



Practical multimodal care for cancer cachexia

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Purpose of review

Cancer cachexia is common and reduces function, treatment tolerability and quality of life. Given its multifaceted pathophysiology a multimodal approach to cachexia management is advocated for, but can be difficult to realise in practice. We use a case-based approach to highlight practical approaches to the multimodal management of cachexia for patients across the cancer trajectory.

Recent findings

Four cases with lung cancer spanning surgical resection, radical chemoradiotherapy, palliative chemotherapy and no anticancer treatment are presented. We propose multimodal care approaches that incorporate nutritional support, exercise, and anti-inflammatory agents, on a background of personalized oncology care and family-centred education. Collectively, the cases reveal that multimodal care is part of everyone's remit, often focuses on supported self-management, and demands buy-in from the patient and their family. Once operationalized, multimodal care approaches can be tested pragmatically, including alongside emerging pharmacological cachexia treatments.

Summary

We demonstrate that multimodal care for cancer cachexia can be achieved using simple treatments and without a dedicated team of specialists. The sharing of advice between health professionals can help build collective confidence and expertise, moving towards a position in which every team member feels they can contribute towards multimodal care.

Keywords

cancer cachexia, clinical education, multimodal care, supportive care

INTRODUCTION

Cancer cachexia is a 'multifactorial syndrome characterized by an ongoing loss of skeletal muscle mass, with or without a loss of fat mass, that cannot be fully reversed by conventional nutritional support and leads to progressive functional impairment' [1]. It is common, especially among patients with advanced solid cancers [1,2], and impacts adversely on function [3,4], treatment tolerability [5], health service use [6], quality of life [7], and survival [8]. The pathophysiology of cancer cachexia is complex but can be characterized by a negative protein and energy balance, driven by a variable combination of reduced food intake and abnormal metabolism [9]. Persistent inflammatory and stress responses, coupled with tumour-derived factors, led to reduced food intake [9], increased resting energy expenditure [10], and net loss of lean tissue [11,12]. The degree of cachexia and the predominant phenotype depends on the tumour and patient characteristics [1,8,13], which can be uncovered with a comprehensive standardized assessment [14].

Given the multifaceted pathophysiology and heterogeneous presentation of cancer cachexia

[15], a multimodal approach to its management has been proposed [16] and advocated for by experts in the field [9,11,14,17–20]. Core treatment goals of the approach include ensuring sufficient energy and protein intake, maintaining physical activity and muscle mass, and reducing systemic inflammation where present [14]. Core component interventions would therefore include nutritional support, physical activity and exercise, and

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KEY POINTS

- A multimodal approach to cancer cachexia management has a strong theoretical rationale, but can be difficult to realise in practice with time and resource restraints, limited guidelines, and the perception that cachexia management requires a specialist team.
- Multimodal care can include nutritional, exercise based, anti-inflammatory and educational components, offered on a background of personalized oncology and nursing practice.
- Tailored multimodal care can be delivered without a specialist team, and starts with simple advice and education, treatment of nutritional impact symptoms (e.g. sore mouth, constipation, and pain), and promoting good health behaviours (e.g. eating well, staying physically active).
- Once operationalized, multimodal care approaches for cancer cachexia can be tested pragmatically, including alongside emerging pharmacological treatments.

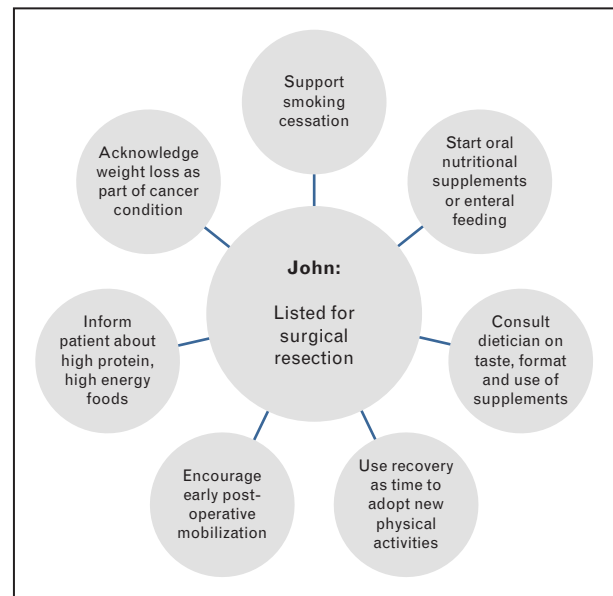


FIGURE 1. John, listed for surgical resection.

anti-inflammatory agents, for example, *n*-3 fatty acids or NSAIDs. These should be offered on a background of personalized oncological and nursing management, and family-centred education [21].

A multimodal approach has a strong theoretical backing but can be difficult to realise in clinical practice [22]. With only a handful of specialized cachexia clinics and limited allied health professionals (AHPs), responsibility falls to those providing routine care, usually the oncologist and/or cancer nurse [23[¶]]. There are time and resource restraints, few guidelines providing recommendations for cachexia management, and there can be the perception that cachexia management demands specialist expertise [23[¶]]. In this article, we use a case-based approach to highlight practical approaches to the multimodal management of cachexia for patients across the cancer trajectory. The cases are based on patients attending a lung clinic in a tertiary cancer centre. The suggested treatments are informed and guided by recent evidence, but have been selected with the generalist in mind and do not require specialist equipment and expertise. The intention is to demonstrate that multimodal care can be implemented into routine clinical practice.

CASE #1: LISTED FOR SURGICAL RESECTION

John, aged 75, has been listed for surgical resection of a T1aNoMo adenocarcinoma of the lung (Fig. 1). His current WHO performance status is 1. He has

concurrent COPD, suffers from severe anxiety, and continues to smoke half-an-ounce of rolling tobacco daily. He reports losing about half a stone and his current BMI is 17.8 kg/m², CRP is 119 mg/L, and appetite is lower than usual. Depending on John's pathological staging, he may need further adjuvant chemotherapy. His oncologist has prescribed post-operative pabrinex and vitamin B12 and is supporting John to stop smoking.

John's BMI is below normal and he is severely malnourished which could impact negatively on the outcome of his surgery in terms of complications and length of stay. His weight loss and associated problems should be acknowledged [24], with an explanation that surgery can cure lung cancer and, with adequate nutrition, the weight can be regained. A nutritional care plan over the next 7–10 days could include dietary intake and oral nutritional supplements or alternatively enteral tube feeding [25]. The latter is not often offered to patients but may be useful given John's anxiety if he is unable to meet his nutritional requirements orally. Food fortification advice would include information about the use of high energy and high protein foods, for example, the use of full cream milk, additional cheese or cream in soup or mashed potato, the use of flavoured oils (olive, nut or vegetable) on foods such as soup, rice or pasta. Use of high energy fluids can add to his energy intake, for example milky coffee, hot chocolate, malted milk drinks, milkshakes or fruit smoothies. High energy snacks between meals are also useful to increase energy intake including nuts, dried fruit, cheese or nut butter on crackers or toast, cake and biscuits,

but dietary counselling must discuss the foods that the patient would be able to eat in addition to usual meals. Talking with and his wife together can facilitate dialogue about sensitive topics, conflicts, and strengths they have developed to manage his COPD that might be helpful now [26[■]]. Oral nutritional supplements may improve overall dietary intake in some patients [27]. Adherence to taking these may be improved with the added expertise of a dietician to discuss taste preference, formats of supplements available and suitable usage in addition to food [28–31]. When introducing them talking about ways other couples have coped in similar situations could be used as an indirect way of normalizing experience, supporting problem solving and reinforcing existing coping strategies [26[■],32].

Without the need for neoadjuvant chemotherapy there is only a short window of opportunity to improve John's pulmonary function and fitness prior to surgery [33,34], so the focus should shift towards enhanced recovery after surgery. Early mobilization is an important aspect of postoperative care, to be encouraged by all the team. There is limited evidence on which protocol to adopt [35[■]], but the patient who can mobilize quickly becomes an active participant in their care [36]. This might again reduce postoperative complications and risk of prolonged stay or readmission. John is a good candidate for pulmonary rehabilitation, which can reduce symptom burden and enhance exercise capacity following lung resection [37,38]. From the first contact this plan can be introduced, along with counselling to find new activities in the recovery phase. Patients often adopt sedentary behaviours despite successful primary treatment of disease, but something as simple as a step counter/pedometer may help them to self-manage this [39,40].

CASE #2: COMMENCED RADICAL CHEMORADIO THERAPY

Doris, aged 65, has COPD and presented with cough and weight loss (Fig. 2). She was diagnosed with a radically treatable T1aN2Mo squamous cell carcinoma of the lung. She commenced radical chemo-radiation therapy but following cycle 1 of chemotherapy was admitted with acute sepsis. Her weight at diagnosis had dropped 13 kg since documented 2 years previously, and has since dropped a further 6 kg despite enteral support. Doris had a current BMI of 14.7 kg/m² and performance status of 2. Her appetite remains poor and she has a high CRP of 280 mg/L. She is a retired landlady, is widowed with no children, and currently lives alone but has supportive neighbours. Her admission might

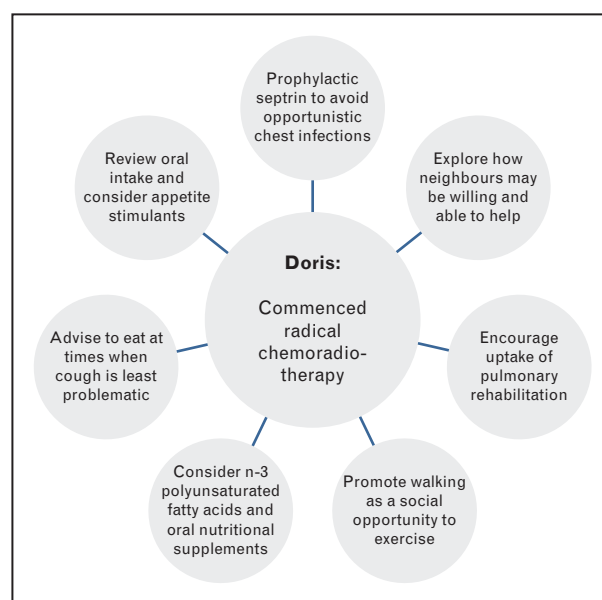


FIGURE 2. Doris, commenced radical chemoradiotherapy.

prompt a change in medical management including stopping her chemotherapy and altering the dose per fraction of radiotherapy. Prophylactic septrin could help avoid opportunistic chest infections while her radiotherapy continues and nutritional support with pabrinex and vitamin B12 could be offered.

This patient has severe malnutrition despite enteral support. The persistent inflammatory response, possibly fuelled by recurrent infection, has contributed to her ongoing weight loss and treatment may have further reduced appetite and food intake. A full review of symptoms is warranted. Ideally this would have occurred prior to her starting treatment to improve tolerance to it. The use of n-3 polyunsaturated fatty acids in addition to protein and energy dense nutritional supplements may have helped support performance status and quality of life [41]. A self-management approach to eating can help retain a sense of control [42,43]. Doris could be advised to eat and drink at times when her cough is least problematic and use nutrition dense snacks and fluids, for example, milk drinks of fortified soups, to increase intake in spite of symptoms. Appetite stimulants may have a role. On completion of radiotherapy proactive monitoring and management of oesophagitis is required to ensure this does not further exacerbate the poor intake. Enteral tube feeding may be required in circumstances if oral intake is particularly compromised and nutritional status deteriorating. Treatment-related anaemia, pneumonitis and physical inactivity might have reduced Doris' exercise tolerance, particularly during her recent hospital admission [3,44]. Studies

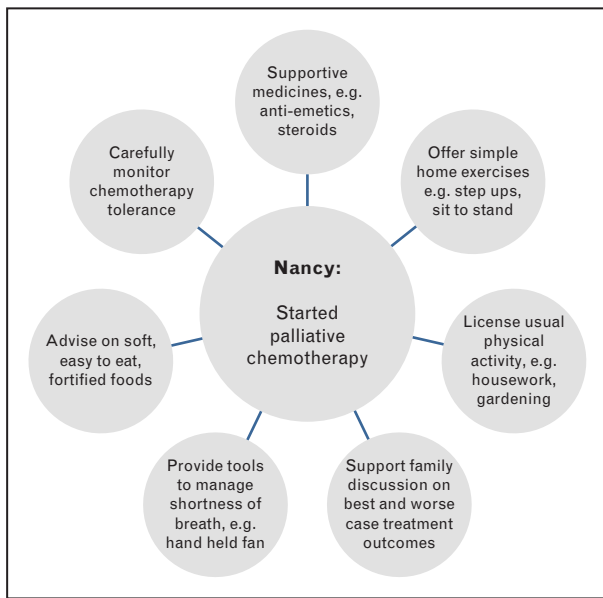


FIGURE 3. Nancy, receiving palliative chemotherapy.

support exercise alongside chemoradiotherapy therapy [45[■]]. Although no study has purposefully selected cachectic patients [46], exercise has an anti-inflammatory effect [47] and can help maintain function. If local rehabilitation services are available a referral should be discussed. With her concurrent COPD diagnosis Doris would be an excellent candidate for pulmonary rehabilitation [48,49] despite her current frailty [50[■],51]. Doris should be encouraged to stay as active as she feels able [52,53], perhaps to start walking with friends or neighbours on a few days of each week as a social activity [54].

CASE #3: RECEIVING PALLIATIVE CHEMOTHERAPY

Nancy, aged 71, was recently diagnosed with stage IV squamous cell lung carcinoma having presented to her GP with breathlessness (Fig. 3). She had a pleural effusion which was drained, and has a medical history of a cardiac pacemaker, small hiatus hernia, and hypercholesterolaemia. She lives with her husband and has four grown children nearby. Her performance status is 1 and she mobilizes with a walking stick, mainly for confidence. Nancy's BMI at diagnosis was 28.5 kg/m². She had lost 5 kg but this did not cause her particular concern as she had been keen to lose weight. Her appetite remains low and her breathlessness persists. She was prescribed palliative chemotherapy with gemcitabine/carboplatin and baseline bloods revealed an ESR of 116 mm/h and CRP of 58 mg/L. Her oncological management included prescribing postchemotherapy supportive medications (antiemetics, proton pump inhibitors

and steroids), treating constipation, and close monitoring of tolerance to chemotherapy.

Breathlessness and poor appetite here will have had a significant impact on the dietary intake for this patient leading to malnutrition. Malnourished patients have a poorer outcome compared with those who are not malnourished at diagnosis [55] so symptom control is a priority. Given Nancy's age and comorbidities, polypharmacy may be contributing to her symptoms and a geriatric assessment is worthwhile. Achieving sufficient dietary intake can be difficult in the older breathless patient, who often reduce the frequency of eating and have dietary profiles with little variety and unusually high proportions of liquids [56]. Consideration should be given to foods and fluids that maximize dietary intake but are easy to eat and drink, for example, foods that are soft and can be fortified. Oral nutritional supplements may be an option if found suitably palatable. The home support from her husband and grown children is important. Families can support or challenge the patient's approach to progressing disease and changing eating habits [57,58] and should be closely involved in management where possible. It can be important to support the patient's plans to tell family about best and worst case scenario from treatment and negotiate with their family. There is also a role in preparing the family in the case of rapidly progressing disease where they may engage in futile attempts to feed that cause distress [43]. Acknowledging the importance of meals for maintaining relationships can be useful, as can suggesting ways Nancy can continue to be part of daily family routines and events without feeling pressure to eat, such as offering 'help yourself' meals.

Nancy's favourable performance status should assist her getting through her palliative chemotherapy, indeed performance status, functional capacity and activity behaviours are all predictors of overall survival [59]. Physical activity level should be seen as a 'vital sign' reflecting current wellbeing. Whilst when Nancy feels in need of rest this should happen, she should be permitted and encouraged to continue usual activity behaviours such as the housework, gardening and hobbies. With her symptoms, advice should be offered on activity planning and pacing 'balancing activity and rest' and 'listening to your body', along with simple way to manage breathlessness, such as using a handheld fan or cooled water spray. Reassuring Nancy and her family about normal exertional responses to activity can also be helpful [60]. They could be directed towards web-based information and guidance to support active living, for example, from Macmillan Cancer Care. Although formal exercise services are not often

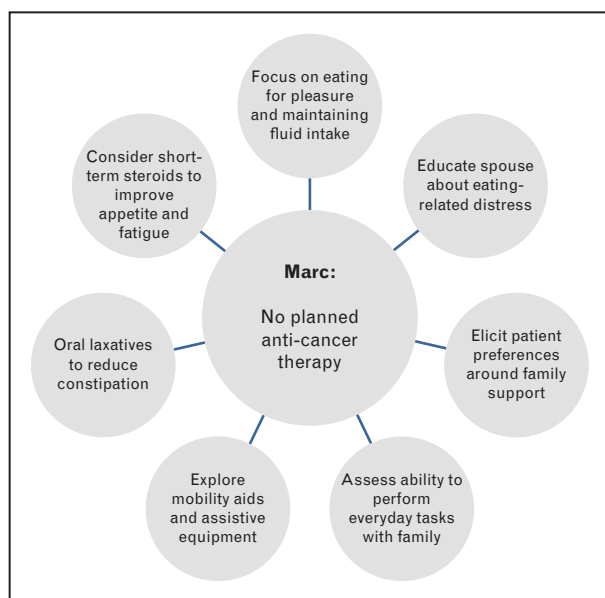


FIGURE 4. Marc, no planned anticancer therapy.

available, many patients report a readiness to take up light self-managed exercise during chemotherapy [61,62]. Simple home exercises that do not require equipment can be taught, for example step-ups and sit-to-stands with a focus on a slow and controlled movement. Furthermore palliative care services, including hospices, may provide rehabilitation services that the patient may be willing to explore [63–65].

CASE #4: NO PLANNED ANTI-CANCER THERAPY

Marc, aged 63, was diagnosed with a Stage IV mixed large cell/neuroendocrine lung tumour following flu-like symptoms that restricted his work as a carpenter (Fig. 4). His performance status had deteriorated rapidly in the last month, from WHO 1 to 3, and he reported significant weight loss. Additional symptoms included chronic fatigue, cough, constipation, peripheral oedema. Marc's BMI was 19.3 kg/m² and blood tests revealed a high CRP of 232 mg/L. His planned management was for best supportive care. The oncologist assessed Marc for palliative radiotherapy to improve his cough, prescribed oral laxatives for his constipation as a nutritional impact symptom, diuretics to improve peripheral oedema, and a short-course of corticosteroids to stimulate appetite and alleviate fatigue. Timely involvement of palliative care was also prioritized.

Marc's nutritional markers (weight loss, poor appetite and increased CRP) suggest refractory cachexia [1] and with such rapid deterioration the provision of nutrition is unlikely to prevent further change in body composition. The deterioration in

performance status and loss of body weight is likely to cause concern and distress to Marc and his family [21]. Therapeutic discussion should cover the causes of weight loss, main symptoms and what changing dietary intake can and cannot realistically achieve. Regarding nutrition, the focus might be to eat for pleasure whilst maintaining an adequate fluid intake – finding foods and fluids that provide best taste, are easy to eat, and taking small portion sizes. The link between constipation and drinking plenty of fluids could also be made. The use of oral nutritional supplements is unlikely to provide clinical benefit so these should only be considered if they are liked by the patient and requested. It can be helpful to include those preparing food in the discussion, often the family, to ensure their role is supportive. A clear explanation of what causes weight loss, for example, there may be a malnutrition component, but it is likely predominantly caused by disease and not anyone's fault, may help to alleviate the anxiety around appetite and eating, and help manage expectations [66]. The reduced performance status will also threaten Marc's physical independence and normal 'role', particularly with regard to his work [23,67]. An intense exercise programme targeting change in body composition is unlikely to be realistic or helpful. Instead the focus should be on maintaining independence in activities of daily living, involving the family who will be at home supporting Marc. The provision of a mobility aid and/or assistive equipment should be considered, to promote independence in and around the home [55,68]. It is common for family members to be uncertain what to do, so a supportive approach that encourages the patient to talk about their preferences and how best to manage change can be useful [69], for example asking: 'how would you prefer them to help?'. Family members sometimes default to doing everything for their loved one in an attempt to preserve their energy levels, including tasks they are capable of doing independently. A reminder that independence is often important to people may help family members to offer care that enables rather than limits daily activity.

IMPLEMENTING MULTIMODAL CARE IN PRACTICE

These cases highlight numerous component treatments to consider, and provide three key messages to support multimodal care for cancer cachexia in practice. First, every member of the clinical team can contribute towards multimodal care. Multimodal care includes addressing nutritional impact symptoms, for example, sore mouth, constipation, pain, which interfere with intake and absorption and

compound cachexia. Assessing and managing these symptoms is an important part of multimodal care within reach of all clinicians. A holistic needs assessment can uncover additional patient and family needs relating to cachexia and prompt appropriate education and management. It is not always possible to refer to specialists, or there can be long wait lists, so simple practical advice should become part of each team member's repertoire. This would be supported by a commitment to inter-professional learning and working. Second, multimodal care for cancer cachexia should be person centred and focus on supported self-management. Treatments to improve or maintain physical, psychological and social functioning often require behaviour change and should be tailored to individual and the surrounding context. The patient's family and social support network are often important, and including them in the promotion and monitoring of health behaviours, for example, preparing meals or being physically active, can be invaluable. In line with this patient reported outcomes also have a role in recognizing successful care [70]. Third, multimodal approaches can ask a lot of the patient and their family. When introducing new treatments it is helpful to remind patients that they are buying-in to an approach to care, rather than signing up to a strict, often challenging treatment regimen. Adherence is key, so new requests or treatments should always be considered and introduced in line with the whole approach.

Once multimodal care is operationalized it can then be tested pragmatically, either alone or alongside pharmacological treatments. Some centres have developed cachexia clinics and offer working models to build an evidence base for multimodal care. Emerging trials also show promise for pharmacological agents, for example, ghrelin receptor agonists, myostatin, SARMs [19,71^{***}]. There may soon be new therapies to prescribe for cancer cachexia, but arguably these should be offered on a background of good multimodal care [23^{*,}71^{***}]. To test this argument trials may be needed to monitor the combined effects of exercise and nutrition, and anti-inflammatory medicines, with or without cachexia drug therapies [20]. Such designs have increasing importance given the regulatory perspective on functional trial endpoints [19,72].

CONCLUSION

This case-based paper highlights practical ways to provide multimodal care for cancer cachexia. Across a range of clinical scenarios, we demonstrate that this can be achieved with simple treatments and without a dedicated team of specialists. As multimodal care is

part of everyone's remit, the sharing of advice and experiences between health professionals can help build confidence and expertise, moving towards a position where every team member feels they can contribute towards cachexia care.

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Conflicts of interest

M.M. and C.S. have received lecture fees from Fresenius Kabi. J.H. is a member of the Scientific Board for the Cachexia Hub, Helsinn Healthcare. KCHF has received lecture fees, consultancy fees, research support or attended advisory boards for Nutricia, Abbot, Fresenius Kabi, Lilly, Helsinn, Chugai, Ono, Novartis and Aveo Oncology. For the remaining authors none were declared.

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