they face at diagnosis [6, 7]: parents are most distressed at the time of diagnosis and early stages of treatment [8–10]. Stress further hinders information retention, making it extremely difficult for parents to relay and translate information to children following diagnosis [11]. Despite the inherent barriers, it is important that parents begin to share information with their child following diagnosis and build up complex information over time.

Nurses are well situated to share information and be a conduit for the translation of complex information [12, 13]. Parents must then choose when and how much of this information to share with their child [14]. Prognostic disclosure is more complex with children, where 'never tell', 'always tell' and 'maybe tell' have been described as a historical continuum, where the individual needs of children and parents have more recently become the priority [15]. There is evidence to suggest that children should be involved in decisions that affect them when they are able to do so and that children would like to be active participants in their healthcare or at least have the choice to participate [16–18]. The desire to gain control has also been described by children, where they reported knowledge and understanding about their illness and treatment that allowed them to participate in their own care [19]. The sharing of information helps children better understand, prepare for and cope with their illness, the procedures they may undergo, discharge from hospital, return to school and, in some cases, relapse or end-of-life care [20]. Children who do not receive this kind of information early on are more prone than others to anxiety and depression during cancer treatment and to long-term psychosocial adjustment problems following treatment [21]. Young children in particular are known to rely on their parents for all of their medical and non-medical information [22, 23]. Many parents report a strong desire to take on information-giving roles within their families and believe they are best positioned to discuss their child's illness with their child [24]. Parents have the onerous responsibility of first understanding the information they are given, assessing the appropriate amount of information that should be available to their child and then disclosing it. Yet the transfer of information to parents can sometimes be problematic [25]. Professionals may find it difficult to judge the amount of information a parent needs, at a particular time, in response to change as treatment and care progresses. Healthcare professionals do have a clearly described role in helping parents to cope [8], and this involves supporting parents in their information-sharing roles [5, 26].

We have a research programme, dedicated to improving communication in children's cancer care, to ensure timely access to high-quality information for parents and their children. Understanding needs and preferences and tailoring information accordingly require appreciation of the triadic encounters between child, parents and healthcare professionals and the roles that each member takes, as well as how these roles change over time. Although not a new reference, Sobo [27] argued that many holes remain in the clinical communication literature. She argued that scant attention has been made to include the voice of children. We might argue that some holes do still exist, and certainly Sisk et al. [28], would confirm our view. We therefore first started to study communication patterns and preferences by talking to children with cancer, aged 4–19 years [29]. Children (primarily between the ages of 4 and 10) were shown to have a reliance on parents for information, therefore giving parents many important communication roles. We then went on to try and understand more about the roles parents play and how healthcare professionals prepare parents for these roles [29]. In our endeavours to understand more about triadic communication encounters, we have also used our research studies to explore how we might best gather data with children and as a result would be encouraging researchers to use participant observation as their primary research method in communication studies with children [30].

In this chapter, I want to share with readers some of these works; I will draw on the words of children, young people, parents and professionals from three of our studies. Our work is based on three assertions: first, we know that children report a desire for information about a number of important treatment-related issues, such as the permanence of the effects of steroids, severity and length of side effects, prognosis and pain [31, 32]; second, we know from our earlier research that professionals might not always communicate complex information to children as effectively as they think they do [23, 33], so, for example, some children told us that:

> 'They could tell me what was going to happen and when it will happen, that would help, they just keep you waiting and don't tell you why' (boy, 9 years old);
>
> 'They tell you the medicine will make you better but they don't tell you how it works' (boy, 12 years old);
>
> 'They told me my hair would come out but they didn't tell me it would be different when it came back' (girl, 10 years old);

Preferences for information, for these children, had clearly not been substantiated. Finally, we know that parents play a pivotal role in communication, with many parents acting in an executive capacity, managing what and how children are told [11]. Other relevant literature will be drawn upon, but the main focus is on the accounts of those involved in this triadic communication process.

Children's Communication Preferences

There is no doubt among the experts that improved communication will help children better understand, prepare for and cope with their illness, the procedures they may undergo, discharge from hospital, return to school, any relapses that may occur

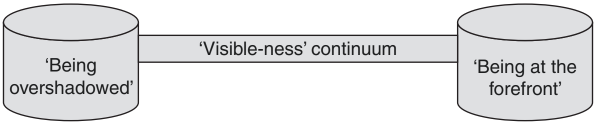

Fig. 20.1 Lambert et al.'s [31] the children's 'visibleness' continuum

and, in some cases, their last weeks of life [20]. Children are recognised as capable of shifting their visibility in their communication roles from being in the 'foreground' or 'forefront' of communication with health professionals to being in the 'background' or 'overshadowed' [34, 35]. Lambert et al. [35] describe children's participation in communication as a continuum (Fig. 20.1) that is determined by four factors:

1. The child's desire to engage in communication
2. The healthcare professionals' level of engagement or marginalisation of the child
3. The parents' recognition of the child as part of the communication process
4. The hospital environment itself

Being overshadowed in communication occurs when healthcare professionals focus on their own agenda and communicate directly with parents. This leads to children being only peripherally aware of what might occur during treatment and hospitalisation and hence might be unprepared and worried about the illness and their future. While being in the forefront of communication appears ideal, it is argued that no one side of the continuum is better than the other because some children do not want to be involved in communication and decision-making, and for some these preferences change over time [16]. It is only when there is a conflict in children's preferences that a shift is made. Children can shift into the forefront when parents and health professionals provide honest, accurate and complete information to children and encourage the asking of questions. It is suggested that instilling confidence in children that they will be able to handle the illness and related situations, they will be able to focus on themselves outside of the illness and find meaning in life and interactions with others. The need to maintain hope and spirit and promote an optimistic identity influenced the amount and type of information shared by parents [16]. Children are known to trust their parents to share information and value their parents' role as interpreters of information, advocates and communication buffers [36]. Children's preferences have been described as either information-seeking or information-avoiding and are often dependent on the situation [37]. Child-parent relationships are complex, changeable and highly individual. Children's preferences for information are also individual set within the family context and influenced by their experiential and developmental level [19]. Many assumptions are made about the benefits of the child 'knowing', but many questions remain about how and when it is best to tell them and whether 'knowing' everything is essential or simply that they trust adults to be honest with them [38]. On the whole, the following is already known that:

1. Some children prefer to hear information directly rather than mediated via their parents.
2. Some children prefer to be included in information-sharing.
3. Children do need information to be prepared.
4. Children can feel angry over lack of information.
5. Many children rely on parents to share and explain information later with them.
6. Some children do not want to receive any information.
7. For many children they become more involved in information and decision-making over time.

Parents' Perceptions of Sharing Information with Their Child

Kazimierczak et al. [39] refer to 'navigating the knowledge landscape' (p. 360), where 'information provision is not a benign intervention, it requires a responsive approach to patients' needs and preference'. What complicates this process is the different information needs and preferences of individual parents and children [40–43]. Parents in our studies have described their communication strategies as intuitive and instinctive. Their stories were often not planned in advance, and they would change the storyline iteratively if their child did not accept or understand certain concepts. However, if their child appeared to understand the storyline, parents continued and built on their initial discussions over time. For example, families created their own understandings of treatment-related side effects, such as hair loss, and linked it to seasonal events throughout the year, such as the leaves falling off of/appearing on trees. Other families drew on annual life events, such as Islamic men shaving their heads during pilgrimage. Information provided throughout treatment was put into a context for children that fitted into their understandings of life outside of illness. Parents translated information to their child based on their assumptions of their child's reactions to emotion-provoking discussions. Parents argued that they knew their child best and had played important information-giving roles with their child in the past. They believed that information should be provided to their child at the right time, with a suitable amount of detail, in the right environment and by the right person. This was different for each child in our studies.

Parents also reported being led by their children's questions and sometimes having little time to plan thoughtful answers, as questions often immediately preceded medical procedures during clinic appointments or after an event (e.g. television news report on leukaemia, overheard 'adult' conversation). One mother described feeling obliged to discuss the illness with her daughter too soon after diagnosis because her daughter was concerned about her crying. Parents have reported a preference to be informed about their child's diagnosis before the child was informed themselves to avoid 'breaking down' in front of their child, as well as to be able to ask key questions [5]. Parents often reported that they and their child felt that they quickly became accustomed to terminology and that everything felt as if it repeated after the initial courses of therapy. The procedures, treatments and medicines stayed the same; hence, a level of comfort was built by most families if the child was reacting to treatment well and was experiencing few new side effects. As children's questions were often led by treatment, over time, they asked fewer questions, and more psychosocial issues become problematic such as when the child should return to school. Some parents discussed their communication roles during this time as simply keeping their child updated with what is going on with treatment and telling the child when days off school should be taken off in advance, for example. Their information-sharing role appeared to be concerned with logistic issues. Although not explicitly discussed in our data collection with parents, our results appear to echo those of Young et al. [5] who suggested that throughout the illness some parents felt that their executive-type roles of information sharing had transformed to more of a partnership with their children, where communication was much more open than during diagnosis and early treatment. Other parents described continuing to orchestrate when and what their child was told.

Parents in our studies wanted to be able to share information with their children in their own time. Conflict between healthcare professionals and parents occurred when parents buffered too much information or took 'too long' to tell their child what was happening. Many parents of older children asked their child, 'are you ready to hear about lumbar punctures?', for example, and were led by the child's response. Exchanging information in this way allowed children to feel constantly supported and parents to feel as if they were satisfying the individual information needs of their child. When parents were asked about how they prepared to share information with their child in our interviews, they said that they were never sure that what they were telling their child was the best information or that the information was given in the best way. Many families justified their unstructured approaches saying, 'no one actually said to us, "right, as parents you need to give guidance in that way"'. They suggested they felt they had very little support from health professionals to share information with their child. This led to worries for parents. One mother doubted herself saying, 'as a parent I worry that I have told him too much. I've told him what's right, but you know like, could I have changed it in any way?'

Parents in our studies admitted feeling more supported in their information-sharing roles when healthcare professionals shared stories about how other parents had translated information to their child at inappropriate times and in insufficient quantities: so real-life stories helped. It appeared healthcare professionals used this technique to encourage open communication within families when parents were unsure about the amount of information to share with their child. Other parents reported feeling much better about communicating with their child when health professionals gave them direct advice. Consistent with other research, parents were a crucial source of information and were key to facilitating children's ability to ask questions [44]. From our work, we would suggest the following:

1. Parents, for themselves, often need time to come to terms with a diagnosis, in order to:
   - Help their child.
   - Provide full information, at the right time.
   - Tailor the information for their child.

  - Assess when providing information on a 'need to know' basis might be the preferred option.
2. Healthcare professionals, their role in these encounters is to:
   - Clarify communication roles in the multidisciplinary team, who gives what kind of information and when and who is there to support parents in their role.
   - Learn from parents about their family communication style, and share this knowledge with the clinical team.
   - Consider conveying new and complicated information to parents in separate consultations before discussing it with a child.
   - Listen carefully for openings when working with children and young people, as many may not raise their concerns directly, and assist parents in responding to such information needs.
   - Help navigate parents in communication encounters, in advance of and post significant encounters.
   - Share stories about how other parents have helped to translate medical and prognostic information to their child.

Health Professionals Sharing Information with Parents and Children

Most healthcare professionals endorse parents' primacy as managers of information but experience some difficulty navigating a restricted stance. Few healthcare professionals in our studies seemed to see their role as providing information direct to children. Many suggested that they were there to make sure parents were 'well informed and as comfortable as they could be' and that parents would pass information on to their child. Healthcare professionals generally viewed speaking with children as the role of the parent and rarely engaged in direct information sharing with them. Parents did not necessarily object to this behaviour, as they saw themselves as the ones guiding conversation, not their child. Some junior staff did not see it necessary to provide information to children under a certain age, 5 years for some and 8 for others; clearly for some judgements are made about children's preferences for information, based on age. Healthcare professionals argued they did not share information with children often because they had a perception that children were scared of them or scared of the information they were sharing. One healthcare professional suggested, 'Obviously children quite often want to know what is happening, but they're too scared to ask doctors. They go their mums and dads first rather than a doctor who's this random stranger who sticks this needle into them'. Healthcare professionals recognised that they did not always offer clear direction to parents and that at times, they were unsure how to best communicate with younger children, and they did not always match level and approach to age/cognitive ability/previous experience. As one healthcare professional suggested, 'So it's giving information, but at the same time, don't scare them so much. I think that's the thing because at the end of the day – yes, they want information and they need to know some information, but they're children, they can get quite scared easily'.

It often appeared in our studies that medical procedures and discussions happened separately, and this should be clearly explained to children. Information provided during these times should be discussed with parents beforehand, and a storyline should be worked out to ensure that it can be built upon over time, making sure children are prepared for such procedures. Our work consistently suggests that healthcare professionals needed to maintain an open mind about information-sharing strategies families may choose, remaining sensitive to parents and children's information requirements and adopting a flexible approach to information provision. Our work, like that of others, reinforces the view that healthcare professionals have a supporting role to reduce the burden on parents who feel responsible for conveying information to their child and other family members [45, 46]. Professionals may find it difficult to judge the amount of information that parents need in response to change as treatment and care progresses, but understanding needs and preferences and tailoring information accordingly require appreciation of the triadic encounters between child, parents and professionals and the roles that each member takes, as well as how these roles change over time. On the whole the following is suggested for healthcare professionals when working with parents:

1. Being honest and sensitive and aware of parents' information overload and understanding of the shock and denial that may come with a diagnosis.
2. Give parents time and space to come to terms with the diagnosis.
3. Explore the reasons behind parents' need to limit information.
4. Help parents to understand that children worry more if not included and that children are perceptive and will worry if not informed.
5. Raise parents' awareness that children know more than they might realise.
6. Raise parents' awareness that children are more resilient than they think.
7. Encourage parents to be open and honest.

Why Is Communicating with Children and Young People Important

To begin this final section of the chapter, I wanted to share with readers some quotes that I have heard from children and young people in some of our other studies, as evidence of why communicating with children is important:

- 'I had my kidney removed but I don't know which one'.
- 'I had ALL, but I don't know what that means'.
- 'I did not know there were long term side-effects, every time I come to clinic I am told to worry about something else'.
- 'When I went to the hospital I saw a stretchy doctor'.
- 'I only come to clinic cos my mum tells me I have to come, I don't know why I come really'.

These quotes highlight a number of factors referred to earlier in this chapter that maybe we, as healthcare professionals, need to get better at, so that in the future children have the right language, to understand what they have experienced and hence make the right health and life choices. We need to work with parents, and children, to make sure they get the right information when they need it and recognise that information needs and preferences for more complex information may change over time. To help us, there is much that we already know about this triadic communication in children's cancer care:

1. Children have articulated clearly the importance of information and communication; parents are described as important in addressing information needs [44].
2. Understanding family preferences is key, where parental information-sharing practice is not fixed, where facilitating and restricting information and preferences shift depending on the situation and health status of their child [47].
3. Tensions arise when health professionals are unaware of these preferences; clearly shared goals are essential and need to be acknowledged across all parts of the cancer journey [48].
4. Parents can be frustrated and overwhelmed when healthcare professionals convey inconsistent messages [49].
5. Uniformly, children and parents prefer communication that is honest, sensitive, empathetic and hopeful. While parents mostly prefer engagement in communication and decision-making, children and young people vary in their desire for inclusion and amount of involvement [28].
6. 'High-quality' communication is associated with parental peace of mind, feeling acknowledged and comforted and greater trust in the medical team [28].
7. Information and communication have been described by children to be essential to their wellbeing and acceptance of treatment [44].
8. While most young people want to be involved in conversations about prognosis, this is an individual and sometimes fluctuating decision, highlighting the importance of continuing discussions regarding preferences to support changing information needs [50].
9. In communication encounters healthcare professionals have expertise at the outset, while parents have less expertise, but this expertise grows over time and this can increase perceptions of a communication 'mismatch' and creates challenges [29].
10. To provide optimal care to children and young people and their parents, healthcare professionals require skills with regard to the therapeutic alliance, involving children and young people in medical discussions, communicating with the whole family unit and engaging in collaborative dialogue in the context of an interdisciplinary approach to care [51].

Communicating Effectively, Translating Evidence into Practice

Key to this area of clinical care is of course education: cancer communication is a complex problem, and effective solutions require multifaceted approaches, of which communication training is one important element [52]. Delivering a dedicated advanced communication training programme around communicating with this population to healthcare professionals is a much-needed development and should be available to all professionals, not just nurses. Training is not however a one-off exercise; maintaining excellent communication skills must be finely tuned and improved constantly. I agree with Salmon and Young [53] that communication training that remains only at the level of skills training does not go far enough. Bringing judgements about communication goals to the foreground of communication training offers a potentially more realistic way to influence communication [53]. This means at some point we have to help families to think about what their goals are and to help children with their goals too, so that together we can scaffold information over time, in response to children's needs. Poor communication outcomes can result from insufficient communication skills training, overreliance on role modelling and failure to utilise best practice [54]: communication skills are teachable and measurable and would benefit from best practice principles of multimodal education. From our own work, [52], and that of others, [55], education should aim to build upon the communication skills that healthcare professionals already have developed, but these dedicated training programmes must be available and sustained once in place. Communication programmes must also find ways to harness the experience of participants, to involve family members in simulated sessions, and find ways to bring creativity and holism into the classroom [56, 57]. In addition, I would argue that the use of case studies and script role plays with 'genuine' content are additional approaches to content that educators should consider as essential.

Conclusion

As one parent in one of our studies stated: 'Being appropriately informed could… promote the opportunity for choice and control in a situation where there has been very little'. Three concepts highlighted by Hentea et al. [49] provide a suitable conclusion to this chapter that seeks to highlight communication as an important component of clinical care. Patient-centred communication consists of:

1. Informed flexibility: the ability of the healthcare professional to adapt any consultation to the changing needs of the child, young person and parent
2. Personalised interactions: where collaboration between parents and healthcare professionals creates a communication experience that is unique in structure and content
3. Team-based communication that focuses on role clarification, which provides what kind of information, and message coordination, to provide consistent information

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Support of Teenagers and Young Adults with Cancer

21

Marion Lucas and Loïc Dagorne

Abstract

Teenagers and young adults (TYA) with cancer (TYAC) are a unique population among people with cancer. Their medical specificities and complex psychological and social needs between the pediatric and adult world are challenges for the carers, from the diagnosis to the posttreatment period. TYAC care units and national multidisciplinary TYAC programs have been developed in the last three decades in several countries, helped by an active collaboration between pediatric and "adult" hematology/oncology teams. Their main mission is to take into account all this complexity to better tailor the medical and psychosocial care to the disease, the treatments, and the specific TYA needs, with the help of several professionals specialized in TYA care (pediatric and medical hematologists/oncologists, facilitators, psychologists, social workers, and coordinating nurses). The role of the coordinating nurses is central both in the TYAC team and for the young people. TYAC coordinating nurses coordinate the patient pathway of care from the diagnosis, all along and beyond the treatments, helping TYAC to understand the disease and its consequences, answering their questions about treatment and everyday life, and accompanying and empowering them to help them be young people. Therapeutic education is an interesting tool to achieve these goals. Single or collective workshops have been built around various themes of specific interests for TYA to help them deal with cancer during this transition period of adolescence and young adulthood (physical changes, relationships,

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M. Lucas
Department of Oncology for Child and Adolescent with Cancer and Young Adult Transversal SPIAJA Team, Gustave Roussy, Villejuif, France
e-mail: marion.lucas@gustaveroussy.fr

L. Dagorne (✉)
Réseau Ile-de-France d'Hématologie Oncologie Pédiatrique (RIFHOP), Paris, France
e-mail: loic.dagorne@rifhop.net

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education/work, etc.). Building this kind of therapeutic educational program is a collaborative work with coordinating nurses, different professionals, and TYA themselves. Such active collaboration between adult and pediatric nurses is still needed and could be the starting point of new nursing researches.

Keywords
Teenager · Young adult · Multidisciplinary team · Coordinating nurse Empowerment · Therapeutic education

Introduction

Teenagers and young adults (TYA) are very special populations among people with cancer. This age group is variously defined among the different countries, ranging from 13–15 to 25–39 [1, 2].

Every year in the European Union (EU), around 20,000 TYA (15–24 years) will be treated for cancer [3], with very different cancer types, either pediatric-type cancers (e.g., leukemia, embryonal tumors) or specific TYA cancers (e.g., lymphomas, bone sarcomas, germ cell tumors) and adult-type cancers (e.g., melanoma, carcinomas, glioblastomas). Although the 5-year overall survival is good, estimated at more than 80%, cancer remains the second leading cause of death in this age group, due to some dismal histology sub-types, metastatic disease at diagnosis, and relapsed disease [3]. Adolescence and young adulthood is a period of life characterized by significant changes either physical related to puberty or psychic and social with the acquisition of psychic, financial, and social autonomy and constitutes a period of transition between childhood and adulthood [4]. Cancer occurrence at this age might disrupt these processes.

Thus, the TYAC population is unique. Through their medical specificities (e.g., unique spectrum of cancer types, specific tumor biology, need for fertility preservation, distinct late squeal, insufficient awareness of cancer that may occur in this age group, etc.), and their complex psychological and social needs (e.g., education, work, autonomization), TYAC represents real challenges in TYAC care.

We will try to highlight how the dedicated TYA coordinating nurses have a critical role in the TYAC care.

Nursing TYA with Cancer: Why Is It So Special?

TYAC support is complex in several ways and requires properly balancing TYA issues and cancer/treatment issues, oscillating between flexibility and frameworks.

No more children, not yet autonomous adults, TYA will face profound changes during this period of construction of themselves and construction of their self-image, their sexual identity, their independence from their family/parents, their new relationships with peers/friends/lovers, defining their own value system, and their new position in the society evolving from a student position toward a professional working life. However, this period might be also a period of doubts and a period of powerfulness that might lead some TYA to test authority, to break boundaries, and to take risks (e.g., experiment with drugs) [5].

Cancer is like an earthquake that will question everything in their everyday lives, from the diagnoses, the treatment period, and even in the posttreatment period (risk of cancer recurrences) and for some for all their lives (long-term sequelae). The confrontation of the sick body with its physical transformation toward adulthood, the loss of a nascent or just acquired autonomy, the projection in a potential parentality not thought before or already effective (fertility preservation), the awareness of a possible death, and the redefinition of scholar and professional projects might become as important or more important for TYAC than the disease and treatment themselves and lead to poor treatment compliance, despite TYAC being aware of the seriousness of their disease.

In addition, depending on the age and the degree of psychological and social maturity, the situation of TYA might be very different from an adolescent at scholar age living with their parents, a young adult with educational occupation but starting an independent life with peers, to a young adult worker with his own partner and children. The TYA cancer might impact not just the TYA but all the surroundings and often in a complex manner, with parent/personal/partner financial problems, educational/professional reorientation (e.g., cognitive or physical sequelae), and return to some dependency to the parents.

In this context, the support by dedicated TYAC multi-professional teams, expert in oncology and trained in communication with TYA, will be crucial to help them in coping with cancer-induced changes, with a minimum of interference in their lives and with the management of cancer [6]. These TYAC dedicated teams should cover all medical, psychosocial, and educational aspects, including pediatric and medical hematologists/oncologists, facilitators, psychologists, social workers, and coordinating nurses. All members of these teams should have adaptability skills to properly balance TYA issues and cancer/treatment issues, oscillating between flexibility and frameworks. The cohesion of the team is as essential as their competences, as TYA might challenge them by choosing the information to be shared and the person to share with some critical information. Although the TYA will still be the main interlocutor of the TYAC team, the interrelation of the TYA with their parents, brother/sister, partner, and friends might be very different, as well as the interaction TYA will allow between the TYA team and these persons. This might lead to very complex and unexpected interactions within the TYA care (Fig. 21.1).

Most of the TYAC mobile outreach units or teams have appropriate facilities, where young patients can meet with each other but also receive visits from family and friends [7]. The nurses, nurse aides, and doctors who care for TYAC must keep in mind that their patients are not only children who will not follow rules they are given without discussing them, nor adults who could understand all illness and treatment issues and accept all their constraints. Caregivers must be able to really listen to them and to consider that they're capable of taking decisions by themselves

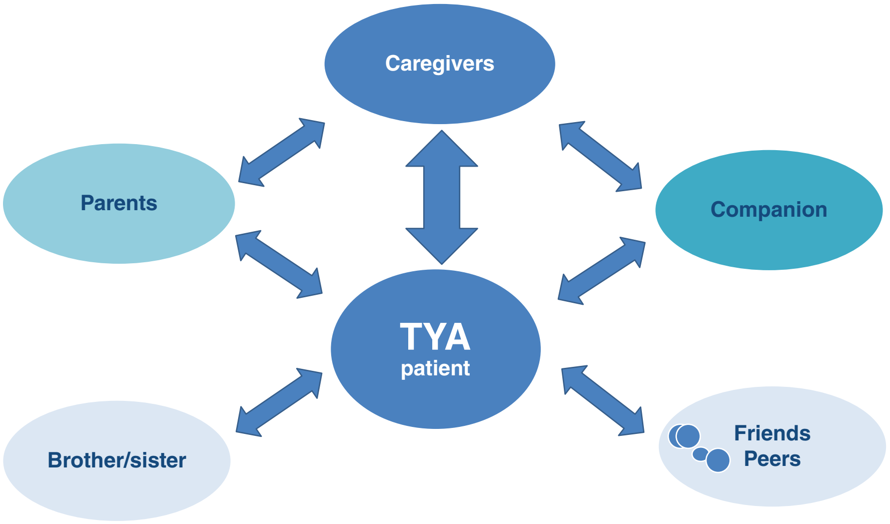

Fig. 21.1 Complex interactions between caregivers and TYA patient involving distinct relatives

while leading them to accept the established guidelines and the rules of the unit. Compromises are part of TYA caregiver's daily routine.

Structuration of TYAC Care Across Europe: Different Models, Same Objectives

Pediatric oncology care units for minor patients have emerged in the 1970s with an age limit of 15–18 years in most countries, while the concept of TYAC care emerged in Europe in the 1990s under patient's impulsion, with a progressive active collaboration between pediatric and adult oncology teams, charity financial help, and now with health authority's support. Different models successively emerged in Europe [8]. In the UK, specific specialized TYAC units were created with the help of the Teenage Cancer Trust [9], and the National Institute for Health and Care Excellence (NICE) issued guidance in 2005 to "improve outcomes in children and young people with cancer," defining standards for service delivery, with currently 28 TYAC units existing across the whole UK. In France, the first TYA unit was created in 2002 in the Department of Oncology for child and adolescent at Gustave Roussy Cancer Campus [10], followed by two other TYA units. But other models of TYAC care were developed based on transversal dedicated TYAC multidisciplinary teams, with the help of the successive cancer plans since 2003 [11], the structuration of a national multi-professional association for TYAC Groupe Oncologie Adolescents et Jeunes Adultes (GO-AJA), and a recent directive of the national authorities to spread at all national level a regional structuration of TYAC care. These different models include transversal team across a same institution, mobile teams at local or regional level, and dedicated program at local or regional level. While in France these units and programs for TYA management developed and expanded under the initial leadership of pediatrics, in other countries the leadership came from medical oncology "adult" teams (e.g., the Netherlands). Italy, more recently developed TYA unit and a national program SIAMO (Società Italiana Adolescenti con Malattie Onco-ematologiche). A TYA unit also exists in Spain, in the Netherlands, and in Denmark. In other European countries, there may be national programs of cooperation between pediatric and adult teams, and plans for the creation of TYA units are emerging.

All these different initiatives for TYA have required reinventing the role of each actor of the TYA team to adapt it to the working context and not just to the TYAC problematic. Sharing these experiences beyond the national level became crucial and was rendered possible by the European Network for Cancer Research in Children and Adolescents (ENCCA) with a working group dedicated to TYAs who created the European Network for Teenagers and Young Adults with Cancer (ENTYAC) in order to develop specific practice guidance. ENTYAC leans on the involvement of patients themselves, caregivers, and charities. ENCCA defined the specific criteria and required facilities in centers that treat TYAC [7]: no restrictive age cutoffs, a multidisciplinary staff (cooperation between pediatric and adult oncologists), a specialist team (dedicated nurses, social workers, psychologists, teachers, activity organizers), dedicated physical spaces with other young people, a fertility preservation program, a transition program, and clinical trial availability.

The Central Role of the TYAC Coordinating Nurses: Example of a French AYA Team

Taking into account all the psychosocial upheavals caused by the diagnosis and the imperatives of treatment is the main mission of the multidisciplinary TYA teams whose programs are developing in hospitals that care TYA with cancer. These teams of specialists usually include coordinating nurses, psychologists, social workers, facilitators, and pediatric and medical oncologists (i.e. a double medical expertise) [12]. Most teams also include teachers, as schooling continuation is a major concern for most patients and more recently help for professional insertion is also proposed in some structures [13]. Other professionals may also be involved such as socio-beautician, psychomotor therapist, nurse specialized in addiction care, adapted physical activity professor, and others to cover all the aspects of TYA problematic (Fig. 21.2).

During many years, the coordinating nurse function has expanded taking a central position to deliver an optimal support to TYA and progressively to coordinate the actions of the different members of the TYAC teams and developed new tools adapted to their always reinvented profession [14].

The main missions of this coordinating nurse remain to coordinate and smoothen TYA pathway of care, starting from the diagnosis up to the end of the treatments and even beyond the post-cancer/treatment period, either within or outside the primary care unit. The first TYA and coordinating nurse meeting should take place at an early stage after the diagnosis is announced, for example, during the first stay in the

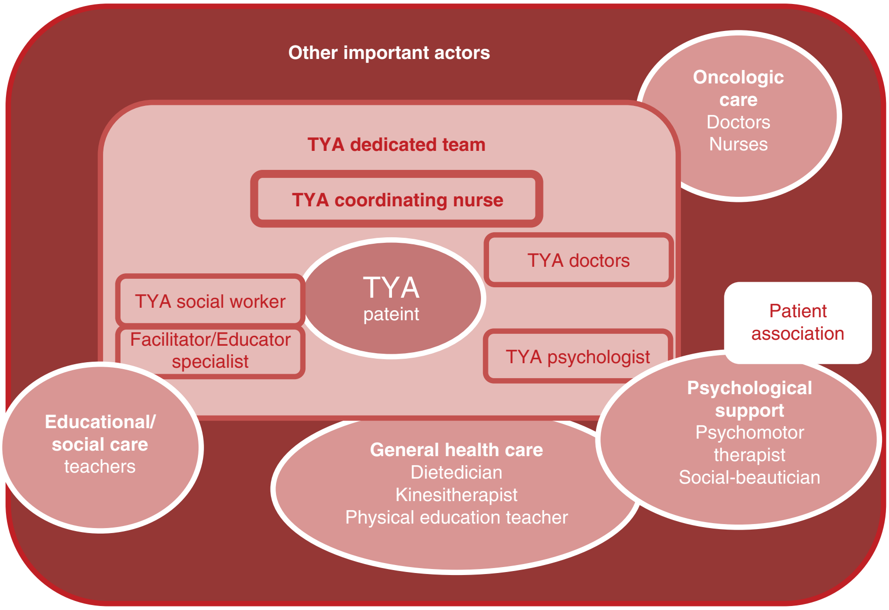

Fig. 21.2 Example of TYAC team

hospital. But, it might be more difficult to meet TYA who receives only outpatient treatment (e.g., radiotherapy, chemotherapy in day hospital) or had just medical consultations for surveillance of oral treatment. This first meeting is the opportunity to collect information on TYA lifestyle, to evaluate his (her) level of understanding on the disease, the treatments, the side effects, and the impacts of all these on his (her) life. This meeting might also help to get a quick overview of the first issues and to inform TYA of the available resources within the department, inside and outside the hospital. This meeting allows introducing the existing facilities and the caring teams, the TYA dedicated team, and the AYA program. When appropriate, the coordinating nurse will organize all appointments with the different TYA care actors, social worker, psychologists, medical personals, socio-beauticians, and many others as required by the TYA (Fig. 21.3). Strong medical knowledge on the disease and the associated treatments are required, along with a good ability to shape his (her) verbal exchanges to the level of understanding of the TYA but also to take into account his (her) lifestyle to define with him (her) the best acceptable disease-tracking process to favor the optima ways to set up the appropriate monitoring rules. A list of emergency phone numbers is also given during this meeting with a specific focus on the importance to report everything that seems abnormal on top of the traditional guidelines (fever, pain, bleeding, local infection signals, etc.). After this first meeting, numerous formal but most often informal meetings might occur all along the medical care pathway as either desired by the young patients themselves or by the medical teams. These intermediate meetings are not always required, but they allow identifying the apparition of new problems and accordingly any required

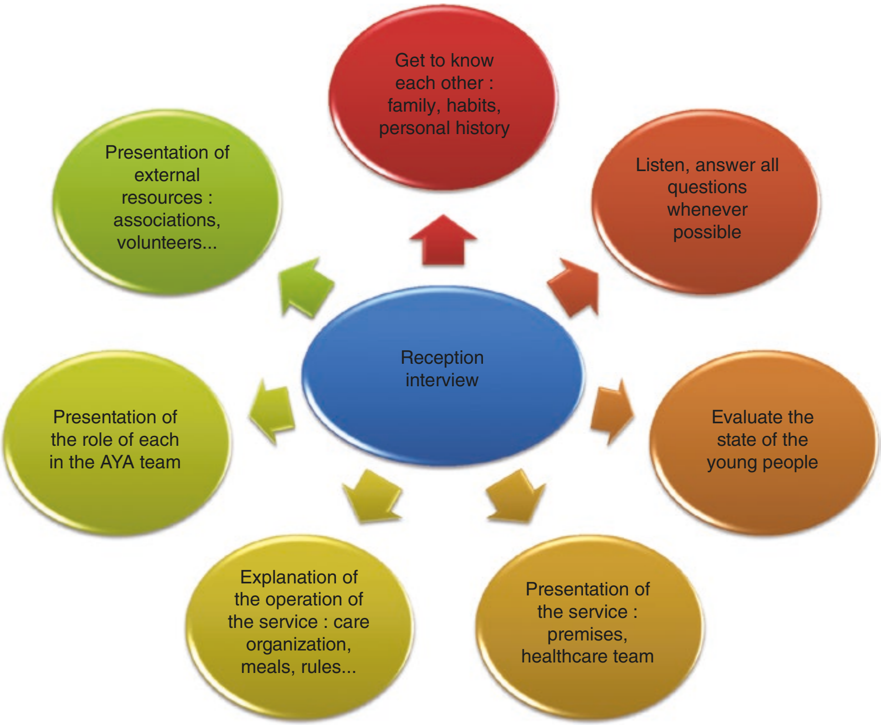

Fig. 21.3 Content of the first interview between the TYA patient and the coordinating nurse

readjustment of the global medical care. This may lead to involve new team members not previously involved. For TYA the coordinating nurse will become a key element of this pathway of care, and this might be facilitated by a "TYA dedicated" hotline (mobile phone number) to directly reach the coordinating nurse (Fig. 21.4).

Coordination function of TYA coordinating nurse will extend to the TYA team. Information sharing with every members of the team is essential. Regular meetings to discuss all new patients are important where the coordinating nurse explains the disease and where the TYA situation can be discussed and analyzed with the different points of view of the whole team. As a result every actor of the TYA support is aware of the issues/needs, allowing appropriate actions and meetings to be scheduled.

Coordination function of TYA coordinating nurse might also extend outside the oncology care hospital. Jointly with the oncologists, the coordinating nurse may properly set up the release from the hospital operations with specific procedures depending on the first chemotherapy and may help to manage the choice of a home visiting nurse who will perform appropriate monitoring (e.g., blood tests, bandages, central line checkups). Additionally the coordinating nurse carries out a meeting with the TYA and his (her) relatives to verify the correct understanding of the treatment protocol, its consequences, and how to handle secondary effects to be able to prevent, to track, and finally to treat them. Coordination with specific structures such as secondary care units, surgical hospital, rehabilitation institution, home

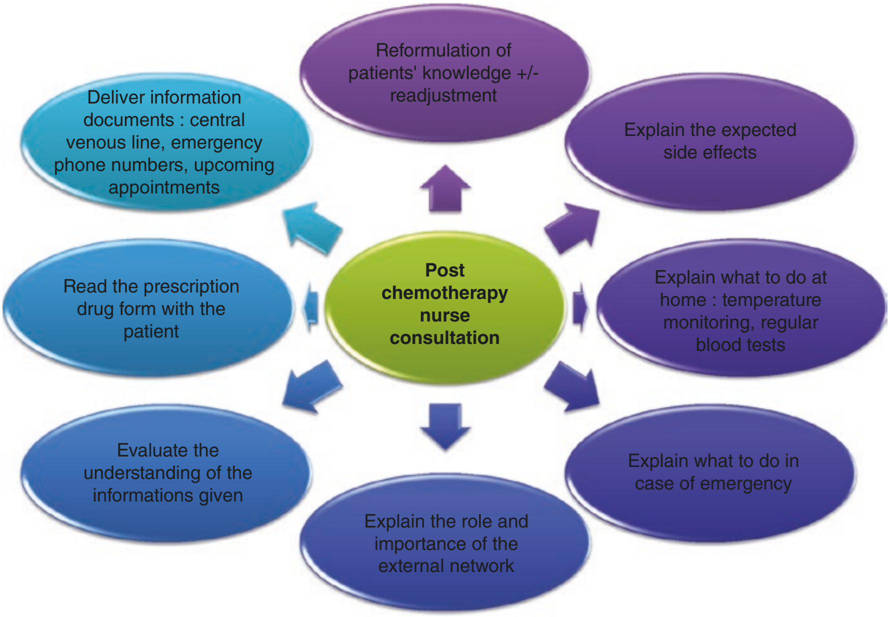

Fig. 21.4 Content of the post first chemotherapy nurse consultation

hospitalization, regional network (e.g., the RIFHOP, Réseau Ile de France d'Hématologie Oncologie Pédiatrique, provides support at home during and after the period of treatment [15]), visiting nurse, or palliative care unit might also be necessary during the follow-up of some patients. A good communication is mandatory among all actors in order to quickly exchange data to tailor at best the cares for each TYA medical and psychosocial needs. The position of the coordinating nurse is really central compared to these various teams and as such is able to establish a focal point to spread the appropriate information between all of them.

Therapeutic Education for TYAC Empowerment: An Innovative and Interesting Tool

In addition to their role to smoothen TYA pathway of care, one of the missions of the TYA support team is to favor the empowerment of the TYA patients. Therapeutic education program is an innovative tool in TYA empowerment, where TYA coordinating nurse had got a crucial role from the development of the program, its setup, and organization and a practical facilitating role.

Therapeutic education has been developed in the last 40 years in order to help the patients with chronic diseases to increase their knowledge and their skills [16]. All along the time, the efficiency of this approach has been largely demonstrated, and therapeutic education is now among national guidelines for chronic disease care [17]. The therapeutic education is divided into four steps. (1) The diagnostic evaluation performed with the patient by a trained staff allows to identify the positioning of the patient regarding the disease. (2) The therapeutic alliance is performed with the patient to make up his mind about what to do regarding the priority objectives. (3) The implementation is the setup phase of all actions driving the learning curve and the empowerment of the patient. (4) The assessment step reviews the needed changes and residual difficulties.

Using therapeutic education programs in acute disease such as cancer might appear difficult but can been seen also as a huge help for TYA during and beyond cancer treatment. In addition, in the last few years, some cancers have evolved toward chronic disease changing medical care approach of the patients, while patient care outside of the hospitals expended. As a consequence the empowerment of the patients has taken an increasing and essential place. All these aspects require a specific support and contribute to justify therapeutic education programs to be developed in oncology. Therapeutic education may come in different varieties of forms, starting from diagnosis up to the post therapy phase and the long-term follow-up. Main objectives are (1) to improve the understanding and acceptance/compliance to treatments and adaptation of the everyday life (e.g., disease knowledge, treatments, pain management, physical appearance), (2) to encourage a healthier lifestyle during the treatment that might extend after the disease and the treatments (e.g., nutrition, well-fitted sports activities, drug abuse dangers), and (3) to anticipate a return to school or work. However, a simple linear therapeutic educational program is not always compatible with TYA cancer pathway of care, and adaptations are required (Fig. 21.5).

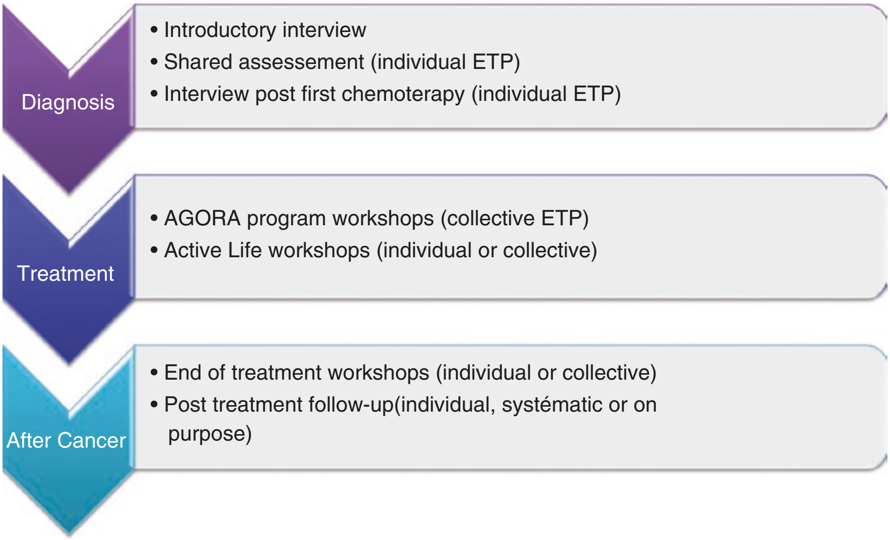

Fig. 21.5 Conceptual process of the complete therapeutic education program. (Adaptations might be required: treatment without chemotherapy, relapse before end of treatment, exclusive day hospital treatment, etc.)

The unique experience on therapeutic education in TYAC of the French TYA unit/programs funded by INCa has been published in December 2016 [18]. Two therapeutic education programs for TYA with cancer were validated by regional health authorities, and a national working group was set up under GO-AJA lead. Several common tools/documents were produced for therapeutic education, further validated at national level and available to all teams developing their own program.

The following are tools for individual therapeutic education to facilitate the different required steps:

1. An interview guide with few open questions allowing a large freedom of speech to the young patient to perform the initial data collection and needs (questions about the knowledge of the disease and associated treatments, lifestyle, occupations, and foreseeable impacts)
2. A table to ease jotting down notes in order to favor verbal and nonverbal exchanges with the TYA and provide a global picture of the situation of each TYA focused on his(her) lifestyle, contact relatives, motivations, projects, resources, self-identified obstacles, and solutions
3. A grid to synthesize the shared educational assessment that can be used to determine with the patient its own primary target goals, with these objectives stated in verbal mode by the coordinating nurse and their validation by the patient to build up the therapeutic alliance, necessary before the implementation of the program
4. A competency framework specific to TYA population, built upon discussions not only between TYA's and medical staff but also between caregivers issued from different medical disciplines, which includes self-care and adaptation competencies (Table 21.1)

Collective workshops have been developed in the AGORA program of Gustave Roussy from 2012, covering seven themes important for TYA with cancer (Table 21.2), and were made available for the TYA community. The pedagogic tools are varied and adapted to attendance expectations. Each workshop is facilitated by two specialists issued from different disciplines according to their specific competencies (oncologist, nutritionist/dietician, coordinating nurse, addiction nurse, TYA nurse, education specialist, physical activity teacher, psychologist, psychomotor therapist) and trained for therapeutic education. TYA's relatives might participate in some specific workshops to involve them more thoroughly: parents, brothers, and sisters may attend with a young patient in workshops dedicated to “disease knowledge,” “nutrition,” and “fatigue management and physical activity.” Other workshops such as the one dedicated to “love life and sexuality” are strictly restricted to TYA and his/her companion and some other only open to TYA, depending on confidentiality (“drug addiction”) or intimacy (“physical appearance,” “pain management”). Other essential issues of TYA lives are discussed in workshops paralleling the therapeutic educational program concerning school and working life reinsertion (How to manage private data on social networks? How to write a CV after a disease?

Table 21.1 Competency framework. Examples of self-care and adaptation competencies identified by the GO-AJA therapeutic education working group

		Self-care	Adaptation competencies
The disease	*Infectious risk*	Know the first signs of aplasia	Restrict the situations of infectious risks
		Understand the blood test results	
	Emergency situations	Know when to call the hospital	
	Treatment	Understand the disease, the treatment mechanism	Identify a contact person at the hospital
		Respect the prescription	Schedule blood tests, medical appointments, etc.
		Manage drug supplies	
	Nutrition	Adapt food in case of constipation, diarrhea, weight loss, etc.	Find tricks to continue to eat with pleasure
		Use a nasogastric tube	
	Side effects	Deal with fatigue, digestive disorders, pain, etc.	Find tricks to deal with physical changes (scars, hair loss, etc.)
		Choose adapted complementary medicine (relaxation, art therapy, etc.)	
Disease and TYA life	*Juvenile development*	Know the risk of the disease on the juvenile development	Be able to talk about fertility
		Know the impact on the fertility	
	Sexuality	Use contraceptive measures during the treatment	Be able to ask for any question about sexual disorder
		Know the impact of the treatment on the sexuality	Manage an intimate relationship during the treatment
	Friendship		Be able to talk about cancer with the friends/relatives
			Use the social networks advisedly
	The don't	Know the drug interactions with toxics	Deal with risk behaviors
	Work/school	Meet a guidance counselor	Choose when and how to return to school/work
		Set up homeschooling with the teachers	

What to tell about the disease after it's over?). Without being formally part of the ETP program, these actions are also keys to the global care of the TYACs. Extending this education therapeutic program to the actor outside the hospital is being discussed with the RIFHOP.

Therapeutic education is an interesting part of a complete TYAC support, allowing them, from the diagnosis to the period after cancer, to be actors of their treatment, to better deal with all the various consequences of the disease and treatment and help them in continuing the autoimmunization process specific of this age group toward adulthood.

Table 21.2 Seven collective workshops in AGORA program

Workshop	Public	Facilitators	Content	Pedagogic support
Le cancer, c'est. quoi? (What is the cancer?)	Patient Relatives	Doctor Coordinating nurse	Better know the disease, its genesis, diagnosis, treatment, and side effects	Interactive slideshow, microscope, interactive quiz
AJA'ime manger (TYA loves to eat)	Patient Relatives	Nutritionist doctor Dietician	Understand balance diet, learn how to eat during treatment	Healthy menu composition game, tasting of dietary supplements
Stop la douleur (pain management)	Patient	Psychomotor specialist Nurse	Understand pain mechanism, its management, medical treatment, or alternate paths	Manipulation of a PCA pump, initiation in relaxation
L'info addicto (addicts information)	Patient	Addictologist nurse Education specialist	Get informations, position oneself regarding toxics	Interactive quiz
Bien dans mon corps, bien dans ma tête (well in my body, well in my head)	Patient	Psychomotor therapist Healthcare manager	Talk about physical appearance, understand changes in image body	Compare physical image in front of a mirror or in front of a pair
AJActiv' (TYA are moving)	Patient relatives	Psychologist Physical activity trainer	Understand fatigue caused by the treatments, discover how sport can help manage fatigue	Interactive quiz, training session
Quand mon cœur fait boum (when my heart skips a beat)	Patient partner	Doctor Psychologist or coordinating nurse	Deal with questions about fertility, sexuality, and love life during treatment	Info/hoax game, watch a part of a movie, read a graphic novel

Toward a Better Nursing Care

The specificity and complexity of TYAC care are challenges that have forced nurses to think their work differently and improve their practices by innovative tools. These efforts made all along in the last decade to enhance the quality of care with these young patients are visible and are the result of a multidisciplinary work where many actors are involved. The collaboration between professionals is essential, and a joint process of reflection may be the starting point of various research works to go further and to further enhance TYAC care.

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Elderlies

22

Sylvie Perrin

Abstract

There are many risk factors that may be involved in being diagnosed with cancer. Some are related to our behaviors (alcohol, smoking, obesity, sedentary lifestyle, ...) and can be avoided by a good lifestyle. Others are not modifiable (the place of birth, sex, family history, ...). Of these, the most important risk factor for developing cancer is age. This is why the incidence increases with age, so cancers are in the vast majority of diseases of the elderly. As a result, new cases of cancer in the world are constantly increasing due to demographic changes on the one hand and improvements in life expectancy on the other, and they differ from one country to another. Often age is a factor of late detection; for several reasons, it is therefore necessary to improve early diagnosis.

Older people do not age in the same way, and when they have cancer, it is important to set up a specific and adapted treatment for each individual. Must be adding to the carcinological expertise, the geriatric expertise that will take into account functionality, comorbidities, social context, and patients' geriatric syndromes. The advice of the geriatrician should be involved in the decision-making process and follow-up of the patient.

In addition, cancer treatments have received little or no attention in patients in this age group. This will require health care staff to acquire geriatric knowledge in order to optimize the management of elderly patients so that they can derive maximum benefit from treatments while maintaining their quality of life.

Keywords

Elderlies · Cancer · Frailty · Treatment · Nursing care

S. Perrin (✉)
Centre Léon Bérard, Lyon, France
e-mail: sylvie.perrin@lyon.unicancer.fr

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Demography and Epidemiology

Worldwide, there were 901 million people aged 60 or over in 2015, an increase of 48% from 607 million in 2000. By 2050, the world's population of older people is expected to have more than doubled by 2015 to almost 2.1 billion.

Globally, the number of people aged 80 and over, the "oldest people," is growing even faster than the rest of the elderly.

In 2000, there were 71 million people aged 80 and over worldwide. Since then, the number of older persons has increased by 77% to 125 million in 2015.

Projections indicate that by 2050, the world's oldest population will be 434 million, more than triple the number since 2015.

The weight of seniors (Fig. 22.1)

As the number of seniors increases, life expectancy increases and will continue to increase by 2050 (Fig. 22.2).

Cancer Incidence

Incidence rates are strongly related to age for all cancers combined, with the highest incidence rates being in older people.

Late Detection

There is a delay in the diagnosis of cancer in people over 75 years of age, for several complex reasons:

Lack of awareness of the problem on the part of health professionals and users
By an observed tendency to do less investigations among seniors
Decreased vigilance among health professionals
By a lack of evidence on treatments, therapeutic strategies, quality of life, drug toxicity, for this population
Constraints on human resources and cancer care capacity
By an apprehension about the disease, by a trivialization of symptoms in the elderly
By sociocultural and generational barriers, fear of death
By fatalism, abandonment of oneself in old age, by a change of heart or even entering an institution
Improving early detection

Signs Not to Be Neglected

Persistent fatigue, weight loss for no reason.
Blood in the stool (or black stool). Constipation or alternating constipation and diarrhea.

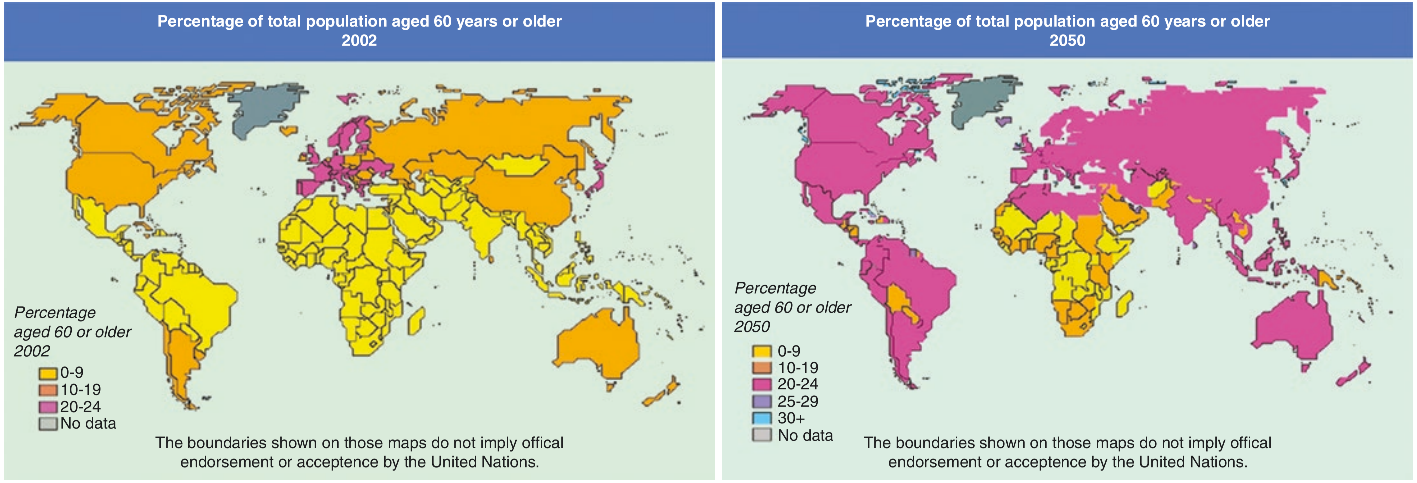

Fig. 22.1 Comparison of the percentage of people aged 60 and over in the world in 2002 and 2050

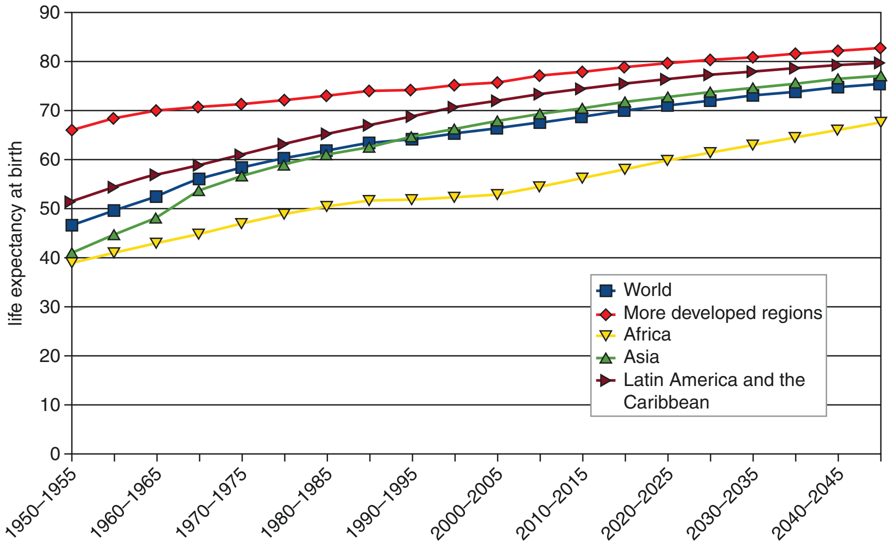

Fig. 22.2 Life expectancy at birth from 1950 to 2050 by continent. (Source: UN World Population Prospects, 2008)

Vaginal bleeding (after intercourse or between periods).

Blood in the urine (or semen), difficulty urinating.

Persistent hoarseness, voice changes, mouth sores, and persistent coughing.

The appearance of lump, redness, change in the shape of the breast, a colored flow (blood) through the nipple.

The appearance of a lymph node in the cervical region, under the arm, in the groin, ...

A nevus (grain of beauty) that evolves wounds or stains on the skin that does not heal.

One size in a testicle.

Human Aging

It is a set of physiological and psychological processes (slow and progressive) in the absence of disease that alter the body’s structure and functions with age.

It is due to intrinsic (genetic) and extrasic (environmental) factors.

Maximum capacities are reduced.

The state of health will depend on the effects of aging and the additive effects of any pathologies. The repercussions will be physiological, psychological, and societal.

Older people do not age in the same way, this population is heterogeneous, and their needs for care and social services can differ significantly.

According to these needs, three types of aging are considered:

1. Successful aging with a reduced likelihood of pathology or disability, significant physical or cognitive abilities, and significant involvement in social and personal life.
2. Habitual or usual aging, where the damage is called "physiological and age-related." There is a high probability of pathologies or disabilities. This population is vulnerable.
3. Pathological aging corresponds to illnesses and/or disabilities.

They are dependent persons in poor health, who have a profile of residents of institutions for dependent elderly people.

The evaluation of the state of health of elderly people allows for a subject with a successful aging process, follow-up, and possible intervention in the event of deterioration of a function.

For a patient with usual or pathological aging, this makes it possible to determine the most altered elements, to envisage one or more interventions, to set up an individualized program of medico-social care, and to differentiate what is related to age from what is responsible for other causes, avoiding excesses in one sense (age) or in the other (it is such a pathology).

Aging is a complex physiological, psychological, and social entity.

Aging will require an in-depth medical-psychosocial expertise of each individual.

In order to identify the major geriatric syndromes and addiction, several domains will be explored most of the time by the cross-eyes of several professionals interacting around an elderly person.

Several scales of assessment currently validated coexist; they will explore the following areas (Table 22.1).

How to Treat Seniors with Cancer

Feasibility of treatment and therapeutic resources:

1. Surgery

   Surgery remains the reference curative treatment for solid tumors.

   The surgical risk is reduced in the event of scheduled surgery.

   Prevention of perioperative risks (respiratory, thromboembolic, nutritional, cutaneous, cognitive, immobilization, ...) must be evaluated according to the severity and duration of the intervention.
2. Radiotherapy

   It is feasible and effective and noninvasive.

   Optimal methods (dose, spread, fractionation, ...) are still under study.

   Need for increased prevention of side effects according to irradiated regions:

   Abdominal: digestive (diarrhea, nausea, vomiting, anorexia).

Table 22.1 Table of the areas to explore and the main screening tools used for a geriatric assessment

Domains	Assessment	Some geriatric screening tests
Socio-environmental situation	Habitat (adapted, accessible) Caregiver (helping or assisted)	MOSS-SS (medical outcomes social support survey) MCSI (modified caregiver strain index)
Functional status	Acts of daily life (toilet, clothing, mobility, ...) Living space management (maintenance, shopping, budget, ...) Vision-hearing Motricity Pain	ADL (activities of daily living) of Katz IADL (instrumental of daily living) of Lawton Visual analogue scale
Cognition	Memory problems Orientation disorders	MMS (mini mental state examination) of Fölstein
Depression	Mood disorders	GDS (geriatric depression scale)
Nutritional status	Nutrition (weight loss) Dehydration	MNA (mini-nutritional assessment) BMI (body mass index)
Fatigue Sleep Quality of life	Cancer-related fatigue(CRF) Sleep disturbance How is it	Fatigue scale: FACT-T (functional assessment of cancer therapy) Visual analogue scale EORTC-QLQ-ELD 14
Polypharmacy	Treatment: number of medications and compliance Drug interaction	STOPP (screening tool of older person's prescriptions) MAI (medication appropriateness index)
Geriatric syndromes	– Dementia: known or unknown? Confusion, delirium – Urinary and/or fecal incontinence Constipation – Falls: numbers? risk? – Skin condition (pessure sore)	– Neuropsychological tests CAM (confusion assessment method) MDAS (memorial delirium assessment scale) – ADL – Tinetti test, time get-up an go test, walking speed, single mode station – The scales of Waterlow, Norton, Braden, ...
Comorbidities	Cardiac; vascular; hematological; respiratory; ENT; digestive; liver; kidney; urinary; genital; muscular; osteoarticular; neurological; psychiatric; metabolic; endocrine	CCI (Charlson comorbidity index) CIRS-G (cumulative illness rating scale for geriatrics)

At the pelvic level: cystitis or rectitis.

At the level of ENT: mucitis, dry mouth, pain.

The effects on the skin are more frequent because the skin is more fragile (fine and dry).

The limitations will be comorbidities, hypertension, diabetes, and inflammatory diseases often poorly evaluated.

Technical conditions may be an obstacle due to immobilization, installation, and restraint.

Also the social environment, remoteness, and transport can create additional difficulties.

3. Chemotherapy

   It is used for curative or palliative purposes.

   It is feasible and effective (especially in hematology, such as lymphomas).

   But it is little or not studied after 70 years.

   The methods of administering drugs (dose, rhythm) are not completely defined and validated beyond the age of 70. Doses and rhythms should be adjusted to suit each elderly patient.

   The side effects are the same as in younger people, but their consequences may be greater, hence the importance of supportive care, which will have a considerable interest in improving the tolerance of treatments.

4. Hormone therapy

   Its effectiveness is recognized especially in breast cancer in women by aromatase inhibitors and in prostate cancer in men by LH-RH agonists.

   But it can lead to or aggravate osteoporosis, arthralgia (sometimes debilitating), musculoskeletal disorders, and venous thromboembolic events.

   It can alter the quality of life through hot flashes and impotence.

5. Targeted therapy

   Targeted therapies have no effect on healthy cells as opposed to chemotherapy, which acts on dividing cells.

   The effects differ from those observed with chemotherapy (their mode of action is not similar) and are quite frequent and sometimes severe, affecting the quality of life and compliance of elderly patients.

   The skin's effects are in the foreground as well as fatigue.

   The other effects are cardiac and vascular not negligible in this age group.

   Moreover, medical information is not always sufficient. Necessity in the coordination of care to reinforce and supplement information with a pharmacist and a nurse.

   They are also poorly studied after 70 years old. The pharmacokinetics of these molecules are specific to the elderly patient in a polymedication context in the senior who may increase drug interactions.

   Oral use in elderly patients can increase medication errors (misunderstanding, difficulty in retaining information) and lead to compliance problems (duration of treatment, psychological disorders, existence of comorbidities).

As a conclusion to all possible treatments, the offer of clinical trials for seniors with cancer 75 years of age and older does not reflect the epidemiology of cancer in this population. They are often excluded from them either directly according to an age criterion or indirectly because of very restrictive exclusion criteria. This very low percentage of inclusions of elderly cancer patients may call into question the place of new anticancer therapies in terms of efficacy and job security for them.

Geriatric Oncology

What are the treatment goals?

In fact, the therapeutic goals differ from a younger person.

Try to answer three questions:

1. Is the patient going to die of cancer or some other cause?
2. Does the patient suffer from cancer during his or her natural evolution?
3. Does the patient have the resources to tolerate cancer treatments?

Most health systems around the world share the common view that oncogeriatrics is an appropriate form of care for the elderly with cancer, possibly suffering from functional deficits (handicaps) or charged pathologies (polypathologies). It may be necessary to adapt their treatment and provide special care for the elderly.

For the SIOG (International Society of Geriatric Oncology)

Geriatric Oncology Is About

- How should oncologists be individualizing their treatment approach based on the risks and benefits of therapy?
- What instruments can help oncologists to have a better view of the patient's overall health situation?
- How do the cancer and the cancer treatment impact the aging process of the patient?

Geriatric Oncology Worldwide

In Western Europe mainly France, Italy, Norway, and the Netherlands, coordinated geriatric oncology and geriatric programs have been established, although an audit shows that they are accessible to only a limited number of patients. Japan's Cancer Control Act aims to further research to improve cancer care and reduce cancer incidence. In Latin America, frailty assessments have been developed and incorporated into treatment strategies for older patients, and use of a simplified geriatric evaluation tool has allowed resource stratification. In other parts of the world, however, geriatric oncology is just becoming recognized and developed.

Geriatric Assessment Helps Oncologists to

- Understand the overall health status of the patient
- Identify previously unknown health problems
- Predict life expectancy of the patient
- Predict tolerance of treatments
- Influence treatment choices
- Identify geriatric interventions that can improve treatment tolerability and compliance

How does this work?

Several models to implement geriatric assessment exist, and it is probably best to use geriatric assessment tools and geriatric expertise according to local/national habits in the geriatric community.

European Model: Many European countries work with geriatric screening tools and only full CGA (Comprehensive Geriatric Assessment) – when the screening test shows a geriatric risk profile. This system has the advantage that a full CGA, which is time-consuming, is done only for those who really need it.

Screening tools (like G8 Fig. 22.3) only take a few minutes and can be used in busy practices to distinguish fit older patients (+/−30% of the 70+ cancer population) versus older cancer patients at risk for geriatric deficiencies (+/−70% of the 70+ cancer population). The latter group requires a full CGA (comprises an evaluation of the most important geriatric assessment domains).

USA Model: Many centers work with patient completed geriatric questionnaires. This has the advantage that the workload is mainly done by the patient (or caregiver).

The geriatric oncology nurse's clinical role is to coordinate the CGA of older patients with cancer, create and manage individualized care plans with the geriatric recommendations, and support patient caregivers while coordinating care with other institutions, teams, and home care suppliers.

Nursing Care of the Older Adult with Cancer

An important aspect in oncogeriatrics; as effective will be the geriatric evaluations, relevant recommendations of geriatricist and his multidisciplinary team, the elderly patient is likely to be poorly managed or even "ill-teated" if the hospital or home care staff does not pocess the fundamentals in geriatrics.

It will be important to develop their geriatric knowledge, as they will then be able to detect situations of loss of independence, prevent dependency, alert caregivers, relatives and doctors, and report them to the appropriate service if necessary.

Its role will be educational in promoting beneficial behaviors.

Empathic and attentive listening to the elderly patient will be essential in order to respect him/her.

G8 questionnaire

	Items	Possible answers (score)
A	Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties?	0 : severe decrease in food intake
		1 : moderate decrease in food intake
		2 : no decrease in food intake
B	Weight loss during the last 3 months	0 : weight loss > 3 kg
		1 : does not know
		2 : weight loss between 1 and 3 kgs
		3 : no weight loss
C	Mobility	0 : bed or chair bound
		1 : able to get out of bed/chair but does not o out
		2 : goes out
E	Neuropsychological problems	0 : severe dementia or depression
		1 : mild dementia or depression
		2 : no psychological problems
F	Body Mass Index (BMI (weight in kg) / (height in m^2)	0 : BMI < 19
		1 : BMI - 19 to BMI < 21
		2 : BMI = 21 to BMI < 23
		3 : BMI = 23 and > 23
H	Takes more than 3 medications per day	0 : yes
		1 : no
P	In comparison with other people of the same age, how does the patient consider his/her health status?	0 : not as good
		0.5 : does not know
		1 : as good
		2 : better
	Age	0 : >85
		1 : 80-85
		2 : <80
	TOTAL SCORE	**0 - 17**

Positive test: G8≤14/17→ Complete CGA

Fig. 22.3 The rapid screening tool in cancerology: the G8 validated by a French prospective study (ONCODAGE). Positive test: G8≤14/17→ Complete CGA

In order to adapt the care approach to the patient's situation, the caregiver will need to know his or her patient:

1. Socio-environmental situation:
   Interrogation of the patient and/or family: family situation, place of life, human environment, recent mourning, ...
   Report or refer patients to a social service if necessary.

2. The state of dependence:

   To know the patient's level of independence for activities of daily living and to maintain and improve the patient's independence in order to allow him/her to return to his/her usual place of life:

   To hydrate and nourish yourself

   To wash

   To look after yourself (teeth, hair, beard)

   To dress and undress and choose their clothes

   Avoiding mothering, letting the patient do what he or she can, educating families in this sense.

3. Nutrition:

   Major role of caregivers, in oncology the majority of elderly patients are undernourished:

   Learn about eating habits (diet, allergies, and preference).

   Beware of abusive regimes to which people have been forced to adhere at a younger age and which are no longer adapted.

   Undernutrition detection and weight monitoring.

   Check if the braces are fitted and adapted.

   Check for oral hygiene and fungal infection.

   Detecting problems of chewing (poor dentition, pain) or swallowing (false routes).

   Detect dry mouth due to salivary gland involution aggravated by psychotropic treatments and dehydration.

   Set up and help with meals, especially if there is a disability (motor and/or cognitive handicap).

   Monitoring the intake of nutritional supplements (outside meals).

   Not more than 12 h of nocturnal fasting.

   Monitor dehydration (access to water at all times).

   Drink (1.5 l) especially in summer (the feeling of thirst no longer occurs with age) and if the patient refuses to drink because of fear of urinary incontinence.

   Report in case of diarrhea, constipation, vomiting, fever, depressive syndrome, pain, and behavioral problems are present.

   Make a statement of meals and drinks if necessary.

   Think about leaving the hospital if access to food will be feasible (report to the dietary and social service)

4. Cognitive and thymic disorders:

   Help the patient to find his or her way in time and space (time, date, name of the hospital where he or she is).

   Do not leave the shutters closed during the day (unless sun ++); to reduce the risk of day/night inversion (especially in winter), dress it if possible with its day clothes (pajama = night!).

   Reassure them; explain what they will do to them, what they have been done, and what they should do (especially if cognitive problems have been diagnosed).

   Advise families to bring a calendar and alarm clock (readable easily).

Report any changes in behavior or suspicions (especially apathetic).
Report any confounding syndrome promptly.
Talk to the patient; see if they are depressed, sad, withdrawn, sleep well, ...

5. The main pathologies:
   Know the patient's pathologies in order to adapt their management (heart problems, diabetes, osteoarthritis, ...).
   Report any disturbances, observe and get to know your patient better:
   Shortness of breath, palpitations, tachycardia, poor blood circulation (hands, cold feet), dizziness, tremors, pain, motor problems, and incorrect renal elimination.
6. The alteration of sensory functions:
   Optimize communication:
   Be careful if wearing glasses or a hearing aid (the forgetting or loss can be the cause of delirium, especially in post-op) and have them brought from home if forgotten.
7. Motor skills:
   Prevent immobilization syndrome (the bed is the enemy of the elderly patient):
   Stimulating older patients to walk
   Putting the patient in the chair
   Early lifting after the operation
   Prevent falls:
   Reduction of catheters and tubes as soon as possible.
   Check that the patient is properly fitted (shoes are now well fitted; advise families to buy appropriate shoes).
   Take care of the room environment (lighting, obstacles, encourage them to call for transfers especially at night).
   Tell the patient to use his cane or walker when he has one, even in the hospital, to have the family bring it home if forgotten.
   Provide advice to families to secure their homes (furniture, lighting, ...), if necessary directing them to competent people who can provide them with information brochures.
   Report falls, do not trivialize them (post-fall syndrome may reeducate).
   In transfers help the person but do not do in his place.
8. Assessment of sphincter functions:
   (a) Urinary tract
   Know the elimination before and after hospitalization:
   Number of urinations per day and distribution.
   Method of elimination: urinal, pot chair, peniflow, protections.
   Existence of acute or chronic incontinence.
   Associated problems (urinary infection, bladder globe).
   Know the patient's degree of independence (walking to the WC, transfers, ...) and autonomy (recall to go to the toilet, need for accompaniment, ...).
   Environment (be careful with obstacles, signage, lighting, ...).
   A patient continent at the entrance = continent at the exit, no unwanted protections.
   Relevance of a DAS.
   Possible urodynamic checkup; talk to the doctor.

(b) Fecal route:

Transit monitoring (diarrhea or constipation can have much more serious consequences in the elderly) and correction of transit problems (walking, if morphine: laxatives).

Know the elimination before and during hospitalization (frequency, mode of elimination, notion of constipation, incontinence, rectorragia, pain, history of pelvic or abdominal surgery).

Degree of independence (accompaniment to the WC) and autonomy (identify behaviors indicating the desire to go bowel movement).

Environment (facilitate access to the toilets which must be adapted: bar, raised seat, pot chair, privacy to be preserved if patient is bedridden)

Conclusion

Nurses need to take a leadership role in integrating gerontological principles into oncology settings.

They must work closely with interdisciplinary team members; they should utilize available resources and continue to build evidence through gero-oncology nursing research.

They can only improve the quality of care in healthcare systems for elderly cancer patients.

Training in oncogeriatrics, whether academic or continuing, for all health professionals will have to be developed, as well as information for users and the public.

Worldwide, the flow of elderly people with cancer can be more serene, as health professionals will be better able to take care of them properly and the financial resources put in place will be used wisely.

Resources

www.msss.gouv.qc.ca
Approche adaptée à la personne âgée en milieu hospitalier
Auteur: MSSS
Publication no: 10-830-15W
No. ISBN (PDF): 978-2-550-60960-5
www.siog.org
www.hartfordig.org
www.ConsultGeriRN.org

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Rare Tumours

23

Paz Fernández-Ortega and Inma Bonilla

Abstract

A total number of two million of persons in Europe are affected today by a rare tumour that makes up one quarter of all malignancies. The classification includes a very heterogeneous group of more than 200 different cancers. Although the increasing precision medicine has led to great advances in treatment and survivor rates of all cancers, because of the rarity of some tumours, patients have lot of difficulties to be diagnosed, to be treated or to follow up care in adequate manner.

The purpose of this chapter is to describe how cancer nurses should be aware of the specific knowledge needed to take care of these patients, which are their main concerns, and the specific needs along the cancer process. It is discussed how few patients have the opportunity to participate in clinical trials or to get the excellent multidisciplinary team that they need because of disparity in equity among countries or regions.

This chapter includes some resources and links of support networks for the patients and professionals.

Keywords

Rare disease · Uncommon tumour · Cancer research

P. Fernández-Ortega (✉)
Nursing Research Institute Català d'Oncologia, University of Barcelona, Barcelona, Spain
e-mail: mfo@iconcologia.net

I. Bonilla
Nuclear Medicine Department, Hospital Universitary of Bellvitge, Barcelona, Spain
e-mail: ibonilla@bellvitgehospital.cat

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Definition of "Rare"

A "rare disease" definition and classification is based on its prevalence and is a condition present in very few persons. Incidence is the number of new cases per year, and prevalence is based on the number of cases out of 100,000 people with the same pathology.

There are more than 6000 types of rare diseases; in the USA are catalogued almost 7000. A majority of them, up to 80%, are of genetic origin. In the last decade, with genomic advances, it has done great efforts, providing many opportunities for better identification of these patients, improving and developing treatments and stabilizing conditions and politics to improve the general care of rare diseases [1].

The terminology of "rare" or "orphan diseases" and their definitions may differ among countries. In Europe, a disease is categorized as "rare disease" when it affects fewer than 1 in 2000 people, which supposes in total 30 million of people living with this condition in Europe.

In the USA, a rare disease is defined as a condition that affects fewer than 200,000 people in all the country which represents 1 in 1500. This definition was endorsed by the US Congress in the Orphan Drug Act of 1983. Rare diseases are also known as an "orphan disease", since pharma companies were not interested in adopting them to develop new drugs or onco-specific treatments. The inform from Food and Drug Administration FDA, by Huron et al. in 2017 *Posted by* Washington, D.C., January 11, 2017, revealed that 9 of the 22 new medications approved in 2016 or the 41% of the drugs are those called orphan drugs for rare diseases [2].

These days, there is a new law in the European Parliament based on the Orphan Drug Regulation 141/2000 that indicates some slightly better attitude to the rare disease, but lot still has to be done locally, nationally or worldwide [3, 4]. More information is available from National https://www.hhs.gov/ and US Food and Drug Administration https://rarediseases.info.nih.gov/diseases/pages/31/faqs-about-rare-diseases.

Still now, as rare patients explain about their rare conditions in www.eurordis.org platform, most of these diseases are life-threatening, chronic and progressive, with a high impact on patients' and families' quality of life (QoL) [2].

Rare Tumours Epidemiology

A rare tumour is considered a rare disease. The RARECARE project defines rare cancers as cancer with an annual incidence of less than 6 per 100,000 people. Rare cancers represent 22% of all cancers, which implicates that slightly more than 4.3 million people live with a rare cancer diagnosis in Europe [4].

Incidence and not prevalence is a more useful indicator to calculate the rare cancers. The RARECANCER, in its rationale and questions for consensus, defined prevalence as the indicator of how many persons previously diagnosed with a rare tumour are alive at the defined date per year. Because prevalence varies considerably depending on life expectancy within the countries, because some cancers occur with such low prevalence and because some are not perceived as rare cancer, data is inconsistent [5].

Differences can also be attributed to cancer registries on both continents. In the USA it is commonly assumed that "rare" is defined by the annual incidence and is around 6 cases per 100,000 people [6, 7]. In Europe, those numbers elevate to 5 cases per 100,000 people, so final numbers rise to a total of 4.3 million persons living with an uncommon cancer diagnosis [4]. Comparing data globally, the incidence for tumour entities is, in general, underestimated [8]. Although rare diseases are not considered a public health priority in developing countries in the world and although in emerging countries the incidence and prevalence of cancers is rapidly increasing, the absolute numbers of all known rare tumours will represent a significant burden to societies with less resource and not prepared.

Each year, from a few hundred to a few thousand persons will be affected by a rare tumour, making the definition of "rare" much more difficult to establish. In the UK, one in five people with cancer will have a "rare and very rare cancer", and of these, one of three will develop a very rare cancer [9] (https://www.macmillan.org.uk/information-and-support/audience/rare-cancers/what-is-rare-cancer.html).

A very recent report on The Lancet Oncology in 2017 by the RARECARE project considers that up to 24% of all new cancer patients have this condition at the moment of diagnosis, and data is increasing, almost doubling, in Europe comparing to the 13% reported in the USA [10, 11].

Facts associated with rare tumours:

– Lack of evidence-based guidelines and solid studies derivate from research to orientate the oncologist and haematologist in the clinical treatment and management of these patients.
– A political decision in the countries that prioritize the research funding for most prevalent cancers rather than to those affecting only small groups of population.
– Insufficient research for treatment and lack of pharmacological and non-pharmacological development on drugs, medications or devices.
– Insufficient coverage by the national health systems and the insurances companies that do not cover adequately their citizens' needs [12].
– Common to all the factors presented is the low prevalence of a disease and the professional perception that it is an uncommon condition.
– Prevention and screening programmes are mostly difficult or impossible [12].
– Delay in time and uncorrected diagnosis are often common.

Another fact takes into consideration the frequency of the condition in onco-haematology. A cancer infrequently seen by professionals is the one that an oncologist may see only three or four times every few years. For the majority, 83.0% of the rare entities, the annual incidence was lower than 1 per 100,000 [13] (http://www.rarecare.eu/resources/RARECARE).

Clinical Characteristics in Rare Cancer (Table 23.1)

Table 23.1 Clinical characteristics in rare cancer

All cancers in children and teenagers are classified as rare cancers Paediatric tumours in adult patients are also considered as rare cancers
A rare cancer might be present in an uncommon localization of the body for the type of cancer. As example melanoma is a type of skin cancer that is not so rare, but uveal or choroidal melanoma that starts in the eye is rare
A rare cancer might be in an uncommon age, generally younger than the average. For example, some colorectal cancers under 35 years, usually associated to hereditary syndromes
A rare cancer might start in a different type of cell than usual, for example, in a bone cell. Most cancers start in certain types of cells, such as skin cells and the cells lining the organs of the body
A rare cancer might be a subtype of a more common cancer. For example, non-Hodgkin lymphoma (NHL) is one of the ten most common types of cancer. There are many subtypes of NHL. Some of these are very rare
Breast cancer in male is considered a rare cancer presentation
The rare cancer might be in an unusual part of the body for that type of cancer. For example, melanoma (a type of skin cancer) that starts in the eye
The rare cancer might have severe barriers in early detection and correct diagnosis and, later, in an effective treatment

Modified by author from Macmillan information web

Classification

A wide typology of cancers could be considered as *rare cancers*. In fact, there is a classification made by Macmillan organization that considers, as a whole picture, which cancer is common or rare or very rare; 53% are common cancers present in more than 50% of the population internationally, like lung, breast, colorectal or prostate; some are less common cancers 27%, such as ovarian or melanoma; and lastly there are rare cancers 20% and very rare cancers in 1.3% of the population [14] (www.macmillan.org.uk/information-and-support/audience/rare-cancers/what-is-rare-cancer.html) (Fig. 23.1).

According to the major families of cancer and localization, the most common rare cancers are haematological conditions with a total of 22% of them, followed by 18% of the female genital cancers and the digestive and the head and neck, both with 14%. The respiratory tract is 8%, and later the rest of the rare cancers are descending to 5% to 2%, enclosing a myriad of very rare cancer presentations.

They are a very heterogeneous group with almost 200 tumours, 2% only for skin localization, and 32% of all are female genital cancers. According to Gatta et al. up to 261 cancers are considered rare and somewhat less common cancers [15]. According to RARECAREnet analyses, commonly it is reported that rare cancers are 196 [5, 14] (Table 23.2).

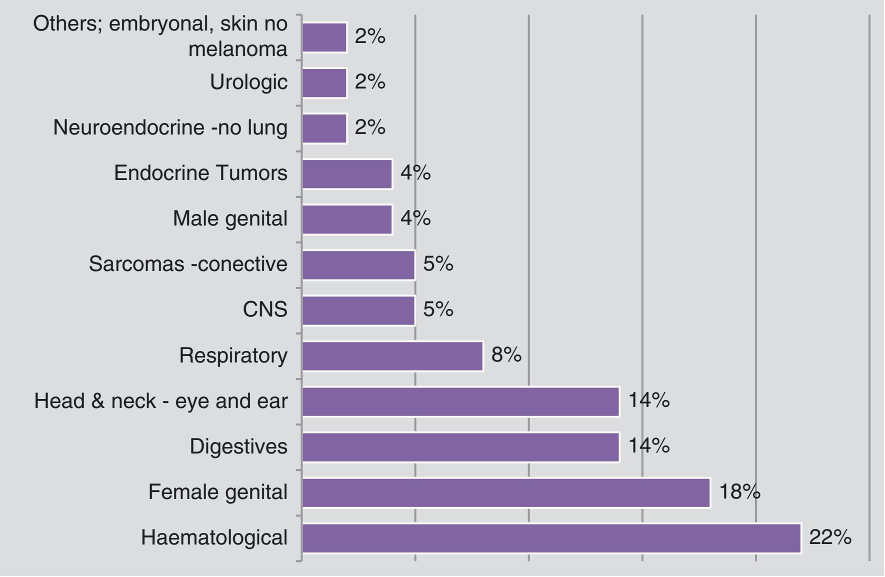

Fig. 23.1 Rare tumour classification in major families of cancers. (Author adapted from Rarecancers.org. Available from: https://www.rarecancerseurope.org/About-Rare-Cancers/Families-and-List-of-Rare-Cancers)

Table 23.2 Rare cancers can be grouped into the following "families"

Families of tumour classification[a] by rarecancereurope.org	Classification by tumour entities[b] version 2, July 2015
Paediatric solid cancers	Central nervous system (incl brain) malignant and non-invasive Hodgkin lymphoma Kidney Leukaemia: acute lymphoblastic Leukaemia: acute myeloid Leukaemia: other (all excluding ALL, AML and CLL) Non-Hodgkin lymphoma Sarcoma: connective and soft tissue
Teenagers and young adults	In teenagers. Paediatric previous and: Cervix Colorectal Female breast cancer Head and neck – thyroid Hodgkin lymphoma Melanoma Ovary Sarcoma: connective and soft tissue Mixed epithelial and mesenchymal

(continued)

Table 23.2 (continued)

Families of tumour classification[a] by rarecancereurope.org	Classification by tumour entities[b] version 2, July 2015
Rare skin cancers and non-cutaneous melanoma	Apocrine carcinoma Atypical fibroxanthoma Dermatofibrosarcoma protuberans Digital papillary adenocarcinoma Eccrine epithelioma Eccrine porocarcinoma Fibro-epithelial tumour of Pinkus Haemangioendothelioma Hidradenocarcinoma Histiocytoma Malignant cylindroma Malignant haemangioendothelioma Malignant pilomatricoma Malignant spiradenoma Microcystic adnexal carcinoma Neuroendocrine Merkel cell tumour Adenoid cystic carcinoma Mucinous carcinoma Mucoepidermoid carcinoma Sebaceous carcinoma Skin appendage Tumours (Muir–Torre syndrome) Unspecified parts of face Mycosis fungoides
Rare thoracic cancers (mesothelioma, thymoma, rare lung cancers, rare breast cancers)	Breast: Male breast cancer Breast nipple and areola Mesothelioma Pulmonary carcinoids Solitary fibrous tumours of pleura Thymomas
Rare urogenital cancers (kidney cancers, bladder cancers, urinary tract cancers)	Urologic: Non-TCC bladder Para-testicular neoplasms Testicular – sertoli cells and Leydig cell Penile cancer Ureter and renal pelvis Urethral cancer
Rare male genital cancers (prostate and testicular cancers)	Prostate: Small-cell prostate

Table 23.2 (continued)

Rare female genital cancers (cervical and ovarian cancers)	Cervical: Neuroendocrine Cervical adenosquamous Cervical adenocarcinoma Cervical unclassified epithelial and other Ovarian: Ovarian clear cell carcinoma Ovarian mucinous carcinoma Ovarian serous carcinoma Ovarian sex cord-stromal Ovarian germ cell tumours Miscellaneous and unspecified Uterine: Clear cell and papillary serous carcinoma Endometrioid adenocarcinoma Mixed epithelial and mesenchymal Unclassified carcinoma Miscellaneous and unspecified Vulva: Squamous carcinoma Adenocarcinoma Melanocytic Other classified and unclassified epithelial Miscellaneous and unspecified Vaginal: Squamous carcinoma Adenocarcinoma Melanocytic Other classified and unclassified epithelial Miscellaneous and unspecified Placenta
Neuroendocrine cancers	Neuroendocrine tumours (NETs) – they are also called carcinoids tumours – vipoma, glucagonoma Neuroendocrine – Merkel cell tumour
Endocrine organ cancers (adrenal cancer, thyroid and parathyroid cancer)	Adrenal cancer Thyroid cancer Parathyroid cancer
Rare CNS cancers (brain cancer)	Meninges Spinal cord and cranial nerves Intracranial endocrine CNS unspecified/unknown
Sarcomas	Sarcoma: connective and soft tissue Bone sarcomas all subgroups Soft tissue: Soft tissue sarcomas all subgroups Gastrointestinal stromal tumours Kaposi sarcoma Leiomyosarcoma Rhabdomyosarcoma

(continued)

Table 23.2 (continued)

Families of tumour classification[a] by rarecancereurope.org	Classification by tumour entities[b] version 2, July 2015
Rare digestive cancers (oesophageal cancers, stomach and small intestine cancer, colorectal and anal cancers, liver cancers, gallbladder cancers and cancers of the intrahepatic/extrahepatic bile tract (IBT/EBT), pancreatic cancers)	Anal: Anal cancer – adenocarcinoma basaloid and cloacogenic carcinoma Squamous-cell carcinoma GI: Ampulla of Vater Biliary tract cancer Duodenal cancer Gallbladder cancer Primary liver (no intrahepatic bile duct cancer)
Rare cancers of head and neck	Bone tumours Lip internal and external Hypopharynx Larynx Middle ear and external auditory canal Nasal cavity and nasopharynx Oral – oropharynx Palate Salivary glands Sinuses Thyroid Head and neck other sites
Rare haematologic cancers (lymphomas, leukaemias, myelodysplastic and myeloproliferative disorders/neoplasms)	Hodgkin lymphoma Leukaemia: acute lymphoblastic Leukaemia: acute myeloid Leukaemia: chronic lymphocytic Leukaemia: chronic myeloid Leukaemia: rarer types Monoclonal gammopathy of undetermined significance Myelodysplastic syndromes

Adapted by authors

[a] First column – families classification. Rarecancereurope.org. Available from: https://www.rarecancerseurope.org/About-Rare-Cancers/Families-and-List-of-Rare-Cancers

[b] Second column adapted from Cancer 52 – less common and rarer cancers 2010 to 2013 Workbook. Published Jun 2015 – classification using ICD-10 codes or morphology codes Public Health England. Available from: http://www.ncin.org.uk/view?rid=2970

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Description of Some Rare Tumours

The *ependymoma* is an intracranial neoplasm of the central nervous system, which commonly appears in the fourth ventricle in children and in the ependymal or spinal canal in the lumbosacral region in adults. These rare tumours are treated surgically, which, with a total resection, are associated with excellent survival rate. At 5 years, 80% is expected, although not all ependymomas can be completely resected, so they receive radiotherapy and chemotherapy.

Adrenal (adrenocortical) carcinoma is a rare and highly aggressive tumour. Its incidence is around 1 to 2 million inhabitants per year. It is presented in a peak before 5 years and in the fourth to fifth decade of life. Although a small percentage of cases are associated with hereditary syndromes, in most cases the cause is not known. More than 50% secrete a hormone, giving the typical symptoms of Cushing's syndrome: glucocorticoid hypersecretion with weight gain, weakness, insomnia and production of androgens.

Surgery is the initial choice of treatment if local and resectable presentation, followed or not by radiotherapy and complementary systemic treatment. In cases of advanced disease, various agents, such as mitotane combined or not with chemotherapeutic agents such as Adriamycin, Cisplatin, Etoposide, Vincristine or Streptozocine, but with poor response.

Neuroendocrine tumours (NETs) are a group of rare cancers that represent 0.46% of gastrointestinal and broncho-pulmonary neoplasm. The overall incidence rate of NET is 25/1,000,000 and somewhat higher in patients over 65 years [16]. They are a heterogeneous group of malignant tumours that can originate in the pancreas, lungs, ovaries, thyroid, pituitary gland and adrenal glands. Most are found in the gastrointestinal system (Hallet et al.). These tumours have the ability to produce peptides causing the carcinoid syndrome. They produce symptoms such as diarrhoea, bronchospasm, facial skin flushing, hot flushes and valvular heart disease [16]. They mimic a wide variety of disorders, making it difficult to diagnose. Some will delay up to 7 years. This facilitates majority progress to metastatic disease up to 71% of patients when undiagnosed, mainly in the liver [16, 17]. In patients with metastases, the combination of slow progression of the disease and hormonal symptoms produces debilitating symptoms with a great impact on the quality of life of these patients [16].

The treatment of NET depends on the size of the tumour, the anatomical location of the primary tumour and the clinical condition of the patient. Radical surgery is the main treatment, including resection of the primary tumour and hepatic metastases if appropriate [16]. In patients with metastases, the combination of slow progression of the disease and hormonal production produces debilitating symptoms with a great impact on the quality of life of these patients [17]. Therefore, there are therapies such as transarterial chemoembolization or radioembolization to treat non-resectable liver metastases. In contrast, liver transplantation is a controversial issue since most of the NETs show low biological aggressiveness and are slow growing [16].

Most NETs express somatostatin receptors and can therefore be treated with somatostatin analogues. Chemotherapy is the treatment for tumours with rapid progression and when other treatments fail. The somatostatin analogues can be labelled with a radiopharmaceutical allowing the performance of somatostatin receptor scintigraphy and in turn the treatment of the tumour if it is positive [16].

Pheochromocytomas and paragangliomas or "extra-adrenal pheochromocytomas" are a group of neoplasms or tumours derived from chromaffin cells located in the adrenal medulla or in the ganglia of the sympathetic that secrete catecholamines. The incidence is approximately 0.8 cases per 10,000 habitants/year, more frequent during the 4th and 5th decades of life, similarly for both sexes. Complete surgical resection is the best treatment with curative intention. When it is not possible or the disease is in advanced stages, the options existing are limited.

Childhood Tumours in Adulthood

Paediatric tumours appearing in adulthood are rare and infrequent tumours. The diagnosis and treatment of paediatric tumours in adulthood are usually extrapolated from that with demonstrated efficacy in the paediatric age, with more than disparate results. Some groups propose to create a national registry of paediatric tumours in adults and develop a network of work with a good intercommunication of professionals.

Eye Cancer Eye tumour is uncommon. It can affect the external, such as the eyelids, muscles, skin and nerves. If it starts inside the eye, it is called intraocular cancer. The most common intraocular cancers in adults are melanoma and lymphoma. The most common eye cancer in children is retinoblastoma, which begins in the cells of the retina.

Skin Rare Tumours

Except for malignant melanoma, skin neoplasms are a heterogeneous group of rare diseases. They can originate anywhere in the body. Complexity in diagnosis, because high degree of difficulty in differentiating from the benign and differentiating between them. There is not always a relationship between morphology and biological response, so the nomenclature is confusing. Regarding their biological response, they can be classified as *low- and high-grade* neoplasm and uncertain response. They are also classified in reference to their origin in the structure of the skin and its differentiation and histopathological characteristics.

To reach the definitive diagnosis, a histopathological examination is essential, after performing a biopsy or after the excision of the probable malignancy lesion. The treatment is also variable, depending on histopathological data and depending on the location and extension. Radiotherapy is the elected treatment if local lesions or systemic treatments if extended. Distant dissemination is highly variable.

Rare Digestive Tumours

Infrequent digestive tumours include a widely heterogeneous variety of pathologies with a very different diagnostic, therapeutic and prognostic focus. Among them, we can find the following: small bowel, appendicular tumours, neuroendocrine tumours, gastrointestinal stromal tumours, anal canal carcinoma and gallbladder and bile duct tumours. Due to the small number of patients in CT, therapeutic management is usually based on the extrapolation of existing neoplasm with similar localization and higher frequency, which is the case of the small intestine and anal cancer. In some gastrointestinal stromal tumours, the study of the molecular basis has allowed to reach an effective treatment with targeted therapies.

Parathyroid

Parathyroid carcinoma is a particularly rare, slowly evolving tumour present in less than 1% of cases of primary hyperparathyroidism. It occurs equally in males and females with a peak incidence in the fourth or fifth decade of life. Most cases are sporadic but may also occur as part of hyperparathyroidism-jaw tumour syndrome (HJTS) or rarely multiple endocrine neoplasia (MEN) type 1 or 2A syndromes. Symptoms are related to the severity of hypercalcemia, more than 90% of the cases are functional, and human chorionic gonadotropin is elevated [18]. There are two prognostic classification systems; Stage III disease in Schulte's staging system, lymph node metastases and a high-risk score in the Schulte risk classification, vascular and lymph node invasion, vital organ or distant metastases are associated with parathyroid carcinoma recurrence.

Surgery is the only curative treatment, but some cases receive adjuvant radiotherapy. In the unresectable cases, some can receive chemotherapy. In advanced and metastatic patients, the hypercalcemia control is the most important. Recurrence is very common [19].

Neuroendocrine Rare Tumours

Thyroid cancer is the most frequent cancer of the neuroendocrine system and represents less than 2% of all solid tumours in adults. The annual incidence of thyroid cancer varies considerably by geographical area, age and sex and has increased in recent decades worldwide, mainly due to a greater detection of the micropapillary tumour (<2 cm) thanks to better diagnostic techniques. In addition, an increase in the incidence of all thyroid tumours has been recently observed, regardless of their size, which suggests that in addition to an improvement in the diagnosis, there are environmental factors that should be considered. To date, the only environmental factor demonstrated for thyroid carcinoma is ionizing radiation, which predisposes mainly to papillary carcinoma, especially if the exposure occurs at an early age.

The World Health Organization (WHO) considers five types of tumours: differentiated thyroid cancer (CDT) is the most frequent, accounting for up to 90% of total thyroid cancer, then papillary carcinoma (75%), follicular carcinoma (10%) and Hürthle carcinoma or poorly differentiated thyroid carcinoma (5%), defined as an undifferentiated evolution of CDT. The other less frequent variants are *medullary thyroid carcinoma (CMT)*, which represents approximately 10% of thyroid tumours, and undifferentiated thyroid carcinoma (1%), also known as anaplastic thyroid carcinoma (CAT).

Surgical resection and ablation with radioiodine are the most effective treatment, achieving a survival at 10 years of over 90%. However, about 30% of patients will present recurrence of the disease. In addition, approximately 10–15% (mainly the most undifferentiated carcinomas) will do distant metastasis. Molecular characterization in these patients has played a fundamental role for personalized treatment and opens a hopeful future for patients.

Medullary Thyroid Carcinoma It accounts for only between 4% and 10% of total thyroid cancers, but it is the cause of 13.4% of the deaths caused by thyroid tumours. About 50% of patients with CMT have tumours that extend beyond the thyroid, mainly at the regional lymph node level, and 13% have metastases at the time of diagnosis. About 90% of patients with metastatic disease will die due to the progression of the disease [6].

The *RET* proto-oncogene encodes a transmembrane receptor with tyrosine kinase domain that is expressed primarily in cells of the neural crest and the urogenital tract.

Approximately 50% of patients with sporadic CMT have somatic mutations in the *RET* gene, and 85% of them have the M918T mutation. The existence of these mutations is also associated with a high probability of lymph node metastasis, recurrence and a lower survival rate [20].

Thymic Tumours A thymoma is a neoplasm of the thymus, specifically formed by epithelial cells of the thymus. It is a rare disease, best known for its association with myasthenia gravis. There are malignant and benign forms, of similar presentation.

Sarcomas are tumours of mesenchymal origin that enclose more than 50 different histological subtypes, which are treated in the same way, not all of them being sensitive to the treatments offered in advanced or metastatic disease. There are rare subtypes resistant to conventional treatments that require a different approach in terms of therapeutic attitude. For this reason, the registry of these subtypes has been created that are not frequent and not sensitive to conventional treatments, to determine their frequency and be able to study individually, in order to offer a more effective individualized therapy in each case.

Prognosis in Rare Cancers

Relative survival in rare cancers is defined as the ratio of the observed survival in a group of cancer patients compared to the expected survival in a comparable group of cancer with similar age, sex and other demographic characteristics. Rarecancer.org gives data by eliminating the effect of mortality due to causes other than cancer. The 5-year survival rate for rare cancers is 47% compared with 65% for more common cancer. In the USA 25% of mortality is for a rare cancer. It can be predicted as well that the increasing fragmentation of “common” cancers into molecular subgroups will effectively proliferate the total data on rare cancers [21].

Comparing with the poor data about overall survival (OS) in the past, today a more aggressive approach has been taken in oncological treatments, and the patient survival has resulted far superior than expected. But, for this approach, there is a need of better coordination and referral inside each country and within European and International arena.

Solids plans for rare cancers are needed, and it is an urgent matter in Europe, so the European Commission wants to enhance the European Reference Networks to reach all EU countries within 5 years, providing a referral system to ensure at least 75% of patients are treated in an accredited centre [2, 3, 15, 21].

It is seeking to improve patient survival, produce communication tools in all languages for patients and physicians and develop multinational databases and tumour banks [21].

Living with a Rare Cancer

Patients with rare cancers face specific challenges. Severe barriers are present during early detection, correct diagnosis and later for an effective treatment.

For a patient and his family, the whole process of diagnosis and treatment usually supposes a great burden that directly affects the relationships, the family dynamic and the financial situation and also impacts on many social and psycho-emotional aspects of his life. This burden may be present more in rare cancers than in other common cancer patients.

Another difficult is the fact that patients with rare tumours, who originally are in rural, small hospitals or community, are often referred towards larger centres, sometimes far away of their homes, especially if there is diagnostic uncertainty or lack of a clear therapeutic treatment protocol.

In addition, experienced oncologist is not always available locally in the same proportion in different regions, or within the countries or within all European countries; Northern, Southern or Eastern European countries present high disparity [2, 22] (www.eurordis.org).

Worldwide, developing countries suffer for a chronic lack of clinical expertise or professionals, driven by economical limitations; cancer nurses, oncologists or radiotherapists are also unequally distributed in hospitals, and both common and less common cancer patients face stigma and inequity [23].

If a condition requires particular expertise or resources as it is a rare cancer, currently the Directive 2011/24 EU, in national law by October 2013, provides a legal framework on access to diagnosis and healthcare in other EU member states, which supposes a challenge country crossing borders [3]. It implicates rules regulations for reimbursement and procedural guarantees and provides the national contact points to cooperate between health systems in the EU [3, 23].

Participating in Clinical Trials and Research

It is a general concern that treatments and research related to a rare specific disease usually are not enough, often inadequate, slow and not well coordinated. The competition for funding for rare cancers is particularly intense adding the lack of trials or commercial interest. Some patients are going back to less expensive drugs, some of which date from the 1970s [8].

In rare cancer research, testing a research question requires the involvement of multiple groups across multiple centres, adding costs and difficulties. But in the clinical environment, although *cooperative groups* exist, they are challenged, with rare diseases, to obtain results and develop trials [24, 25].

As a consensus in all guidelines, the best is to be treated in an experienced centre rather than in a regional cancer unit or small private hospitals. It might happen that misdiagnosis occurs before definitive diagnosis due to the lack of resources or the lack of professional expertise. The number of cases treated in a centre has been considered like a good predictor for survivorship rate. Data from last decade vary from 25% to 48%, resulting from the small comparing with most experienced institutions or cancer centres that presented higher chance to deliver a better protocol [2, 15].

Today, some advantages are present with the possibility of an adequate *molecular classification* of cancers [26] that has considerably changed the approach we had in the past for diagnosis and management of this group of disease. But due to their low incidence, there are still a lot of difficulties due to scarceness of tissue samples and experimental models to facilitate basic research and unsatisfactory patient recruitment or accrual for the clinical trials [27].

In the clinical trial context, the eligibility criteria are established to preserve participants from preventable toxicity or harm, principally for those believed to be at great risk, and also to try to guarantee that participants are quite homogenous and similar. These specific criteria are increasing complexity and avoiding the number of eligible patients [25]. Eligibility in this case results to be too restrictive for patients with rare cancers and is recommended to be expanded to include patients who have exhausted the standard treatment options. If not, patients with rare cancers will never have any or few options to participate in CT [24, 28, 29].

Genomic is opening some new possibilities for future research. Taking a tumour sample will allow to identify those genes with erroneous and relevant models for vulnerabilities and essential genes in rare types of cancer and later to translate this information to many other rare cancers offering new perspective on treatment [27] (Fig. 23.2).

Many challenges are associated to cancers that are less common, with such low incidence. It is a general consensus that treatments and research related to a rare specific disease usually are not enough, often inadequate and not well coordinated [2, 23].

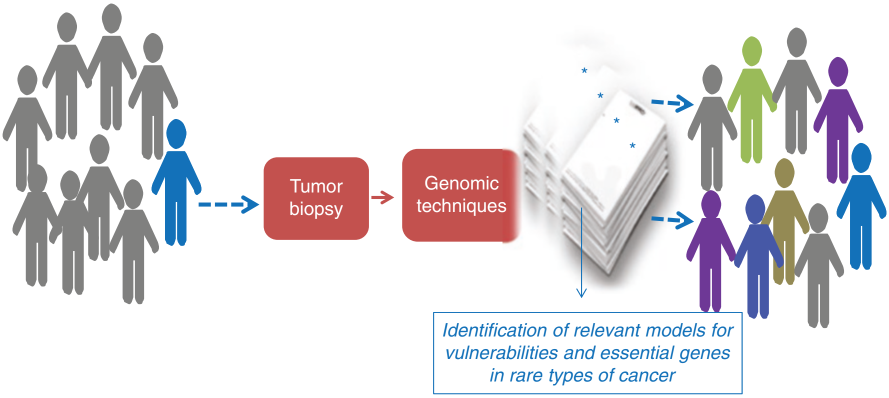

Fig. 23.2 Identification of rare cancer type-relevant vulnerabilities [27]. (Author adapted from Sharifnia et al. [27])

Social Media and Rare Cancers

Another important point to highlight is the lack of information available about the specific condition of a rare cancer and the lack of patient groups or professionals to provide support to patients and families. Patients, and also family members, report the need to talk, to be heard and to share different experiences and concerns with others which will help them in a positive way [21, 30].

Social media platforms, such as Facebook, connect patients with rare cancers. There are some groups in the media that provide support and help patients to avoid the feeling of isolation. If a person has a disease like a rare tumour, life is not limited to taking pills or the medical visits, but conditions disturb his family, his spirituality and his social, emotional and working situation [30].

Now on Facebook, at least one group related to each cancer type is present. *Membership in these Facebook groups* sometimes exceeds the number of new cases of the disease per year in the USA. While members may not all be patients living with disease, these groups reflect disease-specific communities that are amalgamating via online platforms and may increase access to patients for research studies.

Also, social media can be a strong way to connect patients and to disseminate information about the clinical trials existing for different types of conditions. Surprisingly there are eight cancer types, some of the rarest existing with a lot of followers, and they act informing and including well-powered studies in different institutions [21, 31].

Future: Current Initiatives in Matters of Improvement for Rare Tumours in Europe

To meet needs and requests of European patients that wish to improve their access to healthcare and to better disseminate the expertise held by major European centres, Europe has set up reference networks for rare diseases and cancers, the ERNs (European Reference Networks), and launched a year ago a call for applications. In the year 2016, a total of 23 networks were formalized, among which is the EURACAN, dedicated to rare solid cancers of the adult and piloted by the Léon Bérard Centre [32].

Useful Links (Organized by Names)

- ASCO American Society of Clinical Oncology. Doctor approved information for patients at: http://www.cancer.net/
- Cancer Care, Inc Counselling Support Groups. Web: http://www.cancercare.org
- National Cancer Institute Website: http://www.cancer.gov
- Cancer52 represents nearly 100 predominantly small patient support group cancer charities Link: https://www.cancer52.org.uk/cancer52
- ERN-EURACAN (EUropean Rare solid Adult CANcer). ERNs (European Reference Networks). Centre Léon Bérard Center: https://www.centreleonberard.fr/institution/centre-leon-berard-une-vision-internationale/euracan-expertise
- EUROCARE: http://www.eurocare.it
- European Commission Cross-border healthcare directives. Official Journal of the EU. Link: https://ec.europa.eu/health/cross_border_care/overview_en
- EURORDIS 2018. The voice of Rare Disease Patients in Europe. A non-profit alliance of patient organisations. https://www.eurordis.org/about-rare-diseases
- ECPC. European Cancer Patient Coalition
- EUCERD European Union Committee of Experts on Rare Diseases is now available from: http://www.eucerd.eu/
- Genetic and Rare Diseases Information Center at: https://rarediseases.info.nih.gov/
- Genetics Home Reference: https://ghr.nlm.nih.gov/
- Information on clinical trials conducted in Europe. https://www.clinicaltrialsregister.eu/
- Information RARE CANCERS EUROPE: http://www.rarecancers.eu
- Information France cancers rares. Link: www.cancer.ooreka.fr/comprendre/cancers-rares
- HAEMACARE: http://www.haemacare.eu
- National Cancer Institute Website: http://www.cancer.gov
- NORD: Hereditary Breast and Ovarian Cancer Syndrome HBOC- NORD https://rarediseases.org/rare-diseases/hereditary-breast-ovarian-cancer-syndrome/
- NORD website: https://rarediseases.org/for-patients-and-families/information-resources/info-clinical-trials-and-research-studies/

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- Macmillan – UK, Rare cancers information for patients. Link:https://www.macmillan.org.uk/information-and-support/audience/rare-cancers/what-is-rare-cancer.html
- Rare cancers patient support and association in Australia:: https://www.rarecancers.org.au/directory
- Research in rare cancers. Link: www.rarecancer.org

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Supportive Care in Cancer

24

Andreas Charalambous

Abstract
Over the last two decades, significant progress has been made in the management and treatment of cancer; however, the state of science and research development has lagged in targeting the physical, psychosocial and existential elements of living with advanced cancer. Patients and families experience numerous, persistent and depilating physical, psychological and spiritual challenges at this point of the cancer care continuum affecting their human dimension in its totality often leading to poor quality of life and suboptimal treatment outcomes. The supportive model care has been advocated as the mean to help relieve symptoms and improve well-being in patients and their families living with an advanced disease. This is achieved by placing the patient (and the family) at the centre of the care and developing an individualised care pathway to addressing personalised needs that correspond to the dimensions that constitute a human being. The context that informs the provision of supportive care is one that is informed by the interdisciplinary approach where various disciplines work together to achieve a common goal: to provide high-level quality care that is tailored based on the supportive needs of the person that can go beyond the effects of cancer or its treatments.

Keywords
Supportive care · Individuality · Needs · Palliative care · Holistic care

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A. Charalambous (✉)
Cyprus University of Technology, Limassol, Cyprus

University of Turku, Turku, Finland
e-mail: andreas.charalambous@cut.ac.cy

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The Conceptualisation of Supportive Care

Supportive care has been defined by the National Cancer Institute (NCI) as care given to improve the quality of life of patients who are diagnosed with a serious or life-threatening disease. The goal of supportive care is to prevent or treat as early as possible the symptoms of the disease, side effects caused by treatment of the disease and psychological, social and spiritual problems related to the disease or its treatment [1]. In the same line, the Multinational Association for Supportive Care in Cancer (MASCC) describes supportive care as the prevention and management of the adverse effects of cancer and its treatment, including management of physical and psychological symptoms and side effects across the cancer care continuum. Supportive care also promotes rehabilitation, secondary cancer prevention, survivorship and end-of-life care [2]. Although these definitions are similar and encapsulate the essence of supportive care at least in the cancer care context, there appears to be a lack of definitional clarify when it comes to related concepts in the literature often creating confusion among clinicians and patients. It is not infrequent that supportive care and palliative care are seen as 'A rose by any other name would smell as sweet'. A systematic review by Hui et al. [3] revealed that there is a wide range of definitions for these terms, with significant overlaps yet many distinguishing features. The same review identified the concept of 'palliative care' as being more homogeneously defined and in most cases referred to interdisciplinary care focusing on improving patients' quality of life by addressing their physical, emotional and spiritual needs and on supporting their families [3]. The World Health Organization (WHO) defines palliative care as 'an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial, and spiritual' [4]. The WHO also emphasises that palliative care is implemented 'in conjunction with other therapies that are intended to prolong life, such as chemotherapy or radiation therapy, and includes those investigations needed to better understand and manage distressing clinical complications' [4]. This lack of conceptual clarity seems also to have clinical applications as seen in a survey study in the USA that aimed to explore the attitudes and beliefs among medical oncologists and mid-level providers towards the impact of the name palliative care compared with supportive care on patient referral [5]. The researchers found that medical oncologists and midlevel providers were more likely to refer patients at earlier stages of the cancer illness trajectory to a service named supportive care compared with palliative care. They were as likely to refer symptomatic patients at the end of life to a service named supportive care compared with palliative care [5]. In the same study, content analysis showed that most interviewees characterised palliative care as end of life or hospice care. This is only one research example demonstrating that health-care professionals are struggling to clearly identify the differences between palliative and supportive care and identify the context where these two models of care integrate and even how to best implement these in clinical practice.

The Birth of Supportive Care

The model of supportive care has risen as the fusion between the traditional medical model which has its focus on the prolongation and the hospice model that focuses on the palliation of symptoms in people with terminal illness. Despite the fact that these models were developed in isolation, developments in the cancer therapies and the better understanding of the disease and its impact on the person revealed the necessity for integrating these two related but distinct approaches to care. One common element in these two models is that irrelevant to the context that these are provided, the aim is to correspond to the patient's needs. Many of these needs arise from the impact of cancer-related treatments on patients and their families that generate different needs, create expectations and shape beliefs [6, 7]. Therefore there is need to tailor supportive care needs based on the person's individual characteristics which can be managed using individualised care taking into consideration the patient's response to the disease. This is of paramount and fundamental importance within the context of supportive care as patients often correspond differently to the cancer diagnosis, to the treatments and to prognosis and often may come from different cultural backgrounds. Therefore, individualised care does not refer solely on the patient's needs but also takes into account a person's own values, preferences and beliefs related to health in personally meaningful ways [8] and has a positive impact on patient outcomes [9, 10]. The influencing role of the provision of individualised care should also be considered when delivering supportive care as it has been found to be associated with concepts such as quality of life and quality of oncology care. In an international study [11] in Cyprus, Finland, Greece and Sweden, individualised care was associated with trust in nurses, health status and quality of care.

The idea of supportive care echoes the current models of care delivery that call for an integrated model of care where supportive and palliative care co-exists early on at the disease trajectory. For example, the bow tie model [12] is based on the principle of early integration of palliative care with disease management where the possibility of cure is still recognised as well as the possibility of entering a pathway in which death is a possible outcome. The contribution of supportive care is highlighted through the disease trajectory with fluctuations according to the clinical progression of the disease and the needs generated as a result of the disease itself or its related treatments. The model balances between the best and the worst case scenarios; however, it allows for the possibility of dying to be gently introduced at a time when patients' and families' thoughts may be consumed by hope of cure [12]. Increasingly, international organisations such as the European Society of Medical Oncology (ESMO) recognised the need to integrate supportive and palliative services to the care of cancer patient for succeeding better results in managing the disease or the effects caused by its related treatments [13].

Challenges to Implement Supportive Care

Despite the universal acceptance of the value of supportive care and the fact that this approach has gained much headway in some countries, challenges remain that prevent its full deployment in clinical practice and in supportive care research.

Challenges have been identified in the wider context of supportive care but also in disease-specific contexts such as lung cancer [14]. Therefore, the relevant literature has highlighted the disparity in the provision of such comprehensive supportive cancer care to this group of people, an aspect which has been attributed to a number of factors. Such factors include the lack of trained professionals to undertake research and clinical care, a cultural stigma, a paucity of evidence to guide the delivery and dissemination of supportive care services, limited funding for developing and testing interventions to alleviate symptoms and enhance quality of life and a need for well-defined metrics for quality palliative care [15, 16]. As a result of these challenges, the example of supportive care within the childhood cancer context is one area of clinical practice where evidence-based guidelines regarding supportive care are sparse [17]. As supportive care addresses a wide range of disease or treatment-generated effects, such evidence-based guidelines should be available covering all these effects and not prioritising areas of care. In the same example of the childhood cancer context, there is tendency for such guidelines to aim at specific areas of the major supportive care topics, such as nausea, vomiting and febrile neutropenia [18, 19]. As the patient is often faced with a castellation of symptoms (i.e. symptom clusters), the emphasis of the supportive care needs to be holistically delivered addressing his or her needs based on the biopsychosocial model of care and the principles of total patient care.

The challenges associated with supportive care research are also considerable in cancer-specific areas of care. For example, within the lung cancer context, these challenges may include problems in the sample selection that call for more flexibility in recruitment and data collection mechanisms and time frames, problems in selecting an appropriate mode of delivery for the intervention, choice of inadequate length of follow-up and utilization of long questionnaires. Poor management of these challenges has resulted in a paucity of high-quality rigorous randomised controlled trials [14]. Taking into consideration the context of supportive care, many of these challenges can be ameliorated if not overcome with careful planning.

The Way Forward

Early integration of palliative care services with standard oncology care soon after the diagnosis of advanced cancer has been advocated in recent years as a potential effective approach. In this context of care, the interdisciplinary team plays a pivotal role in its successful implementation. Members of the interdisciplinary team can also assume coordinating and management roles to promote the organisation and delivery of supportive care. For example, through patient navigation programs, the nurse can facilitate patients' access to supportive care by providing a smooth transition from oncology to palliative care, promote their adherence to supportive treatment and increase patient empowerment [20]. Coordinated care with a nurse in charge of resource use has been shown to preserve palliative care quality and lower cost [21]. Evidence show that specific nurse-led interventions (e.g. psychosocial and supportive care nursing interventions in breast cancer, gynaecological cancer, etc.) can promote the provision of high-quality comprehensive care to patients within the interdisciplinary context [22]. The Program of Optimization of Chemotherapy Administration (PROCHE) that was implemented at the Georges Pompidou European Hospital presents as an example of optimizing the provision of supportive care [23]. Identifying the timely assessment of chemotherapy-related adverse events as a prerequisite of effective supportive care, the program was developed to optimise the work of the chemotherapy outpatient unit, reduce unnecessary hospital stays, effectively manage adverse events and improve patient quality of life and survival [24]. As part of the PROCHE program, a specialist nurse acts as the liaison with the patient and the other members of the multidisciplinary team. Clinical and biological data are collected from the patient 2 days before chemotherapy is scheduled, allowing time for the MDT to review the data and make any necessary changes to the scheduled chemotherapy prior to the patient's visit. This proactive organisation of the care allows for a thorough assessment of the patient's needs in a timely manner, therefore maximising the treatment's results and minimising the adverse effects and hence the burden of the disease. With the changes in the delivery and the finance of the care around the world, the provision of a significant level of supportive care has been extended to include the home setting. Therefore a supportive care program should extend to include the care delivered at home not only by professionals but also by those who assume the role of the family caregiver. Preceding studies show that the majority of supportive care at the home setting is provided by family caregivers [25]; therefore, adequate preparation and support is needed for the person who assumes this kind of care. In this context, several telemedicine programs have been developed around the world either to provide supportive care remotely or either to support the family members who deliver such care to the patient. A study by Roberts et al. [26] introduced a telenursing intervention as a means to support patients at home during after-hours. As a result of implementing this supportive care program, positive outcomes were recorded such as decreased visits to emergency rooms and enhanced support for families caring for patients at home [26].

With the integration of different models of care delivery within the supportive care context, an integration between traditional and complementary interventions should also be considered as a way to optimise supportive care through an integrative care approach. According to the National Centre for Complementary and Integrative Health (NCCA), "integrative" health care involves 'bringing conventional and complementary approaches together in a coordinated way' [27]. The National Institute for Clinical Excellence (NICE) describes complementary therapies as those which are 'used alongside orthodox treatments with the aim of providing psychological and emotional support through the relief of symptoms' [28]. Although conventional management provides in most cases adequate symptom control, yet it is coupled with some limitations. A number of symptoms however (e.g. xerostomia, palmar-plantar erythrodysesthesia) do not respond to conventional treatments resulting in the patient experiencing poor quality of life and increased disease burden. A growing body of literature however demonstrates that several complementary therapies can have beneficial effects in cancer patients for symptomatic relief [29]. Recent studies also provided evidence on the effectiveness of such complementary interventions in managing cluster of symptoms in patients diagnosed with cancer [30]. The complexity of the symptoms and treatment effects experienced by patients diagnosed with cancer call for an integration of evidence-based complementary interventions in clinical practice alongside conventional treatments.

Conclusion

The supportive care model has risen as the partway to minimise the burden of cancer and of its related therapies throughout the disease trajectory, be it curable, palliative or terminal. Despite the conceptual challenges posed by the concept of 'supportive care', the essence remains that it is a unifying philosophy that bridges the traditional medical model and the palliative care model. The result is what defines supportive care; the provision of supportive care to patients across the cancer care continuum in various contexts, disease stages and prognoses. Supportive care is a concept that utilises the principles of individualised care and multidisciplinary care to achieving its goals of providing support to the needs generated by the disease or the treatment.

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Genetic Counseling

25

Marie Met-Domestici and Anne E. Murphy

Abstract

In this chapter, we describe briefly the cancer genetics field. Basic notions of genetics and mode of inheritance will be summarized first, in order to introduce clinical cancer genetic assessment and, finally, genetic counseling that should go along with any genetic testing.

Keywords

Cancer genetics · Assessment · Genetic counselling

Hereditary Cancer Predisposition

In this chapter, we describe briefly the cancer genetics field. Basic notions of genetics and mode of inheritance will be summarized first, in order to introduce clinical cancer genetic assessment and, finally, genetic counseling that should go along with any genetic testing.

Although different situations can be seen in clinic, we chose here to focus on the well-known hereditary predisposition to cancers: HBOC (hereditary breast and ovarian cancer).

M. Met-Domestici
University Hospital of Lausanne, Lausanne, Switzerland

A. E. Murphy (✉)
University Hospital of Geneva, Geneva, Switzerland
e-mail: anne.murphy@hcuge.ch

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General Approach to Cancer Genetics

Paul Broca was a French surgeon. In 1866, he was the first to describe that breast cancers could run in families. His wife had been diagnosed with an early-onset breast tumor, and he has been able to demonstrate that four generations in his wife's family were concerned, by drawing a family tree [1].

In 1974, Henry Lynch started to inventory familial cancer cases [2].

Some families present more cancer cases than one could expect from the prevalence of tumors seen in the general population. This observation suggests that cancer cases could run in families. Later on, genes that were segregating with the disease have been identified and, it had been undertood that mutations in those genes increase the risk of developing cancer.

More than 100 genes predisposing to cancers have now been identified, and research goes on. It is commonly admitted that 5–10% of all cancer cases can be attributed to a constitutional mutation in such a gene [3].

The identification of those genes was concurrent with the rise of predictive medicine. When a hereditary predisposition to cancers is identified some surveillance protocole or preventive measures are discussed in order to reduce the risk of cancers or detect cancers earlier.

What Are the Implications of Cancer Predisposition Genes in Carcinogenesis?

As discussed in Chap. 1, many of those genes are involved in cell division. It is possible to distinguish two families of genes involved in the carcinogenesis process:

- *Oncogenes*: they encode proteins that favor the process of cell multiplication (growth factors, receptors to growth factors, transcription factors, proteins involved in cell cycle progression, etc.)
- *Tumor suppressor genes*: they encode proteins that will play a role in stopping the process of cell multiplication (proteins involved in cell cycle stop, proteins involved in apoptosis, proteins involved in DNA repair process, etc.).

Cell division is a highly complicated and balanced process. Evolution selected many mechanisms that mitigate the risk of accumulating deleterious mutations by (1) controlling the accuracy of DNA replication, (2) repairing DNA when mutations occur, (3) impeding DNA errors to be passed down from one cell generation to the next, and, at last, (4) triggering cell death when errors are too numerous to be repaired. Ultimately, the immune system is also carefully monitoring for abnormal cells.

Tumorigenesis implies the slow accretion of numerous errors that will be tolerated for a time and which, eventually, may lead to an unwanted, unneeded, and uncontrolled cell growth: a tumor. The last stroke intervenes when tumor cells develop the ability to invade surrounding or distant tissues.

Consequently, cancer genesis takes time and requires the accumulation of many different somatic alterations in genes [4].

What Is a Mutation?: Somatic Versus Constitutional Mutation

As human beings, we carry a lot of mutations in our genes. Most of the time, these variations do not impede our genes to work properly, i.e., they can still be translated into functional mRNA, and the corresponding encoded protein will function normally as well.

However, a mutation that will change the structure of the gene product (protein) or that will impact the normal function of the gene is called pathogenic. Either the resulting protein will be missing or the protein will not operate correctly [5].

Mutations in cancer predisposition genes that lead to cancer genesis:

- Mutations in oncogenes (activation and up-regulation)
- Loss of function mutations in tumor suppressor genes

The gradual accumulation of these mutations is the sine qua non condition for carcinogenesis. Evolution of the tumor also depends on mistakes accumulating in cancer-related genes.

Mutations in genes that are localized to a specific tissue are called **somatic mutations**. Those mutations are found only in the cancerous tissue, not in other cells in the body. In consequence, healthy tissues do not carry those mutations. Somatic mutations are not inherited and can't be passed down to the next generation: they happened by chance because of various endogenic and/or exogenic reasons in a specific tissue.

Unlike somatic mutations, **germline or constitutional mutations** are already present in parental germ cells (eggs or sperm) and can be transmitted to the next generation. Such mutations can be **inherited through generations**. When germline mutations are located in cancer susceptibility genes, the increased risk of cancer can be passed down to the next generation. It means that already at birth, the lifetime risk of some specific types of cancer is known to be increased, because a susceptibility gene already carries a mutation at conception. Less "steps" are required for normal cells to begin into a carcinogenic pathway.

Furthermore, as an inherited mutation is present from the very beginning of the individual's conception, all cells of the body will bear it: the mutation is said to be **constitutional**.

Although some oncogenes have been implicated in hereditary predispositions to cancer, a vast majority of the involved genes are tumor suppressor genes. Hence, we will focus on those to proceed.

The Knudson Model Hypothesis Explains This Process in Tumor Suppressor Genes

Genes exist in two copies: one inherited from the mother and the other one inherited from the father.

The Knudson "two-hit" hypothesis for tumor genesis explains the difference between sporadic and constitutional mutations in tumor suppressor genes.

From a strict genetic viewpoint, mutations in tumor suppressor genes have to concern both copies of the gene to interfere with the normal function of the gene.

When someone carries a constitutional mutation in a tumor suppressor gene, one copy of the gene carries the mutation, and the other one is a normal copy of the gene. Thus, **the "first hit" is already inherited**.

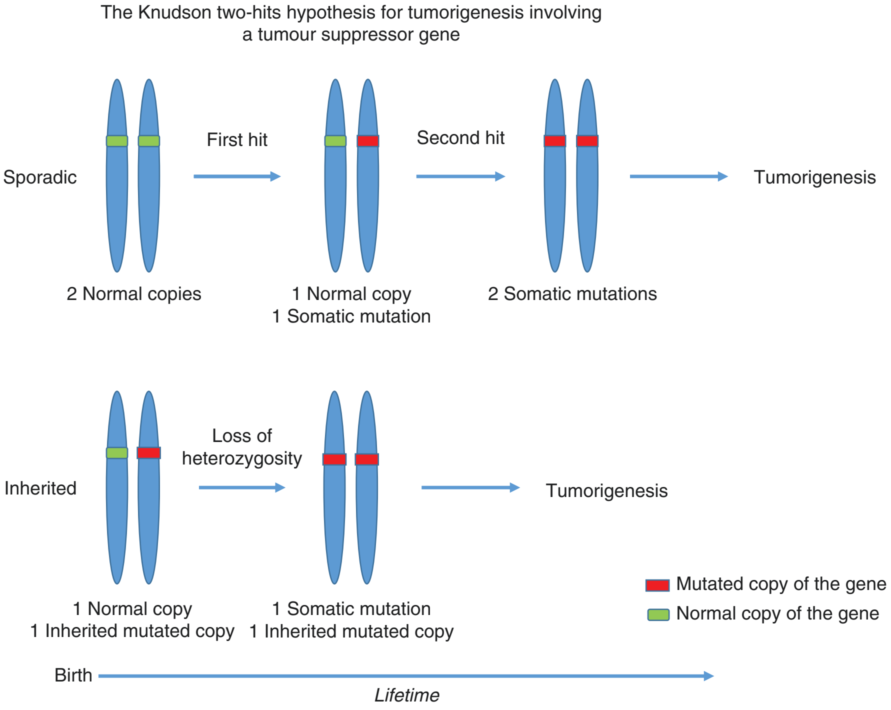
The "second hit" is what will lead to the second allele inactivation. A somatic mutation (in a single cell at first) occurs which leads to loss of heterozygosity. Consequently, the function of the gene will be lost, at first in a single cell but also in every single cell that will descend from this progenitor [6].

The risk of some cancers is significantly increased compared to the general population risk because fewer steps are "needed" to lead to the "second hit."

That's why, from a clinical perspective, the predisposition to develop a cancer in people carrying inherited mutations in tumor suppressor genes is called **autosomic dominant**. A single inherited wrong copy of the gene is sufficient to significantly increase the risk of developing some types of cancers, depending on the gene.

In general population, sporadic cancers arise too. In a *sporadic cancer case*, the two copies of the genes are originally normal. Then, two "mutational hits" have to occur in a cell. It takes more time to cumulate those somatic mutations that might ultimately lead to tumor genesis.

In people who carry a constitutional mutation in a tumor suppressor gene, fewer steps are needed to inactivate the gene. Hence, tumor genesis in that group of people will be a more probable and quicker process. Consequently, cancers in that group of population tend to happen earlier in life. Also, since the constitutional mutation is present in every cell of the body, this explains why people with a hereditary predisposition to cancer may develop more than one tumor (e.g., bilateral breast cancers are seen more often in women who carry a mutation in *BRCA* genes since all breast tissue cells carry the mutation).


The Knudson two-hits hypothesis for tumorigenesis involving a tumour suppressor gene

Autosomic Dominant Mode of Inheritance is Most Common for Mutations in Cancer Predisposition Genes

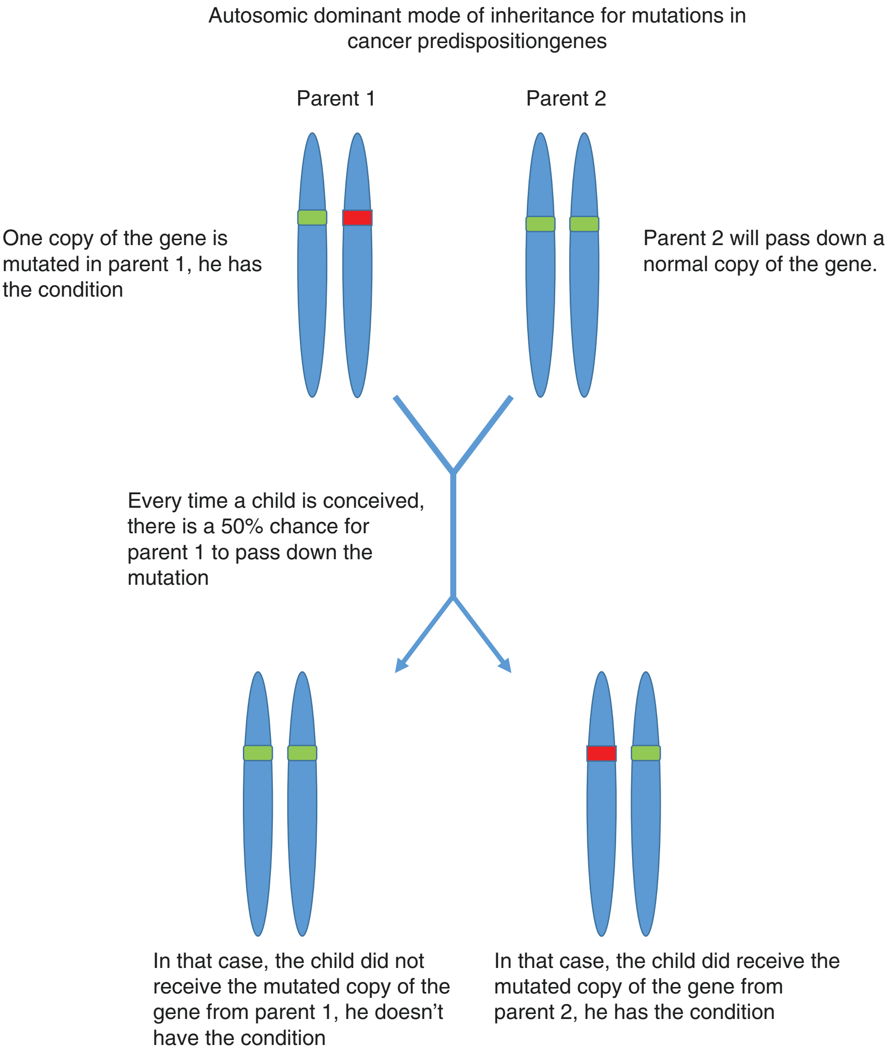
Although autosomic recessive mode of inheritance pattern exists, the most common mode of inheritance for mutations in hereditary predisposition genes is autosomic dominant. It means that the condition reveals when only one of the two copies of the gene is mutated. Patients are heterozygous for the mutation.

To sum up, patients exposed to an increased risk of cancer hold:

- One mutated copy of the gene
- One normal copy of the gene

This Fact Implies Three Crucial Repercussions

- The mutated copy has been inherited (either from the father or from the mother). As a result, *one of the parents* should be also a carrier of the mutation.
- If one of the parents is a carrier, all the *siblings* have a 50% chance to share the mutation.
- The patient who is found to be a carrier of a mutation has a 50% chance to pass it down to every *child*, no matter if the child is a boy or a girl.



Autosomic dominant mode of inheritance for mutations in cancer predispositiongenes

One copy of the gene is mutated in parent 1, he has the condition

Parent 2 will pass down a normal copy of the gene.

Every time a child is conceived, there is a 50% chance for parent 1 to pass down the mutation

In that case, the child did not receive the mutated copy of the gene from parent 1, he doesn't have the condition

In that case, the child did receive the mutated copy of the gene from parent 2, he has the condition

As we stated earlier, those mutations are constitutional. They can be passed down by women as well as by men. It means that eggs or sperm may carry the mutation (parent 1). Since we pass down only one of the two copies of every gene to the next generation, sperm and eggs carry either the mutated or the normal copy of the gene. Since the noncarrier parent (parent 2) will automatically pass down a normal copy of the gene, the fertilized embryo has a 50% chance to carry the mutation.

Cancer Genetic Assessment and Genetic Counseling

Cancer is a common disease. One third of women and 1/2 of men will be diagnosed someday with cancer [7]. Aging is the main factor increasing the risk of cancers, and the majority of cancers are sporadic, i.e., they happen by chance. Various factors lead to somatic mutation accumulation over the years. Those factors can be endogenic and/or exogenic.

For any specific type of cancers, we know:

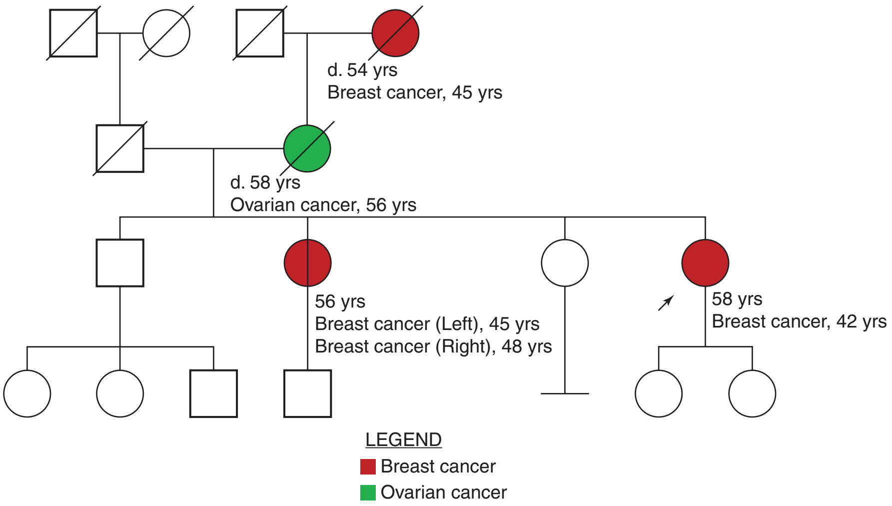
- The medium age at onset
- The proportion of people diagnosed with this type of cancer in general population (incidence)

The whole point of familial and personal history collection is to look for some indication that will seem out of the range of what is normally expected to occur in general population.

Family Tree Drawing

Probands are individuals who come in for a consultation. Proband's personal history of cancer has to be integrated into the familial history of cancers. A precise family tree has to be drawn, gathering relatives over at least three generations. Women are represented by circles, men by squares. The maternal as well as the paternal side of the family has to be pictured. Cancer diagnosis and age at onset of disease are important features that need to be highlighted in such a document so that it is easier to figure out if a hereditary predisposition to cancers can be suspected.

In the following figure, the proband is marked by an arrow. This lady is 58 years old. She has been diagnosed with breast cancer at the age of 42. She has two healthy daughters. She has one healthy sister and a healthy brother as well as healthy nieces and nephews. Her second sister has been diagnosed with bilateral breast cancer at the ages of 45 and 48 years old. Her mother has been diagnosed with ovarian cancer at the age of 56 and her grandmother with breast cancer at the age of 45. Nobody has been diagnosed with cancer on the paternal side of the family.



Genetic Assessment

We shall take this family tree as an example to illustrate a suspicion of hereditary breast and ovarian Cancer (HBOC) predisposition. Based on the personal and familial history assessment, some features will lead the professional in genetic counseling to discuss about genetic testing in the family.

The following situations could evoke HBOC syndrome:

- Personal history of young-onset breast cancer
- Personal history of “triple-negative” breast cancer (a specific subtype of breast cancer)
- Personal history of breast and ovarian cancer
- Bilateral breast cancer with the first tumor before the age of 50
- Close relatives diagnosed with breast and/or ovarian cancers
- Male diagnosed with breast cancer
- Relatives in successive generations with breast and/or ovarian cancers

In the above family tree example, some features are suggestive of a hereditary predisposition to breast and ovarian cancers:

- Breast and ovarian cancer have been diagnosed in close relatives over three generations.
- The proband’s sister has been diagnosed with bilateral breast cancer, both tumors diagnosed before the age of 50.

Personal and familial history assessment is about looking for indication that will lead to offer genetic testing when a benefit in terms of surveillance and prevention is expected for the patient and family members. That is the reason why indications to testing should better be larger than very restrictive.

Recommendations to offer genetic testing to patients may vary from one country to another, mainly based on national recommendations.

In some countries, the government pays for these tests as long as the professional in the field indicates testing. In those settings, such as France, for example, it may be appropriate to use some risk model calculation such as **BOADICEA tool** (French group "Groupe Génétique et Cancer" discuss criteria for testing). **BOADICEA** (Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm) consists of an algorithm that estimates the risk for an individual to carry a mutation predisposing to breast and ovarian cancer. Data about personal and familial history are gathered with age at onset of breast/ovarian/prostate and pancreatic cancers. All family members have to be entered in the program for coding, and thus, computing these data will evaluate the probability for a mutation to be carried by the proband, which could be helpful in some cases to determine if testing is appropriated or not [8].

In some other settings, testing will be supported by private insurance companies or even completely out of the pocket for the patient.

In Switzerland, the mandatory health insurance system in place will cover the testing fees, if testing criteria, elaborated by SAKK group, are met (Swiss Group for Clinical Cancer Research) [9].

With or without risk model calculation tools, the idea is to be able to offer genetic testing to probands when this seems appropriate or reasonable. Testing criteria can always be debated, but the idea is to be able to offer genetic testing to all the patients who may benefit from these test results in order to be able to put in place any recommended management.

Testing: From Targeted Testing to Panel Testing

When genetic testing seems appropriate, *testing should start in a family with an affected individual*. If available, the one who has been diagnosed the youngest in the family would be the best person to offer genetic testing to. In other terms, this person is the most informative one in order to try to explain the family pattern.

If a mutation is found, it is then possible to offer predictive testing to relatives in order to be able to figure out who needs a more intensive screening in a family and reassure those who do not share the mutation and has the general population's cancer risk.

In the past, genetic testing in cancer genetics used to concern only some specific genes. For example, when personal and familial history of cancers evoked a hereditary predisposition to breast and ovarian cancers, only two genes, *BRCA1* and *BRCA2*, were tested. *BRCA1* has been identified by Mary-Claire King's laboratory in 1990 at UC Berkely [10] and *BRCA2* in 1994 [11].

BRCA genes encode proteins involved in a DNA repair process called homologous recombination (HR). When someone carries a BRCA mutation, all cells are heterozygous for the inherited *BRCA* mutation, one copy of the gene performs normally, the other one doesn't. When a cell losses by accident its only functional *BRCA* allele, HR process is disrupted. Some alterative repair processes are then involved but lead to higher chances of genomic instability, which increases the risk of tumorigenesis. Constitutional mutations in those genes have been associated with a significant increase in breast and ovarian cancer lifetime risks [12, 13].

Although mutations in those two genes explain a majority of the situations that could evoke a hereditary predisposition to breast cancer, some other genes, more recently described, are now tested at the same time [12].

These last few years, along with the generalization of *next-generation sequencing*, which allows testing many genes simultaneously, panel testing is getting commonly used worldwide. Hence, more situations can be explained by mutations in some other genes. This will increase knowledge and allow adjusting recommendations over time [14].

Discussion About the Screening: Pretest Genetic Counseling

Genetic counseling is a global discussion with the proband. It has to gather patient education about the suspected condition, as well as explaining basic genetic and inheritance pattern notions. Personal and familial implications of testing have to be detailed. This discussion also focuses on the particular psychological aspects of testing. Altogether, genetic counseling has to give enough tools to the patient for him to be able to make an informed decision about proceeding with genetic testing or not.

Patient education has first to encompass basic genetic and hereditary notions as described earlier. Then, possible test results and implications of testing have to be detailed.

Possible Test Results

Genetic screening varies from any common biological test. If any blood tests will give an "in range" result or "out range" one, genetic screening results are way more complicated than that. And explaining the possible test result is one of the challenges of genetic counseling.

Results may be *positive*. In that case, a mutation is found in the sample. It can give an explanation to the patient's diagnosis, and risk management protocols may be put in place. Also, targeted testing is available for relatives.

Results may also be *negative*. In that case, no mutation is found in the sample. Personal and familial medical history is not explained by test results, and no targeted screening will be offered to relatives. Screening recommendations will be offered based on the familial history of disease.

"Variants of unknown significance" (VUS) can also be found. The likelihood of detecting such variants rises with NGS panel testing. In such a case, the lab finds a change in a gene, but the impact on the gene functioning is unclear: this may or may not impact the gene function. In most of the cases, the lab comes back to the cancer genetics service, when the change is subsequently reclassified, so that the patient can be informed. Until then, VUS will not be used neither to recommend a change in the patient's follow-up nor to offer any targeted screening to relative [14, 15].

Testing Implications

Personal Implications of Testing

Increased Surveillance and Risk-Reduction Surgeries

Pre-test genetic counseling has to describe the implications and limits of testing so that patients may freely decide whether or not they want to go for it. Now that we rather do panel testing, these explanations tend to be more complicated and have to be comprehensive [14]. Informed consent is fundamental to the pre-test counseling process.

Some genes have been associated with cancers for a while, whereas some other genes have been more recently correlated. Since panel testing is only starting to be generally used, that means that we have to gather information over years to increase knowledge on these newly tested genes in clinical settings. When a deleterious constitutional mutation is found, it can be associated to a high or a moderate risk of cancers, depending on the gene [16–19].

Let's focus on *BRCA1/2* genes. Mutations in those genes are associated with a high risk of breast and ovarian cancers in female. Men with a *BRCA2* mutation have a higher risk of prostate cancer. Breast awareness also has to be increased in men. A woman with a *BRCA* mutation has a *60–80% lifetime risk of breast cancer* (risk in general population is around 12%), whereas the lifetime risk of *ovarian cancer rises to 20–40%* (around 1% in general population). Women already diagnosed with breast cancer also have a higher risk of contralateral breast cancer when *BRCA* mutation carriers [12].

Men with *BRCA2* mutations, have a higher risk of getting breast cancer (8 versus 0.05%) and prostatic cancer (20 versus 16%) [12].

Screening recommendations and risk-reducing surgeries are offered to patients. The recommendations represented below are adapted from the NCCN guidelines (National Comprehensive Cancer Network).

Breast Surveillance and Risk-Reducing (RR) Surgery Possibility

Age	Surveillance	Risk Reducing (RR) Surgeries
25–30 years old	- Yearly breast MRI - Clinical palpation every 6 months	Bilateral RR mastectomy is available to patients who choose this option
From 30 years old	- Yearly breast MRI - Yearly breast mammogram and ultrasound - Clinical palpation every 6 months	

Ovarian Preventive Measures

Age	Surveillance	Risk reducing salpingo-oophorectomy (RRSO)
Until RRSO is done	Pelvic ultrasound every 6 months CA-125 blood test every 6 months	
From age 35 (in any case, after childbearing is completed)		Bilateral salpingo-oophorectomy

New Treatment Options and Perspectives

Genetic testing may also have some direct impact on cancer treatment for some patients. PARP inhibitor treatments are now available for women with ovarian cancer tested positive for *BRCA* genes.

As we stated earlier, cells with *BRCA* mutations will not be able to use the HR DNA repair process. Some alterative repair processes associated with higher chances of genomic instability are used by the cell [13].

PARP (poly-ADP polymerase I) is an enzyme involved in those alterative DNA repair processes. In patients with *BRCA* mutation, as discussed earlier, alternative DNA repair processes increase genome instability. If a PARP inhibitor treatment is offered to patients, these alternative routes will not be taken by cells. Cells will remain with DNA double-strand breaks, which will lead to cell apoptosis. This induced process is called synthetic lethality. Two studies showed in 2005 the efficiency of PARP inhibitors on cells with BRCA deficiency [20, 21].

Different subsequent studies showed the expected benefit of PARP inhibitor treatment in patients *BRCA* positive diagnosed with ovarian cancer [22, 23].

Hence, patients diagnosed with ovarian cancer, especially high-grade serous subtype are being referred to cancer genetics clinics in order to define their *BRCA* status so that treatment options may be available.

Also, ongoing researches tend to focus on *BRCA* patients with triple-negative breast cancers (tumors that don’t express estrogen, progesterone, and HER2 receptors) in order to offer them targeted chemotherapies [24, 25].

Familial Implications

When a mutation is found in a family, information should be shared with family members so that relatives can decide if they want to go for predictive testing. Predictive testing is a targeted testing. Either the mutation is found or the mutation is excluded. This allows to offer proper risk management to those in the family who need it and to reassure those who don’t carry the predisposition.

The Limits of the Test

Genetic testing gathers some *psychological issues* that need to be underlined. These psychological issues represent a very important part of genetic counseling. Limits of the tests as well as advantages and disadvantages of the test have to be comprehensively approached.

First of all, patients have to be aware that genetic test results may be more complicated than “yes” or “no” answers.

Positive test results allow entering the predictive medicine area. It has to be a shared decision-making process between the patient and the team to organize a more intensive follow-up or discuss surgical strategies.

On the other hand, a negative or non-informative test result can be more difficult to apprehend, if the patient has already been diagnosed with cancer. The diagnosis is not explained by genetic test results, and many other factors may have played a role in carcinogenesis. As research continues, technical advances may allow us to discover other gene associations with disease. Nonetheless, some patients may expect too much from a genetic test result. Some may experience frustration when no mutation is found, leaving the question “why did I get cancer?” unanswered.

Also, the possibility to find a “variant of unknown significance” may be difficult to accept for some patients.

The Advantages and Disadvantages of Testing

Advantages of Testing

- Knowledge of a mutation allows the medical team to offer some risk-reduction options.
- Results may benefit other family members: children, siblings, and parents have 50% chance to share the mutation if the test is positive. Once a mutation is found in a family, genetic testing can be provided more easily to relatives since testing will be specific for the mutation already found. Test results are obtained faster and either relieve anxiety, if negative, or help to offer risk-reduction strategies, if positive [14]. Consequently testing will rationalize the risk and remove uncertainty.

Disadvantages of Testing

- A negative test result may give a false feeling of security. Some other genes or some other unknown factors may still increase the risk of cancers.
- A positive test result can be stressful. Some individuals may need to find psychological support to deal with anxiety [26].
- It may be difficult for patients to share with relatives that they carry a mutation. Knowledge of a mutation in a family can disturb links between family members. Sometimes, people may feel responsible for passing down a mutation. Those tested negative may also feel guilty toward those who have to face a high risk of cancer [14].
- Since genetic test results are sensitive data, they have to benefit from a very high confidentiality protection. There is a risk of discrimination based on these results.

In conclusion, oncogenetics is an important field nurses have to apprehend in order to be able to answer to their cancer patients who are asking them about the risk for their family members, especially their children. Nowadays most oncology services work along with cancer genetics services, and genetic counselling tend to be part of the therapeutic path.

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Oncology in the Primary Care

Maria Goreti da Rocha Rodrigues and Delphine Lesoin

Abstract

This chapter introduces the general notions and the aims of primary health care and primary nursing care. The focus of this chapter is on the role of nursing care and the promotion of health in the area of oncology along the person's entire health path.

In this chapter particularly attention is paid to oncological care in the home setting, with a description of the targeted care approach among children, adolescents, and elderly individuals. Palliative care is also addressed in connection with primary health care.

This chapter should be of interest to students in the area of nursing care, to caregivers in the area of oncology, in home care or in primary health care.

Keywords

Primary nursing · Oncology nursing · Survivorship · Home setting · Palliative care

Primary Health Care

In 1978, primary health care became one of the key themes of the WHO upon adoption of the declaration of Alma Ata and the strategy of health for all in the year 2000 [1]. Primary care consists of essential health care centered on the needs of the population,

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M. G. da Rocha Rodrigues (✉)
School of Health Sciences, HES-SO University of Applied Sciences and Arts Western Switzerland, Geneva, Switzerland
e-mail: gora.darocha@hesge.ch

D. Lesoin
Home Care Geneva, Geneva, Switzerland

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and it is considered to be the cornerstone of all health systems. It can improve health by providing universal access to care, contributing to a reduction in the costs and a decrease in inequalities in regard to global health [2]. It involves a commitment to equity in terms of health in the framework of development geared toward social justice [3].

Primary care comprises wider access to required services and to optimal quality care. An increased emphasis is given to the prevention and early treatment of health problems, particularly when it applies to everyone. The idea is to reorient health services to promote health by catering better to population needs. The promotion of health is a global intervention strategy for population-based results. It aims to reduce inappropriate recourse to specialists and the adoption of intersectional approaches to health. Primary health care is associated with better health outcomes, and it has proven to be economical. It improves what patients experience [4], and it takes place at the population level.

This care needs to be accessible to all, it should be close to where they live, and it should support self-responsibility of the person undergoing treatment. The emphasis is on its continuity and quality throughout the care process, all the while ensuring a personalized process and “efficacious” care.

The increase in the need for primary care stems from sociodemographic issues linked with aging of the population, the increase in chronic diseases, the complexity of treatments and their monitoring, as well as technological changes.

The role of primary care is particularly important in oncology. Approximately 42,000 new cases of cancer are diagnosed each year in Switzerland. Nearly one out of every two men and two out of every five women develop cancer in their lifetime. Since the beginning of the 1980s, the rate of new cases has increased slightly, while deaths from cancer are declining [5]. More and more people are surviving cancer, and they end up with additional comorbidities that require specific follow-up [5]. As an improvement in the survival rate leads to an increase in the prevalence, primary care is important for addressing upstream pathologies and for decreasing their prevalence.

In light of demographic changes, increased health costs, the development of outpatient care, a decrease in the duration of hospitalization, and the complexity of the pathologies and treatments, primary care has become indispensible for optimal care. A national strategy against cancer was initiated in 2014, and it will be in effect until 2020. It determines the main priority directions, the areas for action, and the associated activities [6]. The priority directions target coordination, quality, and innovation. The areas for action are geared toward prevention, screening, treatment, and follow-up (patient itineraries, health services, and skills) as well as in regard to research and data. Finally, the associated activities include communication, the transfer of knowledge, the coordination with other strategies, and the establishment of an oncology community.

Primary Nursing: Nursing Care in Primary Health Care

Nurses are agents for change for the health system. Primary nursing is a model for providing autonomous nursing care that is evidence-based and that relies on enhanced therapeutic attendance by the nurse. An emphasis is placed on interdisciplinary collaboration and the sharing of responsibilities for the continuity of care. There are four determinant elements: the responsibility of the nurse in establishing a relationship with the person being cared for and the sharing of the decision-making process, the distribution of the work for optimal care and the allocation of resources, communication with the health team, and leadership [7].

The care for patients is the under the responsibility of a designated nurse throughout the patient's trajectory in a hospital or in a care facility. This involves assuming responsibility, planning, and the implementation of care for patients and for their families, as well as planning for the possible delegation of the responsibility for this to other health professionals.

Positive effects have been documented for patients following this approach, and they can be summarized as satisfaction in regard to the care that was received. This translated into a better patient-nurse relationship, better relaying of information, a stronger psychosocial support, facilitation of the coordination and the continuity of the care, as well as involvement of the patient in the decision-making process and the selection of the options for care.

Another effect of this patient-centered approach is that it supports professionalism, development of autonomy, and participation in the decision-making process by nurses. Positive effects have also been noted for the nursing staff that are reflected as a decline in the rate of absenteeism and turnover, as well as an improvement in the quality of the care. For all of the health institutions, these effects led to a decrease in their costs [7].

Oncology Nursing and Primary Care

The professional perspective of primary health-care nurses in oncology is to promote health. The available models for promoting health can provide a useful framework for which the key elements are the community strategies for prevention. The approaches are population-based as they consider the social determinants of health. At the core there are individual actions aligned with the determinants of closeness according to the life trajectory, whereby the relationship with the patient is brought to the forefront. For a holistic approach, nurses need to have good abilities in terms of being able to communicate and show compassion. Interpersonal skills establish relationship skills, and they support the change in behavior in the person being cared for so as to encourage the promotion of healthy ways of living.

In terms of the prevention of cancer, primary prevention is aimed at avoiding risk factors and the known causative factors for the disease, as well as an increase in protective factors to prevent the occurrence of the disease. In secondary prevention, care is centered on early detection in individuals at high risk of developing the disease. Finally, tertiary prevention is focused on assisting individuals facing cancer to manage the long-term effects [8] and after the cancer in those who survive.

The role of primary nursing in the area of oncology also consists of facilitating decision-making and self-determination by the patient [9]. Making decisions requires building a therapeutic relationship throughout the follow-up of the patient. Nurses have a patient advocacy role so as to uphold their interests and whishes among the other members of the multidisciplinary team. They are responsible for coordinating and managing the planning and the care process: whence the importance of effective communication and a clear distribution of responsibilities [10].

The Survivors

Primary care for the population surviving a cancer is a priority in the care continuum against cancer [11]. Survivorship is the experience of living with cancer, since the time of the diagnosis and thereafter, throughout the remainder of one's life and until its end. This population is particularly at risk of suffering from delayed effects of the treatments, as well as the occurrence of relapses or of new cancers [12]. Thus, the care comprises prevention of delayed effects, the detection and monitoring of recurrences, or the appearance of new cancers. Prevention also needs to be undertaken more broadly by screening and monitoring of family members.

Conventional treatments focusing on monitoring of recurrences of cancer have expanded to give more consideration to the well-being and the recovery of the patient. The care involves evaluation, identification, monitoring, and interventions in regard to the consequences of the cancer and the treatments that have an influence on the quality of life. The treatments can trigger a wide range of adverse effects, with consequences that can be physical, psychological, social, as well as financial, both for the patient and their family members. Effective management of these consequences is essential. In terms of physical effects, some injury to normal tissues during the treatment is inevitable, and the impact on the quality of life varies with the type of treatment. While some effects of the treatment can be relatively short-term, for some patients the problems following treatment can persist and become long-term [4].

Health professionals need to ensure that monitoring and management of psychosocial, physical, spiritual, and economic effects takes place. Patients can live in fear of a recurrence, or have anxiety, depression, or a decrease in self-esteem.

Attention is given to the promotion of health by teaching healthy behaviors to the person afflicted with cancer and to their family. Finally, primary oncology care ensures the coordination of care between the various specialized health professionals who participate in the care so as to ensure continuity of the care [13].

Primary health-care nurses need to be involved throughout the continuum of care in order to act as a resource for the survivor. The emphasis needs to be on a better integration of primary care to ensure continuity and support of patients, with the aim of a better quality of life. It also comprises taking into account the impact of the disease on their family, friends, and the caregivers. This experience is accompanied by particular needs in a "new journey," which is that of survival. These individuals can be overloaded from a psychological perspective, and they experience changes in their relationships.

Existential distress is a frequent problem expressed by the patients. On the one hand, in addition to their own experience, they may shoulder that of their loved ones, which increases their burden. Some patients find themselves providing emotional support to their loved ones rather than receiving it [14]. Primary health care can contribute to supporting the patient and relieving this burden by also focusing on the family members and by ensuring that they too receive follow-up care. This approach allows the survivor to be supported. It allows them to again find their role as a parent or spouse within their family environment and to strengthen their need for recognition on the one hand and to support the family in its new reconfiguration on the other.

People who have experienced having cancer face having to battle to rediscover a life that is not the same as before the disease. The uncertainty associated with recurrence of the disease, the impact on family dynamics, and the burden of regular examinations can lead to some very difficult life circumstances. Some patients find themselves in a precarious family situation, and they face social injustices, whereby they have to deal with particularly onerous administrative procedures. For some, it will be difficult or unimaginable to reenter the professional work force, to regain their former job, or to obtain a full-time position, with the consequent risk of social alienation. A struggle to reintegrate professionally and socially then ensues. Thus, the caregiver can then play a key role in supporting the person with their social reintegration, so as to assist them with finding a suitable social integration that avoids exclusion [15].

Different Models of Collaboration

Use of a model of shared care to provide continued care in the area of oncology and to ensure a treatment plan and individualized follow-up is recommended. Several models exist, such as the "nurse-led models" or the "shared care model," for example. Moreover, specific nursing roles have also emerged, such as that of "navigator" or "pivot."

Navigator Role/Pivot Role

Engagement of a pivot nurse is an emerging trend in oncology. The concept of a pivot nurse started in the United States at the beginning of the 1990s [16], and its aim was to improve access to cancer screening by treating delays at the level of clinical follow-up and by removing obstacles to cancer care that may be encountered by poor or destitute people [2]. The concept then soon expanded to Nova Scotia in light of issues with accessibility due to the geography and the availability of specialists.

The term "main root" which is the basis for the term "pivot" truly defines the characteristics of the role of a pivot nurse. This can be pictured as the patient being the root, and they integrate all of the ramifications of the care. The pivot nurse is a contact person who, from the time that the diagnosis is made and in collaboration with the members of the interdisciplinary team, ensures continuous personalized care throughout the care trajectory, between the units and the facilities [16]. They exert clinical leadership, and they have the interpersonal skills to work effectively in a team, thereby ensuring sharing of expertise and coordination of the care [17]. They provide a "common thread" to all of the health workers, in regard to the well-being, the quality of life, and the life project of the patients. They use the results of research and the advice of experts to engage in evidence-based practice.

This role is also described using the term of "navigation" in the Canadian healthcare system.

The Broader Role of the Nurse in Oncology

However, not all cancer care facilities benefit systematically from clearly defined roles of "primary nursing," such as the role of the pivot nurse or navigator. Thus, the role of the nurse in oncology is broadened. The latter is centered on evaluation of the needs of the patients, the education, the management of symptoms, and the support care. They play an essential role in the administration of antineoplastic agents, while they are also responsible for calculating the doses of the medications and for their safe handling. Evaluation of the laboratory results, management of intravenous access, as well as continued and intensive follow-up to treat the potential adverse effects or the medication interactions are also part of their tasks [18].

In light of therapeutic advances and increased complexity of treatment protocols, nurses working in oncology need to broaden their knowledge base both in regard to therapies and new technologies and the adoption of the new guidelines and standards for practice. Surgery, chemotherapy, and radiotherapy constitute the main therapeutic approaches in the treatment of cancer. Scientific and technological advances have, however, given rise to new therapies. Thus, for several years now, immunotherapy has become an option for certain types of cancer, such as melanoma in particular. The aim is to stimulate the immune system to attack the cancerous cells [19]. Innovative and promising research in this regard is currently taking place at the University Hospitals of Geneva, particularly on gliomas and the combination with other therapies (e.g., chemotherapy). Immunotherapy is accompanied by adverse effects that are different from those with other therapeutics. Patients may experience respiratory difficulties, a change in gastrointestinal tract functioning that can be accompanied by diarrhea or gastric pain. Skin rashes can erupt that result in itching. There can also be adverse effects on the hepatic, endocrine, nervous, renal, or ophthalmic systems [20]. Health professionals need to be aware of the importance of follow-up and management of symptoms that can persist for a long time after the end of the treatment. Attention needs to be paid to the various grades of toxicity, with increased monitoring as well as early detection of possible worsening of the condition. The treatment needs to be targeted, while taking into account the various parameters and the relevant professional interventions that are provided as a consequence. In light of these constant developments in the area, continued training of nurses is fundamental if their interventions are to be founded on evidence-based outcomes and if they are to be able to explain it to the patients.

The Home Setting

New technologies and drug-based therapies, a decrease in the duration of hospital stays, a switching to outpatient care, and the chronicity linked with cancerous diseases call for new adaptations in the treatment centered on care at home. The home setting is one of the ways to access the social-health system. Home health care covers a wide area of activities, and it allows for a comprehensive treatment. Long-term continuity and monitoring can be ensured, allowing for early support and diagnosis of a change in the health status of people with cancer.

A holistic approach takes into account the life history and the family dynamics. Inclusion of the goodwill and substitution by family members are also part of the objectives of home care. Taking into account the impact of the cancer on the family is important, as the cancer has repercussions on the family system, with potential negative consequences on spouses and/or other members of the family. Exploring the needs of the family throughout the trajectory of the cancerous disease and survival of the cancer and identification of the mechanisms for coping are extremely important. Indeed, 25–35% of helpers develop symptoms of emotional distress and to a lesser extent (15%) depression [4].

Primary care is fully in line with a strategy of promoting health, while it also contributes to a continuation of care in the preferred framework represented by the living quarters of the client. Indeed, the program of the national strategy against cancer places an emphasis on an integrated treatment, whereby the human being is placed at the center that includes the dimensions of care, the rehabilitation, the psychosocial aspect, the psycho-oncological aspect, and the palliative aspect [6]. Collaboration and interdisciplinary coordination need to be ensured. This treatment allows the trajectory of the oncological care to be "delineated" with the aim of prioritizing a customized quality of life. This change realigns primary care at the core of our health system, and it guarantees a customized process of effective care for the patient and their loved ones.

The challenges at home will become more complex in years to come. There will be a need to add survival care, as well as more and more complex care due to the increase in chronic diseases. The provision of primary care will then have to become diversified in order to meet the growing needs of the population and customized by taking into account the specificities of the participants. Specific treatments will increasingly take place at home. It will therefore be important to develop specific skills in regard to survival care so as to maintain an optimal care trajectory that is linked with the patient's trajectory. Home care nurses in collaboration with oncologists, oncology nurses, and pharmacists at medical centers will provide oncology services, in particular the administration of chemotherapy, at home. Chemotherapy home care should be as efficacious and safe as the care received in health facilities, while continued training and certification of home care nurses are necessary to provide safe and efficacious care [21].

The home remains a preferred site and a valuable source for evaluation of the needs for primary care. It is hence paramount to prioritize survival care in regard to everyone's well-being and values. This role as a care partner will be at the core of the demographic and political challenges of the next years. Improvement of the models of care and the tools, as well as interprofessional collaboration, will therefore be essential for promoting the integration of specialized care in oncology and thereby maintain continuity of care between the various hospital and outpatient care entities.

Features of Home Care for Children and Adolescents

Each year approximately 205 children aged 14 years or less are afflicted with cancer in Switzerland, and approximately 27 die of the disease [22]. In light of the improvement in survival rates, the length of treatments, multidisciplinary approaches, and a decrease in the time it takes to be treated, primary health care at home has led to new issues and challenges in pediatric oncology. The home network is evolving, presenting as an active partner of support and of closeness. Taking care of a child afflicted with cancer results in a substantial level of stress for the parents that can erode family cohesion and generate an imbalance throughout the treatment process due to unforeseeable fluctuations of the disease. Taking heed of the quality of life of the child during this period is paramount. Following the hospitalization, the return home can be a source of considerable anxiety, uncertainty, and loneliness. Some parents are not cognizant of the available support networks. The overall treatment of the child and the parents will therefore be vital for the success of the care project, although other factors are equally decisive, such as forging a partnership relationship, developing an optimal interdisciplinary collaboration (hospital-home), and emphasizing the resources of the health system (respite units, organizations, etc.).

Partnership, alliance, and confidence are important notions in the disease of the child. At home, these all come into play as the health-care professionals have an inside view of the psychosocial changes and of what led to the occurrence of the disease and hence disruption of the entire family structure and cohesion. All of the members of the family are affected by the disease of the child, and the identification of their needs must be part of the objectives and the strategies of the care. It involves decreasing the burden linked to the daily management of the disease, maintaining or even strengthening the family bonds, promotion of the sharing of decisions, and improvement of the sense of safety. A home care visit that is well organized, with a calm and confident atmosphere, allows the members of the family to feel secure and to be relaxed and ready in regard to having health-care professionals attend to the patient in their home [23]. The importance of primary health care at home has been underscored by the strengthening of family life and the promotion of health. However, this provision of home care needs to be aligned with the hospital care. The layout and the scheduling of the care should be discussed and decided jointly with the family, the home care unit, and the pediatrics unit, while paying particular attention to the needs and to the conditions of each member of the family [23].

All of these new issues have a bona fide impact on home treatment. Indeed, this change in the provision of care cannot take place without a minimal degree of skill in oncopediatrics. The specifics of the treatment of a child afflicted with cancer and their immediate family requires increased specific awareness and daily adjustments.

Although it allows access to equitable care to be guaranteed, interdisciplinary collaboration in pediatric primary care facilities remains a weak link, and it is also one the major issues for achieving quality home care.

Features of Home Care for Elderly Individuals

More than 90% of people between 80 and 84 years of age live independently, and 48% of them receive assistance and care at home. Approximately 46% of cancer diagnoses are made in individuals aged 70 years or more [22]. The oncological therapy for elderly patients is different, due to the treatment, the potential complications, and the comorbidities that influence the progression of the disease. Oncogeriatric evaluation allows for an individualized treatment of elderly patients afflicted with cancer, and it takes into account numerous factors such as life expectancy, comorbidities, cognitive functions, and the social environment. It involves not treating the whole population in the same way but rather doing so in a highly individualized manner, through a multidisciplinary approach, so as to provide a customized oncological treatment [24].

The concept of frailty is a key notion in primary health care for this population category. An oncological disease disrupts the home balance and can lead to a cascade of determinant events for the end-of-life period. Once it takes hold, this frailty represents an additional risk factor of contracting acute diseases, recourse to institutionalization, and a potential decrease in survival. Indeed, several factors such as functional decline, comorbidities, and geriatric syndromes are associated with a decrease in life expectancy [25]. Oncogeriatric evaluation takes the heterogeneity of this population into consideration. It is a determinant element of the layout of the personalized care comprising the anticancer treatment, the support care, the treatment of the symptoms, and the end-of-life care. The geriatric population is very heterogeneous due to the change in life expectancy in recent years. Primary health care and support care are again central considerations: promoting elderly individuals being able to stay at home and providing specific oncological treatments or treatments linked with symptoms of the disease, while also fully taking into account the health status of the elderly individual is paramount. An interdisciplinary approach with elderly individuals and their loved ones will allow their specific wishes to be determined, to anticipate risk factors and possible secondary effects, to identify the resources and the means, as well as to personalize a care plan that will contribute to their comfort and quality of life while promoting support as much as possible so that they can remain at home.

Palliative Care and Primary Care

Primary care has a priority status as well as a high potential for offering efficacious palliative care to patients. Indeed, primary health-care professionals can engage with patients afflicted with serious progressive diseases early on in the disease process [26]. Once an advanced cancer has been diagnosed, it is important to introduce palliative care early on in the process. It places an emphasis on relief of the pain, the symptoms, and the stress generated by the serious nature of the disease, and the main aim is to improve the quality of life until the end of their being while also ensuring that their loved ones receive an appropriate level of support [27]. The intervention can address physical, social, psychological, and spiritual needs, thereby ensuring the quality of life of individuals in palliative care [26]. With advanced cancer, the individual realizes that the disease represents a threat to their life. The approach of death seems inevitable, even though its timing cannot be determined precisely [28]. This experience is a burden for the individual and even their loved ones, and it comprises numerous psychological and existential concerns. These are sometimes more important to the patient than the management of their pain or other physical symptoms [29]. Faced with this precarious stage of life, it is paramount that the care is in keeping with the values, the needs, and the preferences of the individual [27]. Working in primary health care allows for interdisciplinary communication and collaboration centered on the needs of the patients. Coordination of the care can allow patients to choose the site where they wish to end their existence, and it allows for dignity at the end to life. Ensuring dignity at the end of life takes into account certain characteristics such as experiencing a minimum number of symptoms and invasive procedures, accomplishing one's existential and spiritual aims, maintaining autonomy, and consolidating the relationship with loved ones during the last stage of one's existence. The recommendations in regard to the end of life are to respect the rights of the patient, their autonomy, and their needs [30], as well as to promote support for them to stay at home and to avoid unnecessary hospitalizations. Ideally, the care is provided at the doctor's office, at the dispensary, at the retirement home, or at their place of residence [26]. It is important that the national strategies support the resources for palliative care so as to ensure that there is a foundation that is efficacious and that covers the health and social systems [26].

Foresight is important for care at home at the end of life. Depending on the oncological history and the trajectory of the patient, the transition toward palliative care needs to be individualized, and it requires constant evaluation of the needs, over time. To satisfy the care objectives and to tackle certain complex situations, for example, when the symptoms are refractory, it is necessary to engage all accessible resources at home so as to collaborate and to construct a mobile, multidisciplinary, and palliative care network. The main aim of optimization of the network and engagement of its full capacity is to improve the quality of the end-of-life experience by ensuring the comfort and the well-being of the patient and of their family until the end of their being.

The adoption of home care may be achieved firstly by informing the patient and his relatives of all of the options for providing care and support that can be made available to them at home. In particular, information should be provided on the treatment of pain or any other symptoms, advance directives, palliative care network resources, associated partner organizations, and resources to support informal caregivers. This first approach allows the primary needs to be screened and to elicit questions regarding their personal and intimate wishes linked with the end of life. However, preserving the right to self-determination is fundamental. At home, family members are an integral part of this process, and they collaborate with the questions regarding this stage of life. The common goal of all of the participants is to ensure a quality end-of-life experience. This first phase of intervention will be a common thread for providing and supporting decisional processes that are informed.

Palliative care at home is achievable when there is a stable network of professional and family members who underpin the full end-of-life project. This allows the management of crises or emergency situations, the prescription of stock analgesics, and the possibility of reaching a doctor of the network for the patient, the family members, or the professionals to be addressed proactively. Such an organization requires an optimal coordination of all of the home care participants, as well as a global and personalized treatment of the patient and of their loved ones so as to create a safe environment and thereby accommodate the common desire of the population to die at home. Primary health care has the advantage of being a resource once it has been implemented early in the oncological trajectory of the patient. Knowledge of the family structure, the life history, and the care pathway are a base to start the introduction of a palliative approach that allows continuity of the care until the end of existence.

Conclusion and Challenges

Primary care in oncology is not yet systematically provided to patients afflicted with cancer in a continuity of long-term care, between the hospital and the place of residence, and with the perspective of customized monitoring to obtain optimal health outcomes over time [31]. New models of care need to be able to meet the challenges of the future. Models of shared health centers and health centers run by nurses could be developed so as to promote the safety, the quality, and the continuity of care. The emphasis needs to be placed on care shared in collaboration with other health professionals. A distinction and recognition of the contributions and expertise of each profession is necessary, as well as skills in interprofessional communication. This collaboration, which is centered on the patient, would allow preservation of the human values of primary care, and it would also ensure the well-being of the care teams [32]. Interventions will need to be tested to determine which model can produce the best results centered on the cancer patient and their loved ones and offer the best coordinated care.

The challenges regarding oncology care will encompass a multitude of care objectives, whether they are preventative and curative, in regard to relationships or coordination of patients diagnosed with cancer and of patients in remission and/or survivorship. To meet these challenges, continuous training of caregivers is paramount in regard to complex care, as is care centered on the individual and their associates, so as to promote high-quality care of patients who have cancer.

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eHealth, ePatient

27

Adam Morse, Ryan Chan, and Richard Booth

Abstract

Over the last two decades, the profession of nursing has experienced a range of technological advancements used to support patient safety and enhance practice and professional development. As patients and organizations continue to utilize technology for health-related purposes, healthcare providers must establish a deeper understanding of various elements related to the use of *electronic health* (eHealth) and *informatics* technologies in healthcare. To do this, a range of various concepts related to eHealth and health technology (i.e., *eHealth*, *electronic health records* [EHR], *telemedicine*, and *ePatients*) will be discussed in this chapter. Consumer applications of eHealth, implications of health literacy related to eHealth, and leadership in the utilization of technology for professional development will also be explored.

Keywords

eHealth · Informatics · Nursing · Patient · Electronic medical record · Electronic health record

Understanding Informatics

Rapid advances in technology over the last two decades have been witnessed in a range of disciplines like business, manufacturing, and communications. Within healthcare, the increased diffusion of technology has also had significant influence

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A. Morse · R. Chan · R. Booth (✉)
Arthur Labatt Family School of Nursing, Western University, London, ON, Canada
e-mail: amorse3@uwo.ca; rchan228@uwo.ca; rbooth5@uwo.ca

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on many aspects of healthcare. From cellular phones, video conferencing, electronic medical records, and other point-of-care technologies used to support patient care, health technology is quickly evolving the profession of nursing and influencing the role of the nurse in new and different ways [1]. Although impressive advances have been made, the healthcare system as a collective has been relatively slow to adopt various forms of technology. While there are a multitude of reasons related to the delay of healthcare to fully embrace various forms of health technology, the topic has become an important area of inquiry for many nursing researchers and scholars [2, 3]. Further, given the wide scale spread of the Internet and related technologies in all aspects of society, understanding various elements related to the use of *electronic health* (eHealth) and *informatics* technologies in healthcare is an important topic for nurses.

eHealth

The terms *eHealth* and *informatics* are both commonly used within healthcare to denote various types of technology, processes, or innovations for the purposes of delivering, managing, and planning healthcare [3]. This may include the use of various electronic record systems, wearable body sensor technology, and any other technologies that involve the collection of data. While these two terms are largely synonymous within many healthcare contexts, this chapter will use *eHealth* as the predominant term to refer to a range of information and communication technologies that exist for, and within, healthcare activities.

Historically, the term eHealth originated during the 1990s, as a product of a popular e-term labeling phase that was commonly applied to various activities of industries (e.g., e-learning, e-banking, e-commerce) [4]. While disagreements related to the definition of eHealth still exist, Oh et al. [5] have suggested that the term eHealth relates to any form of communication technology used in healthcare practice or processes. Further, some authors have expanded on the definition of *eHealth*, suggesting its definition to include aspects related to thinking about technology used in healthcare as a state-of-mind or as a heuristic approach to thinking, acting, and committing to a networked system that assists local, regional, and global healthcare through information and communication technology [3, 6]. Some authors have expanded on the definition of *eHealth*, suggesting its definitions be altered when developing new models in the way users perceive the capabilities of this technology as a means of collecting, monitoring, utilizing, and communicating information across clients and practitioners [7].

Eysenbach [8] has suggested that eHealth encompasses 10 various, interrelated dimensions (Table 27.1). Simply, eHealth is the use of electronic and information-based technologies for the purposes of collecting, analyzing, and disseminating information for healthcare purposes.

Table 27.1 The term *eHealth* is not simply the use of Internet for medical purposes; rather, *eHealth* encompasses a variety of interrelated dimensions, as outlined by Eysenbach [8]

Efficiency	Increase efficiency and reduce cost (e.g., avoiding duplications, irrelevant diagnostics and interventions, enhanced communication effectiveness)
Enhancing quality of care	Reduced cost must also be accompanied with increased quality (e.g., consumers provided power through quality checks, directing patients to most appropriate practitioner, enabling comparisons between various practitioners)
Evidence based	Effectiveness and efficiency should not be assumed; rather, use evidence-based research to support interventions through rigorous scientific evaluation
Empowerment of patients and consumers	Providing access to personal health records and a shared knowledge base will create avenues to develop patient-centered medicine that enables evidence-based patient choice
Encouragement	Creating a true partnership that fosters decision-making in a shared manner between the patient and health practitioner
Education	Encouraging continuous education to patients and practitioners (e.g., consumer health education, individual tailored preventions for consumers, continuing medical education for practitioners)
Enabling	Establish a support means to standardize communication and information exchange between various health networks
Extending	Growing the scope of the healthcare system both conceptually and geographically (e.g., practitioners are able to provide services such as medical advice to pharmaceuticals globally via online services
Ethics	New challenges and threats must be acknowledged with this new form of patient interactions (e.g., privacy, equity, professional practice, informed consent)
Equity	It must be acknowledged that eHealth may create additional barriers to patient populations it attempts to assist. Those assumed to benefit the most from having this level of access may be the least likely to receive any benefit due to various barriers including money, computer literacy, and computer access. This may further worsen the digital divide that currently exists (e.g., rich vs. poor, rural vs. urban populations, male vs. female, young vs. old, and neglected/rare vs. common diseases)

Nursing and eHealth

Nurses represent the largest group of healthcare providers who have direct interaction with eHealth technologies [9]. It is therefore imperative that nurses fully understand the implications of utilizing eHealth technologies to better provide nursing care through increased speed, accuracy, and diminished waste while mitigating risk for patients, public, and the profession as a whole. To understand the implications of eHealth, an understanding of the term is necessary to appreciate the risks and benefits these forms of technology can provide to clinical practice. Currently, nurses utilize (knowingly or unknowingly) a multitude of eHealth systems within many domains of clinical practice. Although the functionality and features of eHealth systems may differ, the main purpose of this kind of health technology is to help healthcare providers manipulate, transfer, and manage various clinical data and information related to clinical or patient encounters [6]. Due to the focus of eHealth toward supporting the management of data and information related to healthcare interactions, the range of technologies that nurses use that can be arguably defined as *eHealth technology* is large. Given this expansive breadth, a range of eHealth technologies that nurses commonly interact with, now and into the future, will be discussed in the following sections.

Clinical Applications of *eHealth*

The rise of eHealth technologies over the last two decades has been most significantly felt within acute care and primary healthcare settings. In these environments, a range of various eHealth technologies have become commonplace to support or extend various aspects of the nursing role [10]. While the availability of these sorts of technology is dependent on several factors related to the environment (e.g., funding, technological infrastructure, etc.), there are a number of common types of systems that can be found in many healthcare environments worldwide.

Electronic Medical Records/Electronic Health Records

Historically, clinical records used by nurses to keep documentation related to a patient's care and treatment have largely been paper-based. With the drive to digitize clinical records, there has been an increased adoption and implementation of various electronic record technologies in a range of environments where nurses work. An *electronic medical record* (EMR) is a system used by clinicians to collect, record, and transmit various health information of patients, including (but not limited to) medical history, allergies, prescribed medications, diagnosis, and other clinically important information related to various episodic interactions with the healthcare system [11]. While there are a variety of EMR systems currently in use globally, all healthcare certified or approved electronic health record systems (which encompass the EMR) share similar characteristics, including (1) the ability to store data in a secure and encrypted manner; (2) allowing audited access to clinical data by only authorized members of the healthcare team and circle of care; and (3) commonly networked to allow multiple users to simultaneously interact with clinical data contained in the record [12]. Data and information in the EMR can be entered and maintained by the users and the organization, but generally not the patient. Although EMRs are digital records of patient information, difficulties still occur related to portability of the clinical record. For example, clinicians at a different clinic or hospital site may not be able to retrieve an individual patient's electronic record from other organization due to a lack of EMR technology interoperability (i.e., compatibility between different technological systems) or other privacy and policy considerations related to transmission of personal health information.

The term *electronic health record* (EHR) has also found traction in the eHealth vernacular. Although regional differences do exist, the term *EHR* is commonly used to denote an electronic record of healthcare information that is more comprehensive and longitudinal than the EMR [13]. The primary intent of EHRs is for information sharing between the patient and healthcare provider across various healthcare organizations and/or institutions [13]. Possessing an EHR provides a patient with a longitudinal record of their healthcare interactions, across various jurisdictions, which can be accessed by healthcare providers over the individual's lifespan. Meanwhile, it has been suggested that EHRs and its related functionalities (e.g., e-prescribing) can serve as a valuable tool in the prevention of medical errors caused by human errors associated with traditional paper-based records and care orders [12].

Developments in EMR and EHR technology have also afforded patients and consumers more abilities to stay connected to their healthcare and related information within their digital records. For instance, *health* or *patient portals* are applications that provide opportunities for patients to directly manage and manipulate their healthcare information stored digitally [14]. In some cases, patient portal technology also enables users to connect to established EMR and EHR databases and view various elements of their clinical or medical record contained within these formalized systems. Other patient portals are stand-alone or adjunct from healthcare-operated EMRs and EHRs. For instance, *Health Myself Patient Portal* (healthmyself.ca, 2018) or Medfusion (Medfusion Inc., 2018) are two platforms that enable patients to enter, upload, edit, and store their health information through a secured patient portal. Based on the services offered by their healthcare provider (i.e., family physician), patients may also be able to schedule appointments or engage in electronic communication with the provider through online health portals. It has been proposed that the use of online patient portals can result in greater communication between providers and patients [15]. Despite the many benefits of patient portals, there remain several unanswered concerns regarding various privacy and confidentiality implications of the technology, as well as the efficacy of these tools [14].

Telemedicine

Telemedicine, with the assistance of ubiquitous telecommunication infrastructures, enables clinicians to provide medical care, diagnosis, and consultation for patients such as through video conferencing platforms, smartphones, and mobile applications [16]. Once considered to be a fictional possibility, the ability of clinicians to provide care to patients virtually is now a reality in many jurisdictions around the world. Historically, various aspects of telemedicine have been introduced in Europe in the early 1905 and have subsequently grown rapidly over the last few decades with the advancements of Internet and communication technologies [16].

Although differences exist, most telemedicine systems contain similar functionalities. At its basics, telemedicine uses various types of information and communication technologies, typically connected to the Internet, to connect individuals together via secured audio and video conferencing environments. Through these virtual connections, clinicians and patients are provided a virtual environment from which medical care (e.g., consultations, assessments, and even in some cases, treatments) can be provided [17]. During remote consultations, patients do not need to travel to the same physical location as the clinician in order to be assessed or receive medical/healthcare treatment. In this model of care, clinicians and patients can be geographically disparate, yet interact in a virtual fashion to accomplish various health and medical tasks. With the ever-increasing advancement of information and communication technologies, telemedicine brings forth both the capacity and opportunity for clinicians to provide a broader range of medical services conducted at a distance and without physical presence. For example, telemedicine has provided effective opportunities for patients who require peritoneal dialysis to undergo the procedure in their own home as they are closely monitored by a team of healthcare professionals who can intervene if necessary [17].

One of the main values of telemedicine is that it can address the various geographical and time constraints related to patients having to travel long distances to receive medical and specialized care [18]. Further, telemedicine also acts as an alternative avenue of care to increase access to healthcare for patients, by affording increased flexibility and the lack of requirement to physically mobilization to a given healthcare institution or clinic. For some patients with mobility issues, cognitive deficits, or lack of access to public transit, the opportunity to receive care virtually without the added burden of having to physically travel to an office or healthcare center can be immensely valuable. Therefore, models of care that utilize telemedicine can provide a valuable opportunity to increase patient-centeredness and engagement in care delivery, by allowing greater flexibility for people who may experience barriers toward accessing healthcare services (e.g., access to health services) [18]. While impressive, telemedicine is still limited in many jurisdictions by cost, technological infrastructure, clinician and specialist adoption, and other contextually driven access issues like Internet connectivity in rural and remote areas.

Consumer Applications of eHealth

With the increasing use of Internet-connected devices and platforms, patients now have increased opportunities to participate and engage in various aspects of managing their healthcare. For instance, mobile applications, smart wearable technologies (i.e., smart watches, fitbit, etc.), online patient discussion forums, and online health portals all now currently exist and can be used by patients and consumers to manage various aspects of individual health and healthcare. While these sorts of technologies and applications are increasingly commonplace now, the use of mobile technology and Internet-based applications for self-management and care is a relatively new innovation. Historically, most healthcare interactions related to an individual's healthcare (e.g., health assessments, monitoring, consultations, etc.) were conducted during in-person visits with a healthcare provider. The wider-scale emergence of various consumer eHealth applications has afforded individuals the opportunity to conduct self-care and management aspects related to their healthcare, including the potential to connect with providers remotely; share and manipulate health information contained on various EMR and EHR systems; and receive personalized healthcare advice generated by these applications. While these forms of consumer eHealth applications may not be uniformly used by everyone, for individuals who are highly motivated and activated to participate in their healthcare, these forms of innovations have been found to be beneficial [19].

For instance, smart wearables (e.g., watches, fitbit, etc.) are capable to monitor an individual's biometric information and transmit them to the corresponding mobile health application. This promotes the accuracy of the information which may be subsequently analyzed and provide related health information, suggestions, and advice to the consumers. In addition to mobile health applications, the surfaces of Internet communities or discussion forums have also served as an alternate source of health information for patients. In 2017, 325,000 mobile health applications were available for consumers to download and use on their mobile devices [20]. The types of mobile health applications range from health monitoring activities such as blood pressure and pulse monitoring, to health management practices such as fitness, dietary applications, and medication reminders. Recent advancements in technology have enabled the connectivity and synchronization for the delivery of health information between mobile applications and smart wearable technology.

Online health information and discussion forums such as *Patient* (https://patient.info), *PatientsLikeMe* (https://www.patientslikeme.com), and Fig. 27.1 (http://figure1.com) offer opportunities for patients to seek health information and suggestions from other patients and healthcare providers. These sorts of online communities enable patients to independently access information related to their specific health conditions and interact with other patients regarding their past experiences, treatments, and results. Further, these health information and discussion forums provide opportunities for patients to enhance their knowledge and understanding of their conditions and may result in increased emotional well-being and feelings of support [21].

Despite the proliferation of various consumer health applications, further research examining the efficacy, safety, and privacy of these alternative modalities

Fig. 27.1 Practitioner utilizing telemedicine technology to conduct a virtual consultation. (Source: Wikimedia Commons (2011). Telemedicine consult. Retrieved from https://commons.wikimedia.org/wiki/File:TelemedicineConsult)

to support health and healthcare management are required [22]. It must be recognized that healthcare providers should not simply dismiss the use of various consumer eHealth applications outlined or described by patients; rather, healthcare providers should be encouraging patients to both meaningfully and purposefully integrate these elements of self-care and management into a patient's plan of care. It is the increasing role of the healthcare provider to become knowledgeable regarding these forms of consumer eHealth applications, to better consult with individuals regarding the efficacy, safety, and evidence base underpinning of these forms of self-care innovations.

Health Literacy

Health literacy refers to "the ability to access, comprehend, evaluate and communicate information as a way to promote, maintain and improve health in a variety of settings across the life-course" [23]. Further, health literacy refers to an individual's understanding of various forms of health information such as medical terminologies including (but not limited to) diagnosis, treatments, medications, and procedures. Without an appropriate level of health literacy, an individual may be prone to experience challenges and barriers during activities of daily living that require a certain level of literacy comprehension (e.g., completing health self-assessment surveys; understanding risks associated with various lifestyle choices; interpreting news from social media sources) [23]. In 2003, the National Assessment of Adult Literacy (NAAL) which surveyed more than 19,000 adults living in the United States revealed that only 12% of those individuals possessed a proficient level of health literacy (e.g., the ability to identify a medical term through searching through a complex document) [24]. Individuals who possess limited levels of health literacy skills are also associated with lower levels of health management abilities, including medication nonadherence, lowered health and well-being, and increased hospitalization [25].

With the introduction of various form health information and applications, including EHRs, social media, mobile health applications, and online health forums, the need for patients to possess adequate levels of health literacy is of significant importance. *eHealth literacy*, though similar to health literacy, refers to an individual's ability to access, interpret, understand, and appraise health information from electronic sources to promote health [26]. Further, the term refers to an individual's ability to locate and use health information from online sources that are both appropriate and valid. Without functional levels of eHealth literacy, patients who attempt to seek health-related information online may misrepresent information or make poor choices based on invalid or false information related to health or healthcare decisions (e.g., vaccination efficacy and safety; nutritional requirements for infants; etc.) Therefore, the increased need for patients to possess functional levels of eHealth literacy provides a meaningful opportunity for healthcare providers to educate and work with patients to assess their levels of literacy, especially surrounding healthcare information derived from Internet sources. Furthermore, patients who possess adequate eHealth literacy may develop a greater sense of autonomy and empowerment as they are better informed through an enhanced understanding of their health condition(s).

Challenges Related to eHealth

The advancement of eHealth in healthcare has provided a number of undeniable benefits for the nursing profession. However, many of these benefits are commonly accompanied by significant challenges faced by both nurses and patients. For instance, cellular phones and wireless Internet have been instrumental innovations that have afforded people worldwide almost ubiquitous access to health- and healthcare-related information. Of 323 physicians questioned in a study from Brazil examining Internet influencing patient relationships, over 85% of patients access information from the Internet prior to seeking medical attention [27]. Without functional health or eHealth literacy levels, patients may make decisions regarding their care that are not evidence-informed or follow established clinical recommendations. As outlined by the Public Health Agency of Canada [28], roughly 88% of older adults lack adequate levels of health literacy. With the increased use of Internet and related technologies by all demographics of society, the role of the nurse must also evolve to help navigate patients through their decision processes related to health information derived from Internet sources (including both credible and non-credible sources). The ethical, privacy, and literacy elements of this emergent nursing role have yet to be fully established but should be subject to further development and recommendations.

The advent of digital records has also generated new issues related to information security and privacy. While there are commonly enhanced digital security measures on all accredited eHealth technology used for clinical practice (e.g., encryption; auditing of records related to access; etc.), the risk of privacy breaches related to the unintentional (or intentional) sharing of personal health information needs to be discussed. Prior to the development of eHealth technologies, most healthcare facilities used a wide assortment of paper-based records to collect and share health information related to patient encounters. The main risk at that time was the misplacement or potential theft of hard copy, paper documents. With the development of eHealth technologies, the potential for data breaches and leakage of personal health information has become a larger issue of concern due to the relative ease related to the transmission and potential sharing of digital media.

Along with the potential of data breaches related to personal health information via eHealth technologies, nurses must also be aware of the potential pitfalls related to social media and other Internet-based technologies. When sharing comments, opinions, photos, and other information to social media networks, nurses must be diligent that they are following both the specific confidentiality/privacy laws and regulatory guidelines enforced by their jurisdiction. Nurses hold the responsibility of being aware of what they share over the Internet, including confidential information describing an incident or information potentially depicted in the background of a photo (e.g., white board outlining a patient roster with names of patients).

eHealth and Leadership

The role of the nurse leader regarding the use of eHealth is an important topic of discussion for future practice. Although the use of eHealth in many clinical environments has been become established over the last decade, there are still many areas of the healthcare system that are undergoing change and adoption of these forms of innovations. Therefore, it is the role of the nursing leader to help guide, shape, and evolve the use of eHealth technologies to both support the roles of nurses and improve the lives and well-being of patients. According to Mintzberg [29], a nursing leader conducts three main activities: (1) *interpersonal roles*, an individual who acts as a *figurehead* to the organization and a network builder among staff and other clinicians; (2) *information roles*, an individual who acts as a spokesperson and disseminator of knowledge in a given environment; and (3) *decisional roles*, an individual who sets and establishes priorities and helps to facilitate or negotiate their execution. It is suggested that many eHealth technologies can help to amplify various roles of a nurse leader including the leveraging of technological innovations that facilitate interpersonal connections between individuals and the refinement of professional networks [30]. Along with allowing nurse leaders to extend aspects of their *interpersonal role*, the use of eHealth can also help to extend the *information* and *decisional roles* of leaders in a variety of ways. For instance, nurse leaders can use specific types of eHealth technologies to more accurately track resource utilization related to their units or organizations. Resource allocation, length of stay trending, and other uses of aggregated clinical data and information arising from various eHealth technologies (i.e., EMR) can be used to help leaders inform their decision-making regarding a variety of clinically focused tasks or activities. Further, by using aggregated data commonly captured through eHealth technology, leaders can better plan for appropriate distribution of resources based on departmental or organizational needs through dashboards and bed tracking systems [31].

Future Directions

Given the increasing complex and data-driven nature of healthcare in modern society, it is almost certain that the use of eHealth technologies within nursing practice will continue to rapidly evolve in the future. Due to the information rich environments where nurses work, the use of eHealth to support decision-making and knowledge management will be essential in the coming decades. With the increasing use of artificial intelligence and automation present in many areas of society, future directions related to the use of eHealth to support patient care will likely become more complex and nuanced [32]. For instance, the increased use of machine learning in various aspects of healthcare (e.g., IBM Watson; the development of precision/personalized medicine approaches) is new areas of eHealth that has yet to be fully studied or examined by nurses for potential within the profession. Further, the increased use of robotics and other artificially intelligent assistive technologies is fruitful directions for nurses to examine regarding using these forms of innovations to safely and proactively generate new models of nursing care that synergize elements of the nursing role and eHealth in functional and meaningful fashions [33].

Summary

This chapter provided an overview related to eHealth in healthcare. The concept of eHealth and its influence on both the nursing role and patients have also been discussed. Various applications of health information technologies such as clinical and consumer applications of eHealth (e.g., EHRs, EMRs, smart wearable technology, online health portals, etc.) have been presented along with the challenges that eHealth and these technologies may bring forth. Potential research and practice implications that may assist in addressing these challenges have also been presented. Given the continuous growth and development in the areas of eHealth and health informatics, opportunities remain in identifying future technological trends and strategies that can be adapted and incorporated in both the management and provision of care for patients and healthcare providers. Further efforts to recognize the benefits of new and innovative forms of eHealth technologies may not only assist in the developments of new models of care but may also empower and engage a new generation of ePatients.

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28

Patient as Actor of His Treatment: Shared Decision-Making

Pascale Breton

Abstract

My own experience of cancer combined with my professional background and the trainer-coach position allowed me to stand in front of nursing staff and indulgently raise their awareness on cancer patient standpoint.

Keywords

BRCA2 · Empowerment · Family · Posture · Diagnosis · Values · Driver seat GPS

Introduction

I survived two advanced-stage melanomas and have inherited a harmful BRCA2 mutation that exposes me to increased risk of breast, ovarian, skin and pancreatic cancer. Most of my close family members have been hit by cancer.

Ten years ago, after a rich and rewarding career in financial services, I have decided to share my experience and contribute to improve survivors' personal and professional lives.

My own experience of the pathology combined with my professional background and the trainer-coach position allowed me to stand in front of nursing staff and indulgently raise their awareness on cancer patient standpoint.

I leave my long-lasting cancer experience as a journey and often use the comparison with a driver on a road trip. Where do we decide to seat in the car? Is the GPS needed and beneficial? I like those metaphors as they can easily be used with patients and are self-explanatory.

P. Breton (✉)
PREVIA, Paris, France
e-mail: pbreton@previa.fr

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From cancer diagnosis announcement to last day of treatment, it's a long way to cover, patient and medical staff travelling together as a team.

A very complex journey, different from a patient to another, successively paved of fear, pain, hope and relief.

A journey I strongly believed is best lived in the driver seat with the medical team besides bringing cares, scientific expertise and support to maximise chances of victory.

However, each one should be left the choice of knowing or ignoring, making decisions or delegating it. Whatever the patient chooses, he exercises his free will, which is a matter of dignity.

Starting Point: Cancer Diagnosis Announcement

I have a vivid memory of my first cancer announcement, and I gathered numerous similar testimonies. My only preoccupation was how to announce it to my husband and mother and how to ease their sorrow and support them in this traumatism. A few minutes later, I was actively shaping plans to support my team during my sick leave. I don't even remember when exactly I realised my life was seriously at threat.

I have also seen patients literally obsessed with what seemed minor to the oncologist (but important to them) like dog or garden care in their absence.

The announcement of cancer diagnosis might generate all sorts of reactions, and some of them might be unexpected or destabilising for the nursing staff.

Whether related to denial, unreadiness to accept the truth or psychological defences, those reactions are part of the process and should be expected and accepted by the nursing staff.

Patient timing is not always synchronised with nursing timing; this is to be known and dealt with. It leads to other possible communication glitches, e.g. patient not remembering key information about diagnosis or treatment, forcing doctors and nurses to repeat and reinforce message several times.

Anyhow, cancer announcement is never insignificant and might be traumatic on both parts. It should be dealt with in an impeccable posture as it will be the foundation of the doctor/patient relationships moving forward.

> *The diagnosis announcement must continuously oscillate between fair distance and proximity while respecting the autonomy, dignity and freedom of patient's choice. The respect of ethical principles will prevent incomprehension phenomena and seal the pact of trust between doctors and patients* (1).
>
> *(1) Bulletin du cancer -95(9):841–7 · November* 2008

After the first announcement, the patient will be repeatedly confronted with the reality of his disease. It will take him more or less time to accept, adapt and adjust. Several members of the nursing staff will have the opportunity to check his understanding of the diagnosis and what comes next.

There are multiple ways to check what the patient knows, understands and feels about the diagnosis, but what seems to work quite well is simply asking the patient to replay his situation in his own words. "Tell me what you heard regarding your health situation and I will complete or amend if you missed or misunderstood anything" will give you a good overview of patient understanding but also where he stands, his feelings and needs moving forward.

In my own experience, this approach efficiently helped me realise what was happening as I talked the nurses and doctors through it.

Friedrich Nietzsche quote, "Silence is worse; all truths that are kept silent become poisonous." (Thus Spoke Zarathustra), says it all.

Travelling in the Driver Seat

I observe it is a challenge sometimes for nursing staff to let patient travel in the driver seat. It means looking at them from a different perspective, grant them more autonomy and consider they have a key role in the healing process.

Being in the driver seat, you feel increased control and empowerment. Your self-esteem raises and some might dare ask questions and make choices and decisions related to treatment strategy.

At the contrary, being in the passenger seat, you tend to live events passively, giving control to the driver and trusting he will know what to do and how to keep you safe.

The collaborative process defined as shared decision-making (SDM) gives the patient a chance to participate actively in his own journey of cancer.

Shared decision-making allows patients and their providers to make health-care treatment decisions together, taking into account the best scientific evidence available, as well as the patient's values and preferences. This process provides patients with the support they need to make the best individualised care decisions, while allowing providers to feel confident in the care they prescribe. It is intended to end as a win-win situation:

> "*We have learned that patients who are active in making decisions about cancer care end up managing their side effects better*" *says Dr. Lidia Schapira, Associate Professor of Medicine at Stanford University School of Medicine*. (2)
>
> (2) *American Society of Clinical Oncology – feb* 2016

In its 2017 report, "The Many Voices of Value," the American organisation CancerCare highlighted how patients participate in their treatment plan and how they view their role and relationships with care providers in the United States (3):

> *Patients often feel they are not active participants in developing their cancer treatment plans*
>
> *Discussions about treatment planning are often overwhelming for people newly diagnosed with cancer*
>
> *Few people realize they can ask questions; even fewer know what questions to ask during these discussions*
>
> *Patients want their providers to recognize and appreciate the effect treatment has on their lives*

> Patients' priorities and perceptions of their treatment change over time.
>
> *Many patients are eager to start treatment as soon as possible, even though for most cancers taking a few weeks to understand the diagnosis and get more than one treatment recommendation would help them make more rational decisions without compromising their prognosis.*
>
> *(3) CancerCare. Patient Values Initiative: The* ***Many*** *Voices of Value, A CancerCare Focus Group Assessment. New York: CancerCare*; 2017.

Very similar results have been shared in 2016 through a French Study "TemA Cancer", run by French organisation "Cancer Contribution" (4):

> *Cancer patients clearly express the desire to be involved in choices related to them. However, they don't feel legitimate to raise their voice in front of doctors who often infantilise them. Patients don't always understand medical information provided and don't feel in a position to make informed decision.*
>
> *Ideally, they would like to be proposed a choice that takes their personal situation, values and culture into account.*
>
> *Others leave it entirely to the medical team to decide for them.*
>
> *Shared decision making is seen as a fundamental act of trust between patient and doctor, that will facilitate communication of doubts, needs and fears on the long run.*
>
> *(4) « La decision médicale partagée à l'épreuve des faits » – Cancer Contribution* 2016

Those results show that behaviours are to be adjusted on a case-by-case basis. Readiness, needs and desires are dependent on patient individual culture and personal situation and might evolve over the course of cancer journey.

This is why open communication, deep listening and adaptability are essential.

> INDIVIDUAL SELF-DETERMINATION IS A DESIRABLE GOAL AND CLINICIANS NEED TO SUPPORT PATIENTS ACHIEVE THIS GOAL, WHEREVER POSSIBLE. SDM RECOGNISES THE NEED TO SUPPORT AUTONOMY BY RESPECTING BOTH INDIVIDUAL COMPETENCE AND RELATIONAL AUTONOMY (5). Entwistle VA, Carter SM, Cribb A, Mc Caffery K. Supporting patient autonomy: the importance of clinician-patient relationships. J Gen intern Med. 2010;25(7):741–5

Travelling Without a Map

Many drivers using a GPS in their car still like to view a map before departure. They prefer to have a complete overview of the journey from starting point to final destination. This is typically what cancer patient cannot benefit from. We can only have a step-by-step view, with key milestones.

Similar to a GPS, you have a narrow view of the road and only the few kilometres ahead are detailed.

The nursing team and doctors have a clearer view of the road from experience but cannot predict final destination either.

This is what often creates frustrations and comes in the way of trustworthy patient/nursing team relationships. Some patients want to see further and others are happy with the GPS set on 500 m view.

This is where nursing team need to adjust and share information as requested, no less no more.

Again, open questioning is the best way to appreciate what the patient wants to know about treatments, side effects and key milestones.

Clarify the Road

Although the word cancer is most often associated with fear and death, it seems that the majority of cancer patients ask for transparency and truth.

Since 2002 in France, it is stated by law that "anyone has the right to be informed on his health condition." However, medical jargon and acronyms are still often used with patients, and some physicians report that they never pronounce the word cancer in front of patients not to worry them.

This attitude raises several questions:

- What if I find out the truth by myself (on the Internet, for instance) with no physician or nurse around to clarify, reassure and explain?
- How can I cope to a situation if I don't have all the information about it?
- Cancer is not named but I have a chemotherapy and am treated with cancer patients; what should I understand?

Clarity helps the patient to take control of his life and his pathology, alleviates fear of the unknown and adjusts to treatments.

With treatment efficiency improvement, "cancer" is not necessarily associated with "death" as it often was in the past. Most practitioners today consider that lie by omission generates more undesirable effects than benefits.

Actually, you cannot effectively fight an enemy you are not conscious of or ignore.

Outside of transparency regarding cancer itself, practitioner and nurse need to be conscious of medical jargon and abbreviations used. Patients and their families might not dare asking for clarifications, and this could lead to misunderstandings and unnecessary worries. I will always remember this patient stressed because he did not know what was this IDE he was supposed to call in case of emergency. In French, IDE is the acronym for state registered nurse (Infirmier Diplômé d'Etat).

Give Up on What You Don't Control

This is probably the best advice I received ever and has been the code of conduct of my life since then.

It worked for me and also made a great difference for many nursing staff members I shared it with.

When a patient is asked what is difficult for him, he will list all sorts of preoccupations. Some of them he can deal with and act upon, some others (most of them) being totally out of his control and he cannot influence.

Interestingly, if you ask the same question to a nurse or a doctor as it relates to their relationships with patients, you will get the same results. They are preoccupied and spend a lot of energy on things out of their responsibility area.

Setting your mindset to focus on what you control and actions depending solely on you allows you to thrive where you are expected to deliver at your best. Your excellence, skills and energy are fully mobilised to serve your purpose in your area of responsibility.

Some other aspects are not fully depending on you, but you can more or less influence the result through your behaviour, mindset or contribution.

Outside of those two areas are all things you have no control nor influence upon and you should give up on Figs. 28.1 and 28.2.

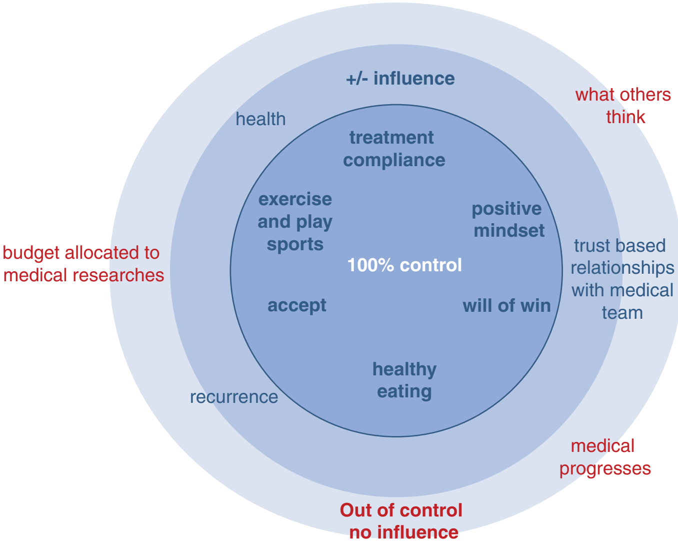

Fig 28.1 Patient circles of influence

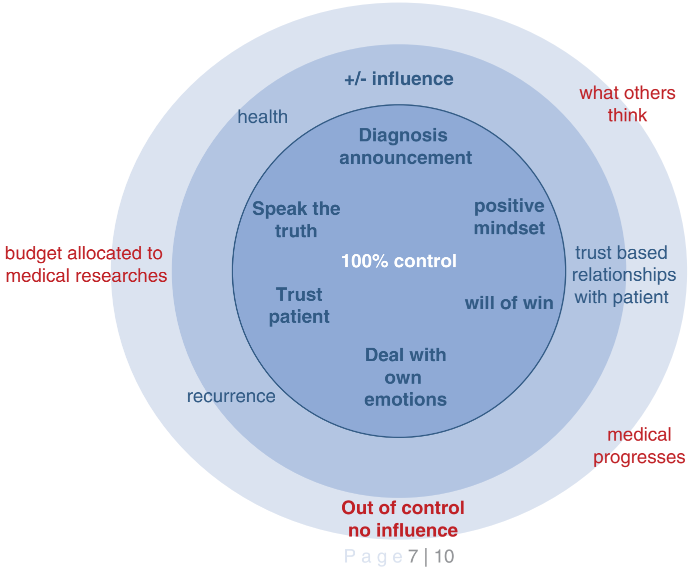

Fig 28.2 Practitioner circles of influence

Patient Position

Preoccupations widely vary from a patient to another and through the cancer journey; however, those are common:

- Other's glance
- Self-esteem
- Job loss
- Relatives' reactions and behaviours
- Uncertainty
- Fear of death
- Fear of recurrence
- Pain

Typically, other's glance and feelings are out of control. How much time do we spend being apprehensive about what others will say, think or do? Who never ambitioned to change someone? It takes time to give up on worrying about other's glance, but, unfortunately, living with a cancer experience might be an opportunity to progress significantly in this matter.

Next are things you cannot fully control but have an influence upon like pain. You can use pain killers but also open your mind to support cares like yoga, sophrology, hypnotherapy, etc. Another example is fear of recurrence: compliance only depends on you and might have an influence and a positive outcome.

Finally, self-esteem, positive attitude and confidence entirely depend on the patient. We are fully and solely responsible for the way we take events. I often use the metaphor of the wave: two kids are side by side on the beach and see a huge wave coming. One takes it as a great amusement and dives under the wave; the second runs away in tears. The wave is not the problem; it's the way we decide to live the experience.

It is therefore important for the nursing staff to let the patient adjust to the event and choose how he will live it. Your inner empathy leads you to encourage the patients to keep positive and move ahead. Don't think you are not doing well enough if the patient keeps crying and being negative, it's a decision he needs to make when he is ready if ever.

Nursing Staff Position

Again, preoccupations vary amongst nursing staff but I often hear:

- Say the right words
- Be reassuring
- Address questions about prognostic
- Keep straight and refrain emotions
- Ease sorrow
- Lack of resources
- Lack of time

Again, there are a number of worries in the above list that are out of control for nurses and doctors.

It is entirely up to you to work on your verbal and non-verbal communication, manage your emotions, focus on your patient and dedicate him quality moments even very short.

You can also influence a positive outcome on physical and psychologic pain by your behaviours and posture.

However, patient's sorrow and fears are under his responsibility and might have their usefulness in his journey.

Also, everything depending on health-care facility organisation and budget allowance, e.g. lack of time and resources, is out of reach. You may decide to focus on what would work better if things were different, but actually there is nothing you can do to change those facts. Time and energy spent in those areas are efficiency loss in your area of responsibility and potential impact on your excellence.

Search for Meaning

Some patients decide that there's no need to search for a deeper meaning in their cancer. They accept the experience without a need to question it.

Others will search purpose in their illness and, sometimes, it helps find a way of healing.

Some will see it as a punishment for their behaviours (smoking, alcoholism, drugs abuse, etc.), and some will attribute it to external factors (stress, loss, environmental factors exposure, etc.) and see it as an injustice.

And a few (like me) will see it as an opportunity to be redistributed a new set of cards to play a better life game.

Beyond meaning given to the illness, a study of Salick and Auerbach (2007) shows that the determining step in the recovery process is the "go-ahead" choice.

Meaning given to illness occurrence is an individual construction and responsibility. Nursing teams might want to prove patients wrong but they have slight chances to be heard.

It is important to be respectful of each individual journey to acceptance and learning of the experience.

Conclusion

In conclusion, the patient timing is very different from yours. If not through you, he will have other interlocutors and opportunities to learn and progress on his journey.

The power of open questioning is unlimited: it gives you an opportunity to build a trusted relationship with your patient and understand where he stands, where he is willing and is prepared to head to. It prevents from making unsolicited or inappropriate decisions for the patients. It helps you evaluate the level of support expected from you and avoid exceed boundaries.

Patients and practitioners have their own areas of influence, control and responsibilities. Being conscious of what you control or influence versus what is out of your control and responsibility area will help you increase efficiency and level of satisfaction.

A balanced and trust-based relationship between patient and nursing team is to be looked for as it is a key element of the healing process.

Patients might request more or less active roles in decision-making regarding their cancer journey. However, they have to be given the choice of the role they want to play and be respected whatever they decide.

Addendum: Useful Links

1. *Professional associations*
    - *EONS* – European Oncology Nursing Society. http://www.cancernurse.eu/
    - *ONS* – Oncology Nursing Society. https://www.ons.org/
2. *National societies*
    - *Austria* – AHOP – Arbeitsgemeinschaft hämatologischer onkologischer Pflegepersonen in Osterreich. http://www.ahop.at/
    - *Belgium* – Société Belge des infirmièr(e)s en Oncologie. http://sioncologie.be/
    - *Belgium* – Vereniging voor Verpleegkundigen Radiotherapie en Onkologie (VVRO). http://www.vvro.be/
    - *Bulgaria* – Bulgarian Oncology Nursing Society. elenfilipova@yahoo.com
    - *Croatia* – Professional Society of Oncology and Haematology. http://hums.hr/word/
    - *Cyprus* – Cyprus Oncology Nursing Society. https://cyna.org//home
    - *Czech Republic* – Czech Nurses Association-Oncology. http://www.cnna.cz/
    - *Denmark* – The Danish Cancer Nursing Society. https://dsr.dk/fs/fs13
    - *Estonia* – Estonian Oncology Nursing Society. http://eons.ee/
    - *Finland* – Finnish Oncology Nursing Society. https://syopasairaanhoitajat.fi/
    - *France* – Association Française des Infirmier(e)s en Cancérologie. https://www.afic-asso.org/
    - *Germany* – KOK Konferenz Onkologischer. Kranken und Kinderkrankenpflege. https://www.kok-krebsgesellschaft.de/
    - *Greece* – Sector of Oncology Nursing of the Hellenic National Graduate Nurses Association. http://www.esne.gr/
    - *Hungary* – Hungarian Cancer Society: Oncology Nursing section. epuskas.gabi@uzsoki.hu
    - *Iceland* – Icelandic Oncology Nursing Society. https://www.hjukrun.is
    - *Ireland* – Irish Association for Nurses in Oncology. http://www.iano.ie/
    - *Israel* – Israel Oncology Nursing Society. http://www.ions.org.il/
    - *Italy* – Associazione Italiana Infermieri di Area Oncologia (AIIAO). http://www.aiiao.it/
    - *Lituania* – Lithuanian Oncology Nursing Society. http://www.lsmuni.lt/

F. Charnay-Sonnek, A. E. Murphy (eds.), *Principle of Nursing in Oncology*,
Principles of Specialty Nursing, https://doi.org/10.1007/978-3-319-76457-3

- *Malta* – Maltese Oncology Nursing Association (MONA). christine.grima@gov.mt
- *The Netherlands* – Verpleegkundigen & Verzorgenden Nederland Oncologie (V&VN). http://www.oncologieverpleging.nl/vvn-oncologie
- *Norway* – Norwegian Society of Nurses in Cancer Care. https://www.nsf.no/faggrupper/kreftsykepleiere
- *Palestine* – Palestinian Oncology Nursing Society. mawad@bethlehem.edu
- *Portugal* – Portuguese Oncology Nursing Association. https://www.aeop.pt/
- *Serbia* – Association of Nurses of Serbia, Nurses Oncology section. http://www.ncrc.ac.rs/
- *Slovenia* – Oncology Nurses Section. http://www.zbornica-zveza.si/sl/
- *Spain* – Sociedad Española de Enfermeria Oncologia SE. https://www.seeo.org/
- *Sweden* – Swedish Cancer Nurses Society. http://www.cancervard.se/
- *Switzerland* – Swiss Oncology Nursing Society – Onkologiepflege Schweiz/Soins en Oncologie Suisse/Cure Oncologiche Svizzera. https://www.onkologiepflege.ch/start/
- *Turkey* – Oncology Nursing Association of Turkey. http://www.onkohem.org.tr/
- *United Kingdom* – United Kingdom Oncology Nursing Society (UKONS). http://www.ukons.org/
- *United Kingdom* – Cancer Nursing Society UK – Royal College of Nursing, Cancer Nursing Forum. https://www.rcn.org.uk/

3. *General information on nursing*
    - *NANDA International* – The International Nursing Knowledge Association. http://www.nanda.org/
4. *General information on cancer*
    - *ACS* – American Cancer Society. https://www.cancer.org/
    - *ASCO* – American Society of Clinical Oncology. https://www.asco.org/
    - *BCCA* – Cancer Management guidelines. http://www.bccancer.bc.ca/health-professionals/clinical-resources/cancer-management-guidelines
    - *EMA* – European Medicine Agencies. http://www.ema.europa.eu/ema/
    - *EORTC* – European Organization for Research and Treatment of Cancer. http://www.eortc.org/
    - *EPAC* – European Association for Palliative Care. http://www.eapcnet.eu/
    - *ESMO* – European Society for Medical Oncology. https://www.esmo.org/
    - https://www.nccn.org/
    - *MASCC* – Multinational Association of Supportive Care in Cancer. https://www.mascc.org/
    - *NCCN* – National Comprehensive Cancer Network
    - *NCI* – National Cancer Institute. https://www.cancer.gov/
    - *NICE* – National Institute for Health and Care Excellence. https://www.nice.org.uk/
    - *SIOG* – International Society of Geriatric Oncology. http://www.siog.org/
    - *WHO* – World Health Organization. http://www.who.int/