

MINI-REVIEW

Sarcopenia in Cancer Patients

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Abstract

Sarcopenia, characterized by a decline of skeletal muscle plus low muscle strength and/or physical performance, has emerged to be an important prognostic factor for advanced cancer patients. It is associated with poor performance status, toxicity from chemotherapy, and shorter time of tumor control. There is limited data about sarcopenia in cancer patients and associated factors. Moreover, the knowledge about the changes of muscle mass during chemotherapy and its impact to response and toxicity to chemotherapy is still lacking. This review aimed to provide understanding about sarcopenia and to emphasize its importance to cancer treatment.

Keywords: Body composition - sarcopenia - cachexia - malignancy - frailty

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Sarcopenia: Definition, Diagnosis Tools, Causes

Definition and diagnostic tools

Sarcopenia is defined as a decrease of skeletal muscle mass (SMI) and function (Kim and Choi, 2013). It is usually associated with frailty syndrome, which common features are physical inactivity, decreased mobility, slow gait, and poor physical endurance (Christensen et al., 2014). The condition is recently described and many clinicians and researchers are still not familiar with the term sarcopenia and its impact to cancer treatment.

The European Working Group on Sarcopenia in Older People (EWGSOP) has proposed an operational definition and diagnostic strategy for sarcopenia that had been used worldwide. Evaluation of muscle mass could be done by various diagnostic methods, but the EWGSOP (Cruz-Jentoft et al., 2010) recommends dual x-ray absorptiometry (DXA), computed tomography (CT), magnetic resonance imaging (MRI), and bio-impedance analysis (BIA) as shown in Table 1.

DXA scan is an accurate and reliable method to distinguish fat, bone mineral, and lean body mass. Currently, DXA is the most widely used method for muscle mass measurement in sarcopenia research. Moreover, there is a guideline developed for sarcopenia in Asian population by the Asian Working Group of Sarcopenia (AWGS) with different cutoff values from EWGSOP. AWGS recommends using 2 standard deviations below the mean muscle mass of young reference group or the lower quintile as the cutoff value determination. The suggested cutoff values were 7.0 kg/m² in men and 5.4 kg/m² in women by using DXA (Chen et al., 2014). However, there is no consensus of CT or MRI scan cutoff value for Asian patients.

Evaluation of muscle function is done by measuring handgrip strength, which is an easy and convenient method. Low handgrip strength according to AWGS is defined as <26 kg for men and <18 kg for women (Chen et al., 2014).

Causes

All cancer patients are generally exposed to several cancer-specific and noncancer-specific factors causing decrease muscle mass and muscle dysfunction including age and comorbidities, malnutrition, physical inactivity, tumor-derived factors, cancer therapy, and supportive care medication (Christensen et al., 2014).

Cancer therapy could affect skeletal muscle change in many means. Surgery and radiation are loco-regional treatment which impair skeletal muscle strength in the treated area. Chemotherapy, hormonal therapy, immunotherapy, and targeted therapy are systemic treatment for cancer which have substantially effect to body composition and muscle strength.

Sarcopenia: Prevalence in Cancer Patients and Associated Factors

The prevalence of sarcopenia in advanced cancer patients was found to vary considerably among various types of cancer, stage of disease, and it also depends on the tools measuring it.

In early cancer patients who underwent curative surgery, the prevalence varies among type of cancer. In a study of breast cancer survivor, the HEAL study, 75/471 (16%) of patients were diagnosed as sarcopenia and it was more common in postmenopausal women (Villasenor et al., 2012). In hepatocellular carcinoma patients underwent curative hepatectomy, 75/186 (40.3%) of patients were

classified as sarcopenia by using CT scan (Harimoto et al., 2013). Sarcopenia was significantly related to female sex, lower body mass index, and liver dysfunction. Also in cholangiocarcinoma patients who underwent major hepatectomy with extrahepatic bile duct resection, preoperative sarcopenia was found in 85/256 (33%) of patients (Otsuji et al., 2015).

As cancer progresses to unresectable or metastatic stage, patients tend to suffer more from cancer cachexia and the treatment is mostly limited to systemic therapy. The goal of treatment in this phase of disease is palliative care involving prolonging survival while maintain good quality of life. In advanced lung cancer patients receiving palliative chemotherapy, using SMCA at the third lumbar vertebrae, the prevalence was as high as 71% (Stene et al., 2015).

Sarcopenia and chemotherapy toxicity are particularly a concern in elderly patients. In a study of advanced solid and hematologic malignancies, chemotherapy significantly worsened muscle mass, fatigue, and functional status in patients who are more than 70 years old (Luciani et al., 2008).

Effects of Sarcopenia to Oncological Outcomes

Survival and disease progression

In many types of cancer, sarcopenia has been shown

to be a prognostic factor for disease progression and survival. Harimoto et al. retrospectively reviewed the operative outcome in hepatocellular carcinoma patients who underwent hepatectomy for curative intent. The 5-year recurrence-free and overall survival rate was significantly lower in sarcopenic patients (Harimoto et al., 2013). Accordingly, sarcopenic patients who underwent radical cystectomy for bladder cancer or curative surgery for esophageal carcinoma also had lower survival rate compared with non-sarcopenic patients (Psutka et al., 2014). In advanced breast and lung cancer, sarcopenia was associated with shorter time to progression and poorer overall survival respectively (Prado et al., 2008) as shown in Table 2.

Treatment complications

Following major hepatectomy and extrahepatic bile duct resection in perihilar cholangiocarcinoma, sarcopenia was associated with higher rate of liver failure, major postoperative complications and intra-abdominal abscess than those without sarcopenia (Otsuji et al., 2015).

Sarcopenia was a predictor for toxicity from capecitabine in metastatic breast cancer. Fifty percent of the patients presenting with sarcopenia suffered from toxicity, compared with only 20% in non-sarcopenic patients (Prado et al., 2009). Similarly, decreased muscle mass was associated with increased risk of grade 3-4

Table 1. Diagnostic Tools for Evaluating Muscle Mass

Measuring techniques	Measurement	Comments
DXA scan	Total skeletal muscle mass	Reliable, low radiation exposure
BIA	Tissue conductivity	Less reliable
CT scan	Muscle cross-sectional area	Radiation exposure, expensive
MRI scan	Muscle cross-sectional area	Expensive, less available

Table 2. Diagnostic Tools for Evaluating Muscle Mass

References	Measuring techniques	Population, N	Results
TTP			
(Prado et al. 2009)	Muscle index (CT scan)	Breast cancer, stages IV, N=55	Sarcopenia associated with -TTP: 101.4 vs 173.3 days (p=0.05)
Mortality			Sarcopenia associated with
(Prado et al. 2008)	Muscle index (CT scan)	Lung and GI cancer, stages I-IV, N=250	-Survival: 21.6 vs 11.3 mo., HR 4.2 (95%CI 2.4-7.2, p<0.001)
(Villasenor et al. 2012)	Muscle mass (DXA scan)	Breast cancer, stages I-IIIa, N=471	-5-yr survival rate: 83.7% vs 92.9%, HR 2.86 (95%CI 1.67- 4.89, p<0.001)
(Hayashi et al. 2014)	Muscle index (CT scan)	Esophageal cancer, stages I-IV, N=204	-5-yr survival rate: 33% vs 66%, HR 1.86 (p=0.006)
(Harimoto et al. 2013)	Muscle index (CT scan)	Hepatocellular cancer, stages I-IV, N=186	-5-yr survival rate: 71% vs 83.7%, p=0.001
(Psutka et al. 2014)	Muscle index (CT scan)	Bladder cancer, underwent radical cystectomy, N=205	-5-yr survival rate: 39% vs 70%, p=0.003
(Jung HW et al. 2015)	Muscle index (CT scan)	Colon cancer, stages III, N=229	Decrement of 1 SD in the muscle index increased over- all mortality: HR=1.85 (95% CI 1.10-3.13)

toxicity in both adjuvant and metastatic colon cancer treatment (Barret et al., 2014; Jung et al., 2015). Likewise, sarcoma patients treated with doxorubicin-based chemotherapy, sarcopenic patients experienced more acute severe toxicity; more grade 4 hematologic toxicity, and more febrile neutropenia (Comte et al., 2014).

Changes in Muscle Mass During Palliative Chemotherapy

Even though chemotherapy has been shown to improve quality of life and survival in advanced cholangiocarcinoma patients, there is limited data regarding alterations in muscle mass and function during chemotherapy and the association with response and survival.

In a study by Stene GB et al., 35 advanced lung cancer patients receiving chemotherapy were assessed for muscle mass change by measuring skeletal muscle cross sectional area (SMCA) at the level of the third lumbar vertebrae using CT images before first cycle and after third cycle of chemotherapy. The mean reduction in SMCA was 4.6 cm² (1.4 kg) loss, patients who maintained or gained SMCA resulted in longer median overall survival (Stene et al., 2015).

In summary, the clinical importance of sarcopenia in cancer patients is apparent from many recent studies demonstrating strong associations to treatment toxicity and survival. Given the increasing incidence of cancer and the aging population, early recognition is beneficial for prevention of sarcopenia-related disability and emphasizing the need for effective strategies.

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