**Supplemental Instruction**

(This is just a supplemental document. These texts, figure or table are not required to appear in formal article.)

Some previous studies calculated negative predictive values at each T stage and recommended the required number of nodes based on more than 90% values [1-4]. But in our research, the NPV (>86.5%) of resection of LNs >21 is slightly lower than 90%. Nevertheless, 86.5% is still a relatively high threshold, and we have demonstrated its effectiveness through survival analysis and Cox regression model.

The reason why our metrics is slightly lower than 90% could be that we did not acquire thresholds on the required number of nodes to be decided on the basis of NPV separately for each T stage. Actually, we had tried like that during the process of building our model, but we finally did not adopt that approach (relevant figure and table are listed in supplementary materials for illustrating).

As expected, the false-omission rate decreased with a higher T stage, and NPV increased with a lower T stage in the same examined node count (Supplemental Figure). According to the method originally proposed by Gönen et al (2009), the number of LNs to achieve negative predictive value > 90% for each T stage was separately 15, 26, 30 and 34. But reviewing our **original** data, most patients did not reach the standard for each T stage (Supplemental Table), even less than 20% of patients with T2-4 stage with could get the criterion. This led that we could not conduct further survival analyses more **precisely to verify the validity of each** threshold. The similar phenomenon also existed in quite a few studies. The minimum numbers of LNs examined in these studies varied from 14 to 30 [5-10]. According to the distribution of LNs examined in each study (such as median, quartiles or others), near or more than half, even higher percentages of patients could not reach their respective standards for optimal or minimum threshold of examined nodes.



**Supplemental Figure A)** The probability of false-negative findings as a function of number of lymph nodes examined in patients with truly node-positive disease for each T stage.

**Supplemental Figure B)** Negative Predictive Value as a function of number of lymph nodes examined in patients with declared node-negative diseases for each T stage.

**Supplementary Table** Distribution of number of LNs removed in pN0 patients.

|  |  |  |  |
| --- | --- | --- | --- |
| T stage | Number of nodes to achieve NPV > 90% | Patient proportion of more than the ideal number of nodes (%) | Median number of nodes (25th, 75th percentiles) |
| T1 | 15 | 50 | 15 (11,21) |
| T2 | 26 | 19.5 | 17 (12,24) |
| T3 | 30 | 14.9 | 19 (13,27) |
| T4 | 34 | 12.8 | 20 (13,28) |

Additionally, this also partly reveals the current situation of surgical quality control in ESCC—the lymphadenectomy numerous patients received might be below the right criterion in practice. This phenomenon reminds clinicians that the quantity of patients with occult nodal disease might be seriously underestimated in the real world.

The discoveries in the process we created our model and consulted literatures remind us that, we should attach more importance to occult lymph node metastasis caused by surgery. With the development and standardization of esophagectomy, surgeons may need to dissect more lymph nodes based on specific situation during operation.

**References**

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