16 Quality of Life and Cancer-Related Fatigue: Prevalence, Assessment and Interventions

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Contents

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16.1 Introduction

Fatigue is one of the most distressing symptoms for cancer patients affecting their quality of life (QoL) in all phases of treatment and stages of the disease. The syndrome of fatigue and exhaustion in cancer patients is commonly described as cancer-related fatigue (CrF). Other terms such as cancer fatigue or cancer treatment–related fatigue are also used in the literature and in educational materials for patients. CrF is commonly defined as a self-recognised phenomenon that is subjective in nature and experienced as a feeling of tiredness or lack of energy that varies in degree, frequency and duration which is not proportional to physical activities and not relieved by sleep or rest [1, 2]. Patients often describe CrF as an unusual feeling of exhaustion, weakness or a loss of activity with sequels to emotional and cognitive functions [1–3]. This chapter gives an overview about CrF as one of the most common side effects of cancer treatment. It will enable readers to understand the characteristics, the aetiology and the epidemiology of CrF. The reader will learn how to screen and assess CrF, and which treatment strategies are most appropriate.

16.2 Definition and Clinical Characteristics

As the most common definition, CrF is defined as a distressing, persistent subjective sense of physical, emotional and cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activities and interferes with usual functioning [4]. Typically, the symptoms do not decrease after recovery periods or sleep, and if at all, improvement only occurs for a short time [5]. CrF is not defined as a disease entity, but a concomitant syndrome of cancer [6].

In most publications, CrF has been described as a multidimensional construct including physical, cognitive and emotional dimensions [4]. The physical domain covers a loss of ability to perform activities due to somatic symptoms of tiredness and loss of energy. Depending on the type and intensity of the CrF, typical subjective perceptions include tiredness, heaviness of limbs, apathy towards external stimuli or even myalgias. Physical symptoms include muscular and metabolic changes, reduced muscle strength, tremor, diminished reflex responses, impaired coordination, electrolyte abnormalities, lactate increase and reduction of glycogen. The cognitive dimension includes loss of concentration, problems of attention, reduced alertness or impairment in short-term memory. The emotional dimension covers symptoms like loss of motivation, negative self-esteem, feeling of frustration and depressive feelings (Fig. 16.1).

Research has shown that fatigue may be a part of a complex regulation aimed to protect the body from harm [7]. The central nervous system may use the symptoms of fatigue and exhaustion as important regulators to ensure that an effort is stopped before it results in damage. Fatigue and increased fatigability are common reactions to physical and psychological distress but may also occur as symptoms in other medical and psychiatric conditions. Therefore, many chronic diseases such as rheumatoid arthritis, cardiovascular diseases or multiple sclerosis are associated with fatigue. Fatigue can occur as a concomitant symptom, or as in the case of depression, represent a main symptom. It is quite possible that fatigue has more than one simultaneous cause, even when it is associated with a clear diagnosis [8].

The clinical manifestation of fatigue in cancer patients (CrF) is multifaceted, and the perceived problems and limitations affect patients in a highly individual manner [9]. In comparison to healthy individuals who experience their fatigue as a normal sensation that is associated with daily activities, with CrF patients, the focus is on the feeling that already after a short time and at minimal exertion levels, physical exhaustion, fatigue, weakness and an unusually strong tiredness occur.

CrF often seriously impacts the QoL of patients and affects daily activities, work, sexuality or family life [10]. Ahlberg and colleagues found statistically significant negative correlations between fatigue and various domains of quality of life, including effects on physical,

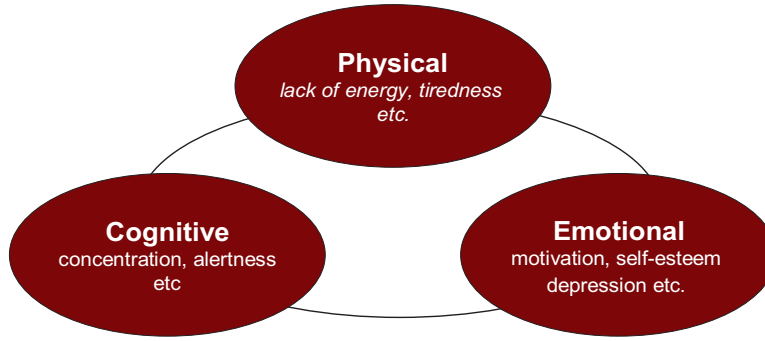

Fig. 16.1 Multidimensional structure of cancer-related fatigue [99]. (Reprinted by permission from Springer Nature: Definition and Prevalence of Cancer-Related Fatigue. In: *Cancer-Related Fatigue* by J. Weis and M. Horneber. Copyright © Springer Healthcare 2015)

emotional, cognitive, social functioning and role functioning [11]. They showed further that physical, role and cognitive functioning remained highly negatively correlated with general fatigue over time [11]. In addition, CrF does not only affect the individual patient but also the patient's partners or relatives [12]. Patients often report that persisting fatigue is not always understood by the people close to them and social conflicts arise which may result in social withdrawal or isolation. CrF has a significant effect on employment and financial status and has been proven to be a negative predictor for return to work after cancer [13, 14].

16.3 Aetiology and Pathogenesis

Until now, all attempts to explain the aetiology and pathogenesis of CrF failed to give a clear understanding about the pathogenesis of CrF. It is assumed that in CrF multicausal processes including somatic, emotional and cognitive factors are mutually dependent and interacting [15]. These factors are induced not only by cancer or cancer therapy but also by genetic predisposition, epigenetic changes, concomitant somatic or mental disorders, as well as through behavioural or environmental aspects [16].

Although the pathogenesis of CrF has not been completely clarified so far, some hypothetical explanations are discussed in the literature [17]. CrF often is associated with symptom clusters including mood disorders, sleep disturbances and cognitive dysfunctions which follow a similar time course in relation to treatment or disease [18, 19]. There is growing evidence that such symptom clusters may follow similar pathogenetic mechanisms.

Inflammation is discussed as the mediating process between the possible causes and the symptoms of CrF [20, 21]. Recently, proinflammatory mediators produced in response to cancer have been associated with fatigue; however, their direct role in pathogenesis of fatigue is controversial [16, 22].

In considering the relationship between immunological factors and CrF, a review of ten clinical trials has demonstrated that patients with CrF had elevated levels of markers for systemic inflammation [23]. In addition, it is known that chemotherapy and radiotherapy lead to an increase of numerous proinflammatory cytokines and chemokines [24–27]. The results of a longitudinal study suggest a link between CrF and increased soluble TNF receptor 1 and IL-6 levels during radiochemotherapy for colorectal and oesophageal cancer [28].

There is an overlapping in symptoms of CrF and clinical depression (e.g. tiredness, concentration, loss of motivation), whereas suicidal ideation, social withdrawal and anhedonia are more specific for major depression. Therefore, in some cases, it may be difficult to distinguish between both. In the literature, potential explanations are discussed: fatigue may cause the cancer patient to become depressed; cancer patients may become fatigued because they are depressed; or experience of cancer may cause both depression and fatigue [29, 30]. There is growing recognition that depression and CrF share common biologic mechanisms [16, 20, 31].

16.4 Epidemiology and Prevalence Rates

CrF is one of the most common symptoms in cancer patients and may occur either during or after medical treatment or as a long-term late effect after cessation of treatment. Based on several epidemiological studies, prevalence rates of CrF range from 59% to 100% depending on treatment modalities, cancer diagnoses or the time when CrF has been measured. In addition, the differences in the various prevalence rates may be explained by how fatigue is assessed, as well as which criteria for fatigue were used [32].

The degree, duration and frequency of CrF may vary over time [2]. Some studies have demonstrated that CrF usually increases during chemotherapy and decreases afterwards but may persist for up to 1 year or longer [33]. Comparing various treatment options, some studies have shown that severe CrF is more prevalent among patients receiving chemotherapy or concurrent chemoradiation compared with patients receiving only radiotherapy [34]. There is some evidence that treatment with opioids, poor performance states and weight loss are the strongest predictors for CrF [35]. In a retrospective study with mixed cancer diagnoses, women show higher level of CrF compared with men, whereas no difference was found comparing older and younger patients [36].

During the last two decades, a considerable number of studies have emphasised the complex problems faced by patients with cancer who experience CrF during treatment or afterwards. The highest prevalence rates were found for CrF as a direct side effect of a combination of medical therapies such as surgery, chemotherapy, radiotherapy, stem cell transplantation and hormone therapy [37, 38]. Higher prevalence rates for CrF are associated with the use of certain treatments such as hematopoietic stem cell transplantation (HSCT) or high-dose chemotherapy. Clinical studies investigating immune checkpoint antibodies, antiangiogenic agents and targeted therapies have reported higher rates of fatigue, ranging from 21% to 71% [39].

CrF has been documented for several specific cancer diagnoses. Lindendoll et al. showed in a systematic review on quality of life in lymphoma survivors that survivors of Hodgkin's lymphoma are at increased risk for fatigue when compared to healthy controls [40]. Heutte et al. found that high levels of fatigue at the end of treatment predicted persistent fatigue into long-term follow-up, but they did not find any differences between the treatment groups [41]. For patients with gynaecological cancer, prevalence rates between 20% and 58% are reported [42–44] and were identified as the most distressing symptom [45]. In a longitudinal study in patients with gynaecological cancer, CrF increased during treatment (chemotherapy, radiotherapy), whereas after completion of therapy, there was a slight improvement of the severity [46].

Previous findings reported that CrF as a long-term sequelae or late effect is estimated to have an average prevalence rate of approximately 30% for up to 10 years or more [35, 47]. In a large review and meta-analysis of 27 studies including 12,327 breast cancer survivors, it could be demonstrated that survivors with stage II or III cancer and survivors treated with chemotherapy were at higher risk for severe fatigue than survivors with lower stages [48]. Survivors treated with surgery, radiotherapy, and chemotherapy and survivors with this combination plus hormone therapy were at higher risk than survivors with other treatment combinations. Hormone therapy and targeted therapy were not significant risk factors. The pooled prevalence of severe fatigue was 26.9% (95% CI 23.2–31.0). According to this review, a relatively large decrease in the prevalence of severe fatigue seemed to occur in the first half-year after treatment completion. Overall, approximately one in four breast cancer survivors suffers from severe fatigue. Risk factors of severe fatigue were higher disease stages, chemotherapy and receiving the combination of surgery, radiotherapy and chemotherapy, both with and without hormone therapy. In addition, it was interesting that having a partner, receiving only surgery, and surgery plus radiotherapy decreased the risk [48].

In a prospective study, Fabi et al. investigated incidence, timing of onset, duration of CrF,

impact on QoL and psychological distress in patients with early breast cancer. The results show that prevalence of CrF was higher at the end of chemotherapy (CT) and lower at follow-up. At the end of CT and at 1 and 2 years after CT, persistence of CRF was associated with anxiety in 20%, 11% and 5% of patients and with depression in 15%, 10% and 5% of patients, respectively. A relationship between CrF and psychological distress was observed; patients presenting depression and anxiety before CT were at higher risk for fatigue onset at a later period [32].

For patients with Hodgkin (HL) or non-Hodgkin lymphoma (NHL), it has been documented that HL survivors showed increasing fatigue level with age, while in NHL survivors mean fatigue level remained constant until age 70 years and then increased with older age. HL survivors showed fatigue changes with age at a higher rate than those of the general population with health disorders, while NHL survivors were in between those of the general population with and without health disorders [49].

Prevalence of severe CrF is higher in patients with incurable cancer [50]. For patients receiving palliative or end-of-life care, CrF is associated with highly limited, or even loss of, body functions and overall quality of life [51].

16.5 Screening and Assessment

Assessment and clinical diagnosis of CrF is an important task of healthcare professionals in cancer care. According to the international guidelines [4, 52, 53], it is recommended to screen all cancer patients for symptoms of fatigue and exhaustion at regular intervals during treatment and after treatment has been completed. As a first step, a simple global numeric scale for assessing the intensity of the fatigue symptoms may be used. This global scale ranges from 0 = no fatigue to 10 = worst fatigue the patient could imagine [54]. For patients with age >12 years, a score of 0–3 has been identified as no fatigue to mild fatigue, 4–6 as moderate level of fatigue and 7–10 as severe level of fatigue (Fig. 16.2). The algorithm of screening and diagnostics of CrF in Fig. 16.2 is the recommended standard procedure for assessment and before planning of any therapeutic strategies.

As CrF is a complex and subjective phenomenon, it can only be measured by self-report assessment tools. Therefore, it has been commonly accepted that self-reports of patients are the most reliable and valid measurements of fatigue [55]. Comprehensive assessment of the fatigued patient includes a careful history to characterise the individual's fatigue pattern and to identify all factors that contribute to its development. To differentiate CrF diagnoses from other types of fatigue, specific diagnostic criteria were developed following the *International Statistical Classification of Diseases* (ICD-11) [3, 6]. The criteria define CrF as a syndrome including the 11 specific symptoms such as diminished energy or increased need to rest. The symptoms must have persisted during a defined period of time, caused significant distress or interfered with activities of daily living.

In addition, physical examination and behaviour descriptions by relatives are important sources for diagnosing CrF. Moreover, a review and adjustment of medications (e.g. cardiac medications, thyroid medications, sedative-hypnotic drugs, antidepressants) are needed, as the medication itself or interactions between different classes of drugs may contribute to increased fatigue [4].

Due to overlapping of symptoms of CrF with symptoms of depressive disorders [29], it is necessary to screen for psychiatric comorbidity, especially depressive disorders. The Patient Health Questionnaire 2-item (PHQ-2) may be used as a brief screening tool for major depression. The PHQ-2 consists of the first two questions of the Patient Health Questionnaire-9 (PHQ-9), which target core symptoms of depression (depressed mood and anhedonia) [56].

Due to the increased interest in fatigue among cancer patients, numerous instruments have been developed [57] using different methodologies. CrF may be assessed by either unidimensional or multidimensional instruments. Unidimensional instruments (e.g. FACIT Fa module [58] or the

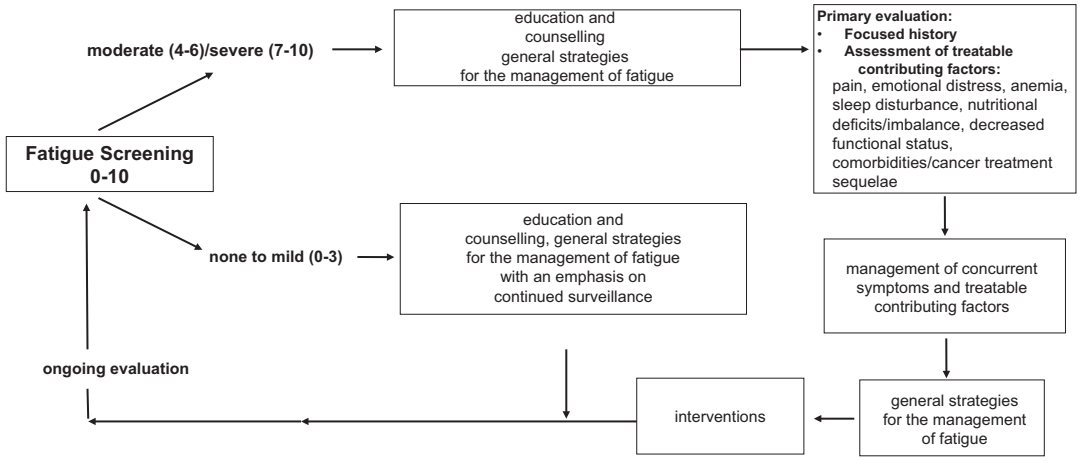

Fig. 16.2 Algorithm for assessment and treatment of cancer-related fatigue according to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) (patients >12 years). (Adapted with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Cancer-Related Fatigue V.1.2021 [4]. © 2020 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines® and illustrations herein may not be reproduced in any form for any purpose without the express written permission of NCCN. To view the most recent and complete version of the NCCN Guidelines, go online to NCCN.org. The NCCN Guidelines are a work in progress that may be refined as often as new significant data becomes available)

Brief Fatigue Inventory [59]) are focusing only on physical symptoms of fatigue, whereas multidimensional instruments are addressing physical, affective and cognitive aspects of CrF. On behalf of the EORTC quality of life group, Weis et al. developed a cross-cultural validated module (EORTC QoL Fa12) [60] which has been proven for sensitivity over time [61] (see also Chap. 5, this volume). Most of the existing cancer-specific questionnaires are using a multidimensional approach to measuring CrF which is in line with an understanding of CrF as a multifaceted syndrome. In most questionnaires, the scaling pertains to intensity, but some are additionally asking for interferences with activities of daily living or quality of life. The existing questionnaires vary largely with respect to the criteria of validity, reliability, sensitivity to change or cross-cultural applicability. Methods used for supporting claims of construct validity include known groups comparisons, analyses for convergent and discriminant validity [52]. Moreover, cultural background is also influencing the way that fatigue issue is considered. In conclusion, while all of the reported fatigue measures have both strengths and limitations, there is no gold standard of which measure is more appropriate. The self-report approach with PRO questionnaires is the most common strategy in research and clinical routine. The decision on which instrument is used to assess CrF should depend primarily on the clinical setting or the research questions that are addressed.

16.6 Treatment Strategies

As mentioned earlier, in most cases there are no clearly diagnosed causes of CrF. Therefore, the treatment approaches are aimed at alleviating any factors that may be worsening the patient's CrF and to help the patient cope with the symptoms of CrF and the distress due to CrF. According to international guidelines, treatment should include strategies activating the patient's strengths and resources and should be initiated as early as possible, to prevent CrF from becoming a chronic problem [52]. The treatment approaches should address the individual needs in terms of physical, mental and cognitive symptoms; the extent of

functional impairment; and the patient's own understanding of the problem. Beyond specificities for subgroups, the following treatment options for CrF are available:

- Physical activity and exercise
- Psychosocial and psychoeducational interventions
- Pharmacological treatment

16.7 Physical Activity and Exercise

Physical activity, exercise and training have been proven as effective strategies to reduce CrF and help against the continuing decrease of physical functional status [62, 63]. Structured exercise programmes designed to improve a patient's skeletal muscle mass and strength and cardiovascular fitness, as well as aerobic endurance, can help the patients to reduce CrF and improve their overall quality of life [63]. Within the last two decades, many reviews and meta-analyses have demonstrated substantial evidence that moderate training in combination with relaxation techniques as well as body awareness reduce subjective fatigue levels and improve patients' quality of life. A Cochrane Review [62] shows moderate effects of physical training, especially for some subgroups of cancer patients and if applied early during ongoing adjuvant treatment. Although all existing guidelines and reviews recommend physical activity to cancer patients, frequency and intensity of exercise and training should be adapted individually depending on patients' age, clinical status of cancer and the level of physical fitness [64, 65].

Several meta-analyses demonstrated a significant reduction of CrF by exercise [66, 67]. In addition, in most reviews, symptomatic relief of depression, anxiety and pain also has been documented. Although there is a persuasive evidence for physical activity and exercise in reducing CrF over the whole trajectory of cancer, there is still a need for randomised clinical trials to investigate the effect of physical exercise in patients with advanced cancer.

16.8 Psychosocial Interventions

Psychosocial interventions for treating CrF include various types of interventions such as psychosocial counselling, psychoeducation, cognitive behavioural therapy and mind-body interventions [52, 68]. The main goals of the psychosocial interventions are to help patients understand the complexity of CrF, restructure their cognitive appraisal of CrF and change their coping strategies. In some of the psychosocial interventions, recommendations for physical activity or training are included.

Information and counselling may be a standalone intervention or a part of psychoeducational or other more comprehensive interventions. Information on the multifactorial nature of CrF and its potential causes and influencing factors help the patients to gain a better understanding of the complexity of CrF. Counselling can support the patients to devise a personalised activity plan, taking into account restrictions due to CrF [69]. Brochures or interactive media, including internet platforms, may be additionally used in the counselling process. Information and counselling also are provided for partners or relatives in order to prevent negative psychosocial implications.

Psychoeducational interventions are focused on empowering patients and enhancing their skills for self-management of CrF. The most important goal of psychoeducational intervention is to facilitate self-management [70, 71]. Against the background that emotional distress is highly correlated with fatigue, psychoeducational interventions help the patients develop problem-oriented coping strategies. Patients are educated to identify sources of psychosocial distress and to reduce stress-producing activities when possible [72, 73]. According to Fabi et al. (2020), psychoeducational programmes have been investigated in several studies demonstrating a significant reduction in CRF with small to moderate effects on CrF [52].

In the field of CrF, *cognitive behavioural therapy (CBT)* focuses on emotions, cognitive processes and maladaptive behaviour. CBT is used to improve adaptation to CrF by reframing dysfunctional thoughts and enhancing

goal-oriented activities (see also Chap. 19, this volume) [74]. CBT is generally used post-treatment and in the long-term, but it may also be used for patients with fatigue undergoing chemotherapy [75].

Corbett et al. identified in their review 33 studies investigating psychological interventions for CrF including a total of 4525 participants. Most interventions focused on psychoeducation, mindfulness, cognitive or behaviour therapy-oriented strategies. Twenty-three of the included studies reported a significant effect of the interventions on reducing fatigue in cancer survivors. However, studies differed widely in terms of measurement tools used to assess fatigue, mode, duration and frequency of the intervention delivery. In addition, RCTs were heterogeneous in nature and the number of high-quality studies was limited, definitive conclusions are not yet possible [76]. In a Cochrane review, only little evidence around the benefits of psychosocial interventions was found to reduce fatigue in adult patients with incurable cancer receiving cancer treatment with palliative intent. Especially for this subgroup, the authors concluded that additional studies with larger samples are required to assess whether psychosocial interventions are beneficial for addressing fatigue in patients with incurable cancer [77]. Recently, app-based psychoeducational interventions demonstrated effects in reducing CrF [78], but there is a need for further studies.

Mind-body interventions include a wide range of interventions classified as complementary medicine and supposed to work on a physical and mental level such as mindfulness-based stress reduction (MBSR) or yoga [79].

MBSR is a specific multimodal programme focused on improving well-being and health. It combines meditation exercises with cognitive-behavioural interventions and movement exercises. A meta-analysis showed effects of MBSR on global mental health of cancer patients [80]. Intervention studies documented improvements in various psychosocial outcomes, but most of the studies do not specifically use CrF as an outcome criterion. Therefore, more prospective randomised studies are needed [81, 82].

Yoga includes specific bodily postures, breath control and meditation, and has been investigated in several studies with cancer patients. Most of these studies addressed multiple outcome criteria including fatigue [83]. Yoga has been shown effective as a treatment to improve several symptoms and overall quality of life [84], but there is a need for more randomised controlled studies addressing CrF specifically.

16.9 Pharmacological Treatments

Among pharmacologic agents for the treatment of CrF, besides hematopoietics (only for anaemia) especially psycho-stimulants are discussed. There are some randomised controlled trials showing effects of methylphenidate [85, 86], especially for patients with severe levels of long-lasting fatigue and in progressive disease without psychiatric comorbidity. As possible side effects, vertigo, increased blood pressure and dryness of the mouth have been described [87]. Due to heterogeneous results [88], the use of methylphenidate is still discussed controversially. Effects seem to depend on the dosage used, the stage of cancer and the treatment setting. In some European countries, methylphenidate is not approved for use in CrF and taken as an off-label use.

Therefore, methylphenidate may not be regarded as a standard medication for treating CrF in the European guidelines [52], whereas National Comprehensive Cancer Network (NCCN) guidelines recommend psychostimulants for patients with moderate or high levels of fatigue during and after cancer treatment when other causes of fatigue have been excluded [4].

Modafinil was approved only for the treatment of narcolepsy, but it has been shown effective for treating CrF in only some studies [89, 90]. According to the European Society for Medical Oncology (ESMO) guidelines, modafinil cannot be recommended as a medication for CrF due to shortcomings in most of the studies [52].

Short-term use of *corticosteroids* is only recommended for PATIENTS with advanced or metastatic cancer, whereas long-term steroid use

should be avoided due to the possible side effects [91].

Moreover, there are some nutraceutical agents that are less well studied for their effects on CrF or have produced heterogeneous results. Among those that are currently the focus of clinical trials, the use of L-carnitine, coenzyme Q10, Wisconsin ginseng, astragalus, guarana and mistletoe are discussed controversially, and no clear recommendations for the control of CrF are given in the ESMO guidelines [52].

16.10 Conclusion

Among cancer-related symptoms, CrF shows the highest prevalence rates during and after oncological treatment and continues to be a substantial issue in long-term survivors. Although intensive research has been carried out within the last decades, a comprehensive model including somatic as well as psychosocial factors for understanding the multicausal development of CrF is still missing. For clinicians it is important to note that CrF is often not recognised and therefore must be routinely screened over the whole trajectory of cancer. For screening and assessment, some standardised unidimensional or multidimensional instruments are available to identify the individual level of CrF. Although many assessment tools have been developed, there is no gold standard for assessing CrF. An algorithm on how to assess and treat patients with CrF has been proposed to improve diagnostic and treatment planning in clinical care. Based on the diagnosis of the fatigue syndrome, international guidelines are available with recommendations for non-pharmacological and pharmacological interventions to reduce CrF. Comparing the various treatment approaches, physical exercise and psychological interventions are effective for reducing CrF during and after cancer treatment, and show significantly better results than the available pharmaceutical options [92]. Although considerable progress has been made in clarifying potential pathways of the pathogenetic mechanism of CrF and in developing treatment strategies, CrF is still to be regarded as a major challenge for research in the near future in order to better understand, prevent and treat CrF.

16.11 Questions That Can Be Used for Learning/Testing

- What are the typical symptoms of CrF?
- Which hypotheses are discussed as potential pathogenetic causes of CrF?
- Over the whole trajectory of cancer, in which phases may CrF occur?
- In which phase does CrF show the highest prevalence rate?
- Which symptoms show an overlapping of CrF with clinical depression?
- Which score in the screening scale is used as a threshold for a clinically relevant level of CrF?
- Which are the most effective interventions to reduce CrF?

16.12 A Topic for Discussion That Can Be Used in Teaching

Discuss the relevant factors that may influence CrF and propose a stepwise procedure on how to assess CrF and how to choose an intervention strategy to support the patient suffering from severe fatigue.

16.13 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.

- Fabi A, Bhargava B, Fatigoni S, et al. on behalf of the ESMO Guidelines Committee. Cancer-related fatigue: ESMO Clinical Practice Guidelines for diagnosis and treatment. Ann Oncol. 2020;31(6):713–23. https://doi.org/10.1016/j.annonc.2020.02.016
- NCCN (National Comprehensive Cancer Network). Clinical practice guidelines in

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16.14 Research in Context

The effective management of fatigue in patients with cancer requires a clear delineation of what constitutes nontrivial fatigue. The authors[a] defined numeric cut-points for fatigue severity based on functional interference and described the prevalence and characteristics of fatigue in patients with cancer and survivors. In a multicentre study, outpatients with breast, prostate, colorectal or lung cancer rated their fatigue severity and symptom interference with functioning on a numeric scale of 0 to 10. Ratings of symptom interference guided the selection of numeric rating cut-points among mild, moderate and severe fatigue levels.

The statistically optimal cut-points were ≥4 for moderate fatigue and ≥7 for severe fatigue. Moderate/severe fatigue was reported by 983 of 2177 patients (45%) undergoing active treatment and was more likely to occur in patients receiving treatment with strong opioids (odds ratio [OR], 3.00), those with a poor performance status (OR, 2.00), those who had >5% weight loss within 6 months (OR, 1.60), those who were receiving >10 medications (OR, 1.58), those with lung cancer (OR, 1.55) and those with a history of depression (OR, 1.42). Among survivors in complete remission or no evidence of disease, 29% of patients (150 of 515 patients) had moderate/severe fatigue that was associated with poor performance status (OR, 3.48) and a history of depression (OR, 2.21).

The current study statistically defined fatigue severity categories related to significantly increased symptom interference. The high prevalence of moderate/severe fatigue in both actively treated patients with cancer and survivors warrants the promotion of the routine assessment and management of patient-reported fatigue.
[a]Wang et al. [35].

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