

## ESPS PEER REVIEW REPORT

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

**ESPS manuscript NO:** 11142

**Title:** The necessity of protective stoma in low anterior resection with TME for rectal cancer: evidence from eleven studies

**Reviewer code:** 00059371

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2014-05-07 16:30

**Date reviewed:** 2014-05-09 06:33

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<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"/> No records	<input type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input checked="" type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

The manuscript/metaanalysis has several major limitations. It is limited to 2 outcomes leak and reoperation after LAR in rectal cancer rather than assess the benefit of stoma in more broad aspects including total morbidity and mortality. This is a complex setting and more thoughtful analysis is needed. The authors selected very simplistic approach to the issue of creating stoma looking at selected outcomes. This is very suboptimal data to me and the conclusions may be overstatements since other problems can occur with stoma creation including additional cost of 2nd surgery, hospital days. 1. Change title to more clear - The role of protective stoma.... for rectal cancer. A metaanalysis. - This is a metaanalysis. 2. Include more important data on mortality and total morbidity if available even lower number of studies 3. provide more detailed analysis of excluded studies 4. broad research with more than 90% irrelevant papers (poor criteria selection to start with). no need to mention those papers. Focus on 32 full text analysis 5. Needs improved wording and language. Ex. Stoma placed 'after' LAR.- the stoma is placed at the time of surgery. 6. Abstract section results- the sentence 4 does not make any sense. There was no obvious between study.... This is repeated in the body of the paper. 7. Review all papers again and run additional data and outcomes.

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

**ESPS manuscript NO:** 11142

**Title:** The necessity of protective stoma in low anterior resection with TME for rectal cancer: evidence from eleven studies

**Reviewer code:** 00042390

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2014-05-07 16:30

**Date reviewed:** 2014-05-29 01:46

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input checked="" type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

The study lacks one of the most important risks for anastomotic leak: Neoadjuvancy or pre op Chemo and Radiotherapy. You should study your data and classify the patients in 2 groups: 1) with and 2) without radiotherapy and study the rate of anastomotic leakage with and without diverting stoma.

## ESPS PEER REVIEW REPORT

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

**ESPS manuscript NO:** 11142

**Title:** The necessity of protective stoma in low anterior resection with TME for rectal cancer: evidence from eleven studies

**Reviewer code:** 00041288

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2014-05-07 16:30

**Date reviewed:** 2014-06-05 22:41

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input checked="" type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

Thank you for allowing me to review this manuscript. This is a review that evaluates the role of a protective stoma in rectal cancer surgery. The authors performed a literature review from 2007 to 2014. 11 studies were included (3 RCTs) with a total of 5612 patients. Comments: - The PRISMA guidelines for systematic reviews should be followed. More details on the excluded articles should be provided. - The manuscript needs English language revision. - Exclusion criteria should include non-rectal cancer proctectomy given your title. Did you also consider adding a minimum of patients to avoid small studies and case series? - The definitions of anastomotic leak should be included. - It would be interesting to know the incidence of anastomotic leak according to level of anastomosis, type of anastomosis (stapled (single or double), handsewn), laparoscopic vs. open, neoadjuvant chemoradiation, tumor stage, and other high-risk patient-related factors (DM, malnutrition, immunosuppression). - To further enhance this manuscript, details regarding the type of fecal diversion and indications for fecal diversion in the non-RCTs should be included. - P values should be added to table 1. - Figures are very helpful. - Not sure than you can conclude that a protective stoma actually DECREASES anastomotic leak but rather decreases its clinical manifestations and need for reoperation. - Overall I think the 2 findings of this study are limited by the narrow literature search and biased by the heterogeneity of the studies reviewed. Adding outcomes such as intra-abdominal abscess, other surgical morbidity, and mortality would further enhance the



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manuscript as well.

## ESPS PEER REVIEW REPORT

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

**ESPS manuscript NO:** 11142

**Title:** The necessity of protective stoma in low anterior resection with TME for rectal cancer: evidence from eleven studies

**Reviewer code:** 00041058

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2014-05-07 16:30

**Date reviewed:** 2014-06-07 22:17

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

This is a metaanalysis study on the necessity of protective stoma in low anterior resection with TME for rectal cancer. Its publication seems important in a time of intense and controversial discussion about the the necessity of protective stoma in low anterior resection with TME for rectal cancer.

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

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**Title:** The necessity of protective stoma in low anterior resection with TME for rectal cancer: evidence from eleven studies

**Reviewer code:** 00058121

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2014-05-07 16:30

**Date reviewed:** 2014-06-18 00:16

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<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"/> No records	<input type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input checked="" type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

Major issues -The major drawback of this meta-analysis is that RCT and non-RCT have been analyzed together. In non-RCT, use of allocation mechanisms other than concealed randomization means that groups are unlikely to be comparable. These potential systematic differences cause selection bias which produces imbalances in prognostic factors associated with confounding. Two separate meta-analyses should be conducted one for RCT and a second for non-RCT. The estimates of these two analyses can be compared by the z-score test. -A second major issue is the observed heterogeneity ( $I^2=77\%$ ). This number discloses that studies were heterogeneous and the Random effects model should have been performed than the Fixed effects model. Additionally, authors do not make clear the percentage of heterogeneity in each of the two outcomes (anastomotic leak - reoperation). -A third major issue is that authors have not addressed confounding. Meta-regression analysis is a power tool to counter bias introduced from confounding by producing 'adjusted' estimates of intervention effects: e.g.: single institution versus multi-institutional study, more sample size vs. less sample size study, community versus university hospital study e.t.c. -Besides, there is an already published meta-analysis [Ann Surg. 2008 Jul;248(1):52-60] including 27 studies (4 RCT) coming to same conclusions: A defunctioning stoma reduces the rate of clinically relevant anastomotic leakages and is thus recommended in surgery for low rectal cancers. -Table 1 should give the observed leak and reoperation percentages clearly. The observed risk ratio would be more



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digestible by the readers and be put in a proper clinical base. Minor issues -The first paragraph of the results contains duplicate information to figure 1. -The last paragraph of the results should be transferred to the discussion.

## ESPS PEER REVIEW REPORT

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

**ESPS manuscript NO:** 11142

**Title:** The necessity of protective stoma in low anterior resection with TME for rectal cancer: evidence from eleven studies

**Reviewer code:** 00058348

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2014-05-07 16:30

**Date reviewed:** 2014-06-20 02:57

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input checked="" type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair		BPG Search:	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

This well-conducted meta-analysis addresses a critical but controversial topic on the “protective stoma” in low anterior resection with TME for rectal cancer. Specific comments: 1. The nature of “meta-analysis” should be reflected in the title of the article. 2. The authors may justify why they only selected articles between 2007 and 2014. It seems that there are some relevant studies including a few well-designed studies that were carried out before 2007. Also, there are a few meta-analyses on the similar or same topic, which should be mentioned and cited. 3. Overall, the manuscript is well presented and organized. However, there are many grammatical and stylistic errors, inappropriate use of abbreviations, and inappropriate expression of rephrases and sentences in the title, abstract and the main manuscript.