## Title

Preoperative paraspinous muscle sarcopenia and physical performance as prognostic indicators in non-small-cell lung cancer

## **Key Points**

- Preoperative sarcopenia and exercise intolerance increased risk of death in patients with non-small-cell lung cancer (NSCLC).
- Patients with both preoperative sarcopenia and exercise intolerance had a 3.38-fold increased risk of medium- to long-term mortality.
- Comprehensive assessment of preoperative overall physical status is important for predicting the postoperative course of patients with NSCLC.

### Summary

Prof. Toyofumi Fengshi Chen-Yoshikawa and Dr. Naoki Ozeki (corresponding author) in Department of Thoracic Surgery, Nagoya University Graduate School of Medicine, Prof. Yoshihiro Nishida and Mr. Shinya Tanaka (first author) in Department of Rehabilitation, Nagoya University Hospital, and their colleagues revealed the relationships between preoperative sarcopenia and exercise intolerance and poor prognosis in patients with non-small-cell lung cancer (NSCLC).

Lung cancer is one of the main causes of death around the world, and its incidence is increasing in Japan. Sarcopenia, defined as a progressive and generalized skeletal muscle disorder characterized by loss of muscle mass and strength, is common among older adults but can also occur in younger individuals. Early detection of this status and appropriate interventions are important as it has been shown to be associated with frailty, falls, disability, reduced quality of life, and mortality.

In the present study, preoperative sarcopenia (low paraspinous muscle mass) and exercise intolerance (short-distance in 6-minute walking distance) were shown to be associated with mortality rate of NSCLC patients, and the coexistence of both conditions had an adverse effect on prognosis in these patients. In addition, the combination of skeletal muscle mass and exercise tolerance had complementary prognostic predictive capability for preexisting prognostic factors such as age, sex, smoking status, progress of cancer, and respiratory function. It is important to accurately assess preoperative sarcopenia and physical performance because both can be targeted for treatment before and after surgery with various interventions, including nutritional recommendations and exercise therapy. The results of this study may contribute to the development of risk stratification and intervention methods to improve the postoperative course of patients with NSCLC.

The study has been published in the scientific journal "Journal of Cachexia, Sarcopenia and Muscle" on March 4, 2021. This work was supported by the Japan Society for the Promotion of Science Grant-in-Aid.

### **Research Background**

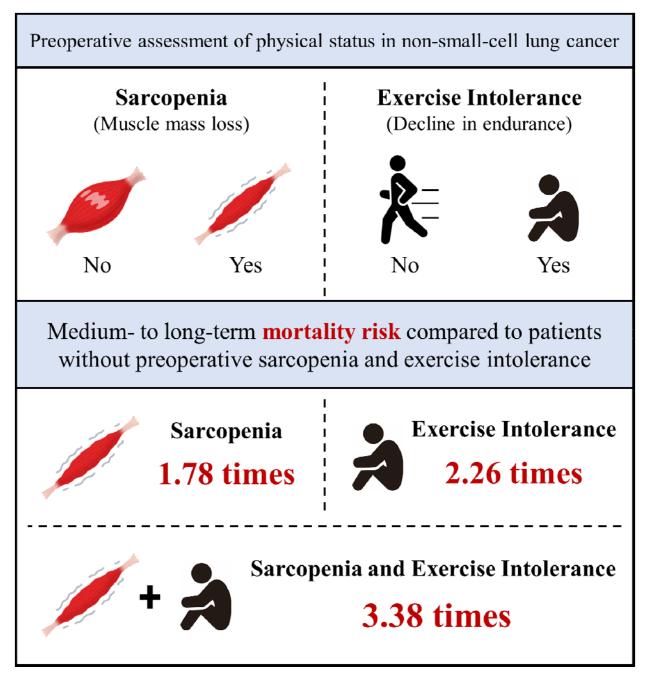
Lung cancer is one of the main causes of death around the world. Non-small-cell lung cancer (NSCLC) accounts for about 80% of cases of primary lung cancer, and surgical resection is the standard treatment of choice for early-stage disease. Although the postoperative survival rate of NSCLC patients is improving due to medical advances, it is still poor in some patients. To improve the postoperative course of these patients, it is necessary to accurately assess their preoperative status and develop a means to predict their postoperative course.

Sarcopenia is a condition in which muscle strength or physical function declines due to a decrease in muscle mass caused by aging or disease, and it has been shown to be associated with frailty, falls, disability, reduced quality of life, and mortality. Exercise intolerance, as well as sarcopenia, is known to cause poor postoperative outcomes in patients with NSCLC. The research group investigated the prognostic significance of preoperative sarcopenia and physical performance status in patients with NSCLC.

#### **Research Results**

This retrospective cohort study was performed in NSCLS patients divided into four groups according to skeletal muscle index (SMI) (sarcopenia [lowest sex-specific tertile] and non-sarcopenia) and 6-minute walking distance (6MWD) (short distance [< 400 m] and long distance [ $\geq$  400 m]). Sarcopenia was assessed by preoperative cross-sectional areas of right and left paraspinous muscles at the level of the 12th thoracic vertebra on computed tomography images and physical performance was determined by preoperative 6MWD. The primary endpoint was postoperative overall survival.

The 587 patients (mean age:  $68.5 \pm 8.8$  years, 399 men [68%]) included in the study were divided into the normal group (58%), sarcopenia group (26%), short-distance group (9%), and sarcopenia and short-distance group (7%). Body mass index < 18.5 kg/m<sup>2</sup> was associated with greater likelihoods of positivity for both sarcopenia and short-distance 6MWD. A total of 109 (18.6%) deaths were observed over a mean follow-up of 3.1 years. The risks of death for patients with sarcopenia alone, short distance on 6MWD test alone, or both conditions were 1.78, 2.26, and 3.38 times higher, respectively, compared to patients with neither sarcopenia nor short distance on 6MWD test (Figure 1). In addition, the combination of SMI and 6MWD had complementary prognostic predictive capability for preexisting prognostic factors such as age, sex, smoking status, progress of cancer, and respiratory function, except within 2 years of surgery. These observations emphasize that a comprehensive evaluation taking into account both preoperative sarcopenia and physical performance is required in patients with NSCLC.



**Figure 1. Effects of preoperative sarcopenia and exercise intolerance on postoperative mortality.** Preoperative sarcopenia and exercise intolerance are associated with higher risk of medium- to long-term mortality in patients with non-small-cell lung cancer.

## **Research Summary and Future Perspective**

Our results showed that preoperative sarcopenia and exercise intolerance were correlated with overall survival even after adjusting for preexisting risk factors in patients with NSCLC. Preoperative screening for sarcopenia and physical performance status may allow more accurate prediction of prognosis and facilitate targeted interventions in these patients. It is unclear whether improvements in sarcopenia and exercise intolerance can improve prognosis. Therefore, further studies addressing these issues are required to facilitate future clinical decision making regarding the treatment of NSCLC.

# Publication

Journal of Cachexia, Sarcopenia and Muscle

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Shinya Tanaka,<sup>1</sup> Naoki Ozeki,<sup>2</sup> Yota Mizuno,<sup>1</sup> Hiroki Nakajima,<sup>1</sup> Keiko Hattori,<sup>1</sup> Takayuki Inoue,<sup>1</sup> Motoki Nagaya,<sup>1</sup> Takayuki Fukui,<sup>2</sup> Shota Nakamura,<sup>2</sup> Masaki Goto,<sup>2</sup> Tomoshi Sugiyama,<sup>2</sup> Yoshihiro Nishida,<sup>1,3</sup> Toyofumi Fengshi Chen-Yoshikawa<sup>2</sup>

<sup>1</sup> Department of Rehabilitation, Nagoya University Hospital, Nagoya, Japan

<sup>2</sup> Department of Thoracic Surgery, Nagoya University Graduate School of Medicine, Nagoya, Japan <sup>3</sup> Department of Orthopaedic Surgery, Nagoya University Graduate School and School of Medicine, Nagoya, Japan

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