Editorial

Editorial: refining the estimation of fitness for surgery

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Lung cancer is the second most common cancer in both men and women and remains the leading cause of cancer death worldwide. Non-small cell lung cancer (NSCLC) accounts for approximately 80% to 85% of new cases of lung cancer (1), with surgical resection serving as a potentially curative treatment for patients with early stage disease. The 5-year post-operative survival rate of patients with stage 1A NSCLC has ranged from 73% to 82% (2), with recurrence rates ranging between 20–30% (2). Numerous risk factors for recurrence and unfavorable prognosis after surgical resection of NSCLC include tumor-specific factors such as pathological stage, lymphatic involvement, and patient characteristics including age, sex, and cardiopulmonary comorbidities.

Recently, there has been increasing recognition of the potential role of measuring a patient's physical status when risk stratifying for postoperative outcomes. Low body weight and low body mass index (BMI) have been identified as important predictors of postoperative complications and mortality (2-4). Physical status is of particular concern in syndromes such as cachexia, which has been reported to account for 20% of cancer related deaths and is frequent in patients with lung cancer (5). Sarcopenia, an age-associated syndrome that is characterized by a progressive loss of skeletal muscle mass, muscle strength, and physical performance, has been studied as an important aspect of cancer cachexia syndrome and its potential prognostic role in a wide range of malignancies including breast, upper gastrointestinal, hepatocellular and colorectal cancers (6). However, there is limited research on the prognostic role of sarcopenia in patients receiving treatment for NSCLC.

Nakamura and colleagues conducted a single institution, retrospective study to investigate the relationship between sarcopenia and treatment outcomes after surgical resection of NSCLC (7). In this retrospective study, 328 patients who underwent lung resection at the National Hospital Organization Mito Medical Center between January 2005 and April 2017 were assessed for sarcopenia using preoperative CT scans obtained within two months before surgery. The assessment of sarcopenia was evaluated by measuring muscle volume and manual tracing of the cross-sectional area of the right and left psoas muscle at the level of the caudal end of the third lumbar vertebra. A psoas muscle index (PMI) was then calculated. The prevalence of patients with sarcopenia as defined by a PMI cutoff value established by Hamagushi *et al.* (6.36 cm^2/m^2 for men, 3.92 cm^2/m^2 in women) was 55.8%. Postoperative complications were assessed using the Clavien-Dindo classification system, with major complications classified as grade 3 or higher. Additional clinical and pathological characteristics were analyzed including smoking status, type of cancer, BMI, FEV_1, sex, age and pathological stage of the cancer. This study demonstrated that the prevalence of sarcopenia increased from the age of 64 to 84, with patients over the age of 85 having a lower prevalence of sarcopenia.

The study demonstrated a significantly worse overall survival in patients with sarcopenia (P<0.001). Postoperative complications were significantly higher (P=0.036) in patients with sarcopenia than in patients without sarcopenia. In an analysis of the relationship between sarcopenia and clinical

characteristics of patients, BMI, age, sex, smoking habit and postoperative complications were significantly different in patients with and without sarcopenia. BMI in the sarcopenia group was significantly lower than that in the group without sarcopenia. Although lower BMI in the presence of sarcopenia would seem expected, recent studies have shown that BMI alone may not be an accurate assessment of sarcopenia. Age-related changes in body composition including an increase in body fat and decline in skeletal muscle may not be reflected by a change in BMI (8). This concept has been termed sarcopenic obesity; a condition in which obesity and low muscle mass occur simultaneously (9). Characteristics that were shown to be poor prognostic factors for overall survival included age above 70 years, male sex, smoking habit, vital capacity <80%, and elevation of CEA.

Recent data investigating the prognostic value of skeletal muscle measurement in patients with advanced NSCLC by Sjøblom *et al.* showed that skeletal muscle radiodensity (SMD) was an independent prognostic factor for overall survival, whereas muscle mass measured by cross sectional muscle area of the lumbar level (as was performed in this study) was not (5). Nonetheless, Sjøblom *et al.* demonstrated the deleterious effect that severe muscular depletion can have on the survival of patients with advanced NSCLC. A similar study performed by us demonstrated that sarcopenia was predictive of peri-operative mortality and length of stay, but not other peri-operative outcomes (10). The contradictory data on the prognostic value of muscle mass in recent studies demonstrates the need for further research into the most accurate method of measurement of skeletal muscle mass as it pertains to evaluation of sarcopenia. Current studies have used several modalities for measuring body composition, including dual x-ray absorptiometry, CT, MRI and bioimpedance analysis (BIA) Additional studies are needed regarding how to best define sarcopenia and the most accurate means by which to assess it.

Sarcopenia is a potentially modifiable risk factor which has been demonstrated to have significant prognostic value in patients undergoing treatment for lung cancer. However, a standard first-line therapy for remediating sarcopenia has not been established. Future directions must include how to best assess patients for sarcopenia and what subsequent clinical interventions can mitigate its effect. Nakamura *et al.* suggest that therapy for remediating sarcopenia, such as with nutrition management and rehabilitation, has the potential to improve postoperative outcomes. A better understanding of the molecular and metabolic factors associated with muscle mass depletion as it relates to postoperative complication risk will be essential in establishing appropriate preoperative interventions. The limitations of the study should also be considered. First, it was a single institution retrospective study with a limited sample size. Secondly, PMI was assessed by manual tracing on preoperative CT scans and this may have some operator error.

In summary, for patients undergoing therapy for NSCLC, preoperative evaluation for sarcopenia should be considered potentially useful as it has been shown in recent studies to correlate with significantly poorer overall survival and higher risk of complications. It may allow for improved selection of surgical candidates and risk stratification for expected surgical outcomes. Clinical treatment planning pertaining to surgery or use of adjuvant versus neoadjuvant therapy may need to be adjusted for preoperative optimization in sarcopenic patients.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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