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Flat C, 23/F., Lucky Plaza,  
315-321 Lockhart Road,  
Wan Chai, Hong Kong, China

## ESPS Peer-review Report

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

**ESPS Manuscript NO:** 5771

**Title:** HISTOLOGICAL HEALING FAVORS LOWER RISK OF COLON CARCINOMA IN EXTENSIVE ULCERATIVE COLITIS

**Reviewer code:** 00503404

**Science editor:** Gou, Su-Xin

**Date sent for review:** 2013-09-26 18:09

**Date reviewed:** 2013-09-26 22:32

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 type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<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	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

## COMMENTS TO AUTHORS

This is an interesting manuscript investigating the possible importance of histologic inflammation in the development of HGD/CRC in UC. Although single center and retrospective it certainly adds to the current evidence. Comments; 1. Calculate ORs for patients with and without a significant inflammation and HGD/CRC. Accepting the limitations this would be still of importance. Probably none/mild inflammation should be compared to moderate/severe. and in a sensitivity analysis authors could compare none vs any inflammation. 2. Please also compare the diagnostic era and HGD/CRC association since this looks to be positive (Table 1) 3. Please revise Table 1 decade of diagnosis section since patients with a diagnosis after 1993 could not fulfil the criteria for a follow-up (at least 20years) 4. Please add details on medical therapy and analyse possible association with the above outcome. 5. Please add data on HGD/CRC prevalence within 10-years from diagnosis in the full cohort (even if none) as well as it would be nice to have a comparison with patients with left-sided disease/proctitis. Do you have HGD/CRC data in that patient group with long follow-up?



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**Reviewer code:** 00030998

**Science editor:** Gou, Su-Xin

**Date sent for review:** 2013-09-26 18:09

**Date reviewed:** 2013-10-06 22:35

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 type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<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"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

This retrospective study was to determine if there was a relationship between histological disease activity and risk for colon cancer (CC) and high grade dysplasia (HGD) in the absence of gross endoscopic inflammation in patients with extensive ulcerative colitis of long standing. Another purpose was to define the incidence of histological disease activity in the absence of gross disease activity, possibly predisposing to the later development of HGD or CC. The authors suggested that progression to HGD or CC was more frequently encountered among patients who demonstrate persistent histological inflammation in the absence of gross mucosal disease. Their findings support including the elimination of histological inflammation in the definition of mucosal healing, and may support this endpoint as an appropriate goal of therapy. They stated that a Microsoft excel spreadsheet was constructed documenting each surveillance colonoscopy, recording the presence or absence of gross endoscopic disease, and the presence or absence of microscopic inflammation in those macroscopically normal in each colonic segment to include the cecum, ascending colon, transverse colon, descending colon, sigmoid colon and rectum. 1. This is a single-center cohort study. Inevitably the sample size is relatively small. This is one of limitations in this study. 2. No specific index system for histological inflammation was used since none was available during most of the study period. But, please state the definition of gross endoscopic disease and microscopic inflammation used in this study in more detail. 3. During the observation period, the policy of medical treatment has changed with time. The impact of the change in medical treatment should be presented. Immunosuppressive therapy with immunomodulators and biologic may impact the incidence of malignancy.



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**Title:** HISTOLOGICAL HEALING FAVORS LOWER RISK OF COLON CARCINOMA IN EXTENSIVE ULCERATIVE COLITIS

**Reviewer code:** 00503405

**Science editor:** Gou, Su-Xin

**Date sent for review:** 2013-09-26 18:09

**Date reviewed:** 2013-10-11 00:06

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"/> Existed	<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)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

The authors examined the connection histological colonic inflammation and dysplasia/UC-associated CRC. Their result i.e. the persisting inflammation usually lead to cancer is not surprising. In case of mild longstanding inflammation factors leading to epithelial cell proliferation (like IGF1R) are usually overexpressed. This may let the genetically defected cells (i.e. cells with defected telomerase activity) to survive, hence the basis of a possible uncontrolled cell proliferation may be high. These facts must be discussed in the discussion. The scoring system for the inflammation is not clear, it would enhance the strenght of teh manuscript to use a well-defined histological activity score. How was the medical treatment of the examined patients? Was there any connection between medical treatment and the development of malignancies? English language needs minor polishing. After major revision I suggest to accept the manuscript for publication in WJG.