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Review

Association between cachexia, chemotherapy and outcomes in older cancer patients: A systematic review

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SUMMARY

Background & aims: The aims of this systematic review were (i) to determine the prevalence of malnutrition and cachexia in older cancer patients in a chemotherapy setting, and (ii) to report the chemotherapy-related causes of malnutrition and (iii) the consequences of malnutrition on the outcomes of these patients.

Methods: We searched MEDLINE for articles published in English or French between 2005 and 2016 and which reported retrospective or prospective, observational or interventional studies of the prevalence of malnutrition and its consequences in patients 65 years or older with solid tumors and chemotherapy-related causes of malnutrition.

Results and conclusion: Malnutrition is prevalent up to 83% in older patients with cancer scheduled to receive chemotherapy. One third or more of patients were malnourished before receiving chemotherapy. A weight loss of 10% or more during the past three or six months was reported in 8%–40% of cancer patients, while a body mass index <21 kg/m^2 was found in 10.7%–23%. Malnutrition was more prevalent in digestive (28%–75%) than in non-digestive cancers (8%–46.9%), and also in metastatic cancers (64%–76.5%). During the course of chemotherapy, weight loss was observed in 40%–91.6% of patients, depending on cancer location. The most frequently reported chemotherapy-related digestive symptoms likely to impair nutritional status were dry mouth, nausea, stomach pain, diarrhea and constipation. Low Mini-Nutritional-Assessment score was an independent predictor of early discontinuation of chemotherapy and increased the risk of mortality.

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1. Introduction

The care of older patients accounts for a major part of everyday oncology practice. Comorbidities and disabilities become increasingly prevalent with advancing age and are associated with side effects related to treatment and poor outcomes [1,2]. A major issue for oncologists is determination of optimal treatment in older patients, who have widely varying comorbidities, physical reserve,

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disabilities and geriatric conditions [3]. One major comorbidity that affects outcomes of older cancer patients is malnutrition [4,5].

For many years, the terms "malnutrition", "undernutrition", "weight loss" and "cachexia" have been used interchangeably in the literature [6]. Malnutrition and undernutrition criteria include weight loss, low body mass index (BMI) and/or low albuminemia, together with composite tools such as the Mini-Nutritional-Assessment (MNA) or Nutritional Risk Screening (NRS), but which make no reference to body composition. Cachexia defines a complex metabolic situation observed in chronic diseases associated with systemic inflammation and includes decreased muscle mass and strength, fatigue, anorexia, and markers of inflammation [7].

Recently, referring to cancer patients, there is a consensus to prefer the term of cachexia for two main reasons [7]. First, the term "malnutrition" suggests that the cause of weight loss in cancer patients is mainly due to low food intake; it implies that weight loss may be resolved by adequate nutrition and/or by overcoming problems of absorption of nutrients. Although nutrient intake is often inadequate in cancer patients, the variety of metabolic and endocrine changes and the activation of catabolic pathways account for some of the weight loss and explain why it cannot be fully reversed by conventional nutritional support [8]. Secondly, the term "cachexia" emphasizes the complexity and importance of muscle wasting in the pathophysiology of nutritional alterations associated with cancer. However, in most studies, the tools used to assess cachexia are limited to nutritional parameters.

Malnutrition and cachexia have long been well known in cancer patients [9] and are a major cause of morbidity and mortality [10]. However, the prevalence of malnutrition/cachexia is less reported in the geriatric oncology setting, especially in older patients who are scheduled for chemotherapy. Its prevalence varies depending on the criteria used to define malnutrition, the location of the tumor and its extension [9]. It is also affected by the anticancer treatments. Chemotherapy may cause adverse effects that have a negative impact on nutritional status, such as anorexia, altered perceptions of taste and smell, food aversions, nausea and vomiting, mucositis, constipation, diarrhea and early satiety. Chemotherapy may also have a direct erosive effect on muscle and produce significant loss of body mass [11]. Several studies have investigated nutrition of older patients and many others, nutrition of cancer patients, but relatively few are devoted to nutrition in older cancer patients and still fewer to the relation between chemotherapy and malnutrition in these patients.

The objectives of this review were to determine the prevalence of malnutrition and cachexia in older cancer patients in a chemotherapy setting, the chemotherapy-related causes of malnutrition and cachexia during cancer treatment, and the consequences of malnutrition on patient outcomes.

2. Materials and methods

2.1. Data sources

We conducted three systematic comprehensive searches of MEDLINE (PubMed) for articles in English or French published between January 1, 2005 and September 30, 2016.

Because "malnutrition" is still often used instead of "cachexia" in the literature, for this systematic review we used both "malnutrition" and "cachexia".

2.2. Study eligibility criteria

We selected studies that focused on older patients (65 years or older) with solid cancer (excluding hematologic malignancies) who were seen in oncology or geriatric oncology clinics (as outpatients or inpatients) and involved retrospective or prospective data collection and observational or interventional design. We excluded editorials, case studies, and studies published as abstracts. Review articles were considered as potential sources for bibliographic references. If review articles contained relevant data, the original articles were analyzed and included in the present article if they fulfilled the eligibility criteria.

We designed a specific algorithm for each objective:

1) Algorithm 1, to assess the prevalence of malnutrition/cachexia in older cancer patients scheduled for chemotherapy: ("Cachexia"[Mesh] OR "Malnutrition"[Mesh]) AND ("Neoplasms"[Mesh] OR "Cancer"[Text Word]) AND ("Aged"[Mesh] OR "Geriatric Assessment"[Mesh] OR "Elderly"[Text Word] OR "Older"[Text Word] OR "Geriatric"[Text Word]) AND ("Antineoplastic Agents"[Mesh] OR "Chemotherapy"[Text Word]).
2) Algorithm 2, to assess the nutritional decline related to chemotherapy during cancer treatment in older patients: ("Cachexia"[Mesh] OR "Malnutrition"[Mesh]) AND ("Neoplasms"[Mesh] OR "Cancer"[Text Word]) AND ("Aged"[Mesh] OR "Geriatric Assessment"[Mesh] OR "Elderly"[Text Word] OR "Older"[Text Word] OR "Geriatric"[Text Word]) AND ("Antineoplastic Agents"[Mesh] OR "Molecular Targeted Therapy"[Mesh] OR "Chemotherapy"[Text Word])
3) Algorithm 3, to assess the clinical consequences of malnutrition/cachexia on outcomes in older cancer patients scheduled for chemotherapy: ("Cachexia"[Mesh] OR "Malnutrition"[Mesh]) AND ("Neoplasms"[Mesh] OR "Cancer"[Text Word]) AND ("Aged"[Mesh] OR "Geriatric Assessment"[Mesh] OR "Elderly"[Text Word] OR "Older"[Text Word] OR "Geriatric"[Text Word]) AND ("Treatment Outcome"[Mesh] OR "Mortality"[Mesh] OR "Morbidity"[Mesh] OR "Treatment Feasibility"[Text Word] OR "Treatment Toxicity"[Text Word] OR "Hospitalization"[Text Word])

For the three algorithms, we used the following limits: Article types: Clinical Trial, Systematic Review, Review, Clinical Trial, Phase I, Clinical Trial, Phase II, Clinical Trial, Phase III, Clinical Trial, Phase IV, Comparative Study, Multicenter Study, Observational Study, Meta-Analysis, Randomized Controlled Trial – Publication date from 2005/01/01 to 2016/09/30 – Humans – English OR French – Cancer – Aged: 65+ years. However, to limit the number of citations for this study in accordance with the guidelines for authors, only recent studies between January 1, 2010 and September 30, 2016 were considered in part 1 to assess the prevalence of malnutrition/cachexia in older cancer patients scheduled for chemotherapy.

When several studies had been published on the same cohort, we analyzed the most relevant study presenting nutritional data in accordance with the purpose of our review. We excluded studies that did not clearly report the nutritional assessment tools used to define malnutrition or cachexia or if the results were not detailed according to these assessment tools.

2.3. Study selection

Articles were selected initially by three senior specialists in geriatric oncology (PC, EL and EP) on the basis of the titles, abstracts and the eligibility criteria described above. When one or more of these investigators were uncertain about whether the article fulfilled the eligibility criteria, the abstract was included and the full-length article was analyzed by the same three physicians. Disagreements were resolved by consensus. We also reviewed the reference lists of all selected articles and related contents of the MEDLINE search, to search for relevant articles.

The three investigators used the PRISMA® (Preferred Reporting Items for Systematic Reviews and Meta-analysis) guidelines (http://

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