Reply to reviewers' comments

We thank all the reviewers and the Science Editor for reviewing the manuscript and giving us opportunity to revise the article. Please find our reply to the comment raised by all the reviewers and editor.

Reviewer 1: Very good educational article. Some figures lack names, just "Figure x"

Reply: Thank you very much for your comment. We have checked the entire manuscript and have made corrections wherever required.

Reviewer 2: This is an interesting review aiming to assess risk factors for major complications in laparoscopic cholecystectomy. There has been a great deal of interest on this topic and much effort has been devoted to avoiding the devastating complications, such as bile duct injury. This review article seems informative and educational. Nonetheless, I would prefer to be informed about potentially important issues in brief comments, as follows. #1 How do the authors think about the clinical relevance of preoperative imaging, such as MRCP or CT, to evaluate anatomical variances or severity of inflammation? #2 How should the cases of suspected or incidental gallbladder malignancy treated? The intraoperative spillage of the gallbladder contents into the abdominal cavity could lead to the dissemination of tumor cells if a malignant lesion were present.

Reply:

#1: We agree with you that preoperative imaging besides USG e.g. CT scan or MRCP is useful to assess severity of inflammation or anatomical variations. However, these special imaging are not part of routine work up for cholecystectomy thus are not performed routinely. There are specific situations where these imaging (CT/MRCP) may be informative and useful in further planning e.g. suspected common bile duct stone, gallbladder perforation/gangrenous cholecystitis, thick wall gallbladder with

suspicion of xanthogranumatous cholecystitis or gallbladder cancer, suspicion of Mirizzi syndrome, and cases with previous subtotal cholecystectomy with stump cholecystitis.

#2: If gallbladder cancer is suspected preoperatively based on USG, then this should be investigated further with CT scan and treated appropriately. Simple laparoscopic cholecystectomy is not recommended in such situations as it might be an inadequate/non curative procedure, and there would be risk of peritoneal dissemination in case of bile spillage as you have mentioned. True incidental gallbladder cancer is diagnosed only on histopathological examination of resected gallbladder when there was no pre- or intraoperative suspicion of malignancy. Further management depends on the stage of tumor. We have not discussed these points as the management of suspected or incidental gallbladder cancer was not the aim of the current review. However, all the surgeons performing cholecystectomy must rule out gallbladder cancer preoperatively as much reasonably as possible, and if doubt persists, these patients should be referred to specialist center for further management. In addition, bile spillage should be avoided as much as possible in all the cases especially in the high incidence regions for gallbladder cancer.

Reviewer 3: Dear Author, It was interesting to assess this review, which I found complete and excellent in scientific quality, with interesting algorithms and pictures.

Reply: Thank you very much for your encouraging comments.

Editorial comments

Reply: We have included audio core tip. Language editing has been done by a native English speaker, and certificate for it has been provided. Rephrasing of sentences has been done wherever it was asked for (highlighted in red fonts). Correction in references has also been done.