Reviewer's report

Title: Tumor Budding as a Risk Factor of Lymph Node Metastasis in Submucosal Invasive T1 Colorectal Carcinoma: a retrospective study

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Reviewer: Frank Pfeffer

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The present study deals with the question if tumour budding is a risk factor of lymph node metastasis in T1 colorectal cancer.

To clarify this question, the authors perform a retrospective analysis of 55 patients who underwent curative radical resection. Data for tumour budding and other risk factors are available in 44 patients.

As the main result, the authors found lymph node metastasis in eight patients (14.5%). Analyzing their data by univariate (p= 0.047) and multivariate analysis (p= 0.042) the authors conclude that tumour budding was an independent factor for predicting lymph node metastasis.

This is a well-written manuscript and the question of risk factors for lymph node metastasis in T1 colorectal cancer is of ongoing interest and clinical importance. However, I have some concerns not allowing me to recommend this paper for publication in BMC Surgery.

1. The question posed by the authors is well defined.

2. The method is not appropriate. This is a retrospective study with 55 patients. In eleven patients (20%) data regarding risk factors are missing. The number of 6 patients with lymph node metastasis is too small to perform appropriate statistical analysis.

3. The data are not sound. 15 patients with tumour budding had no lymph node metastasis. What does it mean? Data for tumour size, circumference ratio, depth of invasion, Kudo`s classification are confusing. Is this effect of small sample size?

4. Percentages in table 1 are unclear and confusing. Percentages should be reported as percentage of the total group. Another opportunity to present the data could be logistic regression and odds ratio.

5. The discussion and conclusion are well balanced. Some aspects are not highlighted. 75% of patients with tumour budding had no metastasis. It would have been interesting to discuss sensitivity, specificity, negative and positive predictive value of tumour budding. Although not appropriate due to small sample size, tumour budding seems to have a high sensitivity (83%), acceptable specificity (61%) and a high negative predictive value (0.96). If these results could be
confirmed in a larger study, tumour budding seems to be a promising risk factor. But the discussion is not supported by the present data. In addition, the authors findings to other risk factors (tumour size, Kudo`s classification and depth of invasion) are discordant with previous reported data. The authors should discuss these discrepancies in findings.

6. The limitations are not clearly stated. The authors mention only missing data in 2 patients with lymph node metastasis.

8. The title and abstract do not accurately convey what has been found. The title reveals tumour budding as risk factor, whereas the abstract is focusing on all risk factors although there is no statistical significance.

In summary: The minimal sample size of six patients with lymph node metastasis and available data to risk factors is too small to allow appropriate statistical analysis. The data could be presented as a series of individual cases.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests