



**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 35158

**Title:** Prognostic value of lymph node metastasis for patients with T1-stage colorectal cancer in multiple-centers of China.

**Reviewer’s code:** 00505440

**Reviewer’s country:** India

**Science editor:** Yuan Qi

**Date sent for review:** 2017-07-21

**Date reviewed:**2017-07-23

**Review time:**2 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	GoogleSearch:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

**COMMENTS TO AUTHORS**

This is a very important manuscript that is likely to be very well cited in the years to come. The information presented is very pertinent. My only concern is that there are too many typographical and grammatical errors that must be sorted out.

**Answer:**

Thank you very much for your valuable suggestions. We have revised typographical and grammatical errors according to reviewer suggestions.



## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 35158

**Title:** Prognostic value of lymph node metastasis for patients with T1-stage colorectal cancer in multiple-centers of China.

**Reviewer's code:** 02682861

**Reviewer's country:** United States

**Science editor:** Yuan Qi

**Date sent for review:** 2017-08-14

**Date reviewed:** 2017-08-15

**Review time:** 1 Day

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	GoogleSearch:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

### COMMENTS TO AUTHORS

1) The introduction does not explain the role of tumor markers (moreover already known - Chao-Xu Zheng WJG, 2001) and vascular infiltration which in the discussion are cited as independent possible risk factors for lymph nodes metastasis (reference is missing) 2) The paragraph of chemotherapy and radical surgery is incomplete and unclear. Why is stage III-chemotherapy described? The focus is early stage (I/II). There is evidence for using adjuvant treatment in T1? How many lymph nodes were removed during the surgery (< o > 10 lymph nodes?). Possible bias of selection patients for different hospital/surgery and different time of surgery (2001-2011)?. A lot of heterogeneity of population study? 3) The results are encouraging but not conclusive 4) Unable to access to references and many missing references into manuscript 5) Many syntactic and grammar errors

**Answer:**

1. The introduction does not explain the role of tumor markers (moreover already known - Chao-Xu Zheng WJG, 2001) and vascular infiltration which in the discussion are cited as independent possible risk factors for lymph nodes metastasis (reference is missing).

Answer: We added the following sentence between the eighth and ninth sentences of paragraph 1 in the manuscript: First of all, thank you very much for your valuable suggestions. Actually, studies reported that elevated serum levels of tumor markers indicate high risk of cancer recurrence and poor survival, yet the relationship between tumor markers and lymph node metastasis in T1-stage CRC remains unknown[1]. Meanwhile, we added necessary references into the first two sentences of paragraph 4 in discussion, indicating that vascular infiltration is an independent possible risk factor for lymph nodes metastasis[2]. Meanwhile, we added necessary references into the two sentences.

1. Chao Xu Zheng, Wen Hua Zhan, Ji Zong Zhao, Dong Zheng, Dong Ping Wang, Yu Long He and Zhang Qing Zheng. The prognostic value of preoperative serum levels of CEA, CA19-9 and CA72-4 in patients with colorectal cancer. *World J Gastroentero*, 2001;7(3):431 - 434.

2. Messenger DE, Driman DK, Kirsch R. Developments in the assessment of venous invasion in colorectal cancer: implications for future practice and patient outcome. *Hum Pathol*. 2012 Jul;43(7):965-73. doi:10.1016/j.humpath.2011.11.015. Epub 2012 Mar 9.

2. The paragraph of chemotherapy and radical surgery is incomplete and unclear. Why is stage III-chemotherapy described? The focus is early stage (I/II). There is evidence for using adjuvant treatment in T1? How many lymph nodes were removed during the surgery (< o > 10 lymph nodes?). Possible bias of selection patients for different hospital/surgery and different time of surgery (2001-2011)?. A lot of heterogeneity of population study?

Answer: We added the following one sentence into paragraph 1 in the Chemotherapy and radical surgery: According to the NCCN Guidelines, colorectal cancer with lymph node metastasis is defined as IIIrd stage, postoperative chemotherapy was performed for colorectal cancer with lymph node metastasis, regardless of T stage. We added the following one sentence into paragraph 2 in the Chemotherapy and radical surgery: All the patients received scheduled surgery, not emergency surgery. More than 12 lymph nodes were removed during the surgery.



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In addition, 321 cases of T1-stage CRC were screened from 10132 patients with CRC receiving surgical therapy in 6 large-scale hospitals of China (the First Affiliated Hospital of Zhengzhou University, the Affiliated Tumor Hospital of Xinjiang Medical University, Sun Yat-sen Memorial Hospital of Sun Yat-sen University, the First Affiliated Hospital of Xinjiang Medical University, the Third Xiangya Hospital of Central South University and the Affiliated Hospital of Traditional Chinese Medicine of Xinjiang Medical University) from June 2001 to June 2011. Because the sample size is large enough, we selected 321 cases of T1-stage CRC were screened from 10132 patients with CRC receiving surgical therapy, The bias of selection patients for different hospital/surgery and different time of surgery (2001-2011) was avoided as much as possible.

### 3. The results are encouraging but not conclusive

Answer: Thank you very much for valuable suggestion.

In the study, firstly, we performed univariate analysis and multivariate analysis of correlation between lymph node metastasis with clinicopathological parameters of T1-stage CRC patients, we demonstrated that lymph node metastasis was associated with preoperative CA724, vascular invasion and differentiated degree. Furthermore, univariate analysis and Cox regress analysis of the correlation between clinicopathological parameters and 5-year OS, univariate analysis demonstrated that age, preoperative CEA, preoperative CA199, vascular invasion, differentiated degree and lymph node metastasis ( $\chi^2=24.180$ ,  $P < 0.001$ ) were associated with 5-year overall survival (OS, all  $P < 0.05$ ). Cox regress analysis showed that preoperative CA199 and lymph node metastasis (RR:5.117,  $P:0.024$ , CI:0.058-0.815) were associated with 5-year OS (both  $P < 0.05$ ).

The results concluded that preoperative serum CA724, vascular invasion and differentiation degree were independent risk factors for lymph node metastasis. Lymph node metastasis was an independent prognostic factor of OS for patients with T1-stage CRC.

### 4. Unable to access to references and many missing references into manuscript

Answer: This is a valuable suggestion. We added necessary references into the manuscript, like the followings:

1. Siegel RL, Miller KD, Fedewa SA, Ahnen DJ, Meester RGS, Barzi A, Jemal A. Colorectal cancer statistics, 2017. *CA Cancer J Clin.* 2017; 67(3):177-193.
2. Chen WQ, Zheng RS, Baade PD, Zhang SW, Zeng HM, Bray F, Jemal A, Yu XQ, He J. Cancer Statistics in China, 2015. *CA-Cancer J Clin.* 2016; 66(2):115-132.



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**5. Many syntactic and grammar errors**

Answer: Thank you very much for your valuable suggestions. We have revised syntactic and grammar errors according to reviewer suggestions.



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**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 35158

**Title:** Prognostic value of lymph node metastasis for patients with T1-stage colorectal cancer in multiple-centers of China.

**Reviewer's code:** 03086186

**Reviewer's country:** Taiwan

**Science editor:** Yuan Qi

**Date sent for review:** 2017-08-14

**Date reviewed:** 2017-08-26

**Review time:** 12 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	GoogleSearch:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input checked="" type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input checked="" type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> Plagiarism	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		[ Y ] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

### COMMENTS TO AUTHORS

Dr. Zhen-Qiang Sun and the other authors used patient information from 6 hospitals in China, collected 321 cases of T1-stage CRC, and retrospectively analyzed factors related to survival with emphasis on the status of lymph node metastasis. They found preoperative serum CEA, CA199, CA724, vascular invasion and degree of differentiation were associated with lymph node metastasis in T1-stage CRC. Survival analysis showed that age, CEA, CA199, vascular invasion, degree of differentiation and lymph node metastasis were risk factors for 5-year overall survival. The findings are significant for surgeons to predict patient's prognosis. Unfortunately, the authors are careless in spelling and I strongly recommend that they ask for help from an expert in English language editing.



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**Answer:**

Thanks to the reviewers for the appreciation of our research, your approval is our greatest encouragement! The suggestion above was meaningful. We have revised syntactic and grammar errors according to reviewer suggestions. At the same time, we chose Editing Service to deeply improve the quality of the manuscript.