



# The Influence of Strength and Speed on Survival in Esophageal Cancer

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Clinicians have long discussed the importance of a general bedside inspection of the patient in predicting their ability to withstand the stress of a surgery or complication. Colloquially termed the “foot of the bed” or “eyeball” test, this intuition involves a subjective assessment of a patient’s functional status. While frequently considered in practice, it is important to objectify these observations by determining what is measurable. Data supporting the value of these measurements can be useful by allowing us to quantitatively prognosticate, develop interventions, and then test their impact.

In this issue of *Annals of Surgical Oncology*, Kanemura and colleagues from the Osaka International Cancer Institute examined the utility of preoperative measures of sarcopenia on prognosis in esophageal cancer.<sup>1</sup> This retrospective cohort study reports the outcomes of patients aged 65 years or older who underwent esophagectomy for esophageal cancer. Twenty-three patients (20%) had sarcopenia based on the Asian Working Group for Sarcopenia (AWGS) 2019 criteria. These patients were slightly but significantly older (73 versus 69 years) and had a significantly higher T stage than those in the nonsarcopenia cohort. There was no difference in the incidence of postoperative complications between the two groups. When analyzing the incidence of complications on the basis of skeletal muscle index (SMI), hand grip strength, and gait speed individually, gait speed was found to be associated with Clavien–Dindo  $\leq 2$  and Clavien–Dindo  $\leq 3$  complications, although the number of patients with slow gait speed was low ( $N = 6$ ). The sarcopenia group did have

significantly worse overall survival. Those with slow gait speed had significantly worse overall survival than those with fast gait speed, but once again with only six patients meeting the criteria for slow gait speed. On univariate analysis, significant predictors of overall survival included postoperative complications (HR 2.20), pT3–4 (HR 2.40), sarcopenia (HR 2.68), and pN2–3 (HR 4.07). However, on multivariate analysis, only pN2–3 remained an independent predictor of worse overall survival.

Although the studied population showed a statistically nonsignificant result when examining the association between sarcopenia and postoperative complications, it is important to note that there were in fact fewer complications observed in the nonsarcopenia group (29.3% versus 39.1%). This result could be due to lack of sufficient power in this specific study to detect a weaker association, and perhaps larger studies could confirm the merit of this definition of sarcopenia for predicting complications in these patients. However, as the authors themselves have pointed out, perhaps there exist measures that exhibit a stronger association and that may be more important. The definition of sarcopenia used in the literature is varied and has changed over time. The authors mention the paper by Nambara et al.<sup>2</sup> that concluded that the European Working Group on Sarcopenia in Older People (EWGSOP) definition of sarcopenia was a better independent predictor of postoperative pneumonia in patients undergoing esophagectomy. It would be interesting to see other definitions of sarcopenia explored for their association with postoperative complications in this cohort. The authors should be applauded for their exploration of SMI, muscle strength (hand-grip strength), and physical function (gait speed) independently. Similar to sarcopenic status, we see a similar phenomenon in the data when examining these subgroups. Fewer postoperative complications were observed in patients with high SMI versus low SMI, high hand-grip strength versus low hand-grip strength, and high gait speed versus low gait speed; however, none of these

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reached statistical significance for association with postoperative complications overall. These could represent weaker associations that could be confirmed with larger studies. One of the striking findings of this paper is the observation that low gait speed had a significant association with Clavien–Dindo  $\leq 2$  and  $\leq 3$  complications as well as decreased overall survival. Although only six patients met this criterion, low gait speed should be considered an indicator for an overall poorer prognosis. Further studies with more patients are required to elucidate the optimal threshold values for what constitutes low and high for SMI, hand-grip strength, and gait speed. This could allow a more accurate prediction of postoperative complications. Additionally, in future datasets, it would be interesting to see a more granular breakdown of specific complications, as well as data regarding length of stay and discharge destination.

Interestingly, despite observing only a statistically insignificant difference in complications between sarcopenic and nonsarcopenic patients, sarcopenia was associated with significantly worse overall survival. Perhaps this implies that nonsarcopenic patients with esophageal cancer are more likely to survive when faced with a complication. As stated in the text, this survival difference has been observed in previous studies including a metaanalysis by Deng et al.<sup>3</sup> in 2019. Other studies<sup>4–6</sup> have failed to replicate these results except when confined to specific subgroups, namely those without lymph node involvement,<sup>4</sup> patients aged 65 years or greater,<sup>5</sup> or those receiving neoadjuvant chemotherapy.<sup>6</sup> The authors cite the difference in the definition of sarcopenia as the possible cause for these varying results, given that diagnosis in those studies was based purely on SMI from CT imaging. In the current study, no significant difference in overall survival was found based on SMI alone; however, when using the AWGS 2019 definition, sarcopenia was a strong predictor of overall survival. Specifically, gait speed alone was a predictor of overall survival on univariate analysis. Given the retrospective nature of this analysis, care must be taken when interpreting these results. Both pT and pN were also found to be significant predictors of overall survival on univariate analysis. Given that sarcopenic patients were more likely to have higher T stage at baseline in this cohort, this begs the question of whether the decrease in overall survival is simply related to more advanced disease rather than directly sarcopenia. Cause and effect cannot be sorted out here. Likewise, we see that sarcopenia and gait speed fall out in the multivariate analysis, leaving only pN stage as an independent predictor of overall survival in this cohort.

The authors conclude that “improvement in sarcopenic status may have some preferable effects on the prognosis of patients.” Indeed, other research demonstrates that

prehabilitation can improve or maintain physical function in patients who are scheduled to undergo esophagectomy or other treatments.<sup>7,8</sup> But once again, care should be taken with conclusions from the present study data. The question remains: although prognosis and sarcopenia may correlate, can you decrease complications and/or improve survival by improving sarcopenic status, muscle strength, and physical function? Fortunately, their ongoing clinical trial (jRCTs051190016) examining the usefulness of nutritional support and prehabilitation on outcomes in esophageal cancer may shed light on this question, so we look forward to their report.

**DISCLOSURE** The authors declare no conflicts of interest.

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