

Dear Colleagues,

First of all, thank you for taking the time to review our article **“Laparoscopic Ultrasonography as an Alternative to Intraoperative Cholangiography during Laparoscopic Cholecystectomy”**. We also appreciate the supportive comments from the majority of the reviewers as to the value and interest of this topic.

We now provide a point-by-point response to the reviewer's comments. Each comment is provided in full (black text) with our reply in blue text. We note that reviewer 3 stipulated that LUS “may be performed on a routine basis. And it is written in textbook”. While we have no objection to this point of view, it doesn't appear to reflect the reality, which is that very few surgeons are currently using this technique. Our assertion would also be supported by the scant literature on this topic. In contrast, there is an abundance of recent literature for intraoperative cholangiography, discussing its value in preventing common bile duct injury, and in detecting common bile duct stones. We have amended our text to highlight the potential benefits of laparoscopic ultrasonography, which is probably even more relevant today due to the commonplace use of the laparoscopic approach, even in technically demanding situations.

We believe that the corrections made to our text have strengthened our manuscript considerably, and we look forward to hearing your opinion as to its suitability for publication.

Sincerely yours.

Alexandra DILI

Claude BERTRAND.

Comments

1. A good topic for LC.

2. The core tips should describe more concisely the essence of the reviewed results. \$

We have now modified the core tips section in response to reviewers 1 and 3.

3. In the main results section –

The collected data should be cited individually in the text to help reading, such prospective non-randomized, retrospective trials or meta-analysis.

We have now modified our text appropriately, with indications throughout the main text as to the study type.

Typical images of “Mickey mouth sign” and “four tube sign” will be preferred than the image of Fig 1.

The authors are more accustomed to the longitudinal analysis, which is why we presented that view. We also find that view to be of use in demonstrating the integrity of the bile duct. However, we have now also added technical aspects of LUS with a transverse analysis, which is particularly useful prior to dissection. See new Fig.1

Several questions about Fig.1:

1)in a,b,c figures, there is a prominent intra-hepatic bile duct. It is my common sense that intra-hepatic bile duct is not depicted, unless there is a bile dilatation caused by the proximal bile duct obstruction.

The accurate identification of the convergence of bile ducts (left duct, right posterior sector duct, right anterior sector duct) would appear to be an important step. Although potentially difficult, we chose a case with a small dilatation of the bile duct to improve visualization. We also chose this case for instructional purposes given the presence of a common bile duct stone. In providing the requisite correction, Fig. 1 now becomes Fig. 2.

2) a longitudinal images of various condition of extra-pancreatic CBD will be more essential for the educational purpose of this review, especially in difficult GB. ?

Other longitudinal images are now shown in fig 2 (i.e. low implantation of cystic duct which is parallel to the intra-pancreatic common duct, low pre-papillary CBS).

Original publication should be cited for the “four tube sign”.

A citation is now provided for this. We could find no other relevant reference.

In “LUS And Anatomy”: 5th section, citation of the mentioned surgeon or article should cited to help understanding.

All authors are now cited in table 2.

7th section, can the data of 73%~100% be indicated in Table 3

As requested, these data (73% -~100%) are now cited in the table (given more precisely as 73.8-98%).

In LUS and Inflammation: Is there any data of analysis rate of the fibrotic state, which is more important than inflammation state to use LUS.

A comment about this issue is deserved in the abstract.

Unfortunately, in the reports analyzed, data for “difficult situations” involving acute/chronic inflammation and Mirizzi’s syndrome were presented collectively. The authors agree with this reviewer that using LUS before dissection, when the anatomy is obscured, is probably the most useful aspect of this technique. More detailed reports concerning specific complex scenarios would help in assessing the usefulness of LUS. These comments have now been added to the text (3rd and 4th sections, and abstract).

Again, citation should be offered to the sentence of “avoiding conversion in 91% of patients” and the results of avoiding conversion should be implemented in the abstract. This is most attractive function of LUS for LC.

This citation was not originally included as we were describing an observation made by Gwin that was already cited at the beginning of the paragraph. However, the citation has now been added.

In LUS and BDI: 3rd section, high recognition rate of BDE using LUS should be more precisely described.

The percentage recognition of bile duct injury (100%) by LUS is now mentioned in the text. However, we also note that this experimental study is limited by a non-blinded design, with surgeons knowing that they had to search for a BDI.

The conclusion of this article was “in cases of iatrogenic occlusion of the bile duct involving hemoclips”.

An example is given of a BDI (from stenosing hemoclips) that can occur with normal perioperative IOC. Performing LUS just before finishing the operation could help to recognize an injury that would otherwise go unnoticed.

In LUS and CBDS: 3rd section, -- sentence of “confirmed a sensitivity and sensitivity rate for LUS”, the latter sensitivity should be corrected for specificity.

We have now made this correction.

4. There is no “Discussion” section.

We have now added the discussion section as suggested by the reviewer.

Can LUS detect aberrant ducts, such as right posterior segment or others, from cystic duct? ?

Can LUS detect the ultra-short, short cystic duct or disappeared cystic duct from CBD?

Can the author discuss about its use in most needed case of fibrotic state of difficult GB.

As mentioned in the text, even when the authors describe the anatomical segments analyzed, few reports provide specific data for each biliary segment. Indeed, aberrant bile ducts, ultra-short cystic ducts, and Mirizzi’s syndrome, have all been described in the literature, as now explained in our report.

Reviewer 2 - 03474672

Review Time 2017-02-22 08:47

Dear authors,

I enjoyed reviewing this paper. Well done and written. Very few studies have been investigated the ultrasonography as an alternative to intraoperative cholangiography during laparoscopic cholecystectomy to evaluate the anatomy.

Otherwise I believe that some details could help you to do better.

First more illustrated figures will clarify the technique.

We now complement the original ultrasound figures with laparoscopic images of the same clarity for instructional purposes (see fig.1).

Other important information is mention in the kind of study it is: prospective non-randomized, retrospective trials or meta-analysis.

Table 1 details the type of study for each paper. To clarify, we have also now inserted this information into the main text.

I miss the discussion part and the study's limitation. I believe you could re-write the specific scenarios and the speed of the process, learning curve and cost building a discussion.

We now mention our study limitations in the discussion section, taking care to address the remarks made by the reviewers, as well as their advice.

It would be interesting if the authors could considerer these suggestions. These constructive criticisms should assist the authors in improving their manuscripts and I will be pleasure in indicate this manuscript to publication.

Laparoscopic ultrasonography may now be performed on a routine basis. And it is written in textbook. What is the different idea current article? There are a lot of review about this topic. I think this issue is not very topical.

We would agree that LUS is a well-established, useful, and cost-effective procedure, which has already been described in the context of cholecystectomy (open or laparoscopic) for more than 30 years. Yet, curiously, on review of the literature, we found relatively few published trials and reports of either its role or effectiveness. Further, no randomized trials have been conducted, and the available reports are heterogeneous in nature with no standardized results. This finding possibly reflects a chronic underuse of this technique. Instead, newer procedures that are more expensive and rarely performed, are used as substitute evaluative techniques in helping the surgeon to map the biliary tract and hilar structures.

A review of the role of LUS as a tool to guide dissection, especially in difficult scenarios, appeared to be relevant, important, and long overdue. LUS is inexpensive, and neither time consuming, nor dangerous in terms of irradiation. Further, the relevant apparatus are commonly found in most operating theatres. Lastly, up until now, many surgeons have been reluctant to perform LUS given their perception that adequate training necessitates too great a time investment. However, as ultrasound and laparoscopy become "everyday" techniques in modern surgery, we find that most surgical trainees and junior surgeons have been exposed to these techniques and are in the habit of using them. Consequently, reluctance in terms of embarking on the "LUS" learning curve is likely to become an historic issue.

Intraoperative cholangiography is an even older technique. However, the importance of accurately detecting the common bile duct in order to prevent injury remains a hot topic. Consequently, there is still a considerable volume of literature on this subject and we feel that it is of value to highlight the potential benefits of laparoscopic ultrasonography, especially in difficult situations. We hope that this type of review will not only enhance the use of LUS, but also stimulate a greater number of studies on the subject. These points are now included in the "Comments" section of the article.

Reviewer 4

Review Time 2017-03-24

The paper describes a literature review of laparoscopic ultrasonography for delineation of the biliary tract and detection of common bile duct stones during laparoscopic cholecystectomy. The paper is well-written, covering all relevant publications on the topic.

Comments:

The authors suggest that LUS is a substitute for intraoperative cholangiography. Could it not be used as an additive to IOC? What is the sensitivity if both techniques are used in combination? There are situations, in particular during surgery for cholecystitis, where either of the techniques may turn out to be impossible to perform

We agree, and this has become our strategy (LUS used initially, with recourse to IOC in the case of anatomical confusion or suspicion of a CBDS). This point is now made (with 2 specific references) in the last part of the section "LUS and common bile duct stones". We also now reiterate this point in the discussion.

The abstract is too long (325 words). It should be shortened and more focused.

The abstract has now been re-written in accordance with the guidelines.

Please give explanations to the abbreviations A-PL and P-AL under "LUS and Anatomy"

We have now amended our text in response to this criticism.

Figure legend 1: CBD is an abbreviation of "Common Bile Duct" -

We have now made this correction to our text.