



Yiola Marcou

Contents

22.1 Introduction	374
22.2 Risk Factors	374
22.3 Treatment of Breast Cancer	375
22.4 Modalities of Breast Cancer Treatment	375
22.4.1 Surgery	375
22.4.2 Chemotherapy	376
22.4.3 Biological Agents	376
22.4.4 Radiotherapy	376
22.4.5 Hormonal Treatment	376
22.5 What Is Quality of Life?	377
22.6 Age	377
22.6.1 Age and Fertility	378
22.6.2 Stage of Disease	378
22.6.3 Breast Surgery and Breast Reconstruction	379
22.6.3.1 Mastectomy and Breast Conservative Surgery	379
22.6.4 Hormonal Treatment	380
22.6.5 Chemotherapy Treatment	380
22.7 Type of Cancer	381
22.8 Carers and Environment	381
22.9 Conclusion	382
22.10 Questions That Can Be Used for Learning/Testing	382
22.11 A Topic for Discussion That Can Be Used for Teaching	382
22.12 Further Reading List	382
22.13 Research in Context	382
References	383

Y. Marcou (✉)
Bank of Cyprus Oncology Centre, Nicosia, Cyprus
e-mail: yiola.marcou@bococ.org.cy

22.1 Introduction

Breast cancer is the commonest female cancer. According to global cancer statistics, in 2020, more than 2 million patients were affected by this disease [1]. Worldwide, there are currently millions of women that are either undergoing treatment or have survived from their disease.

The median age of breast cancer patients is around 60. One in eight women will be diagnosed with breast cancer during their life span.

Despite the anxiety seen in younger women, the incidence of breast cancer in the younger population is much lower (Fig. 22.1). Nevertheless, one could argue that the impact of this disease on the younger patient groups is more profound, as it is affecting a major part of the workforce, it is affecting parenthood, partnership, relationships and social stability.

Nowadays, breast cancer is the leading cause of death in women less than the age of 50.

So, what is the cause of this otherwise common disease? What is our answer to this young

and healthy patient who walks into our clinic with a diagnosis of breast cancer? Why me doctor? What have I done wrong? What have caused my cancer? For the majority of our patients there is no answer, as breast cancer is a multifactorial disease with many risk factors involved.

This chapter will enable readers to familiarize their selves with this very common disease, analysing risk factors, current management options, and how all these treatment options affect the quality of life of the patients.

22.2 Risk Factors

One of the strongest risk factors is age. It is clear that the aging breast has more chances to be affected by mutations causing neoplasia. Aging and prolongation of life are the prices societies are paying to carcinogenesis [2].

There are many other risk factors that play an important role in breast cancer development [2, 3]. The exposure to radiation at a younger age, as

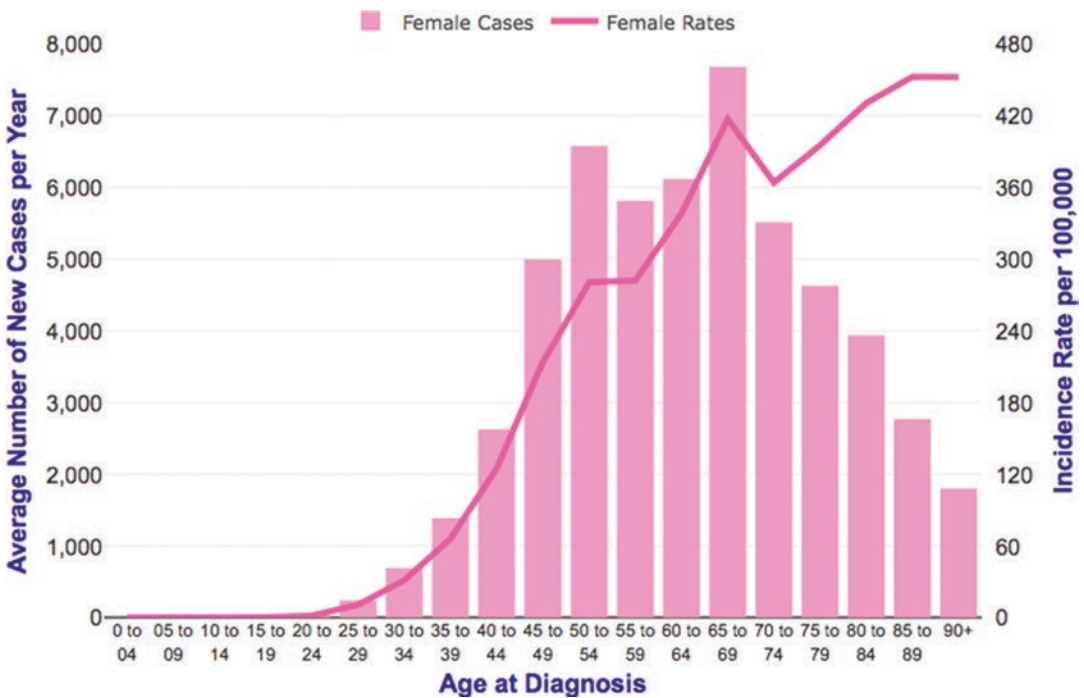


Fig. 22.1 Breast cancer (C50), average number of new cases per year and age-specific incidence rates per 100,000 females, UK, 2015–2017. Breast cancer research UK

part of treating an underlying malignancy, is a significant risk factor, with the anticipated risk of developing breast cancer 10 years post the completion of radiation being significantly higher compared to that of individuals with no radiation exposure.

External hormonal treatment is another risk factor, and many studies have shown that prolonged exposure to HRT (hormone replacement treatment) increases the risk [4]. As the exposure of the female breast to longer hormonal manipulation has been shown to increase the risks of neoplasia, it is clear that early menarche and late menopause are also among the risk factors.

Genetic factors are among the contributing factors and despite the fact that they exist in less than 10% of the patients, their role is clear. Genes like the BRCA1 and BRCA2, located in chromosomes 17 and 14, when mutated, increase the risks of patients significantly. Patients with BRCA1 and 2 have a lifetime risk of developing breast cancer that could be up to 70% [5]. Other genes like PTEN, CHEK2, p53 are also associated with breast cancer and other malignancies, such as ovarian carcinoma, brain tumours and pancreatic disease.

In recent years, obesity, the ‘disease’ that has become a pandemic in the Western societies, has been associated with postmenopausal breast cancer. Alcohol consumption is one of the newest environmental and dietary associations with breast cancer. There is nowadays a clear dosage level of alcohol consumption and breast cancer risk increase [6].

Other risk factors like previous benign breast disease [7], history of previous trauma and increased breast density, as seen on mammography, have also been recognized.

22.3 Treatment of Breast Cancer

Once the diagnosis of breast cancer is made, the patient will undergo treatment that today incorporates surgery, radiotherapy, biological agents, chemotherapy and hormonal treatment. What have changed in the last decade is the individualization of cancer treatment and the recognition

that better survival comes with expertise and multidisciplinary approach [8].

Since the discovery of the different molecular profiles of breast cancer and the publication by Peru [9], we know that every patient fits a different disease model and the approach and the sequencing of the treatment vary significantly, depending on the molecular profile of the tumour. We have today recognized at least four different subtypes of breast cancer like Luminal A, Luminal B, her-2 enriched and triple negative. Depending on this profiling, patients might have a completely different approach and disease outcome is different. As an example, patients with her-2 enriched breast cancer, or triple negative will today be offered chemotherapy prior to surgery (neoadjuvant approach), and that will be followed by surgery and then radiotherapy. Hormonal-driven breast cancers remain the commonest group in all ages, and within this group there is the tendency of offering less chemotherapy with the help of the genomic and prognostic assays. Every single breast cancer patient that presents in the oncology clinic is unique, and any treatment intervention should be decided by the multidisciplinary team that includes radiologist, medical and radiation oncologists, histopathologists, breast and plastic surgeons. All patients should have an initial core biopsy that defines their molecular subtype before any decisions about further treatment are taken.

22.4 Modalities of Breast Cancer Treatment

22.4.1 Surgery

Surgery remains one of the most important treatments in breast cancer. Throughout the years, surgery has moved from the very radical and mutilating approaches of total mastectomies with removal of the whole breast and the muscular structures, to less invasive and minimal surgery. Depending on the size of the lump, the majority of patients today will have conservative surgery with minimal surgery in the axilla. The axillary clearance, which is surgery to remove a signifi-

cant amount of lymph nodes from the axilla, will be offered only to patients with significant volume of involved nodes in the axilla. Today the most standard surgical approach in the axilla is the removal of the sentinel lymph node, the 'guardian' node of the axilla, or the targeted axillary clearance in patients with a small number of metastatic nodes. This approach spares patients from the future development of lymphoedema and aims to avoid post-surgery deformities in the breast area and the axilla.

If mastectomy is needed, reconstructive options, either with implants or autologous grafts, have significantly improved the cosmetic outcome. Patients nowadays, in contrast with the past, will be given the option of immediate reconstruction during the breast cancer surgery.

22.4.2 Chemotherapy

Chemotherapy remains one of the most stressful treatments around malignant disease. Any new patient that walks into an oncology centre will have the fear of chemotherapy, which is associated with the fear of hair loss, nausea and fatigue.

Chemotherapy is mainly offered to very young patients, patients with more advanced nodal disease or patients that have special breast cancer subtypes like triple negative or her-2 enriched. In recent years, molecular profiling of the tumours especially the ones that are oestrogen receptor positive, have added tremendous assistance in the correct identification of the cohort of patient that will have a gain from the adjuvant chemotherapy, thereby avoiding overtreatment of patients with a favourable tumour profile.

Chemotherapy remains one on the main treatment options in patients with metastatic disease.

22.4.3 Biological Agents

The major innovation in treating malignant disease during the last 2 decades has come with the discovery of the molecular subtypes and the use of the targeted monoclonal antibodies. Breast cancer and haematological malignancies have

been the pioneers in the use of targeted treatments in neoplasia, completely changing the traditional treatment field in cancer care. Since the FDA approval of Trastuzumab in 1998, newer biological agents have been approved, not only in breast cancer but also in lung and bowel malignancies, improving considerably the overall survival of patients.

Nowadays, in a breast oncology clinic, there is a number of new anti-her-2 agents, immunotherapy for the triple negative tumours and cyclin-dependent kinases, CDK 4/6, for the advanced metastatic ER positive breast cancer. All of these agents have been associated with improved survival and disease-free survival (DFS) in the adjuvant and metastatic setting.

22.4.4 Radiotherapy

Among the oldest and commonest cancer treatments, widely used in breast cancer, radiotherapy has also seen considerable improvements in the recent years with the application of shorter courses over few weeks compared to the more prolonged regimes of the past. Modern radiotherapy planning techniques with the incorporation of better imaging equipment, like CT scan and MRI, have helped in improving the cosmetic outcome but more importantly in avoiding unnecessary toxicities to the surrounding healthy structures.

22.4.5 Hormonal Treatment

Hormonal treatment remains the cornerstone of the treatment of the ER (oestrogen receptor) positive group. In a proportion of patients in the adjuvant setting, hormonal treatment has been prolonged to up to 10 years. Women will either be offered Tamoxifen an ER modulator, or aromatase inhibitor, like anastrozole, letrozole and exemestane.

Despite the major advances in disease understanding and the major and innovative treatments that have been used, not only in the early stage of disease but also in the metastatic setting, a per-

centage of breast cancer patients will relapse during the course of the illness and will succumb from the disease.

Through this long patient journey from the initial diagnosis, the initial emotions of the patient facing the new breast cancer disease, the treatment journey, the prognosis and its risks, one has to try and maintain one important aspect: quality of life.

For this complex disease, quality of life has to be measured not only around the patient but also around its carers and the environment.

22.5 What Is Quality of Life?

Although frequently used today, quality of life is not that easy to define (see also Chap. 1, this volume). As per WHO, it is ‘the perception of an individual of their position in life in the context of culture and value system and in relation with their goals, expectations, standards and concerns’.

Patients with breast cancer will be faced with many challenges throughout their prolonged journey with the disease. Comparing breast cancer with other malignant disorders, one needs to realize that there are major challenges and major differences. Hormonal-driven breast tumours (the commonest group) have a very good 5-year survival, but they still maintain a small but real risk of relapse for the rest of the life of the patients, making the need for prolonged drug treatment. This is almost unique for this disease. Unfortunately, this disease is so heterogeneous that quality of life might be completely different from one breast cancer subtype to another.

We will analyse in points all these challenges of the different treatment approaches offered in breast cancer and how these factors influence the quality of life.

22.6 Age

Life challenges and quality of life are different for an elderly breast cancer patient when compared to a younger individual. Challenges will

always be there, but the impact on living with a serious and chronic disease can be different across lifespan [10]. Younger age was one of the major sociodemographic characteristics associated with distress on a systematic review from 42 studies published in 2017 [11]. A patient with a young family and young children, a patient planning to start a family and a young professional have many challenges to face when embarked with the cancer diagnosis. Suddenly there is the need of postponing, or even halting current plans, reviewing relationships and family roles. A mother of two with a full-time job might struggle to go through a 6-month chemotherapy treatment. Struggling will not only be because of financial difficulties, but also because career might be put on hold, job and travelling opportunities need to be adjusted. For very young patients, their family planning process will also be affected, they will review their interpersonal relationships, they will have fear for the risks on their fertility from the ongoing treatments. Breast cancer treatment can change body image, affecting sexuality. Marital strain is not uncommon and alienation from society with depression are often observed.

Sexual dysfunction is also common [12]. A high percentage of patients reported sexual dysfunction not only when they were receiving treatment but also after the completion of treatment [13]. In many societies, discussing sexual dysfunction remains a taboo. Even in more advanced societies, patients and healthcare professionals infrequently bring up the issue of sexuality. This is most of the times superseded by other stressful toxicities a patient might report during the clinic visit.

Is the sexual dysfunction associated only with the fear of the new and life-threatening diagnosis? Although the psychological issue is one factor, another important factor is the toxicity associated with the treatment patients are undergoing. Chemotherapy causes early menopause with associated vaginal dryness and loss of libido. Similar toxicities are frequently seen with the use of the hormonal treatment either alone like Tamoxifen or AIs (aromatase inhibitors) or in association with LHRH agonists. Hormonal

treatment causes dryness, amenorrhoea, dyspareunia and poor performance in sexual life.

A third important factor affecting sexual life is surgery, and it seems that any form of surgical intervention to the breast can have a negative impact on sexuality. Surgical treatment entails physical changes to the body that can have adverse effects on the patient, affecting mainly intimate relationships. There is a reduction in the self-perceived attractiveness following mastectomy with negative impact on sexuality. Despite the fact that breast conserving surgery offers better aesthetic outcome, it seems that any form of surgical intervention can affect sexuality. It is vital to discuss all the issues of surgical treatment with the patient so they have a better understanding on what it means to their body, helping them to have acceptance of their new look.

What about quality of life in the elderly patients? In this group, other issues need to be addressed [14]. Struggling with even simple things, for example, cleaning, cooking, looking after an elderly partner could create major stress. The adjustment to the new reality of the disease can be more difficult, and depression and suicidal thoughts are common with advancing age.

QoL in elderly seems to be worse when offering chemotherapy. Chemotherapy toxicities are more profound, and there is evidence that there is a drop in their QoL [15]. Old age is associated with other comorbidities, and older patients are often receiving concurrent medication, thereby making the score of QoL from cancer treatment difficult.

Old age might be a factor for not offering all the best possible treatments, and this is why the incorporation of geriatric assessment tools [16] is important when discussing cancer treatments in this population. Unfortunately, elderly people are sometimes offered less treatment, as, until recently, they were excluded from many clinical trials.

22.6.1 Age and Fertility

Child-bearing has changed considerably over the last few decades, with couples postponing the initiation of family. It is therefore not uncommon

for any young breast cancer patient walking in the clinic not to have children. Not only do breast cancer treatments affect fertility but the diagnosis itself demands postponing any pregnancy plans to a safe time frame of at least 2 to 3 years from the initial diagnosis, depending of course on many patient and disease factors [17]. This is a considerable progress from the past when pregnancy was almost forbidden post cancer diagnosis, or was only allowed after many years of being disease free.

Nevertheless, fertility post cancer treatment is not guaranteed, and this is why appropriate counselling of the young woman is vital as she will need to be given the option of fertility preservation. There is enough data to suggest that this is another stressful event that compromises quality of life in this group [18].

22.6.2 Stage of Disease

The stage of breast cancer is associated strongly with disease prognosis. Disease stage is an independent factor of poor quality of life across ages. The number of involved lymph nodes at presentation associated with more advanced stage disease was associated with depression and anxiolytic prescription [11]. During the course of this disease, patients will have the anxiety of surviving. One of the most important aspects of patients' psychology is to educate them to accept their disease, and to also accept the small risk of developing metastatic disease. Having a breast cancer diagnosis today at an earlier stage with the help of the screening, patients need to realize that their prognosis in early stage remains very good. It needs though enormous mental discipline from the patients to bypass the fears of the disease and to continue living life as normal.

And what if the cancer is back, and what if suddenly in a clinic environment the patient is given the bad news of disease progression, disease relapse, disease metastasis, or even found to have metastatic disease upfront [19]. For any patient, this terminology is irrelevant! Of relevance is now the realization that metastatic breast cancer in 2020 remains an incurable disease.

It is a fact that progress has been made, and 30% of this group will manage to live for more than 5 years. But what quality of life assessment tool will capture this fear? Most probably none! The sadness, the panic, the vulnerability and the fear of a disease that could cause disabilities are emotions encountered frequently in the metastatic setting.

And indeed, when we assess quality of life in early breast cancer, there are many tools and the consensus is easier. In the metastatic setting though quality of life is less clear, here progress needs to be made.

There is enough data to suggest that women with metastatic breast cancer will have reduction in their quality of life not only because of the fear of death from their incurable disease but also, as they move through the combination of palliative treatments, they will experience fatigue, neurotoxicity, neurocognitive impairment, etc. Every effort should be made in assessing the needs of this special group of patients and try to offer support. Patient-centred communication and shared decision-making between any metastatic patient and the physician are vital. There are many patients' stories on how they handle the fear of death. This fear as expected is different among different ages.

22.6.3 Breast Surgery and Breast Reconstruction

22.6.3.1 Mastectomy and Breast Conservative Surgery

For the majority of the patients, wide local excision with breast conservation remains the standard approach. For a number of reasons, a patient might be offered mastectomy instead of wide local excision. Multifocality, very large central tumours, inability of the surgeon to achieve clear margins, very young age and genetic predisposition are among the commonest reasons for offering mastectomy.

Breast reconstruction post mastectomy has improved considerably over the last decade, and nipple- and skin-sparing mastectomies are frequently offered, achieving excellent aesthetic results.

There is enough data to suggest that women that have undergone mastectomy score lower in their quality of life. Body image, future perspective and also acceptance of the systemic treatment toxicity were worse in the mastectomy group in accordance to a recently published meta-analysis [20]. As expected, there are limitations in the analysis as many factors could play a role, that is, mastectomy was associated with larger tumours, therefore worse prognosis, so any impairment of the quality of life might have been due to stage of the cancer and not the type of surgery! There is a universal acceptance though, that the less surgery is done, either in the breast or the axilla, the better the cosmetic outcome, and that will extrapolate to a better quality of life.

Plastic reconstructive options have improved nowadays, but the fear and the acceptance of the new body could be difficult among patients. Even with the better reconstruction, patients might run into problems with the implants with capsular formation post radiotherapy or pain associated with surgery. Immediate breast reconstruction (performed at the same time as the initial breast cancer surgery) was associated with better quality of life compared with the delayed option.

There is a trend nowadays for younger women to request more mastectomies even on the healthy breast as the fear of the initial diagnosis, and the fear of future relapses make the radical approach extremely appealing. Clear discussion with the patient regarding the post-surgery quality of life should always be raised at the initial consultation therefore enabling the patient to make the correct decisions judged by scientific facts and not emotions.

Another factor that has improved considerably is the surgery done for the axilla.

Surgery has moved from axillary dissection with removal of a large number of nodes to minimal axillary surgery and removal of the sentinel node.

Even with this minimal surgery, a significant percentage of patients will suffer from lymphoedema. It is estimated that up to 30% of breast cancer patients might suffer with lymphoedema pain and arm swelling. Quality of life is impaired as lymphoedema is a debilitating condition with a long-term negative impact on a patient [21].

22.6.4 Hormonal Treatment

Hormonal treatment is a major component of breast cancer treatment with the majority of the women having to take it for a prolonged period of time. Five to 10 years of either Tamoxifen (mainly used in the premenopausal women) or aromatase inhibitors (first choice in the postmenopausal group) are the standard of care for all Luminal A and Luminal B breast cancer subtypes. A big percentage of all breast cancer patients either with early or advanced disease will be offered a form of hormonal manipulation at some point during their treatment.

Toxicity profile differs among the antioestrogens like Tamoxifen, and the aromatase inhibitors like letrozole and anastrozole.

Tamoxifen causes hot flushes, weight gain, mild hair loss and mood swings, whereas the use of AIs is associated with bone and joint aches, raised lipids, hot flushes and osteoporosis. Vaginal dryness is commoner in women on AIs compared to Tamoxifen.

Drug adherence could be compromised as these group of drugs need to be taken for long, and sometimes patients are abandoning them without informing their physician.

Few reports have exclusively analysed the quality of life with the use of hormonal treatment, but it seems that there is a compromise and reduced quality of life.

Antioestrogens might affect the mood of patients and compromise their libido and sexual function. Drug adherence could be compromised as these group of drugs need to be taken for long, and sometimes patients are abandoning them without informing their physician. The negativism around taking a treatment that might cause a young patient to dive into menopause, might lead to a disturbed doctor-patient relationship, as there is enough data on patients not taking their treatment but never reporting it!

Aromatase inhibitors are prescribed in up to 60% of patients and prescription is increasing, as there is an increase in their use among the premenopausal group. Musculoskeletal toxicity is well documented and indeed a percentage up to 50% will report joint and muscular pain within a year of use. This is a contributing factor on the lower QoL seen with this class of drugs [22].

Beyond the oral treatments, younger patients with higher risk disease will be offered a gonadotrophin-releasing hormone agonist (GnRHa) on a monthly basis, for up to 2 or 5 years in conjunction with their oral treatment. GnRHa is a monthly subcutaneously administered treatment that is offered to many premenopausal patients, in accordance with the results of the SOFT and TEXT study suggesting a benefit to the premenopausal hormone receptor positive higher risk group [23]. With this treatment, an immediate effect of castration is seen in this younger group changing their hormonal status from premenopausal to postmenopausal. Handling of the menopausal symptoms that appear in such an abrupt way could be difficult especially in the younger groups.

22.6.5 Chemotherapy Treatment

Chemotherapy is commonly offered to younger women with the disease, and it is a major part of the treatment in the metastatic setting. Among all cancer treatment modalities, chemotherapy remains the most fearful of all.

From various studies, it seems that quality of life is compromised during and after chemotherapy. Not only does the patient have to deal with its own fear of the unknown pathway of chemotherapy, there is anxiety about the future, anxiety about the impact of chemotherapy on the rest of their family, like children and spouses. While a patient is receiving chemotherapy, abandonment of routines might be seen. Patients might need to modify their work activities, and they might be off sick from their work environment for a while with social and financial consequences.

Chemotherapy is associated with acute treatment toxicities seen when the patient is receiving the treatment, and late toxicities that appear months to years from the completion of treatment. Among the acute toxicities, nausea, vomiting and myelosuppression are seen within days of offering the treatment. Hair loss is a common side effect in breast cancer patients as the cytotoxic agents commonly used are anthracyclines and taxanes, agents with high incidence of alopecia. Appearance-related side effects during che-

motherapy especially the hair loss, the loss of eyebrows and eyelashes could have a negative impact on social engagements and could compromise the quality of life [24].

Long-term toxicities from chemotherapy are not negligible, and they are associated with a small cardio toxicity risk, infertility with gonadal suppression and small risk of secondary malignancies. Other long-term toxicities that are extremely important have to do with the neuro-cognitive impairment, with the condition referred by patients as 'chemo brain', an entity that has been clearly reported and documented. As per the American Cancer Society, 'chemo brain' is a decrease in the mental 'sharpness' seen post cancer treatment. In science, it is defined as cancer-related cognitive impairment (CRCI) and includes impairment of short-term and working memory, attention, executive function and processing speed. Some of the toxicities can be difficult to go through, and sometimes they appear at the completion of the treatment or years later. Up to 50% of breast cancer patients will report this CRCI, and it can be a cause of distress to the patients as it can impair their day-to-day activities [25].

22.7 Type of Cancer

Little is known about the influence on quality of life among the breast cancer subtypes and the analysis on this is less clear. In the majority of the published data, the analysis on breast cancer is done with breast cancer been mentioned as one unique disease. Having the clear recognition of the breast cancer subtypes, their different treatment pathways, different chemotherapy and monoclonal antibodies and clearly different survival, we do expect to see in the future more analysis on quality of life based on the molecular tumour characteristics. Triple negative breast cancer and her-2 enriched are the two subtypes that women are commonly offered chemotherapy. Most of the times, patients with these two groups present with larger tumours [26]. Patients with these two subtypes have increased anxiety as they are aware of the more complex treatment options. The fear of negative future perspectives

is very high and reduced quality of life with anxiety regarding the prognosis and treatment that accompanies the patient. There are reports on the anxiety caused by the finding of a less favourable breast cancer type, like triple negative. Inevitably patients will associate the certain breast cancer subtypes with the worsening prognosis and that will compromise their quality of life.

22.8 Carers and Environment

Any new diagnosis of cancer, and the treatment that will follow, creates a major stress not only for the patient but also for their carers. Adaptation to the new diagnosis of a chronic disease is not merely to the patients but affects spouses and extended family environment. The carers involvement in all aspects of the patient's treatment from the early stage of disease to the end-of-life care can be diverse and could also be influenced by cultural differences around the globe. Negative effects from the cancer treatment are experienced not only by the patient but also by its carers in a form of dyadic effect [27]. Understanding the carers needs in a breast cancer clinic could be challenging. In recent years, more attention has been paid in the carers needs, as a more holistic environmental approach will empower both the patients and their caregivers.

The fear of metastatic disease affects enormously the patient's environment and his/her carers and does so in amplified way compared to the early stage of the disease. There is lack of data on the impairment of quality of life on the carers of patients with incurable disease as the patient remains at the centre of the oncologist's attention, but it seems that caregivers report higher distress and less quality of life [28].

Scoring the emotions of the carers can be extremely hard. Emotionally they have to deal with fear of the loss of their loved ones. Beyond their emotional stress, the depression and anxiety they experience, they are also faced with physical and social stress. As they provide physical help to the patients, they might experience fatigue, lack of sleep and exhaustion [28]. There is increased anxiety around social circumstances, upbringing of offspring's and financial concerns.

22.9 Conclusion

As breast cancer is the commonest disease seen today in women and as it is one of the leading causes of death, scientific forces should be directed in offering new and pioneer treatments that will help prolonging the life of the patients. The ultimate target should be to cure this disease achieving longer survival and almost zero deaths. As with any other malignant disease, preservation of the quality of life in a holistic approach should walk alongside any treatment interventions. Throughout the spectrum of the ages affected, there are different concerns around the treatment options and associated toxicities. The ultimate goal should be to identify all the different treatment options offered in this heterogeneous disease during the lifespan of patients and act proactively so quality of life is maintained. High-quality research is needed in an attempt to improve holistically the life of breast cancer patients.

22.10 Questions That Can Be Used for Learning/Testing

1. Breast cancer affects women during their lifespan. What are the challenges faced among the different age groups affected by the disease?
2. What are the different molecular subtypes of breast cancer and how treatment gets differentiated?
3. What are the surgical options in a patient with a new diagnosis of breast cancer?
4. Quality of life in carers. A new topic with many challenges.
5. Sexual dysfunction in association with hormonal treatment.
6. Which genes are affected in breast cancer?

22.11 A Topic for Discussion That Can Be Used for Teaching

As survival in metastatic breast cancer is increasing with innovative new treatments, the social consequences of living with metastatic disease

are enormous. Work environment, work absences as a result of treatment and toxicities, financial insecurities, cost of new treatments, raising up a young family, relationship and many more are all put aside, as patients and medical teams need to concentrate on the metastatic disease. What actions societies, patients advocate groups, policy makers and medical teams should undertake to try and improve in a more holistic approach the quality of life of the breast cancer patients beyond the actual medical treatment?

22.12 Further Reading List

The following list presents literature that extends the contents of this chapter. Readers looking for in-depth information and further material are advised to consult the following sources.

- Nardin S, Mora E, Varughese FM, D'Avanzo F, Vachanaram AR, Rossi V, Saggia C, Rubinelli S, Gennari A. Breast Cancer Survivorship, Quality of Life, and Late Toxicities. *Front Oncol.* 2020 Jun 16;10:864. doi: <https://doi.org/10.3389/fonc.2020.00864>. PMID: 32612947; PMCID: PMC7308500.
- Invernizzi M, Kim J, Fusco N. Editorial: Quality of Life in Breast Cancer Patients and Survivors. *Front Oncol.* 2020 Nov 18;10:620574. doi: <https://doi.org/10.3389/fonc.2020.620574>. PMID: 33312961; PMCID: PMC7708334.

22.13 Research in Context

Despite the realization that quality of life is among the most important factors in malignant disease, there is not a uniform tool to measure it. The different treatment options offered to breast cancer patients and their different molecular patterns make identification of factors that cause distress extremely difficult. The publication by Syrowatka et al. from Canada in *Breast*

Cancer Res Treat, in 2017, identified a large number of articles published in literature examining causes of distress in breast cancer patients. Only 42 studies were eligible and collected from the period of 2001 to 2016, either using a prospective cohort, retrospective chart review or they were with a cross-sectional design. The majority of the studies measure depression, anxiety, post-traumatic stress disorder and general distress. The most commonly evaluated predictors were related to breast cancer characteristics, patients' sociodemographic features and treatment-related symptoms. As anticipated on the analysis of breast cancer characteristics, the more advanced cancer at the initial diagnosis and treatment with chemotherapy were associated with distress. Sociodemographic features of younger age, being single and being from lower socioeconomic status were associated with reduction in quality of life. Analysing the treatment-related effects, menopausal symptoms that appear post cancer treatment, pain, fatigue, sleep disturbances and lymphoedema were also associated with distress. As with other studies around quality of life, there are limitations and indeed the authors conclude the need of assessing a larger cohort of breast cancer survivors prospectively to identify distress using time-to-event analysis. Survivorship-related issues in breast cancer are common, and with this systematic review a set of evidence-based predictors could identify the population that is at higher risk and offer them the support they will need in their long survivorship journey [11].

References

1. Ferlay J, Colombet M, Soerjomataram I, Parkin DM, Piñeros M, Znaor A, et al. Cancer statistics for the year 2020: an overview. *Int J Cancer*. 2021 <https://doi.org/10.1002/ijc.33588>. Online ahead of print
2. Rojas K, Stuckey A. Breast cancer epidemiology and risk factors. *Clin Obstet Gynecol*. 2016;59:651–72.
3. Holm J, Eriksson L, Ploner A, Eriksson M, Rantalainen M, Li J, et al. Assessment of breast cancer risk factors reveals subtype heterogeneity. *Cancer Res*. 2017;77:3708–17.
4. Type and timing of menopausal hormone therapy and breast cancer risk: individual participant meta-analysis of the worldwide epidemiological evidence. *Lancet*. 2019;394:1159–68.
5. Neibergs H. Breast and ovarian cancer risks due to inherited mutations in BRCA1 and BRCA2. *Women's Oncol Rev*. 2004;4:59–60.
6. Liu Y, Nguyen N, Colditz GA. Links between alcohol consumption and breast cancer: a look at the evidence. *Womens Health*. 2015;11:65–77.
7. Figueroa JD, Gierach GL, Duggan MA, Fan S, Pfeiffer RM, Wang Y, et al. Risk factors for breast cancer development by tumor characteristics among women with benign breast disease. *Breast Cancer Res*. 2021;23
8. Waks AG, Winer EP. Breast cancer treatment: a review. *JAMA*. 2019;321:288.
9. Eisen MB, Jeffrey SS, Rees CA, Pergamenschikov A, Williams C, Botstein D. Molecular portraits of human breast tumours. *Nature*. 2000;533:747–52.
10. Campbell-Enns H, Woodgate R. The psychosocial experiences of women with breast cancer across the lifespan: a systematic review protocol. *JBI Database System Rev Implement Rep*. 2015;13:112–21.
11. Syrowatka A, Motulsky A, Kurteva S, Hanley JA, Dixon WG, Meguerditchian AN, et al. Predictors of distress in female breast cancer survivors: a systematic review. *Breast Cancer Res Treat*. 2017;165:229–45.
12. Miaja M, Platas A, Martinez-Cannon BA. Psychological impact of alterations in sexuality, fertility, & body image in young breast cancer patients & their partners. *Revista de Investigacion Clinica*. 2017;69:204–9.
13. Kedde H, Van De Wiel HBM, Weijmar Schultz WCM, Wijzen C. Sexual dysfunction in young women with breast cancer. *Support Care Cancer*. 2013;21:271–80.
14. Sharma N, Purkayastha A. Factors affecting quality of life in breast cancer patients: a descriptive and cross-sectional study with review of literature. *J Mid-Life Health*. 2017;8:75–83.
15. Mokhatri-Hesari P, Montazeri A. Health-related quality of life in breast cancer patients: review of reviews from 2008 to 2018. *Health Qual Life Outcomes*. 2020;18:338.
16. Scotté F, Bossi P, Carola E, Cudenneq T, Dielenseger P, Gomes F, et al. Addressing the quality of life needs of older patients with cancer: a SIOG consensus paper and practical guide. *Ann Oncol*. 2018;29:1718–26.
17. Valachis A, Tsali L, Pesce LL, Polyzos NP, Dimitriadis C, Tsalis K, et al. Safety of pregnancy after primary breast carcinoma in young women: a meta-analysis to overcome bias of healthy mother effect studies. *Obstet Gynecol Surv*. 2010;65:786–93.

18. Deshpande NA, Braun IM, Meyer FL. Impact of fertility preservation counseling and treatment on psychological outcomes among women with cancer: a systematic review. *Cancer*. 2015;121:3938–47.
19. Müller V, Nabieva N, Häberle L, Taran FA, Hartkopf AD, Volz B, et al. Impact of disease progression on health-related quality of life in patients with metastatic breast cancer in the PRAEGNANT breast cancer registry. *Breast*. 2018;37:154–60.
20. Ng ET, Ang RZ, Tran BX, Ho CS, Zhang Z, Tan W, et al. Comparing quality of life in breast cancer patients who underwent mastectomy versus breast-conserving surgery: a meta-analysis. *Int J Environ Res Public Health*. 2019;16:4970.
21. Dominick SA, Natarajan L, Pierce JP, Madanat H, Madlensky L. The psychosocial impact of lymphedema-related distress among breast cancer survivors in the WHEL study. *Psycho-Oncology*. 2014;23:1049–56.
22. Laroche F, Perrot S, Medkour T, Cottu PH, Pierga JY, Lotz JP, et al. Quality of life and impact of pain in women treated with aromatase inhibitors for breast cancer. A multicenter cohort study. *PLoS One*. 2017;12:e0187165.
23. Saha P, Regan MM, Pagani O, Francis PA, Walley BA, Ribí K, et al. Treatment efficacy, adherence, and quality of life among women younger than 35 years in the international breast cancer study group TEXT and SOFT adjuvant endocrine therapy trials. *J Clin Oncol*. 2017;35:3113.
24. Richard A, Harbeck N, Wuerstlein R, Wilhelm FH. Recover your smile: effects of a beauty care intervention on depressive symptoms, quality of life, and self-esteem in patients with early breast cancer. *Psychooncology*. 2019;28(2):401–7.
25. Williams R, Müller M, Harewood R, Stanway S, Bhaskaran K, Carreira H. Associations between breast cancer survivorship and adverse mental health outcomes: a systematic review. *J Natl Cancer Inst*. 2018;110:1311.
26. Vadaparampil ST, Christie J, Donovan KA, Kim J, Augusto B, Kasting ML, et al. Health-related quality of life in Black breast cancer survivors with and without triple-negative breast cancer (TNBC). *Breast Cancer Res Treat*. 2017;163(2):331–42.
27. Hu Y, Liu T, Li F. Association between dyadic interventions and outcomes in cancer patients: a meta-analysis. *Support Care Cancer*. 2019;27:745–61.
28. Krug K, Miksch A, Peters-Klimm F, Engeser P, Szecsenyi J. Correlation between patient quality of life in palliative care and burden of their family caregivers: a prospective observational cohort study. *BMC Palliat Care*. 2016;15:4.