

Peer Review File

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Reviewer A:

A good compact narrative review. Comments to improve the manuscript:

1. Although M.Gagner was one of the pioneers of laparoscopic liver surgery and has made a tremendous contribution in its popularisation among general and HPB surgeons, it was H.Reich who first reported laparoscopic liver resection (He was actually a gynecologist). This should corrected. See a reference below:

Reich H, McGlynn F, DeCaprio J, Budin R. Laparoscopic excision of benign liver lesions. *Obstet.Gynecol.* 1991 Nov;78(5 Pt 2):956-8.

Reich H, McGlynn F, DeCaprio J, Budin R. Laparoscopic excision of benign liver lesions. *Obstet.Gynecol.* 1991 Nov;78(5 Pt 2):956-8.

Reply: thanks for your comment, H.Reich et al were also cited.

Pag. 4 - From these years on, several cases were reported. In 1991, Reich et al, (1) describes is first experience with superficial lesions of the liver edge found incidentally during laparoscopic surgery for gynecologic symptoms managed by a laparoscopic approach.

2. It is important to mention the manuscript below in the section about laparoscopic parenchyma-sparing liver resections. That manuscript demonstrated a superiority of multiple parenchyma-sparing concomitant liver resections over early widely performed single major resection for multiple colorectal liver metastases.

Kazaryan AM, Aghayan DL, Barkhatov LI, Fretland ÅA, Edwin B. Laparoscopic Multiple Parenchyma-sparing Concomitant Liver Resections for Colorectal Liver Metastases. *Surg Laparosc Endosc Percutan Tech.* 2019 Jun;29(3):187-193

Reply: thanks for the suggestion, it was cited. Pag 6 Later described by Kazaryan et al., (11), multiple concomitant liver resections provide surgical and oncologic outcomes comparable with single greater resections for multiple lesions

3. Although this review is about laparoscopic techniques, I would recommend mentioning in the section "Discussion" about robot-assisted laparoscopic liver resections (or simplified cold robotic). This technique has an increasing trend and its benefits and disadvantages should be concisely mentioned. Some words about hand-assisted laparoscopic liver resections should be said too. Beside expected future of laparoscopic liver surgery and its modifications (pure laparoscopic liver surgery / robot-assisted laparoscopic liver surgery / hand-assisted laparoscopic liver surgery / 3D

laparoscopic liver surgery) should be outlined.

Reply: thanks for your suggestion, 3D is mentioned at pag 18; robotic surgery in mentioned at pag 19 both in the section "Discussion".

Reviewer B:

Overall, the authors summarize the results of laparoscopic hepatectomy in colorectal liver metastases. However, I believe the article should focus more the current shortcomings and some of the future directions being investigated to help bridge the gaps that currently exist. There are a couple of issues that need addressing.

Major Consideration

Comment 1: Title

The liver is a common site for metastatic disease. The authors should add "colorectal cancer" to the title.

Reply: thanks for your suggestion, title has been changed. LAPAROSCOPIC HEPATIC RESECTIONS FOR COLORECTAL CANCER METASTASES: A NARRATIVE REVIEW

Comment 2: Introduction

The authors have divided the Introduction into two parts: "Development of Laparoscopic liver resection" and "OBJECTIVES". The structure is very clear. However,

- (1) As stated in comment 1, the authors do not present any information on "colorectal liver metastasis".
- (2) Why focus on this minimally invasive surgery instead of the traditional open surgery? This is also not explained clearly.
- (3) The section "Development of Laparoscopic liver resection" seems to be more appropriate after the section "Method": the authors search the literature to help the reader sort out the history and development of "Laparoscopic liver resection".
- (4) Last but not least, the manuscript fails to provide a persuasive rationale for publication this review in the introduction. There have been several similar reviews in this field (e.g., PMID: 27294144, 34869559, 30510936, 28451728, etc.), what does this review add to existing knowledge? How does this review differ from previous reviews?

Reply:

1. Pag.8 Colorectal cancer (CRC) remains a leading cause of tumor-related morbidity and mortality worldwide (12); it is ranked as third in terms of incidence (10.2% of all cancer cases worldwide) and is considered the second most common cause of cancer mortality (9.2% of all cancer mortality) in the world. However, tremendous improvements were reached in term of survival in patients with CRC (13) when considering that the reported

2-year overall survival (OS) for stage IV CRC was only 21% in the 1990s (14) In the last 2 decades, the 5-year OS progressively increased from 9.1% to 19.2%, mostly thanks to an increase in the patients eligible to hepatic resection and to the improvement in systemic chemotherapy (15). The hematogenous spreading via the portal circulation of cancer cells from CRC makes the liver an easy target for metastatic dissemination. The presence of liver metastasis represents the most critical prognostic factor considering that the reported incidence of synchronous metastases is 15–25% (16) and up to 18–25% patients will develop distant metachronous metastases within 5 years from the first diagnosis

2. Pag. 9 and 10- section: MINIMALLY INVASIVE SURGERY AND LOCOREGIONAL THERAPY OF CRLM
3. The section “development of laparoscopic liver resection” has been put in the introduction because it’s more on the historical point of view.
4. We think it’s a quite complete narrative review, concerning the history of laparoscopic liver surgery, the state of art and the potential future developments. The limits of laparoscopic liver surgery has also been described. Last, but not least, we tried to make it accessible to everybody.

Comment 3: Methods

Line 46: “select articles of interest”. This inevitably leads to a rather narrow view. Two suggestions:

- (1) Specify in the "Methods" what is "of interest".
- (2) In the Discussion, add the reasons for doing so and how readers should interpret the review.

Reply: thanks for the suggestion, it has been done.

Comment 4: Discussions & Conclusion

If available, it is suggested the authors could consider presenting the treatment strategies in different situations visually using tables or diagrams.

Reply: thank you, we tried to insert some pictures and a diagram.

- (2) It would be better to present guidelines for future directions as well as personal suggestions.

Reply: thank you for the suggestion, a diagram has been inserted.

- (3) L421-422: ""morbidity and mortality ... is nowadays acceptable". Careful should be taken with the words used.

Reply: thanks, it has been modified.

Minor suggestions

Comment 5: Abstract

(1) Lines 38, 47: Abbreviations "CRC" and "CRLM" can be removed as otherwise not used in Abstract.

Reply: thanks you, we modified it.

(2) Line 45: "PubMed" not "Pub-Med".

Reply: thank you, we changed it.

Comment 6: References

(1) Citations are missing in several places in the manuscript (e.g., line 38, 96). Please cite the reference to back up the claims and check the entire manuscript to address similar concerns.

(2) Line 58: I would use the reference numbers after each author, rather than put them at the end of the sentence. e.g., "Gagner et al (2)".

(3) Line 349: "first introduced by Gold et al. in 2008 (39)". References and citations should check one by one, have wrong numbers.

Reply: Thank you, everything has been changed.

Comment 7: Abbreviations

Please define all abbreviations mentioned for the first time in the text, such as CRLM (line 121).

Reply: thank you, we changed it.