Editorial Commentary

Risk factors of post-esophagectomy-induced malnutrition

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Weight loss (WL) and its related-malnutrition remain crucial problems both before and after esophageal surgery for cancer that might have a potential negative impact on survival (1). Before surgery, near 80% of those patients present significant WL associated to substantial sarcopenia at the moment of the diagnosis directly due to the tumor-related obstructive effects into the esophagus (or cardia) and more generally due to the consequences of a cancer-associated catabolism. After esophagectomy, the WL is common. Half of the patients present a severe WL within 12 months after surgery (i.e., WL >10% of the initial body weight) (2-4). Reasons of this malnutrition are likely multifaceted but can be mainly attributable to the post-esophagectomy effect inherent to the gastric interposition with subsequent gastric volume reduction, changes in postprandial gut hormone profiles, delayed food intake and secondary symptoms due to surgery including reflux and stenosis-related dysphagia. Besides the impact of the surgery, post-esophagectomy-induced malnutrition within the first year might have others patients-related risks factors but studies investigating this aspect are scarce. In western countries, overweight patients have been identified as a subgroup of patients with the higher risk of 1-year WL, suggesting that esophagectomy for cancer might have the same nutritional effect as a bariatric surgery for morbid obesity (4,5).

The recently published study by Wang *et al.* (6) aimed at investigating the risk factors for WL within 12 months after minimally invasive esophagectomy (MIE). Based on a prospective assessment during a very short contemporary study period (7-month period of inclusion between January to July 2017), the authors included a homogeneous cohort of 44 patients submitted to first-line McKeown-MIE without any neoadjuvant therapy. Based on an exclusive Asian population, majority of patients were operated for squamous cell carcinoma and all had a R0 complete resection. Locally advanced esophageal cancers were excluded from the study. With nil anastomotic leakage rate and nil postoperative mortality rate, the authors demonstrated their important experience in esophageal cancer surgery. Based on the "no tube no fasting" fast track protocol whenever possible (70% of adherence rate), the length of hospital stay was short with a mean delay of 9 days. Based on a rigorous assessment of patient's body composition, WL and quality of life assessment, the authors depicted body weigh changes during the 12-month period and analyzed risk factors of such severe WL. Of interest in their methods is the reliable analysis of body composition making distinction between fat-free mass and sarcopenia (depletion of skeletal muscle mass). Moreover, the authors analyzed separately the body weight changes according to gender, to Chinese population and to Asian-specific BMI cut-off. The paper from Wang *et al*. highlights two important results that can be summarized as follow.

First, the authors showed that WL was maximum within the first 4 weeks after surgery with an important effect at 12 months. More specifically, they found an accelerate WL during the first 2 weeks after discharge. Considering a median length of hospital stay of 9 days and considering that WL observed within the first week was neglectable, the

maximum of WL occurred within 4 weeks after discharge participating to 46% of the maximum WL within the 12 months after esophagectomy. They also found that 40% of patients had sarcopenia before surgery with a mean WL of 4.3 kg. This first result suggests that every effort should be made to maintain adequate body weight within the first month in order to have a beneficial effect on the body weight at 12 months. The logical answer to this assumption is undoubtedly the use of an optimized perioperative nutritional support within the first 4 weeks after hospital discharge and probably when the patient goes back home. However, the current study fails to provide evidence on the best options for perioperative nutritional management. Moreover, this study reflects the current change in perioperative management where two strategies are competing: on the one hand, an optimized enteral nutritional support with a feeding jejunostomy but with the risk of the tube-related morbidity; and in other hand, the strategy of an early oral intake illustrated by the "no tube no fasting" protocol figuring the tendency worldwide to adopt more and more the enhanced recovery after surgery (ERAS) protocol. This study highlights that, nowadays, with the introduction of an early oral intake, the routine use of an enteral nutrition through jejunostomy is matter of discussion and should not be recommended routinely. The two arguments against jejunostomy come from its own morbidity and debatable efficiency. Incidence of jejunostomy-related complications is estimated between 30% to 50% with a 2% rate of specific revisional surgery (7-10). Despites its own morbidity, home-tube feeding does not affect WL or readmission rate (9). At last, results comparing enteral nutrition to early oral intake after esophagectomy are encouraging. Early oral intake resulted in same morbidity rate, same anastomotic leakage rate, same rate of aspiration accidents observed in enteral nutrition protocol (9-11). Further randomized controlled trials comparing early oral feeding to routine jejunostomy are needed.

The second main message of the study remains on the factors associated with WL after esophagectomy. Based on logistic regression multivariate analysis, the authors investigated the risk factors associated with WL at 4 weeks and at 1 year after surgery. Surprisingly, the authors identified different risk factors for short and long-term severe WL.

At 4 weeks, with a cut-off WL >7.5% rate (representing 45% of the whole cohort), the authors found four significant and independent variables: age ≥70 years, preoperative sarcopenia, vocal cord paralysis and the first surgery in the daily schedule. If the three first factors are easily understandable (age, sarcopenia, vocal cord) and must be seen as potential targets to select patients for enhance perioperative nutritional support, the fourth one remains questionable. Why patients submitted to the first surgery in the daily schedule are more at risk of WL at 4 weeks? Reasons are not clear and may represent a potential bias as a surrogate factor in the multivariate analysis. The authors advocated more preoperative anxiety but data are not sufficient to support this hypothesis. This deserves further investigations.

At one year, with a cut-off WL >13% rate (representing 47% of the whole cohort), the authors found three significant and independent variables: vocal cord paralysis, ASA score 3–4 and high fat free mass. Because of the related-swallowing problems due to vocal cord paralysis, this complication remains a common risk factor for both short and long-term WL. Vocal cord paralysis is associated with an increased risk of respiration complications such as aspiration pneumonia, increased length of hospital stay, and increase of residual symptoms requiring additional surgery during mid-term outcome (12). This finding pleads for an early and aggressive management of such complications with speech pathologist management or early glottis closure with vocal-cord injection (13). Others factors such as ASA 3–4 score and high fat free mass (determining resting energy expenditure that is consumed during recovery) can be seen as understandable variable markers figuring a global health deterioration in risk patients. Unfortunately, the authors did not investigate in their logistic regression if 4-week WL was *per se* an independent factor of 1-year WL. At last, and in contrast to western series where overweight patients are known to be the most exposed to malnutrition (4,5), Wang *et al.* investigated body weight change in an exclusive Asian population where overweight is less frequent. Thus, results of the current study should be extrapolated to western countries with cautions.

In conclusion, Wang *et al.*, based on a prospective study of a homogenous group of McKeown MIE during a short contemporary period, provide an excellent description of body weight change during the 12 months after esophagectomy. They found an accelerate WL during the first 4 weeks and especially during the first 2 weeks after discharge. Using an ERAS "no tube no fasting" protocol, they provided some keys to identify and to select targeted patients who will benefit from an enteral nutritional support. We can reasonably conclude that for

patients treated with surgery alone without any neoadjuvant treatment and proposed for MIE, a jejunostomy would be recommended when age is over 70 years, when preoperative sarcopenia is present and when patients are at risk or present postoperatively laryngeal nerve paralysis. In other cases, further investigations are needed for a best management of WL after esophagectomy.

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Footnote

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

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