

Nodal skip metastasis in oesophageal cancer: different definition and different prognostic role

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Recently, we read with great interest the article by Xu *et al.* [1], which focused on the prevalence rate and prognostic role of nodal skip metastasis (NSM) in mid-thoracic oesophageal squamous cell carcinoma (ESCC). NSM was defined as positive lymph node in the abdominal or cervical region without lymph node metastasis in the thoracic region. They found that the occurrence rate of NSM was 22.0% and was associated with pathological N stage and sex. Meanwhile, NSM was proved to be an independent factor favouring overall survival. We congratulate Dr. Xu and his colleagues for their innovative and excellent study and want to share some opinions over the issue of NSM.

Currently, the definition of NSM still reached no consensus according to different guidelines including American Joint Committee on Cancer (AJCC), Japanese Society for Esophageal Disease (JSED) and anatomical compartment criteria. The incidence of NSM varied depending on different criterion, ranging from 20% to 64.0% [2–4]. Notably, the frequency of lymph node metastasis was dependent on the lymphatic drainage system rather on the anatomical distance from the primary tumour. In the study by Xu *et al.* [1], most patients underwent two-field lymphadenectomy and more lymph nodes were harvested in NSM (-), which might influence the incidence rate. Intriguingly, the prognostic significance of NSM in ESCC was still controversial. Zhu *et al.* [3] reviewed 207 thoracic ESCC patients and found that NSM was not a predictor of survival. Wang *et al.* [4] retrospectively analyzed 1026 ESCC patients and demonstrated that NSM was associated with a relatively poor prognosis in individuals with solitary node metastasis. Prenzel *et al.* [2] investigated 128 oesophageal cancer patients and verified that NSM was associated with a favourable prognosis, which was similar to the study by Xu *et al.* [1]. The possible reasons underlying the conflicting results included different pathological types, different lymphadenectomy methods and some confounding baseline characteristics. In the future, more prospective multicentre clinical studies are needed to establish the most meaningful definition and to clarify the clinical significance of NSM.

Besides, the second 'NSM (+) ($N=51$)' in Fig. 1 should be 'NSM (-) ($N=51$)' after propensity score matching.

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Reply to Zhang *et al.*

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We appreciate Zhang *et al.* [1] for their interest in our article [2]. As they pointed out, the definition of nodal skip metastasis (NSM) still was controversial. We agreed with them and we further elaborated on the reasons for our selection of the anatomical-region criterion here.

The regional nodes in Japan Esophageal Society system vary according to tumour location and are too sophisticated to be fully adopted to define NSM. For example, in the study by Wang *et al.* [3], they classified the curvature lymph nodes along the branches of the left gastric artery (No. 3a), the right and left paracardial lymph nodes (Nos. 1 and 2) as distant lymph node stations for mid-thoracic oesophageal squamous cell carcinoma (MT-ESCC), which was classified as N1 in 11th Japan Esophageal Society guideline [4]. As for the American Joint Committee on Cancer (AJCC) criterion, all the lymph nodes were defined as regional lymph nodes from the upper oesophageal sphincter to the coeliac artery without consideration of tumour location since the 7th edition AJCC system. All the lymph node stations shared the same prognostic meaning and there was no NSM of oesophageal cancer according to AJCC. We believed the anatomical-region criterion was the most appropriate method to explore the clinical significance of NSM for its feasibility in clinical work.

We also realized that most patients underwent two-field lymphadenectomy in our article would influence the incidence rate of NSM although no cervical lymph node metastasis detected by preoperative ultrasound. More prospective and multicentre clinical studies are warranted. However, we do not agree Drs Zhang's view that more lymph nodes were harvested in NSM(-) might influence the incidence rate. On the contrary, in our opinion, the more lymph nodes were dissected in NSM(-), the more accurate lymph node state and NSM state would be defined. For the error in Figure 1, we had noticed it before we received this letter, and we had contacted the editor of the European Journal of Cardio-Thoracic Surgery (EJCTS) to correct it. The corrigendum has been accepted for publication in EJCTS. Once again, many thanks for your letter and interest on this topic.

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