Reviewer's report

Title: Young Age Increases the Risk for of Lymph Node Metastasis in Patients with Early Colon Cancer

Version: 0 Date: 31 Dec 2018

Reviewer: Thomas Curran

Reviewer's report:

The authors have done a fine job evaluating the intersection of two recent trends in colon cancer epidemiology and management. First, colon cancers are being identified more commonly in younger patients in recent years. Second, EMR/ESD is being increasingly used to resect advanced polyps and even early stage cancers in select patients. The decision making regarding need for radical resection is predicated on the probability of lymph node involvement for patients with cancers that have been completely excised via EMR/ESD. The authors utilized the SEER database to identify the impact of patient age on lymph node status in T1/T2 colon cancer. They found that age, as well as other pathologic factors, was associated with lymph node status. They then used this information to construct a nomogram to inform risk of lymph node involvement based on clinicopathologic factors.

Overall, this study contributes meaningful data to our management of colon cancer. I have made several specific comments below though will review general comments here. This study demonstrates that T-stage for T-stage, younger patients with T1 or T2 cancers appear to have a higher probability of lymph node positive disease as compared to older patients. This informs gastroenterologists and surgeons as to the disease pattern in younger patients. However, in regard to the clinical utility of this information, these findings should be provided additional context. The benefit of the nomogram should be to provide guidance in management. Yet, because the nomogram includes T-stage as a parameter, it is only applicable after either EMR/ESD or radical surgery (procedures that would yield such information). With EMR/ESD, if a T2 cancer is identified, standard of care would suggest that all such patients should receive radical surgery. Thus, the nomogram really only influences management for patients found to have a T1 cancer after EMR/ESD. Stratification according to Haggitt or sm level would be helpful though is not available in the database. The nomogram could theoretically provide some degree of guidance though a C-statistic of 0.65 is not particularly strong. Again, this is useful information but the tone of the discussion should be edited to reflect the specific population for whom this information may influence management.

Overall:

- Grammar/language is awkward at points throughout the manuscript. This should be reviewed prior to publication.
Abstract:

- "colon cancer with mucosal invasion" is an odd statement; by definition T1 cancers invade the submucosa. Another term should be used to describe Tis to T2 as described in the manuscript.

Introduction

- Page 7, Line 12-20; "positive outcomes" appears to be misused here.

- The last paragraph should be revised. The detailed information regarding SEER should be moved to the methods section. The last sentence of the last paragraph is also confusing; I assume the authors are referring to the current study as the "recent study?"

Methods

- The abstract suggests that patients with Tis were included while the results section does not demonstrate any such patients. Please specify.

Discussion

- NCCN guidelines recommend evaluation of 12 lymph nodes for colon cancer resections in general; not just for early stage (reference 17). This should be clarified.

- Page 15; "regional resection" should be clarified. "Aggressive regional resection" should also be clarified.

- Page 15; the suggestion that adjuvant chemoradiation might be an appropriate strategy for young patients with early stage colon cancers is not supported by the data. Post-resection, TNM stage is known through pathologic evaluation. Adjuvant chemotherapy certainly has a role in the treatment of stage III colon cancer and select stage II cases though adjuvant radiation is generally reserved for cases with positive margins, if at all.

Conclusions

- The data do not necessarily support aggressive screening for young patients. While screening guidelines are certainly open for debate, this study does not relate to that debate. All patients studied here have documented colon cancer. It is difficult to make statements about screening without analyses that involve rates of disease in a population.

- The statement that younger patients should be considered for more aggressive treatment strategies has merit. Specifically, with the broader adoption of EMR/ESD, these data suggest that younger patients would be at greater risk of lymph node positivity T-stage for T-stage
relative to older patients. The hazards associated with EMR/ESD for younger patients should be more explicitly stated as I believe this is a powerful finding of your work.

Table 1
- Two decimal places is an unnecessary degree of precision for the percentage column. Consider revising.
- P-values should be included in this table
- the data for left vs. right sided LN positivity should be included

Table 2
- the reference group should be specified.
- Tumor location (left vs. right) appeared to be associated with lymph node positivity per the text yet it did not make it to the final model. Please explain.

Figure 2A
- contains minor typos

Figure 3
- Would benefit from more explanation in the text and/or caption.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No
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If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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Please indicate the quality of language in the manuscript:

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