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LETTER TO THE EDITOR OPEN ACCESS

Response to Letter to the Editor

Lisa van der Schee[1] | Petur Snaebjornsson[2] | Miangela M. Laclé[1]

[1]Department of Pathology, University Medical Center Utrecht, Utrecht, the Netherlands | [2]Department of Pathology, The Netherlands Cancer Institute, Amsterdam, the Netherlands

Correspondence: Miangela M. Laclé (M.M.Lacle@umcutrecht.nl)

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We would like to thank Ichimasa and colleagues for their letter to the editor in which they raised several questions about our study on variation in LVI detection rates in T1 CRC and its impact on clinical decision-making and patient outcomes [1]. We are pleased to address these concerns.

Our nationwide study demonstrated that in centres with high LVI detection rates, the proportion of completion surgery following local excision of T1 CRC is higher than in centres with low or average detection rates. More importantly, there was a greater proportion of lymph node metastasis (LNM) negative surgeries, and no benefits regarding cancer recurrence. In their letter, Ichimasa and colleagues requested further information regarding the correlation between LVI detection rates and lymph node metastasis (LNM) in addition to cancer recurrence. In our dataset, which demonstrated no differences in cancer recurrence among patients from centres with low, average, and high LVI detection rates, the percentages of T1 CRCs that had LNM after completion of surgery were 14.4%, 14.3%, and 10.3%, respectively. As the proportion of completion surgery is significantly higher in centres with high detection rates, yet without a higher incidence of LNM-positive surgeries, this results in a greater number of surgeries with no clinical benefit (LNM-negative surgeries).

We understand the authors' proposal to incorporate depth of invasion into the multivariable analyses, in which we evaluated the correlation between LVI detection rate and surgical resection rates or LNM-negative surgeries. In many countries, deep submucosal invasion has long been considered as an indication for surgery, until recent evidence confirmed that in the absence of other risk factors, the risk of LNM in these cases is low [2]. We agree with Ichimasa and colleagues that the exclusion of this parameter as an indication for completion surgery has a profound impact on the proportion of T1 CRCs that could be treated with local excision alone. However, at the time of the study, the Dutch guideline already did not (and still does not) recommend completion surgery following local excision of a T1 CRC with clear margins based on depth of invasion alone [3]. Moreover, depth of invasion was missing in 18.8% of pathology reports of locally resected pT1 CRCs. For these reasons, we chose to exclude this parameter as a potential confounding variable in the multivariable analyses. Nevertheless, for the purposes of this response letter, we have repeated the multivariable analyses in the subset of patients for whom depth of invasion was reported in the pathology report, and included it as a confounder. These analyses confirm that deeper invasion is indeed associated with higher surgical resection rates. However, it does not influence the strength and significance of the association between the LVI detection rate and surgical resection rates or the rate of LNM-negative surgeries.

It is important to emphasise that we do recognise the pivotal role of LVI as a predictor of LNM in T1 CRCs and that the identification of LVI in a local resection specimen should prompt consideration of completion surgery in these patients. Given the pivotal role of LVI in clinical decision-making, we believe it is essential to demonstrate the significant practice variation in its detection, which has implications for the treatment of T1 CRC patients. In our manuscript, we present our perspective on the potential causes of the observed practice variation and suggest ways to reduce it. It is our belief that it is of utmost importance to raise awareness of the extent of practice

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variation in the detection of LVI and its implications. We hope that this will facilitate further discussions to standardise LVI assessment.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The authors have nothing to report.

Lisavan derSchee
Petur Snaebjornsson
Miangela M. Laclé

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