

Reviewer(s)' Comments to Author:

All corrections in the main text have been highlighted in yellow color.

Reviewer: 1

This manuscript is more like a narrative review of ICG application in identification of extra-hepatic biliary system and its benefits to cholecystectomy. Personally, I also have some experience of ICG application. This review is comprehensive and authors mentioned different aspects of ICG application. I only have one opinion. For the figure 1, please add a photo of pre-dissection. According to the original image, that case seemed to be a simple case of laparoscopic cholecystectomy. I would not like to use ICG in this case. I suggested author should put a photo of pre-dissection, then ICG illustration of biliary tree, and a photo of complete dissection of critical area. In that way, it will be more persuasive. I suggested minor revision and then accept this work. Thank you.

Answer: many thanks for your suggestion and comments. As requested, we put a photo of pre-dissection by white light alone compared to ICG fluorescence (Figure 1A), then a picture of complete dissection of hepatocystic triangle according to CVS method and the complete identification of biliary structures by fluorescence (Figure 1B). So, it will be more persuasive and clearer for readers.

Reviewer: 2

This is an interesting review aiming to describe recent studies regarding near-infrared fluorescent cholangiography (NIFC) for laparoscopic cholecystectomy (LC). In a few years, there has been an increasing body of literature for the fluorescent cholangiography as a promising tool to avoid bile duct injury. It is still unclear whether this procedure provides any additional security during LC with a meticulous dissection to achieve a critical view of safety (CVS). Nonetheless, I agree with the authors in the point that NIFC is a useful teaching tool for young surgeons, because the real-time cholangiography can show them how close to the dissecting site the bile duct is running in the laparoscopic view. This review article seems useful to update our knowledge of the published evidence concerning this topic. Nonetheless, I would prefer to be informed about potentially important issues as follows. #1 The method has a potential to be used in a large population of patients. Therefore, a comment for the risk of rare anaphylactic reaction to iodine would be needed in this kind of article. #2 As the authors mentioned in the manuscript, cholecystitis and obesity potentially hamper the visualization of the bile duct by NIFC. Then, can we say that there is sufficient thickness between the dissecting site and the bile duct when the fluorescence of the bile duct cannot be detected? How is the possibility of “false-negative” cases of fluorescent cholangiography to delineate the bile duct?

Answer: many thanks for your comments and we are grateful to have the possibility to revise our manuscript.

We added a short comment concerning the risk of adverse events and, in particular, anaphylactic reaction to ICG dye with the relative reference (ref. 77), according to available literature data. This confirmed the safety of ICG fluorescence in clinical practice.

We detailed how to dissect the critical area even in cases where CBD cannot be detected. In general, our opinion is to use fluorescence to perform a complete dissection of the hepatocystic triangle in overweight and obese patients and in patients with acute cholecystitis to obtain a good quality visualization of the biliary anatomy. In difficult cases where the surgeon is not able to clearly check the biliary anatomy, the surgeon should respect a sufficient thickness between the dissecting site and the main bile duct by working close to the gallbladder infundibulum to avoid unexpected biliary lesions.