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315-321 Lockhart Road,  
Wan Chai, Hong Kong, China

## ESPS Peer-review Report

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

**ESPS Manuscript NO:** 3932

**Title:** Acute arterial mesenteric ischemia with and without reperfusion: macroscopic and MRI findings

**Reviewer code:** 00069137

**Science editor:** Zhai, Huan-Huan

**Date sent for review:** 2013-06-03 19:48

**Date reviewed:** 2013-06-04 02:38

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)	<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

The authors present an interesting MRI study on a rat model of mesenteric ischemia/reperfusion. The group evidently has experience in the field. The manuscript is well written, concise, but could use some minor editing. I have some minor issues with the study design. 1- The number of animals studied is quite low (only 4 animals per group), and due to the design, only 1 rat was studied at each timepoint. this makes generalizations difficult. 2- The study is mostly observational: due to low animal number, no statistical methods are used to differentiate between groups, and so findings should be taken with caution. 3- The authors claim to study "pathophysiology", but MRI findings are indirect markers of edema, necrosis, or perfusion changes, and give no insight into mechanisms. In other papers they include histopathological analysis, which would have been interesting. 4- The MRI findings in acute models of intestinal ischemia/reperfusion in rats have been studied before by other groups. Given that the issue is controversial, the study is welcome, but given the methodological limitations, its originality could be called into question. 5- The authors published recently a very similar study but in a model of venous mesenteric ischemia; I worry about fragmented publication of results (a single paper could have included both findings and the discussion made comparative) Due to these concerns the authors should consider revising the discussion: stating the limitations, speculating on mechanisms further (they discuss vasoactive substances but what about inflammation, no-reflow phenomenon, neural dysfunction, oxidative stress, intravascular coagulation, systemic alterations etc.). They should also focus the discussion on comparing their results to other similar studies (many in the references) and possibly explaining the differences. The design of the study does not allow to draw strong conclusions on the clinical utility



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of MRI imaging in the setting of mesenteric ischemia.



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## ESPS Peer-review Report

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

**ESPS Manuscript NO:** 3932

**Title:** Acute arterial mesenteric ischemia with and without reperfusion: macroscopic and MRI findings

**Reviewer code:** 00055095

**Science editor:** Zhai, Huan-Huan

**Date sent for review:** 2013-06-03 19:48

**Date reviewed:** 2013-06-04 19:12

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[ Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ Y] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ] Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[ ] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ Y] Major revision
		[ ] No records	

## COMMENTS TO AUTHORS

The goal of this descriptive study was to detect and characterize ischemia or ischemia-reperfusion-induced changes in the rat GI tract by MRI technique. Although the possible clinical relevance of such investigations would merit publication, there are several points of criticism, which should be considered by the authors. My main concern with the general conduction of these experiments arises from the fact that the survival rate of 1 or 8 hrs mesenteric ischemic injury was 100%. 1. In this study complete mesenteric ischemia was maintained for 1 or 8 hrs (with or without 8 hours of reperfusion) by tourniquet placed around the superior mesenteric artery. Our group has conducted large series of experiments with the exact same rat species, weight, and SMA occlusion times ranging from 15 mins to 6 hrs. Our short-term mortality rate after 4 hrs non-resuscitated ischemia reaches 50% and in the 6 hrs group nearly 100%. The authors state, correctly, that the average mortality of acute human mesenteric ischemia is very high, usually exceeding 60%. If this experimental study produces 0 (zero !) mortality in a group of 4 animals after 8 hrs complete mesenteric ischemia, this suggests that model does not replicate clinical practice. 2. Alternatively, the distinctively higher survival rate in the authors approach may be caused by the lack of ischemia. Did you check the presence of intramural flow during these experiments (e.g. 2-3 etc hrs after tightening the tourniquet)? How did you verify the presence/lack of collateral microcirculation or the presence/lack of blood flow? 3. Another important fact is the need of comparable volume status in IR models. In this protocol the authors used 250-340 g rats in two groups (4/4). Circulatory studies with rats require tight control of body weight (for a reference see Gainer et al. Hemorrhagic shock in rats. Lab Animal Sci 1995) because the blood volume, which is a significant determinant of survival in



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hypovolemia, depends on body weight. It is very easy to overlook small differences in body weights between groups (n=4!) and we can conclude that a treatment protects, when it is just that the animals are slightly lower in body weight. Please comment and provide exact weight data/group. 4. It appears that fluid resuscitation was not performed in this study. The authors do not present any data on hemodynamics, but if fluid therapy was not given, there is no doubt that in this situation the animals were under-resuscitated. Were any assessments of intravascular volume performed in these animals (hemoglobin or hct)? Please comment. 5. According to the authors "the chronological sequence of early mesenteric ischemia has not been described". In fact, these data are available (Boros M et al: Ischemic time-dependent microvascular changes and reperfusion injury in the rat small intestine, J Surg Res 1995) and these results should be discussed in the manuscript. Minor 1. There are no page numbers. 2. There are several typos and formatting errors: semeiological (page 2), pre-exixting (page 4), was was (page 9), preivolusly (page 9), boldface (page 10, first para), capital letters (Mesenteric Ischemia), etc. Please check and correct.



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## ESPS Peer-review Report

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

**ESPS Manuscript NO:** 3932

**Title:** Acute arterial mesenteric ischemia with and without reperfusion: macroscopic and MRI findings

**Reviewer code:** 00038529

**Science editor:** Zhai, Huan-Huan

**Date sent for review:** 2013-06-03 19:48

**Date reviewed:** 2013-06-13 19:47

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 submitted paper presents some new methodology concerning the detection of subtle changes that occurs during the acute arterial mesenteric ischemia and ischemia-reperfusion pathological process. The paper is well designed and the results are meaningful and conceivable. However, some shortcomings still deserve further improvement. Major comments: 1. Were there any quantitative datas concerning the parameters detected by MRI or macroscopic analysis compared to the different treatments? 2. There are so many mistakes in grammar and spelling throughout the manuscript, which should be revised carefully. Minor comments: 1. What is the rationale of the time point selected (i.e. ischemia for 8 hours)? 2. In discussion, the author should provide some more information about the underlying mechanisms of the results and the differences between ischemia and ischemia-reperfusion. 3. Several blank space between digit and unit are missing. Please add. 4. Please give the whole name instead of abbreviation alone when first used.



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## ESPS Peer-review Report

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

**ESPS Manuscript NO:** 3932

**Title:** Acute arterial mesenteric ischemia with and without reperfusion: macroscopic and MRI findings

**Reviewer code:** 00502892

**Science editor:** Zhai, Huan-Huan

**Date sent for review:** 2013-06-03 19:48

**Date reviewed:** 2013-06-25 23:06

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 type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input checked="" type="checkbox"/> Rejection
<input checked="" 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 current unavailability of noninvasive imaging techniques is a significant impediment to the timely diagnosis of intestinal ischemia. This manuscript reports a small study in a rat model of intestinal ischemia imposed by occlusion of the superior mesenteric artery (SMA). Two groups were studied: permanent (8 hour) SMA occlusion, and 1 h SMA occlusion + 8 h reperfusion. The goal was to compare invasive, macroscopic evidence of intestinal ischemia with noninvasive magnetic resonance imaging, in order to demonstrate the utility of MRI as a means of detecting intestinal ischemia and the resultant structural injury. The study demonstrated that SMA reperfusion hastened intestinal injury and caused hypercontraction of the intestinal wall. The study addresses an important clinical problem and is well within the journal's scope. The quality of the prose is generally acceptable. The major concern is the limited size of the study and the lack of statistical analysis. Only 4 rats were studied in the ischemia and ischemia + reperfusion groups, respectively, and only 1 rat in each group completed the full protocol. Therefore, this report must be considered preliminary. Firm conclusions regarding the accuracy and reliability of MRI to detect and monitor intestinal ischemia and ischemia-reperfusion will require larger numbers of animals and appropriate statistical analyses. In the first sentence of Materials and Methods, please identify the institution: "...Institutional Animal Care and Use Committee of \_\_\_" The silicon "pipe" would more correctly be termed "tubing." On the third page of Materials and Methods, reword the last sentence: "...was performed in order to verify SMA reperfusion."