

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastrointestinal Surgery

**Manuscript NO:** 61126

**Title:** Colorectal Cancer of the Young Displays Distinct Features of Aggressive Tumor Biology: A Single-Center Cohort Study

**Reviewer's code:** 05445382

**Position:** Peer Reviewer

**Academic degree:** FRCS (Gen Surg), MBBS, MD

**Professional title:** Surgeon

**Reviewer's Country/Territory:** United Kingdom

**Author's Country/Territory:** Switzerland

**Manuscript submission date:** 2020-11-24

**Reviewer chosen by:** Lian-Sheng Ma

**Reviewer accepted review:** 2020-11-25 18:44

**Reviewer performed review:** 2020-11-29 21:29

**Review time:** 4 Days and 2 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## **SPECIFIC COMMENTS TO AUTHORS**

The manuscript is well written and meets most criteria on the check list , however, there is no new message from the manuscript about colorectal cancer in the young, except that the incidence of colorectal in the young is highest in Switzerland. In addition, to drawn a more cogent conclusion on such a topical issue, I think a multi-centre study with larger population size would have been more appropriate. However, I have few comments for the authors.

1. I would have expected a comparison on the 5 years survival in the <50 and >50 we if were discussing aggressive biology of CRC, which is highly predicated on prognosis. There is no data on CRC recurrence , or why was it not discussed.
2. In discussing colorectal cancer, the author made allusion to the fact the rectal cancer may have a different biology as a result of the different embryological origin, which I agree its true. However, nothing was mentioned about the use of MRI in rectal cancer to further describe the radiomic features such as the EMVI, perineural invasion and Circumference resection margin involvement which would have helped to distinctly characterise rectal cancer in both age groups and give us some clue on the need for neo or adjuvant chemotherapy which is another surrogate maker for aggressiveness of the rectal . in question.
3. Why didn't the author use Prealbumin and ferritin level which are more reliable and reflective of nutritional status.
4. Could the high nodal yield in young patient be a function of the immunocompetency in the that age group, knowing that younger patients a more likely to show higher lymphoproliferative ability.
5. This a statement from line 210 " The fact that lymph node dissection was reported to be far more extensive in young patients [27], a result that is concordant with operations performed at our institution, suggests a more aggressive surgical approach in younger patients. Obviously, younger patients have fewer comorbidities and a better physical/nutritional status, which also make them more



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7041 Koll Center Parkway, Suite  
160, Pleasanton, CA 94566, USA  
**Telephone:** +1-925-399-1568  
**E-mail:** [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
**https://**[www.wjgnet.com](http://www.wjgnet.com)

suitable to more aggressive operations associated with increased perioperative morbidity.- Is the author suggesting that age plays a factor in the degree of radicality of the surgery offered". Isn't this a bias already against the over 50yrs. 6. In line 226 "A better understanding of the molecular make-up of young-onset cancers is being achieved by recent advances in decoding the genome with next-generation sequencing, which I agree that is correct. However, the other correlation that would have been more interesting is to see if the molecular mutation has any correlation with CRC metastasis in either group.

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**Title:** Colorectal Cancer of the Young Displays Distinct Features of Aggressive Tumor Biology: A Single-Center Cohort Study

**Reviewer's code:** 03547237

**Position:** Peer Reviewer

**Academic degree:** MD, PhD

**Professional title:** Assistant Professor, Doctor

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** Switzerland

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**Reviewer chosen by:** Lian-Sheng Ma

**Reviewer accepted review:** 2020-11-26 00:53

**Reviewer performed review:** 2020-12-01 16:34

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<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

#### **SPECIFIC COMMENTS TO AUTHORS**

This manuscript is an interesting paper. The study shows that the patients with CRC of young-onset have more frequently with locally advanced tumors, lymphatic invasion and with more frequent lymphatic metastases. It suggests the importance of early diagnosis and treatment in young patients with colorectal cancer, so it is important for clinical practice.

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**Name of journal:** World Journal of Gastrointestinal Surgery

**Manuscript NO:** 61126

**Title:** Colorectal Cancer of the Young Displays Distinct Features of Aggressive Tumor Biology: A Single-Center Cohort Study

**Reviewer's code:** 04163041

**Position:** Editorial Board

**Academic degree:** FACS, MBBS, MNAMS

**Professional title:** Professor

**Reviewer's Country/Territory:** India

**Author's Country/Territory:** Switzerland

**Manuscript submission date:** 2020-11-24

**Reviewer chosen by:** Lian-Sheng Ma

**Reviewer accepted review:** 2020-11-25 15:10

**Reviewer performed review:** 2020-12-08 18:08

**Review time:** 13 Days and 2 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## **SPECIFIC COMMENTS TO AUTHORS**

The authors have chosen a shorter period of time from 2013 to 18 and state that the trend is increasing based on the percentage of patients below 50 years, which may not be true unless either one compares this data with data of a previously defined period (eg. 2008 to 2013) or a joinpoint regression analysis of data of a longer time frame analyzed to arrive at this conclusion. That would have been a more authentic data to incur that the trend is increasing. This is especially true since Fanny ER Vuik et al report that there was no change in the trend of CRC incidence in young in Switzerland in their article(1). While analyzing the colorectal cancer trend, the authors could also have provided the trend for colon and rectal cancers separately too. In those younger than 50 years, the authors could have provided data about those with family history of colon cancer, with IBD , with hereditary colon cancer syndromes, who already have established guidelines for screening. Only data from those with sporadic colorectal cancer in young may help to decide about initiating screening at a lower age than agreed upon. Again to imitate screening programme or to advice preventive measures in those below 50 years, no risk stratification has been attempted by the authors, based on the clinical data. though they state that “parameters of interest included clinical as well as histopathological characteristics”. Also the authors have not provided the regional incidence ( within Switzerland) based on data from more than 400 patients seen in their institution, to direct the preventive measures to those regions with significantly higher incidence. Having brought out obesity as risk factor the authors could have indicated the temporal relationship of CRC in young and obesity in this population. They state that “young patients showed a similar stage-dependent overall survival and recurrence-free survival” and attribute this to more aggressive surgical treatment, though there cannot be different oncological procedures for colorectal cancer management in young



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**Telephone:** +1-925-399-1568  
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and older. It is quoted that higher Percentage of poor tumor grade and signet ring cell type histology was seen in those below 50 years. However the table show that only 17 out of 411 had signet ring cell type histology. It is also noted that out of 411 patients, histological grade was not available in 120 patients. 1. Increasing incidence of colorectal cancer in young adults in Europe over the last 25 years Fanny Er Vuik , Stella Av Nieuwenburg , et al . Gut - 2019 Oct; 68(10):1820-1826



## RE-REVIEW REPORT OF REVISED MANUSCRIPT

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**Reviewer's code:** 05445382

**Position:** Peer Reviewer

**Academic degree:** FRCS (Gen Surg), MBBS, MD

**Professional title:** Surgeon

**Reviewer's Country/Territory:** United Kingdom

**Author's Country/Territory:** Switzerland

**Manuscript submission date:** 2020-11-24

**Reviewer chosen by:** Han Zhang (Part-Time Editor)

**Reviewer accepted review:** 2021-01-04 22:27

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**Review time:** 18 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## SPECIFIC COMMENTS TO AUTHORS



**Baishideng  
Publishing  
Group**

7041 Koll Center Parkway, Suite  
160, Pleasanton, CA 94566, USA  
**Telephone:** +1-925-399-1568  
**E-mail:** [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
<https://www.wjgnet.com>

The authors have responded well to the critiquing of the original manuscript and have shown great insight to the subject of colorectal cancer in the young which is a very topical issue .