



Contents lists available at ScienceDirect

Critical Reviews in Oncology / Hematology

journal homepage: www.elsevier.com/locate/critrevonc

Review

Integration of palliative, supportive, and nutritional care to alleviate eating-related distress among advanced cancer patients with cachexia and their family members

Koji Amano^{a,*}, Vickie E Baracos^b, Jane B Hopkinson^c^a Department of Palliative Medicine, Osaka City General Hospital, 2-13-22 Miyakojima-hondori, Miyakojima-ku, Osaka city, Osaka, 534-0021, Japan^b Division of Palliative Care Medicine, Department of Oncology, University of Alberta, Cross Cancer Institute, 11560 University Avenue, Edmonton, Alberta, T6G1Z2, Canada^c School of Healthcare Sciences, College of Biomedical and Life Sciences, Cardiff University, 35-43 Eastgate House, Newport Road, Cardiff, Wales, CF24 0AB, UK

ARTICLE INFO

Keywords:

Advanced cancer
Palliative care
Supportive care
Nutritional support
Nutrition impact symptoms
Eating-related distress

ABSTRACT

Advanced cancer patients with cachexia and their families can suffer from *eating-related distress*. This complex entity encompasses patients' struggle to nourish themselves, emotional and social consequences of their inability to maintain food intake, and profound disturbance in family relationships. With evidence-based nutritional care, as well as symptom management to enable food intake, cachexia can be mitigated to some degree. In addition, patients and families require psychosocial support and education to understand and cope with this condition. Only by taking an integrated approach can health care teams alleviate eating-related distress, improve quality of life (QOL), reduce interpersonal conflicts, and alter perceptions of nutritional neglect for patients and families. However, few studies have investigated eating-related distress among patients and families. The aim of this narrative review is to describe what is known about eating-related distress and the roles of integrated palliative, supportive, and nutritional care in improving QOL of patients and families.

1. Introduction

Cachexia is particularly prevalent in patients with cancer of advanced stage and has been linked to deteriorations in quality of life (QOL), performance status, treatment outcomes, and survival (Radbruch et al., 2010; Fearon et al., 2011; Tisdale, 2009; Fearon et al., 2013; Amano et al., 2016a; Arends et al., 2017; Amano et al., 2017; Baracos et al., 2018; Sadeghi et al., 2018). Cancer cachexia is defined as a syndrome of body weight loss driven by “a variable combination of reduced food intake and altered metabolism” (Radbruch et al., 2010; Fearon et al., 2011). Reduced food intake is an important and, in some cases, dominant driver of this body weight loss. A diminished central drive to eat (anorexia) is pervasive, and additionally accompanied by an obstacle course of symptoms that impede food intake (Table 1A). Owing to the importance of reduced food intake, cachexia is classified as a form of (disease-associated) malnutrition and is considered to be partially mitigated by nutritional support (Radbruch et al., 2010; Fearon et al., 2011; Tisdale, 2009; Fearon et al., 2013; Arends et al., 2017; Baracos et al., 2018; Sadeghi et al., 2018).

Patients with cachexia and their family members may suffer from

profound psychosocial distress. Prior qualitative research have identified *eating-related distress* as a significant contributor to overall psychosocial distress (Strasser et al., 2007; Hopkinson et al., 2011; Oberholzer et al., 2013; Hopkinson, 2014; Reid, 2014; Cooper et al., 2015; Hopkinson, 2016; Wheelwright et al., 2016). Eating-related distress encompasses a myriad of intersecting factors including patients' and family members' struggles to cope with cachexia, gross impairment of food intake, disturbance of relationships, and changing roles (Table 1A) (Strasser et al., 2007; Hopkinson et al., 2011; Oberholzer et al., 2013; Hopkinson, 2014; Reid, 2014; Cooper et al., 2015; Hopkinson, 2016; Wheelwright et al., 2016; Amano et al., 2016b, c; Amano et al., 2018a, b; Koshimoto et al., 2019). The current management of cancer cachexia is primarily focused on pain and symptom management, nutrition interventions, as well as, development of novel drugs with appetite-enhancing actions. However, to adequately address eating-related distress, future clinical practice guidelines must consider holistic, multimodal care including education and psychosocial support (Table 1B, Fig. 1) (Strasser et al., 2007; Hopkinson et al., 2011; Oberholzer et al., 2013; Hopkinson, 2014; Reid, 2014; Cooper et al., 2015; Hopkinson, 2016; Wheelwright et al., 2016; Amano et al., 2016b,

* Corresponding author.

E-mail addresses: kojiamano4813@gmail.com (K. Amano), vbaracos@ualberta.ca (V.E. Baracos), HopkinsonJB@cardiff.ac.uk (J.B. Hopkinson).

Table 1

. Integration of palliative, supportive, and nutritional care for eating-related distress.

A Problem: Eating-related distress in patients and family members

Nutrition impact symptoms impairing food intake (Amano et al., 2018b; Koshimoto et al., 2019; Kubrak et al., 2010; Anandavadevelan et al., 2018; Martin and Kubrak, 2018; Del Fabbro et al., 2017; Kubrak et al., 2013; Del Fabbro et al., 2011; Omlin et al., 2013; Blum et al., 2014)

- Unpredictable occurrence and course
- Lack of appetite, early satiety, fatigue, pain, shortness of breath, nausea, vomiting, constipation, diarrhea, abnormal taste, abnormal smell, dry mouth, difficulty swallowing, dental problems, drowsiness, anxiety, depression
- Physical and psychosocial consequences: body weight loss, altered body image, impaired activities of daily living, reduced well-being

Unsuccessful coping strategies of patients and/or family members (Strasser et al., 2007; Hopkinson et al., 2011; Oberholzer et al., 2013; Hopkinson, 2014; Reid, 2014; Cooper et al., 2015; Hopkinson, 2016; Wheelwright et al., 2016; Amano et al., 2016b, c; Amano et al., 2018a, b; Koshimoto et al., 2019; McClemen et al., 2003; McClement et al., 2004; McClement and Harlos, 2008; Hopkinson, 2018)

- “Fighting back” against the cancer cachexia
- Gaps between reality and expectation
- Shortage of correct information about cancer cachexia and nutrition
- Insufficient nutritional support by health care teams
- Feelings of loss of control, helplessness, frustration

Conflicts over food between patients and family members (Strasser et al., 2007; Hopkinson et al., 2011; Oberholzer et al., 2013; Hopkinson, 2014; Reid, 2014; Cooper et al., 2015; Hopkinson, 2016; Wheelwright et al., 2016; Amano et al., 2016b, c; Amano et al., 2018a, b; Koshimoto et al., 2019; McClemen et al., 2003; McClement et al., 2004; McClement and Harlos, 2008; Hopkinson, 2018)

- Changes in both patients’ food preferences and eating habits of whole families
- Challenges to spousal and family roles and traditions
- Family members’ pressure on patients to eat
- Differences in beliefs and perceptions between patients and family members

A Solution: Integration of palliative, supportive, and nutritional care (Fig. 1)

Manage nutrition impact symptoms (Amano et al., 2018b; Koshimoto et al., 2019; Kubrak et al., 2010; Anandavadevelan et al., 2018; Martin and Kubrak, 2018; Del Fabbro et al., 2017; Kubrak et al., 2013; Del Fabbro et al., 2011; Omlin et al., 2013; Blum et al., 2014; Gagnon et al., 2013)

Provide psychosocial support for coping of patients and family members (Strasser et al., 2007; Hopkinson et al., 2011; Oberholzer et al., 2013; Hopkinson, 2014; Reid, 2014; Cooper et al., 2015; Hopkinson, 2016; Wheelwright et al., 2016; Amano et al., 2016b, c; Amano et al., 2018a, b; Koshimoto et al., 2019; McClemen et al., 2003; McClement et al., 2004; McClement and Harlos, 2008; Hopkinson, 2018)

Provide nutritional support according to evidence-based clinical practice guidelines (Radbruch et al., 2010; Fearon et al., 2011, 2013; Arends et al., 2017; Baracos et al., 2018; Sadeghi et al., 2018; Amano et al., 2013, 2016d)

Provide evidence-based information and advice on nutritional care for patients by family members (Strasser et al., 2007; Hopkinson et al., 2011; Oberholzer et al., 2013; Hopkinson, 2014; Reid, 2014; Cooper et al., 2015; Hopkinson, 2016; Wheelwright et al., 2016; Amano et al., 2016b, c; Amano et al., 2018a, b; Koshimoto et al., 2019; McClemen et al., 2003; McClement et al., 2004; McClement and Harlos, 2008; Hopkinson, 2018)

Educate patients and family members about cancer cachexia (Strasser et al., 2007; Hopkinson et al., 2011; Oberholzer et al., 2013; Hopkinson, 2014; Reid, 2014; Cooper et al., 2015; Hopkinson, 2016; Wheelwright et al., 2016; Amano et al., 2016b, c; Amano et al., 2018a, b; Koshimoto et al., 2019; McClemen et al., 2003; McClement et al., 2004; McClement and Harlos, 2008; Hopkinson, 2018)

Initiate end-of-life discussion with patients and family members (Hopkinson, 2014, 2018)

A Outcome: Effectiveness of integration of palliative, supportive, and nutritional care

Alleviating eating-related distress of patients and family members (Amano et al., 2016b, c; Amano et al., 2018a, b; Koshimoto et al., 2019)

Improving quality of life in patients and family members (Amano et al., 2016b, c; Amano et al., 2018a, b; Koshimoto et al., 2019)

Mitigating conflicts between patients and family members (Amano et al., 2016b, c; Amano et al., 2018a, b; Koshimoto et al., 2019)

Promoting advanced care planning among patients and family members (Hopkinson, 2014, 2018)

c; Amano et al., 2018a, b; Koshimoto et al., 2019).

Few studies have investigated eating-related distress among patients and family members; furthermore, the segmentation of palliative, supportive, and nutritional care services complicates the matter (Strasser et al., 2007; Hopkinson et al., 2011; Oberholzer et al., 2013;

Hopkinson, 2014; Reid, 2014; Cooper et al., 2015; Hopkinson, 2016; Wheelwright et al., 2016; Amano et al., 2016b, c; Amano et al., 2018a, b; Koshimoto et al., 2019). Therefore, the aim of this narrative review is to describe eating-related distress and the roles of integrated palliative, supportive, and nutritional care in improving QOL of patients and family members. In particular, we will focus on nutrition impact symptoms, perceived need for nutritional support, and conflicts over food among patients and family members in palliative and supportive care settings.

Adequate management of nutrition impact symptoms, i.e., cancer-associated symptoms as well as side effects of cancer treatments, is essential to enable food intake. Psychosocial and nutritional support, provision of evidence-based information and advice, and education enable patients and family members to cope and alleviate eating-related distress. In addition, end-of-life discussion also contributes to optimizing coping strategies and advanced care planning. Interdisciplinary cooperation among oncologists, palliative care physicians, nurses, dietitians, and others is needed to provide the integrated palliative, supportive, and nutritional care.

2. Problems

2.1. Nutrition impact symptoms

Individuals with incurable cancers experience a diverse and complex burden of symptoms. Many of these are deemed *nutrition impact symptoms*, because they compromise food intake and in turn drive body weight loss (Table 1A). However, a consensus on the definition of nutrition impact symptoms in cancer patients does not exist. These symptoms may be owing to the cancer itself, cancer treatment, or comorbidities (Kubrak et al., 2010; Anandavadevelan et al., 2018). Although lack of a central drive to eat (anorexia) is among the most pervasive of cancer-associated symptoms (Amano et al., 2017; Martin and Kubrak, 2018), many others are implicated in impaired food intake. Other symptoms implicated include early satiety, fatigue, pain, shortness of breath, nausea, vomiting, constipation, diarrhea, abnormal taste and smell, dry mouth, difficulty swallowing, dental problems, anxiety, depression, and drowsiness. Due to the complex symptom burden of advanced cancer, medical management of pain and symptoms is considered a principle component of cancer cachexia management (Fearon et al., 2013; Arends et al., 2017).

An important aspect of cancer cachexia management is the identification and evaluation of symptoms interfering with food intake. The Edmonton Symptom Assessment System-revised (ESAS-r) (Bruera et al., 1991) and Patient-Generated Subjective Global Assessments (PG-SGA) (Bauer et al., 2002) are widely used for symptom assessment, some of their components pertain specifically to reduced food intake (Amano et al., 2018b). While the ESAS-r is able to assess the severity of symptoms such as lack of appetite and nausea, other symptoms impeding food intake, such as early satiety and diarrhea, are not included. On the other hand, although the PG-SGA is a validated tool that can identify several nutrition impact symptoms, the binary outputs (yes/no) do not allow for assessment of symptom severity (Del Fabbro et al., 2017). A comprehensive nutrition impact symptom tool specific to cancers of the head and neck has been developed (Kubrak et al., 2013), but this has not been validated in other cancer sites. Other tools used to capture reduced food intake include food/fluid records and Visual Analogue Scales (Martin and Kubrak, 2018), however, the nutritional impact symptoms are not captured by these tools. Given the weaknesses of the aforementioned assessment tools, further investigation is needed to develop a comprehensive tool that captures the both the breadth and severity of nutrition impact symptoms. Only then, can the association between impaired food intake and nutrition impact symptoms be adequately explored.

Despite the limitations described above, several previous studies have attempted to characterize symptom profiles of patients with

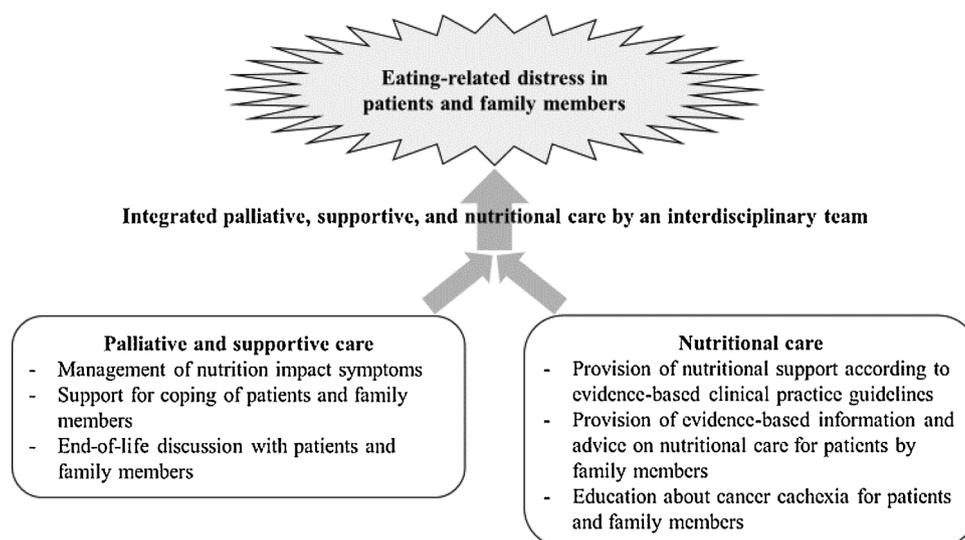


Fig. 1. Integrated model of palliative, supportive, and nutritional care for eating-related distress.

advanced cancer. A study conducted at a cancer cachexia clinic indicated that most patients who experienced body weight loss had three or more uncontrolled symptoms. The most common symptoms were early satiety (62%), constipation (52%), nausea or vomiting (44%), and mood changes (42%) (Del Fabbro et al., 2011). A study in a nutrition fatigue clinic reported that the five most frequent symptoms were abnormal taste and smell (27%), constipation (19%), abdominal pain (14%), difficulty swallowing (12%), and epigastric pain (10%) (Omlin et al., 2013). A large, European cohort study of patients from palliative care in- and out-patient units, hospices, and general oncology wards compared 9 symptoms of the ESAS-r between a non-cachexia group and the cachexia group, categorized using cachexia criteria from the international consensus (Fearon et al., 2011; Blum et al., 2014). Their analysis revealed that the frequency of 6 symptoms, i.e., lack of appetite, fatigue, pain, nausea, drowsiness, and reduced well-being, were significantly higher in the cachexia group (Blum et al., 2014). Finally, a survey of advanced cancer patients in palliative and supportive care settings demonstrated that the severity of 16 symptoms, i.e., 9 symptoms of the ESAS-r and 7 of the PG-SGA, were rated moderate in severity with the top 3 being reduced well-being, lack of appetite, and fatigue. The severity of 8 symptoms, i.e., lack of appetite, early satiety, fatigue, diarrhea, abnormal taste, difficulty swallowing, drowsiness, and reduced well-being, were significantly greater in the cachexia group than in the non-cachexia group based on cachexia criteria from the international consensus (Fearon et al., 2011; Amano et al., 2018b). In summary, due to the heterogeneity in the patient populations, study settings, and assessment tools used in the studies above, direct comparison of the severity and frequency of nutrition impact symptoms would be challenging. Thus, development of a comprehensive assessment tool is urgently needed to identify and evaluate nutrition impact symptoms in palliative and supportive care settings.

2.2. Eating-related distress and perceived need for nutritional support in patients

Eating-related distress experienced by the patient has been substantially informed by qualitative studies involving in depth interviews (Strasser et al., 2007; Hopkinson, 2014; Reid, 2014; Hopkinson, 2016), and this body of work has been systematically reviewed (Hopkinson et al., 2011; Oberholzer et al., 2013; Cooper et al., 2015; Wheelwright et al., 2016). Some questionnaires have been devised based on this information, however these require validation (Amano et al., 2018b). Patients experience many distressing symptoms that reduce food enjoyment and make eating unpleasant. Indeed, lack of appetite, reduced

food intake, and ongoing body weight loss could lead patients to feel that their survival is threatened (Strasser et al., 2007; Hopkinson et al., 2011; Oberholzer et al., 2013; Hopkinson, 2014; Reid, 2014; Cooper et al., 2015; Hopkinson, 2016; Wheelwright et al., 2016; Amano et al., 2016b, c; Amano et al., 2018a, b; Koshimoto et al., 2019). Nevertheless, patients often become resolute in their desire to maintain adequate food intake, forcing themselves to eat despite pain, nausea, and other symptoms. An ensuing challenge is the continued body weight loss in spite of varied efforts to maintain intake (Radbruch et al., 2010; Fearon et al., 2011; Tisdale, 2009; Fearon et al., 2013; Arends et al., 2017; Baracos et al., 2018; Sadeghi et al., 2018). The unsuccessful attempts by patients to increase their body weight widens the gap between reality and expectation resulting in escalation of patient distress (Hopkinson et al., 2011; Oberholzer et al., 2013; Hopkinson, 2014). This phenomenon is called the “Calman gap” (Calman, 1984), and it can escalate or de-escalate depending on patient’s knowledge of cancer cachexia and individual coping strategies (Oberholzer et al., 2013). For example, in a small survey of advanced cancer patients in a palliative care unit, the four most frequent eating-related distress items belonged to “coping strategies”. It also suggested that patients had strong concerns over “lack of appetite”, “inability to eat”, and “body weight loss” and that “hopelessness”, “fretting”, and shortage of “correct information” aggravated their distress (Amano et al., 2016b). Another potential exacerbating factor of eating-related distress may be the inability to halt the body weight loss, as surveys suggest that patients with cachexia had significantly greater eating-related distress than those without cachexia (Amano et al., 2018b).

Lack of credible, proven strategies to manage body weight loss and impaired food intake is a concern expressed by patients (Amano et al., 2016b, a; Amano et al., 2018b). In a survey conducted in an inpatient palliative care unit, 76% of patients felt that they had unmet needs that could have been addressed by unit staff, e.g., physicians, nurses, and dietitians, with specific knowledge of nutritional support for cancer cachexia (Amano et al., 2016b). A survey in palliative and supportive care settings suggested that patients with advanced cancer wished to receive support from a health care teams, including nutritional counselling (94%), ideas to improve food intake (88%), and oral nutritional supplements (83%). In the case that they became unable to take sufficient nourishment orally, patients expressed needs for parenteral nutrition and hydration (77%), and tube feeding (23%) (Amano et al., 2018a). Expressed needs for these forms of nutritional support were higher in patients with cachexia versus the non-cachexia group. Of note, tube feeding was regarded as generally undesirable, and almost all respondents to a survey did not wish to receive tube feeding even if they

could not eat enough (Amano et al., 2018a). Finally, it has been shown that patient-perceived need for nutritional counselling is significantly associated with reduced QOL and eating-related distress, particularly in regard to “conflicts over food”, “concerns about food”, and “self-motivated effect related to nutrition” (Koshimoto et al., 2019).

In conclusion, when patient attempts to combat cachexia, many are disappointed with gaps between reality and expectation. This disappointment can be intensified by a shortage of correct information, lack of provision of nutrition intervention by health care teams, poor coping strategies, and unmet need for nutritional support (Table 1A). Unmet, perceived need for nutritional support is significantly associated with cachexia and increased eating-related-distress and contributes to reduced QOL.

2.3. Eating-related distress and perceived need for nutritional support in family members

Eating-related distress experienced by family members has been studied by interview-based qualitative approaches (Strasser et al., 2007; Hopkinson et al., 2011; Oberholzer et al., 2013; Hopkinson, 2014; Reid, 2014; Cooper et al., 2015; Hopkinson, 2016; Wheelwright et al., 2016), and also by questionnaires-based quantitative approaches (Amano et al., 2016c, b). It is known through previous studies that family members suffer when negative impact of cachexia becomes apparent in the patient (Strasser et al., 2007; Hopkinson et al., 2011; Oberholzer et al., 2013; Hopkinson, 2014; Reid, 2014; Cooper et al., 2015; Hopkinson, 2016; Wheelwright et al., 2016; Amano et al., 2016c, b). A systematic review of qualitative studies reported 5 particular themes expressed by family members of advanced cancer patients: “impact on everyday life”, “taking charge”, “need for outside help”, “conflict with patient”, and “emotions” (Wheelwright et al., 2016). Additional topics that arose from previous studies included the role of female caregivers, sub-processes of “fighting back”, caregiver depression, and association between eating-related distress and progressive cachexia. A unique mixed methods study of male patients and their female partners also suggested that female caregivers may express feelings of deep concern, frustration, and insufficiency, as well as, making innovative efforts to prepare appealing food (Strasser et al., 2007). The sub-processes: “fighting back”, “letting nature take its course”, or “waffling” have been explored through previous qualitative studies (McClement et al., 2003; McClement et al., 2004; McClement and Harlos, 2008), and further characterized in the most recent quantitative study (Amano et al., 2016c, b). Specifically, in a 2016 survey of 702 bereaved family members of patients who had received care in palliative care units, the five most common items relating to eating-related distress were all categorized as “fighting back”, and the sixth item was classified as “letting nature take its course” (Amano et al., 2016c). The authors offered the following four domains for how the “fighting back” sub-process can cause eating-related distress of family members: (factor 1) “feeling that family members forced the patient to eat to avoid death”, (factor 2) “feeling that family members made great efforts to help the patient eat”, (factor 3) “feeling that eating was a cause of conflict between the patient and family members”, and (factor 4) “feeling that correct information was insufficient”. Next, the authors also identified being a patient’s spouse, fair/poor mental status, factor 1, and factor 4 as independent prognostic factors of major depression in bereaved family members. Insufficient care for eating-related distress among family members, especially spouses with weakened mental status, might be associated with major depression among family members after the patient’s death (Amano et al., 2016c). Finally, a 2018 survey in palliative and supportive care settings suggested that family members of patients in a cachexia subgroup had significantly greater eating-related distress than those in the non-cachexia group. Additionally, the results of this study seem to show that cancer cachexia is more distressing for family members than for patients in some items, such as those relating to information about the patient’s diet. The questionnaire used in this study

has not yet been validated (Amano et al., 2018b).

Similar to patients, family members also express concerns of unmet needs for credible, proven strategies to manage body weight loss and meals. In an exploratory qualitative study, advanced cancer patients with prognosis of a few months were interviewed with their family members. The results revealed family members’ desire to maintain a nourishing role supported by professional advice on nutritional care (Hopkinson, 2018). Another quantitative study showed that 73% of bereaved family members believed that advanced cancer patients treated at palliative care units require nutritional support. Furthermore, 41% of bereaved family members would like to have received sufficient explanations about the reasons for the patient’s body weight loss (Amano et al., 2016c).

In conclusion, eating-related distress in family members is multifaceted, comprising of themes of caregiver roles, attempts to fight back against the cancer, and caregiver mental health and well-being. Like patients, when family members fight back, many are disappointed by the futile attempts, which is compounded with lack of information, education as well as the perception of caregiver neglect of nutritional support. These experiences coalesce to generate and propagate family member’s eating-related distress (Table 1A).

2.4. Conflicts over food between patients and family members

Reduced food intake is frequently a source of conflict within families in palliative and supportive care settings (Strasser et al., 2007; Hopkinson et al., 2011; Oberholzer et al., 2013; Hopkinson, 2014; Reid, 2014; Cooper et al., 2015; Hopkinson, 2016; Wheelwright et al., 2016; Amano et al., 2016b, c; Amano et al., 2018a, b; Koshimoto et al., 2019). Changes in patients’ food preferences, changes in eating habits of whole families, challenges to spousal and family roles and traditions, family members’ pressure on patients to eat, and differences in beliefs and perceptions between patients and family members can result in conflicts which worsen eating-related distress (Table 1A). A systematic review extracted “conflict with patient” as one of five themes of concern in family members (Wheelwright et al., 2016). Patients often feel pressured to eat by family members, and distress may be generated when patients eat solely to satisfy family members. This can make patients feel dejected and harassed. As a result, patients may choose to isolate themselves or lie to family members to avoid such conflicts. Family members can experience feelings of rejection when food is refused, as well as, feelings of guilt when they argue with patients over patients’ lack of dietary intake (Strasser et al., 2007; Hopkinson et al., 2011; Oberholzer et al., 2013; Hopkinson, 2014; Reid, 2014; Cooper et al., 2015; Hopkinson, 2016; Wheelwright et al., 2016; Amano et al., 2016b, c; Amano et al., 2018a, b; Koshimoto et al., 2019). Family members’ pressure may be applied unintentionally or due to a lack of insight into patient’s evolving cachexia, symptom burden, food preferences, and eating habits (Strasser et al., 2007; Hopkinson et al., 2011; Oberholzer et al., 2013; Hopkinson, 2014; Reid, 2014; Cooper et al., 2015; Hopkinson, 2016; Wheelwright et al., 2016; Amano et al., 2016b, c; Amano et al., 2018a, b; Koshimoto et al., 2019). In summary, patients’ desire and ability to eat are sometimes incongruent with their family members’ expectations. Thus, contrary to family members’ intentions, their approach to diet and eating problems may become a barrier to increased food intake for patients, should the patient resist well-intentioned encouragement to eat (Strasser et al., 2007; Hopkinson et al., 2011; Oberholzer et al., 2013; Hopkinson, 2014; Reid, 2014; Cooper et al., 2015; Hopkinson, 2016; Wheelwright et al., 2016; Amano et al., 2016b, c; Amano et al., 2018a, b; Koshimoto et al., 2019).

Despite evidence offered by prior qualitative studies showing significant eating-related distress among patients and family members, quantitative studies suggest that overt conflicts over food between patients and family members occur less often than covert distress. In two earlier studies, the actual conflicts over food was reported in only 6–8% of patient and family members, whereas the perception of need for

intervention in such conflicts was higher (18–28%) (Amano et al., 2016b, c). In a more recent study, patients and family members quoted eating-related distress originating from interpersonal conflict to range between 50–60%. However, overt conflicts over food occurred much less frequently, at 20–30% (Amano et al., 2018b). Although the proportion who experience such conflicts may be small, the impact is big in the family. Unfortunately, because the quantitative studies were carried out for palliative care patients in one cultural setting, the observed dichotomy between overt conflicts and covert distress may not be applicable to other cultures and traditions, as well as, patients across varying stages of cancer cachexia. Further research is required to establish universality of this observation.

3. Treatment approaches

3.1. Role of palliative and supportive care

Palliative and supportive care is usually considered as an all-encompassing service providing care from cancer diagnosis to bereavement. The role of palliative and supportive care is for controlling symptoms and improving QOL for patients and their family members (Hui et al., 2013). These services are invaluable to cancer patients as they are subjected to many nutrition impact symptoms, and potentially reversible causes of body weight loss. Some of these factors include intestinal motility disorders, esophageal/bowel obstruction, malabsorption, endocrine and metabolic disorders, and inability to sleep. Among them, pain (including oral pain due to mucositis), lack of appetite, early satiety, fatigue, drowsiness, nausea, vomiting, constipation, diarrhea, abnormal taste and smell, and difficulty swallowing may be particularly important (Amano et al., 2018b; Koshimoto et al., 2019; Kubrak et al., 2010; Anandavivelan et al., 2018; Martin and Kubrak, 2018; Del Fabbro et al., 2017; Kubrak et al., 2013; Del Fabbro et al., 2011; Omlin et al., 2013; Blum et al., 2014). These symptoms need to be systematically assessed and treated, according to clinical practice guidelines, in order to minimize their impact on food intake. As evidence of this, a prospective trial in 2013 demonstrated that cancer patients receiving effective symptom management from a multidisciplinary palliative care service experienced concurrent improvement of appetite (Gagnon et al., 2013).

Although palliative and supportive care advocate for holistic, multimodal care for cancer patients, several limitations exist within this field. Despite clinicians' best efforts, up to 50% of patients with cancer have symptoms that have not been addressed (Basch, 2016). Furthermore, eating-related distress has not been investigated in previous robust interventional studies. Once again, it is evident that a comprehensive assessment tool is needed to assess nutrition impact symptoms and related distress. Next, palliative and supportive care teams typically do not yet offer psychosocial interventions for cachexia-related distress. As such, communicative and educational interventions, tailored to patient's prognosis and severity of cachexia, need to be developed (Strasser et al., 2007; Hopkinson et al., 2011; Oberholzer et al., 2013; Hopkinson, 2014; Reid, 2014; Cooper et al., 2015; Hopkinson, 2016; Wheelwright et al., 2016; Amano et al., 2016b, c; Amano et al., 2018a, b; Koshimoto et al., 2019). These interventions may help patients and family members to cope with refractory cachexia, defined by the presence of rapidly progressive cancer unresponsive to anticancer therapy, and cachexia, characterized by intense catabolism and the presence of factors that render active management of body weight loss no longer possible or appropriate. End-of-life discussion and advanced care planning are an integral part of this conversation (Table 1B, C, Fig. 1).

3.2. Role of nutritional care

Gaps in the availability or access to nutrition care is a major source of distress for patients and family members. Despite the best intentions, health care professionals may be unable to reliably identify the

presence of insufficient dietary intake and implement active nutritional management (Hébuterne et al., 2014). Thus, evidence-based clinical practice guidelines for nutritional care in the setting of advanced cancer are established to serve as health care professionals' road maps for identification of malnutrition and the application of nutritional therapy. The 2017 European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines are of high quality based on their scope and purpose, rigor of development, applicability, and editorial independence (Arends et al., 2017; Shen et al., 2018). Specifically, the ESPEN strongly recommends: 1) Screening/monitoring for nutrition risk in all patients with cancers of advanced stage, with in depth nutritional assessment for patients who screen positive. 2) Providing nutritional counselling and oral nutritional supplements as the 1st line approach, with escalation to artificial nutrition and hydration according to specified criteria.

There is some evidence that body weight loss can be stabilized or even reversed to some degree by nutritional intervention. A 2017 prospective randomized controlled trial demonstrated that nutritional support resulted in a trend towards body weight gain in adult females with cancer cachexia (Kapoor et al., 2017). A 2018 retrospective study demonstrated that food, energy, and protein intake are associated with body weight gain in patients with advanced cancer referred to a multidisciplinary clinic for management of cachexia (Nasrah et al., 2018). A 2018 meta-analysis demonstrated that intake of high energy, high protein supplements enriched with n-3 fatty acids resulted in body weight gain in patients undergoing chemotherapy or chemo-radiation with palliative intent (de van der Schueren et al., 2018). In the very advanced cancer patients, only preliminary studies have shown that nutritional support may be associated with beneficial effects, i.e., prevented bedsores, improved performance status (Amano et al., 2013, 2016d).

The use of artificial nutrition is controversial for a variety of reasons. Patient and family members' views on artificial nutrition are difficult to capture because views on artificial nutrition are often enmeshed with views on artificial hydration. It is also unclear whether patients and family members can distinguish between the two (Amano et al., 2018a). There are profound cultural and ethnic differences in perceptions of artificial hydration during the last weeks of life (Torres-Vigil et al., 2012). For example, in Japan, a large study of the general public and bereaved family members showed that 33–50% of the respondents thought that artificial hydration should be continued until death (Morita et al., 2006). In Germany, a survey of cancer patients revealed that 23% wished for both artificial nutrition and hydration at the end-of-life. Increasing age was significantly correlated with a decision to forgo artificial nutrition and hydration (Bücker et al., 2014). Finally, many patients and family members may attach significant meaning, hope and dignity to artificial hydration which substantially increases the difficulty of discontinuation of this treatment (Cohen et al., 2012). In summary, these studies suggest that the practice of artificial nutrition is complicated by perceptions and beliefs, cultural background, and age of patients.

According to the ESPEN guideline on ethical aspects of artificial nutrition and hydration, decisions on artificial nutrition and hydration have to consider social, cultural, emotional, and existential aspects as well as the patients' spiritual and ethnic background (Druml et al., 2016). However, the ESPEN guidelines on nutrition in cancer patients also suggest that artificial nutrition and hydration are unlikely to provide any benefit for most patients in very advanced terminal phase (Arends et al., 2017). Thus, initiation or discontinuation of artificial nutrition must be accompanied by acceptable explanation of benefits versus risk to patients and family members, while taking into account patients' prognoses and goals of care.

3.3. Integration of palliative, supportive, and nutritional care

Multimodal care has been recommended as a treatment approach

for advanced cancer patients with cachexia (Fearon et al., 2013; Arends et al., 2017; Aapro et al., 2014; Balstad et al., 2014; Maddocks et al., 2016; Hall et al., 2019). A systemic review demonstrated that multimodal rehabilitation program incorporating exercise and nutritional support improved many outcomes, e.g., improvements in physical endurance and depression, in patients with incurable cancer. Although the authors slightly described symptom management, there were no description about effects of management of nutrition impact symptoms on such outcomes (Hall et al., 2019). Effective multimodal care is predicated on a seamless integration of symptom management, psychosocial support, nutritional support, and rehabilitation. There is relatively little research evaluating the efficacy of these combined interventions and their ability to simultaneously improve symptoms, distress, food intake, body weight, physical function, and QOL (Gagnon et al., 2013; Hall et al., 2019; Glare et al., 2011; Parmar et al., 2013, 2017; Uster et al., 2018). The most encouraging data comes from clinical observational studies (Gagnon et al., 2013; Nasrah et al., 2018). In these studies, a team-based approach, involving palliative care physicians, nurses, dietitians, and occupational therapists, is associated with significant improvement in food intake, nutritional indices, distress, concurrent with successful management of pain and symptoms. These results suggest that multimodal care needs to be managed by an interdisciplinary team consisting of specialists e.g., trained physicians, nurses, dietitians, pharmacists, and physical/occupational therapists.

In spite of the merits of multimodal care in advanced cancer patients, several limitations are evident. Some patients with high symptom burden only achieved moderate improvement in their symptoms (Gagnon et al., 2013; Nasrah et al., 2018). Moreover, there often exists a gap between the ideal team environment and reality. Innovative local programs, such as a nurse-led walk-and-eat intervention, should not be discounted, as it could also improve patient outcomes, i.e., preserving functional walking capacity and nutritional status (Xu et al., 2015). Finally, nutrition impact symptoms and eating-related distress are often not evaluated systematically. One recently developed instrument is the Quality of Life Questionnaire-Cachexia 24 (QLQ-CAX24), which offers a cachexia specific module for the assessment of QOL (Wheelwright et al., 2017).

Adapting from previous successes in multimodal care research, we would like to propose an integrated model of palliative, supportive, and nutritional care to alleviate eating-related distress (Table 1, Fig. 1). Our strategy is predicated on the adequate management of nutrition impact symptoms, psychosocial and nutritional support, provision of evidence-based information and advice, education about cancer cachexia, and initiation of end-of-life discussions. Anticipated outcomes from our integrated strategy include improvement in QOL, mitigation of conflicts, and promotion of advanced care planning among patients and family members by supporting for adaptation and coping with nutritional impact symptoms and eating-related distress. Integral to the success of this strategy is the involvement and cooperation between oncologists, palliative care physicians, nurses, dietitians, and other healthcare professionals.

4. Conclusions

We summarized knowledge of eating-related distress in patients and family members and identified some potential priorities for future research. We found limited information about this important detriment to QOL for patients and family members, and there are effectively no well-developed educational tools or psychosocial interventions to alleviate this distress. There is a lack of validated tools for the clinical assessment of eating-related distress and its response to interventions. More robust evidence regarding breadth and depth of nutrition impact symptoms and their association with distress are needed. Palliative, supportive, and nutrition care have varying availability and in many contexts are implemented in isolation of one another. To inform and support patients and family members to cope effectively, health care professionals

must appreciate the complexities and intricacies of eating-related distress. We propose that this will be facilitated by close coordination of palliative, supportive, and nutritional care.

5. Limitations

The scope of the review was confined to caring for nutrition impact symptoms, eating-related distress, need for nutritional support, and conflicts over food among patients and family members. There might be studies on the other aspects of cancer cachexia and the management of symptoms and malnutrition during/after cancer treatments, which were not included.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

Contribution

Study concept and design: KA and VB.
Data acquisition: KA, VB, and JH.
Data interpretation: KA, VB, and JH.
Manuscript preparation: KA, VB, and JH.
Manuscript editing and review: KA, VB, and JH.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The authors have read and complied with the principles of ethical authorship of the journal. We would like to thank Dr Catherine Kubrak, Dr Lisa Martin, and Dr Zhimeng Jia for review and discussion of the manuscript.

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