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Review

Prevalence and predictive value of pre-therapeutic sarcopenia in cancer patients: A systematic review

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SUMMARY

Background & aims: To assess the prevalence of sarcopenia before cancer treatment and its predictive value during the treatment.
Methods: We searched MEDLINE via PubMed for articles published from 2008 to 2016 that reported prospective observational or interventional studies of the prevalence of pre-therapeutic sarcopenia and its consequences in adults with cancer who were 18 years or older. Two independent reviewers selected articles based on titles and/or abstracts before a complete review. Sarcopenia had to be measured before cancer treatment. Methods recommended by consensuses (CT scan, MRI, dual X-ray absorptiometry or bio-impedancemetry) to assess sarcopenia were considered. Characteristics of the studies included the prevalence of pre-therapeutic sarcopenia and the prognostic value for outcomes during the cancer treatment.
Results: We selected 35 articles involving 6894 participants (in/out patients, clinical trials). The mean age ranged from 53 to 69.6 years. Pre-therapeutic sarcopenia was found in 38.6% of patients [95% CI 37.4 −39.8]. Oesophageal and small-cell lung cancers showed the highest prevalence of pre-therapeutic sarcopenia. Pre-therapeutic sarcopenia was significantly and independently associated with post-operative complications, chemotherapy-induced toxicity and poor survival in cancer patients.
Conclusions: Pre-therapeutic sarcopenia is highly prevalent in cancer patients and has severe consequences for outcomes of cancer patients.

1. Introduction

The issue of sarcopenia in cancer patients has been a focus over the last decade. Three consensus statements have been reported: European Working Group on Sarcopenia (EWGOS) in 2010, International Working Group on Sarcopenia (IWGS) in 2011, and Asian Working Group on Sarcopenia (AWGOS) in 2014 [1–3]. These consensus statements agreed to define sarcopenia as a syndrome characterized by the age-associated loss of skeletal muscle mass (quantitative impairment: skeletal muscle index [SMI]) and function (qualitative impairment: loss of muscle strength and/or physical performance) associated or not with increasing fat mass (sarcopenic obesity). These consensus statements had a similar approach to assess the syndrome: a measurement of gait speed to screen for sarcopenia and an objective measure of SMI with different methods. CT scan, MRI, dual X-ray absorptiometry (DXA) or bio-impedancemetry (BIA) were the most recommended methods to measure the SMI.

Sarcopenia must be distinguished from cachexia, which may be involved [2]. Sarcopenia is physiologic with ageing but may be associated with some aetiologies. The European consensus

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distinguished primary sarcopenia when no aetiology is found from secondary sarcopenia when associated with physical inactivity or some chronic conditions: chronic diseases, inflammatory disease, endocrinopathies, malnutrition or cancer [1]. Moreover, this consensus defined pre-sarcopenia as an isolated loss of skeletal muscle without impaired muscle function [1].

The prevalence of sarcopenia varied by the population studied and methods used. It ranges from 1% to 30% in a community-dwelling older people [4–12], 14% to 68% in long-term care institutions [13,14] and was found to be 10% in older inpatients [15]. Moreover, this prevalence seemed to be independent of gender [12]. In addition, sarcopenia has been independently associated with adverse outcomes such as poor survival, disability, falls and nosocomial infections in the geriatric medicine setting [1,2].

Cancer is a major cause of secondary sarcopenia and was recently highlighted in numerous studies of cancer patients. The prevalence and consequences of sarcopenia in the oncology setting might differ from those in the geriatric medicine setting. Furthermore, the cancer population is heterogeneous in terms of cancer type, cancer stage and treatment trajectories. To our knowledge, few reviews have investigated the overall prevalence of sarcopenia and its consequences for cancer patients. In a recent systematic review of 38 studies published from 2008 to 2015, the prevalence of pre-therapeutic sarcopenia (defined by only low SMI) in cancer patients ranged from 15% to 74%. This review focused on only survival predicted by pre-therapeutic sarcopenia in cancer patients, with other outcomes during cancer treatment not considered [16].

The objectives of this review were to determine the overall prevalence of sarcopenia before cancer treatment (i.e., surgery, chemotherapy, targeted therapy, hormonotherapy or radiotherapy) and its predictive value during the treatment.

2. Material and methods

2.1. Data sources

This review was based on a systematic comprehensive search of only MEDLINE via PubMed for articles published in English or French between January 1, 2008 and March 31, 2016. The MeSH term “Sarcopenia” was combined with “Cancer” or “Tumors” or “Malignancies”. We followed the recommendations of the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) method for reporting this systematic review [17].

2.2. Study eligibility criteria

For this review, the following issues were discussed:

a) What is the prevalence of sarcopenia before a cancer treatment modality in adults?
b) What are the definitions used to screen for pre-therapeutic sarcopenia in adults with cancer?
c) Is pre-therapeutic sarcopenia associated with post-operative complications?
d) Is pre-therapeutic sarcopenia associated with toxicity related to chemotherapy and targeted therapy and dose-limiting toxicity during the cancer treatment?
e) Is pre-therapeutic sarcopenia associated with toxicity of hormonotherapy or radiotherapy during the cancer treatment?
f) Is pre-therapeutic sarcopenia associated with overall survival, progression-free survival and relapse-free survival?
g) Is pre-therapeutic sarcopenia associated with disability or nosocomial infections during the cancer treatment?

To answer these questions, we pre-defined eligibility criteria of articles by using Patient, Intervention, Comparator, Outcome, Study (PICOS) criteria (summarized in Box 1). We included all studies of adults aged 18 years and over. Sarcopenia had to be measured before starting a treatment, whether surgery, chemotherapy, targeted therapy, hormonotherapy or radiotherapy. The term “sarcopenia” had to be mentioned in the title and/or abstract. The measurement of sarcopenia had to use methods recommended by consensus statements: CT scan, MRI, DXA or BIA. We included only observational prospective cohort studies and clinical trials and excluded editorials, case studies, studies published as an abstract, retrospective studies and review articles.

Hence, the MeSH terms “death,” “overall survival,” “progression free survival,” “relapse,” “chemotherapy,” “targeted therapy,” “radiotherapy,” “hormonotherapy,” “surgery,” “toxicity,” “disability,” “infection,” and “NOT review” were combined with the initial search.

2.3. Study selection

Two independent senior specialists in geriatric oncology (FP, EP) evaluated the selected articles. Articles with the eligibility criteria

Box 1
Eligibility criteria of studies by the PICOS criteria.

Criteria	Included	Excluded
Population	Adults 18y and over with cancer In/out patients, patients from clinical trials	
Intervention	Pre-therapeutic sarcopenia defined by using a consensual method: CT scan (muscle area or muscle volume or skeletal muscle index), MRI (muscle area or muscle volume or skeletal muscle index), DXA (skeletal muscle index), BIA (skeletal muscle index).	Sarcopenia defined by other methods not recommended by consensual method: Urinary creatinine measured over 24 h, Total body potassium, Arm circumference, Skin fold thickness. Cachexia
Comparison	Not assessed	
Outcomes	Prevalence of pre-therapeutic sarcopenia Survival: overall survival, progression-free survival, relapse-free survival Surgery: post-operative complications Chemotherapy/targeted therapy: toxicity, dose limiting toxicity Radiotherapy: toxicity Hormonotherapy: toxicity Nosocomial infections Disability	
Study design	Clinical trials with randomization Observational prospective cohort studies	Retrospective studies with no consecutive inclusion Systematic and narrative reviews Letter to editor Case report Abstract of congress

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