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Management of fatigue in patients with cancer – A practical overview

Rutger H.T. Koornstra [a,*], Marlies Peters [a,1], Stacey Donofrio [b,2], Ben van den Borne [c,3], Floris A. de Jong [d,4]

[a] Radboud University Medical Center, Nijmegen, The Netherlands
[b] University of Groningen, Groningen, The Netherlands
[c] Catharina Hospital, Eindhoven, The Netherlands
[d] Amgen BV, Breda, The Netherlands

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ABSTRACT

Cancer-related fatigue (CRF) is a serious clinical problem and is one of the most common symptoms experienced by cancer patients. CRF has deleterious effects on many aspects of patient quality of life including their physical, psychological and social well-being. It can also limit their ability to function, socialise and participate in previously enjoyable activities. The aetiology of CRF is complex and multidimensional, involving many potentially contributing elements. These include tumour-related factors and comorbid medical/psychological conditions and also side effects associated with anti-cancer therapies or other medications. Barriers to the effective management of CRF exist both on the side of physicians and patients, and as a result CRF often remains unrecognised and undiscussed in clinical practice. A change of approach is required, where fatigue is treated as central to patient management during and after systemic anti-cancer treatment. In this review we summarise factors involved in the aetiology of CRF and the barriers to its effective management, as well as factors involved in the screening, diagnosis and treatment of cancer patients experiencing fatigue. Pharmacological and non-pharmacological approaches to its management are also reviewed. We suggest an algorithm for the process of managing CRF, guided by our experiences in The Netherlands, which we hope may provide a useful tool to healthcare professionals dealing with cancer patients in their daily practice. Although CRF is a serious and complex clinical problem, if it is worked through in a structured and comprehensive way, effective management has the potential to much improve patient quality of life.

Introduction

Cancer-related fatigue (CRF) is a serious and complex clinical problem [1] and is one of the most common symptoms experienced by oncology patients [2–4]. The proportion of patients experiencing CRF varies widely in the literature, but has generally been reported as affecting between ~40–100% of those with cancer overall [4–9]. The variation in rates is likely due to the fact that fatigue is impacted not only by disease stage and status, but also because there is a lack of commonly accepted diagnostic criteria and assessment tools. However, rates can still vary between studies when the same diagnostic criteria are used, reflecting a lack of consistency in how these criteria are applied [10]. CRF can occur before, during and even long after anti-cancer treatment has been completed [4]. Up to 40% of patients report fatigue at diagnosis and virtually all patients experience fatigue at some point during cancer therapy [4]; reported rates are 80% and 90% for patients being treated with chemotherapy or radiotherapy, respectively [4]. In the post-treatment population, reported CRF rates range from 17% to 21% when strict ICD-10 criteria are applied [11] and

* Corresponding author. Address: Radboud University Medical Center, Department of Medical Oncology, PO Box 9101 (intern nr 452), 6500 HB Nijmegen, The Netherlands. Tel.: +31 (0)24 3610 353; fax: +31 (0)24 3540 788.

E-mail addresses: rutger.koornstra@radboudumc.nl (R.H.T. Koornstra), Marlies.Peters@radboudumc.nl (M. Peters), s.m.donofrio@rug.nl (S. Donofrio), ben.vd.borne@catharinaziekenhuis.nl (B. van den Borne), f.a.dejong73@gmail.com (F.A. de Jong).

[1] Address: Radboud University Medical Center, Department of Medical Oncology, PO Box 9101 (intern nr 452), 6500 HB Nijmegen, The Netherlands. Tel.: +31 (0)24 3610 353; fax: +31 (0)24 3540 788.

[2] Address: Department of Psychology, University of Groningen, Grote Kruisstraat 2/1, 9712 TS Groningen, The Netherlands. Tel.: +31 (0)50 3637 034; fax: +31 (0)50 3636 304.

[3] Address: Catharina Hospital, Department of Pulmonology, Michelangelolaan 2, 5623 EJ Eindhoven, The Netherlands. Tel.: +31 (0)40 2397 280; fax: +31 (0)40 2399 111.

[4] Address: Merck KGaA, Merck Serono Division, HQ Medical Affairs, Mail code F133/302, Frankfurter Strasse 250, 64293 Darmstadt, Germany. Tel.: +49 (0)6151 725 5191; fax: +49 (0)6151 726 1781.

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from 33% to 53% when other criteria are used [12]. A further study found that 22% of cancer survivors had persistent, severe fatigue in the year following anticancer therapy [13]. Although there is no universally accepted definition of CRF, the National Comprehensive Cancer Network® (NCCN®) defines it as 'a distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or cancer treatment, that is not proportional to recent activity and interferes with usual functioning' [9].

Impact of CRF on patients

In comparison to the fatigue experienced by healthy individuals, CRF is differentiated by its severity and the fact that it is often not alleviated by rest or sleep [14]. CRF has deleterious effects on many aspects of patient quality of life [4,5,15,16]. Specifically, it can significantly impact on a patient's physical, psychological, social and spiritual well-being, as well as limiting their ability to function, socialise and participate in previously enjoyable activities [16]. It is not only a cause of stress and anxiety for patients but can also have an impact on their family members/caregivers [17].

The aetiology of CRF

The aetiology of CRF is complex and multidimensional and involves a vast array of potentially contributing factors (Fig. 1) [14]. Anaemia has been linked with poor prognosis and fatigue [18] and is a condition commonly encountered in cancer patients. Fatigue and anaemia are sometimes used interchangeably in the literature but anaemia is actually only one of many possible causes of CRF [14]. Other potentially contributing tumour-related factors include electrolyte abnormalities, dehydration, cachexia, thrombosis/pulmonary embolism, renal failure, liver failure, hypoxia, adrenal insufficiency, neurological deficit, etc. Physical symptoms caused by the underlying tumour or its treatment can also have an impact; the symptoms most strongly correlated with fatigue are pain and dyspnoea. Loss of appetite commonly occurs in cancer patients and can lead to malnutrition and fatigue. This can be exacerbated in patients with more advanced disease who may also experience difficulty with swallowing. The possible impact of any comorbid medical (e.g., hypothyroidism, diabetes mellitus, chronic obstructive pulmonary disease [COPD], cardiovascular disease, etc.) and psychological conditions (e.g., anxiety, depression, sleep disorders, etc.) also need to be considered. In our opinion, decreased physical activity may also be a factor leading to fatigue. Furthermore, anti-cancer treatments such as chemotherapy, targeted therapies, radiotherapy or surgery and other commonly prescribed medications (e.g., opioids, psychiatric drugs, antihistamines, beta blockers, and corticosteroids) are all associated with side effects that may result in fatigue.

As management of CRF is currently sub-optimal, ideally a change of approach is required, where fatigue is treated as central to patient management both during and after systemic anti-cancer treatment. The ultimate aim would be to develop a management programme including information and tools relevant to the screening, diagnosis and potential treatments/interventions for CRF, and combine these onto one platform for use by the wider oncology community. Various programmes and management tools are already available locally, which could perhaps guide best practice more widely. For example, www.oncoline.nl is a website produced by the Comprehensive Cancer Centre in The Netherlands (IKNL), which facilitates the development, implementation and evaluation of guidelines for oncological and palliative care. This comprehensive site includes guidelines on the diagnosis and treatment of patients with various tumour types. It also contains guidelines for the diagnosis and treatment of many symptoms and health complaints caused by the disease itself or its treatment – including fatigue.

Integrated management of CRF

In this section we will overview key factors involved in the screening, diagnosis and treatment of cancer patients experiencing fatigue. We also suggest an algorithm for the process of managing CRF in clinical practice (Fig. 2), which has been guided by our experiences in The Netherlands. This includes key stages involved in the

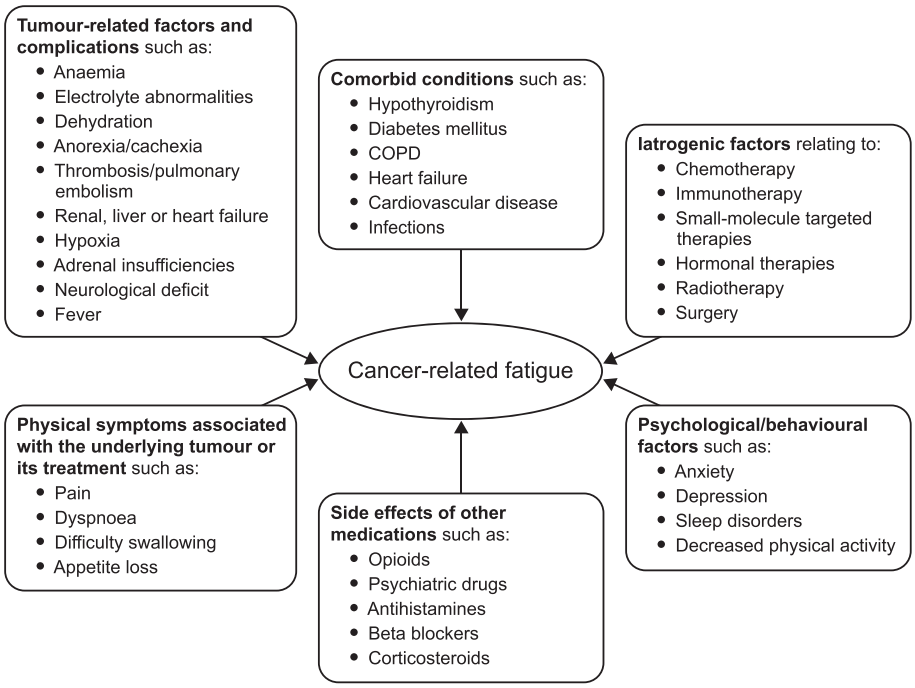

Fig. 1. Aetiology of cancer-related fatigue.