

Editorial



Lymph Node Ratio System for N Staging of Gastric Cancer: Challenging for Universal Application But Useful for the Prognostic Prediction of Individual Patients

Seong-Ho Kong

Department of Surgery, Seoul National University Hospital, Seoul, Korea

OPEN ACCESS

Correspondence to

Seong-Ho Kong

Department of Surgery, Seoul National University Hospital, 101 Daehak-ro, Jongno-gu, Seoul 03080, Korea.

E-mail: seongho.kong@snu.ac.kr

Copyright © 2021. Korean Gastric Cancer Association

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<https://creativecommons.org/licenses/by-nc/4.0>) which permits unrestricted noncommercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ORCID iDs

Seong-Ho Kong

<https://orcid.org/0000-0002-3929-796X>

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

- ▶ See the article “The prognostic value of lymph node ratio after neoadjuvant chemotherapy in patients with locally advanced gastric adenocarcinoma” in volume 21 on page 49.
- ▶ See the article “A novel approach for gastric cancer staging in elderly patients based on the lymph node ratio” in volume 21 on page 84.

Lymph node (LN) dissection is not only a crucial component in the treatment of gastric cancer, but also important for the proper staging and accurate prediction of cancer prognosis. Its clinical implications are relatively high compared to that of other types of cancer in the gastrointestinal organs.

The tumor-node-metastasis (TNM) staging of the American Joint Committee of Cancer (AJCC) is being practically used for its simplicity and reproducibility; however, it has been challenged for its limitation of possible stage migration in gastric cancer.

In response, the LN ratio has been suggested to overcome this problem of staging for patients with a limited number of examined LNs, with the hypothesis that the LN ratio can represent the actual burden of LN metastasis [1]. It has also been shown that N staging by the LN ratio can be superior to the AJCC TNM N staging from a cohort of extensive standard LN dissection [2].

In this issue of the *Journal of Gastric Cancer*, the usefulness of the N staging by the LN ratio has been examined for elderly patients by Park et al. [3]. and for patients who received neoadjuvant chemotherapy by Zhu et al. [4] In both situations, there were concerns about the limited number of total LN counts.

For better understanding, I would like to define the nomenclature of the total LN count. In both articles, the number of the examined LN was expressed as “retrieved LN,” which implies that the number is solely correlated with the extent of the LN dissection. However, the number of examined LNs was affected not only by the extent of surgery, but also by how diligently the pathologists scrutinized the LN, as well as the innate number of LNs of the individual patient. Therefore, I would like to request the reader to understand that the “retrieved LN” be defined as the “examined LN” harboring all these aspects.

Additionally, the “ratio” is the relationship between independent categories (e.g. male-to-female ratio=2:1). Therefore, the term “LN ratio,” which was already widely accepted for many clinicians, should be interpreted as the “proportion” of the number of metastatic LNs among the number of examined LNs.

Contrary to expectations, the number of retrieved LNs in elderly patients and patients who underwent neoadjuvant treatment was not as low as expected, with a proportion of the “D2 or over” LN dissection reaching over 50%. The mean number of retrieved LNs was as high as 38.2 in elderly patients and 32 in those who underwent neoadjuvant chemotherapy. These high numbers of LNs reflect a higher quality of the surgical and pathologic examinations as compared to a limited number of examined LNs.

We conjecture that the usefulness of the LN ratio system has a higher value when there is wide variation in the number of total retrieved LNs, which is mostly affected by the individual variation of the innate number of LNs, and supported by high quality surgical and pathologic examinations, which can minimize the error of missing LNs. We tried to apply the LN ratio in the remnant gastrectomy, which has a smaller number of retrieved LNs; however, we failed to find frequent stage migration between the TNM N staging and LN ratio system due to the limited variation in the number of retrieved LNs [5].

Zhu et al. [4] suggested a special approach to define N0 staging including patients with 25 or fewer retrieved LNs despite the absence of pathological metastatic LNs. We suspect that the poor overall survival of these patients was because of an insufficient extent of surgery or missed metastatic LNs during examination by a pathologist. Far from our common expectations, a large number of metastatic LNs were smaller than 1 cm; therefore, it required special effort by the pathologist to find all the metastatic LNs [6]. We also think that the underlying disease of the patient might have affected the extent of the surgery and could have resulted in poor overall survival directly by itself; however, we should be also cautious about the frequently encountered possibility that the number of LNs in an individual is small by nature. In such cases, the newly suggested staging can cause over-staging and even the implementation of unnecessary adjuvant chemotherapy.

Determining the cut-off value of the LN ratio for each stage is challenging, considering the differences in the retrieved LNs among the institutes. Interestingly, the 2 articles in this issue have suggested the same value of “0.1” for dividing stages I and II, which is particularly important because it is related to the indication for adjuvant chemotherapy. Despite the relatively high number of patients in the two studies, the number of patients with a high LN ratio was limited, with less than 10 patients in each group. Further multicenter studies are necessary to determine the universal cut-off values.

Despite the remaining difficulties in the universal application of the LN ratio, these two articles showed that the LN ratio was not affected by the number of retrieved LNs and identified the superiority of the LN ratio in predicting prognosis. Previously, we have shown that the different N stages by the LN ratio result in different overall survival in the same TNM N stage, but the different TNM N stages showed similar overall survival in the same LN ratio in patients who underwent standard LN dissection [2]. The same result was reproduced for patients who underwent neoadjuvant treatment in the study by Zhu et al. [4]. This phenomenon implies that statistical graphs for overall survival involving many patients could be similar for both TNM and LN ratio systems, but we may minimize and correct the staging

migration in TNM N stage by using the LN ratio system at an individual level and obtain a more accurate prediction for each patient.

Considering that the paradigm of cancer treatment is shifting to the prediction of prognosis and treatment of individualized patients, the value of the LN ratio is expected to increase significantly in the near future. As discussed, the LN ratio may thus be more valuable when a sufficient extent of LN dissection and thorough seeking of LNs by the pathologist are guaranteed, rather than when it is used only for adjusting the inappropriate surgical or pathologic examination.

REFERENCES

1. Marchet A, Mocellin S, Ambrosi A, Morgagni P, Garcea D, Marrelli D, et al. The ratio between metastatic and examined lymph nodes (N ratio) is an independent prognostic factor in gastric cancer regardless of the type of lymphadenectomy: results from an Italian multicentric study in 1853 patients. *Ann Surg* 2007;245:543-552.
[PUBMED](#) | [CROSSREF](#)
2. Kong SH, Lee HJ, Ahn HS, Kim JW, Kim WH, Lee KU, et al. Stage migration effect on survival in gastric cancer surgery with extended lymphadenectomy: the reappraisal of positive lymph node ratio as a proper N-staging. *Ann Surg* 2012;255:50-58.
[PUBMED](#) | [CROSSREF](#)
3. Park J, Jeon CH, Kim SJ, Seo HS, Song KY, Lee HH. A novel approach for gastric cancer staging in elderly patients based on the lymph node ratio. *J Gastric Cancer* 2021;21:84-92.
[CROSSREF](#)
4. Zhu K, Jin H, Li Z, Gao Y, Zhang Q, Liu X, et al. The prognostic value of lymph node ratio after neoadjuvant chemotherapy in patients with locally advanced gastric adenocarcinoma. *J Gastric Cancer* 2021;21:49-62.
[CROSSREF](#)
5. Son SY, Kong SH, Ahn HS, Park YS, Ahn SH, Suh YS, et al. The value of N staging with the positive lymph node ratio, and splenectomy, for remnant gastric cancer: a multicenter retrospective study. *J Surg Oncol* 2017;116:884-893.
[PUBMED](#) | [CROSSREF](#)
6. Kim DJ, Kim W. Is lymph node size a reliable factor for estimating lymph node metastasis in early gastric cancer? *J Gastric Cancer* 2018;18:20-29.
[PUBMED](#) | [CROSSREF](#)