Dear Reviewers,

On behalf of my co-authors, we thank you very much for the reviewers' comments concerning our manuscript entitled "Contrast-induced ischemic colitis following coronary angiography: A case report" (Manuscript NO. 84813). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our research. We have studied all the comments carefully and have tried our best to make the correction. There are still a few problems in our study that can not be solved at present. We will continue to pay attention to them in further research according to your suggestion.

The main corrections in the paper and the responses to the reviewer's comments are as follows:

Reviewer #1:

1. An interesting and original case report proposing an association between contrast exposure during coronary angiography and ischemic colitis and providing reliable evidence of this. The manuscript is relevant and well-written, the case well described with an interesting discussion. This could be clinically important raising awareness for this possible adverse event.

Response: Thanks for your professional comments. We will continue to pay attention to these rare and interesting cases.

Reviewer #2:

1. The clinical sequence is not easy to follow and some gaps are present (the patient was gradually worsening and then suddenly had a quick and excellent recovery).

Response: Thanks for your professional advices. The clinical sequence is important for us to review the cause of ischemic colitis in this case. At 3 hours

post-CAG, the patients complained of epigastric pain and nausea. On the 2nd day after CAG, the patient complained abdominal pain transferred to the right epigastric and subxiphoid. On the 3rd day after CAG, the patient complained of gradual reduction of abdominal pain. On the fourth day after CAG, the patient's abdominal pain changed from persistent pain to paroxysmal pain. After 4-day treatment of antibiotic and supportive management, the patient had a quick and excellent recovery with disappearance of abdominal pain on the fifth day after CAG. In most cases of contrast-induced adverse events, the prognosis was excellent and the patients rapidly recovered after supportive management only. We have added this information in **Treatment section.**

2. The hypothesis that ischemic colitis was provoked by contrast infusion is neither adequately proven nor substantiated in the discussion. I have found no previous descriptions in this regard. How would have ischemia occurred? On the other hand, we cannot rule out that ischemic colitis was induced by the comorbidities of the patient that were numerous.

Response: Thanks for your important comments. The common causes of IC include thromboembolism, haemodynamic insufficiency, iatrogenic factor and drug-induced. Iatrogenic factors should be excluded firstly for the abdominal pain occurred only 3 hours after CAG, which was performed via right radial artery access without further coronary interventional procedure. Therefore, the embolism caused by interventional operation can be ruled out. Abdominal enhanced CT confirmed that there were no evidences of mesenteric artery and vein thrombosis. This patient always remained normal vital signs. The patient also had no previous history of paroxysmal atrial fibrillation and no abnormal right-to-left (R–L) cardiac shunt. The time course of events suggested that the IC had been precipitated by the CAG procedure. As the common causes including iatrogenic factor, haemodynamic insufficiency and thromboembolism were excluded, we can speculate that IC

here was related to the administration of the contrast agent, Omnipaque, which induced mesenteric artery spasm and local diminution of blood supply. In this case, Omnipaque-induced IC remains the most likely diagnosis on the basis of the complete resolution of symptoms with antibiotic therapy and supportive management only. We have carefully discussed in **paragraph 3-6 of Discussion section.**

3. If suspicion of ischemic colitis was raised, why was IV contrast given again twice for CT scan?

Response: This is a very important point. First, the patient underwent emergency abdominal CT scan without contrast when the patients complained of epigastric pain after CAG, and then underwent only once abdominal CT scan with intravenous iodixanol in order to make a clear diagnosis of unexplained abdominal pain. Second, the time course of events suggested that the IC was precipitated by the CAG procedure. And timely abdominal CT examination in this case contributed to the early diagnosis of IC. Finally, according to previous literature reports, different contrast agents may have different adverse reactions.

4. While the discussion is too long, still the possible causes of ischemic colitis are not thoroughly discussed (for instance, ischemic colitis induced by colonoscopy is not mentioned)

Response: Thanks for your professional suggestion. We have added this information in **paragraph 2 of Discussion section.**

Reviewer #3:

1. Post-cardiovascular surgery and coronary angioplasty are well-known etiologies to cause ischemic colitis, although most of the time the thrombi cannot be appreciated in imaging studies since they may only involve small vasculature. The imaging study did not see mesenteric vascular thrombi

cannot exclude this possibility.

Response: Thanks for your professional advices. Iatrogenic factors should be excluded firstly for the abdominal pain occurred only 3 hours after CAG, which was performed via right radial artery access without further coronary interventional procedure. Therefore, the embolism caused by interventional operation can be ruled out. Another striking feature of this case is isolated right colon ischaemia (IRCI). Colonic ischemia can affect any part of the colon but the left colon, particularly the splenic flexure, is involved in two-third of petients. IRCI might be caused by local contraction of vessels that supply the right colon rather than small vasculature thrombosis. We have carefully discussed all these aspects in **paragraph 3 and 7 of Discussion section.**

2. Vascular spasm due to reasons such as medication also can cause ischemic colitis, the authors need to exclude this possibility.

Response: Thanks for your valuable suggestion. Iatrogenic intestinal ischemia can occur secondary to use of certain medications including estrogen, digoxin, danazol, alosetron, pseudo ephedrine, vasopressin, psychotropic drugs, sumatriptan, serotoninergic agonists and anatagonists immunomodulators, laxatives and non-steroidal anti-inflammatory drugs. The patient denied a history of these drug use. Here we speculate that IC here was related to the administration of the contrast agent, Omnipaque, which induced mesenteric artery spasm and local diminution of blood supply. We have carefully discussed this aspect in **paragraph 5 of Discussion section.**

3. The authors contributed the ischemic colitis to the contrast use. There is no direct evidence to show this.

Response: Thanks for your question. We really have no direct evidence that ischemic colitis is caused by contrast use. The time course of events suggested that the IC had been precipitated by the CAG procedure. As the common causes including iatrogenic factor, haemodynamic insufficiency and thromboembolism were excluded, we can speculate that IC here was related

to the administration of the contrast agent.

4. The diagnosis of ischemic colitis was only based on CT imaging study. The imaging findings in this case was not specific for ischemic colitis. The evidence of ischemic colitis was missing from endoscopic finding and pathology biopsy diagnosis.

Response: Timely abdominal CT examination in this case contributed to the early diagnosis of IC. Colonoscopy with biopsy is the next step to confirm the diagnosis of IC. As there is evidence to suggest that the diagnostic yield reduces over time, early endoscopic examination is recommended within the first 48 hours. Considering the symptoms of this patient improved significantly 24 hours after diagnosis and antiplatelet drugs were taken before CAG, further colonoscopy was not performed. So unfortunately, we can't supplement the colonoscopy results.

We appreciate for Editors/Reviewers' warm work earnestly and hope that the correction will meet with approval. Once again, thank you very much for your comments and suggestions.