

A “perfect” lymph node staging system requires a “perfect” surgery

Laura Ruspi, Federica Galli, Francesco Frattini, Chiara Peverelli, Giuseppe Di Rocco, Francesco Martignoni, Francesca Rovera, Luigi Boni, Gianlorenzo Dionigi, Stefano Rausei

Department of Surgical Sciences, University of Insubria, Varese, Italy

Correspondence to: Laura Ruspi, MD. Department of Surgical Sciences, University of Insubria, Ospedale di Circolo, Viale Luigi Borri 57, 21100 Varese, Italy. Email: laura.ruspi@libero.it.

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Lymph node metastases are well known predictors of poor prognosis in gastric cancer patients after curative surgery.

AJCC/UICC TNM staging system is the most commonly used scheme to predict prognosis in oncologic patients, and in 2010 its latest edition revised criteria to assess severity of disease, especially for gastric cancer (1).

Nonetheless, concerning lymph node involvement, different alternative systems have been proposed with the aim to identify the optimal manner to use lymph node status to predict survival among patients with resected gastric cancer. At the moment, none of them has demonstrated to be “perfect” yet.

By a retrospective analysis recently published on *Annals of Surgery*, Spolverato *et al.* compared survivals of more than 800 patients underwent surgery for gastric cancer (2). This paper is the first in evaluating the prognostic ability of the four most commonly cited lymph node staging systems: AJCC/UICC seventh edition TNM, lymph node ratio (LNR, ratio of metastatic lymph nodes relative to total number of examined lymph nodes), log odds of metastatic lymph nodes (LODDS, natural logarithm of the ratio of the probability of a lymph node to contain metastasis versus the probability of a lymph node to be free of metastatic disease) and N score (a prognostic model that takes into account the differential impact of total number of examined lymph nodes among patients with and without lymph node metastasis, as well as the possible nonlinear interaction between total number of examined lymph nodes and the number of metastatic lymph nodes) (3-5).

In this analysis, all of the tested staging systems well discriminated different groups of patients according to

nodal involvement, but some peculiarities emerged: LNR was the most powerful tool to stratify patients’ survival; additionally, the Authors specified that LODDS was a better survival predictor when lymph node status was modeled as a continuous variable.

Actually, this is an obvious detail, because N status is a continuous variable, despite any model. Probably, the need to underline this finding derives from the evidence that these reports aim to solve statistical problems more than concerns in clinical practice.

An ideal staging system should be easily reproducible and should not be influenced by type of treatment. But this does not allow us to play with statistic in order to repair obvious understaging due to suboptimal surgery.

In fact, in order to sustain their conclusions, Spolverato and colleagues selected patients who did not always receive radical surgery with a convincing lymphadenectomy. Their analysis includes patients underwent surgery only with a curative intent (not necessarily R0) and more than one third of patients with limited lymphadenectomy with a low median number of retrieved nodes. The Authors themselves admit that total number of examined lymph nodes has a significant impact on the prognosis (so that according to LNR they included N0 with <15 nodes in subgroup N1), and an insufficient number of retrieved lymph nodes was described in more than 20% of the sample. Nevertheless, this result is still described as a limit of the staging system and not as a consequence of an inadequate surgery.

Again, even if such papers present only statistical speculations, anyway they are affected by relevant biases conditioning results reliability: for example in the paper by

Spolverato *et al.* neither neoadjuvant nor adjuvant therapy are prognostically evaluated (6,7) and quality of surgery improved along the time. Hence, the way towards the definition of the best possible staging system remains very hard. In any case, this cannot justify an undertreatment.

Similarly, Will-Rogers' stage migration phenomenon does not require elegant manipulations to be denied, but it strongly needs an accurate surgical approach to be minimized: this is a due for all involved clinicians and not a mere speculation for statistics.

This underlines the importance of an accurate analysis of the specimen from surgical pathologist too, depending on node retrieval technique, enthusiasm to find more lymph nodes, fat volume of the specimens, nodal status (8).

Generally, we might say that LNR and LODDS have the great advantage of taking into account the total number of examined nodes (which could be a measure of the extent and of the adequacy of lymphadenectomy and respond to inter-individual anatomical variability) (9), although the problem of a minimum number of nodes (16 according to latest TNM, and not 15 as reported in the paper) should be easily overcome if we consider that an extended (D2) lymphadenectomy has to be performed in every cT >1 any N gastric adenocarcinoma, according to Japanese guidelines (10).

Revising conclusions by Spolverato and colleagues, consistently with our previous suggestion (11), we confirm that AJCC/UICC TNM does not seem to offer the best prognostic stratification according to lymph node status in gastric cancer patients if compared with LNR, N score and LODDS. Its main advantage of being easily applicable and reproducible is contrasted by a suboptimal stratification in patients with less than 15 nodes, which, as demonstrated in this report, seems to be still a great part of gastric cancer population in the Western world.

Both surgeons and pathologists should make a great attempt to minimize this defect of the staging system improving their surgical performance and their search for lymph nodes in the specimen, waiting for a further TNM edition where the classic numeric criterion could be improved by other reasonable factors.

We remark that any effort should be towards a standardization of surgery and, above all, an effective treatment for a reliable staging.

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Footnote

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