Lymph node staging in gastric remnant carcinoma

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While different definitions of gastric remnant carcinoma (GRC) still exist (1,2), many accept the one proposed by Tanigawa *et al.*, which defines GRC as the cancer developing in the remnant stomach at least 10 years after distal gastrectomy, regardless of whether the resection was performed for benign or malignant disease (3).

Much interest and debate regarding the prognosis of GRC evolve over past years with different results. While some claimed the prognosis of GRC was poor because of its low resectability, extended lymph node metastasis and infiltration of adjacent organs (4-6), others found the prognosis and resectability were not significantly different between GRC and conventional primary gastric carcinoma (PGC) (7,8).

In pathophysiology, important changes in GRC include the subsequent alteration of lymphatic drainage after resection, and lower numbers of harvestable and/or metastatic lymph nodes, especially if the resection was performed for gastric malignancy with prior extensive node dissection (7,8). It remains unclear and unaddressed if less retrievable lymph nodes in GRC could potentially influence accurate nodal stage which carries a predictive power in terms of survival rate.

Li *et al.*'s recent article in the *Journal of Cancer Research and Clinical Oncology* studied the pattern of lymph node metastasis in GRC and questioned if the lymph node staging according to the Union of International Cancer Control (UICC) TNM classification (7th edition) was appropriate for GRC (9). Because the number of harvestable lymph nodes was generally less in GRC than the ones in PGC due to prior resection of stomach, Li *et al.* suggested that 15 positive lymph nodes as cutoff point for N3b in the 7th UICC N staging system may not be suitable for GRC. Based on their analysis of median survival time (MST) in 83 patients with GRC from a single institution, they concluded that the N stage would be more appropriately classified in GRC if N3a represents 7 to 9 positive nodes (instead of 7 to 15), and N3b represents 10 or more positive nodes (instead of over 15), while N0, N1 and N2 remain same as 7th UICC N staging. Their conclusion was based on the data analysis of MST from 11 patients out of a total 83. Among these 11 patients, 8 were staged as N3a and 3 as N3b per 7th UICC classification, but per Li's protocol, there would be 5 as N3a and 6 as N3b. In that very small patient sample, Li *et al.* found a statistically significant difference in MST between N3a and N3b (P=0.014) if N was staged according to their proposal, which would otherwise not exist if classified according to 7th UICC N stage (P=0.18).

Fewer retrievable lymph nodes and/or less total positive nodes in GRC have been noted in several reports. Rabin *et al.* found the mean number of lymph nodes harvested per patient was 8.3 in GRC compared with 16.7 in PGC, and mean number of metastatic lymph nodes in GRC were 0.7 per patient compared with 3.7 in PGC (P=0.03, statistically significant) (7). While no significant differences in overall 5-year survival were identified between GRC and PGC, An JY *et al.* did notice that in some patients in GRC, especially in those with prior resection of gastric malignancy, the number of retrieved lymph nodes was insufficient for accurate staging of nodal metastasis (8). While those findings support Li *et al.*'s claim in that retrievable lymph nodes in GRC are lower and therefore, it may be difficult to have 15 or more positive lymph nodes, it is too early to draw a conclusion regarding the suitability of the cutoff number of lymph nodes proposed by Li *et al.*

First, Li *et al.*'s conclusion was derived from a very small patient sample in a retrospective or post hoc study.

Therefore, no difference in MST between N3a and N3b when staged per 7th UICC scheme might have occurred because the sample was too small to reach statistic power. The effect of this underpowered study due to small patient sample is evident in that no differences in MST were noted between N1 and N2 in their analysis. In addition, the results from a retrospective or post hoc study with small patient sample such as Li's may be interpreted with bias when confounding factors are not fully addressed. Therefore, the claimed significant difference in MST between N3a and N3b per Li's protocol may not be noted among general population of the patients. It is generally accepted that the stage combining T, N and M, or TNM group stage would have much better predictive value for overall survival and MST than a single T or N stage. Yet, the study did not reveal the T stage associated with those 11 patients in their proposed N3a and N3b subgroups. Additionally, the study failed to reveal if these 11 patients had history of neoadjuvant or adjuvant therapy, because these subjects should generally be excluded from study such as this. Finally, some other studies have shown the ratio of positive to negative nodes in gastric cancer may have a better predictive value for survival (10). It remains to be tested if that finding can also apply to N stage in GRC in which it is more difficult to harvest adequate number of nodes. Therefore, studies with a much larger patient population to exclude potential confounding factors and incorporate alternative way to calculate positive lymph nodes such as the ratio of positive to negative lymph nodes are needed before the modified N stage in GRC proposed by Li *et al.* can be accepted.

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