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Review

Laparoscopic vs. open left lateral sectionectomy: An update meta-analysis of randomized and non-randomized controlled trials

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ABSTRACT

Background: Left lateral sectionectomy (LLS) is thought to be the anatomical liver resection most suitable for the laparoscopic approach. Despite increasing popularity, comparative analysis of laparoscopic and open LLS are mostly limited to retrospective, underpowered studies with small sample size. Recent population-based studies and prospective trials have generated new data; however, this new body of knowledge has not been submitted systematic reviews or meta-analyses and high quality evidence regarding the actual benefits of minimally invasive LLS is lacking.

Methods: Systematic review of studies published until December 31st, 2017 and indexed in Medline, EMBASE, Cochrane Library Central and Scielo/LILACS databases. Randomized controlled trials and observational studies comparing perioperative results of laparoscopic and open LLS were included. Studies with patients submitted to LLS for living donation were excluded. Treatment outcomes, including conversion rates, estimated blood loss, transfusion rates, operative time, length of in-hospital stay, morbidity and mortality rates, were evaluated.

Results: The primary search yielded 2838 articles, 23 of which (21 observational studies and 2 randomized controlled trials; 3415 patients) were included in the meta-analysis. Overall conversion rate was 7.4%. Patients submitted to laparoscopic LLS had less blood loss (mean difference, MD = −119.81 ml, 95% CI = −127.90, −111.72, $P < .00001$, $I^2 = 32\%$, N = 618), lower transfusion rates (4.1% vs. 10.1%; risk difference, RD = - 0.06, 95% CI = - 0.08, - 0.05, $P < .00001$, $I^2 = 13\%$, N = 2968) and shorter length of in-hospital stay (MD = - 2.02 days, 95% CI = - 2.15, - 1.89, $P < .00001$, $I^2 = 77\%$, N = 3160) compared to those undergoing open surgery. Marginally decreased overall complication (21.4% vs. 27.5%; RD = - 0.03, 95% CI = - 0.06, 0.00, P = .05, $I^2 = 0\%$, N = 3268) and perioperative mortality (0.3% vs. 1.5%; RD = - 0.01, 95% CI = - 0.02, - 0.00, P = .01, $I^2 = 0\%$; N = 3332) rates were also observed. Operative time and biliary, cardiac or pulmonary complication rates did not differ significantly between groups.

Conclusion: Current evidence supports the safety and feasibility of laparoscopic LLS. The laparoscopic approach is associated with reduced blood loss, lower transfusion rates and shorter length of in-hospital stay and should be considered the gold-standard for LLS.

1. Introduction

Laparoscopic liver resections consisting of wedge resections of small peripheral lesions were first described by Reich et al. [1] and Gagner et al. [2] in the early 1990s. Left lateral sectionectomy (LLS) was the first anatomical liver resection to be performed via a minimally invasive approach, and was simultaneously reported by Azagra et al. [3] and Kaneko et al. [4] in 1996. Subsequent case series and comparative studies confirmed the safety and feasibility of laparoscopic LLS [5–11].

Laparoscopic LLS has become increasingly popular after the 1st International Consensus Conference on Laparoscopic Liver Resections held in Louisville in 2008, where it was considered a safe and straightforward liver resection procedure in expert hands [12]. In fact, the left lateral sector of the liver has unique anatomical features that

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favor the laparoscopic approach, such as midline position in the abdominal cavity and small parenchymal volume, which facilitate resection using energy devices. Also, access to segment 2 and 3 pedicles alongside the umbilical fissure is relatively easy and allows pedicle control using vascular staplers [13,14]. Laparoscopic LLS is therefore amenable to complete standardization; also, it is thought to be a feasible and reproducible procedure even in the hands of less experienced surgeons and has a shorter learning curve compared to major liver resection [15].

Despite increasing acceptance of laparoscopic LLS, comparative analysis of open and laparoscopic procedures are mostly limited to single center, retrospective, underpowered studies with small sample size. Only recently have population-based studies [16,17] and randomized clinical trials (RCTs) been published [18,19], and the most recent RCT (ORANGE II trial) failed to randomize a sufficient numbers of patients.

Given the emerging body of research, systematic reviews and meta-analyses including larger numbers of cases are warranted to generate high quality evidence regarding the actual benefits of minimally invasive LLS.

This study set out to perform an updated systematic review and meta-analysis of studies comparing perioperative outcomes of patients submitted to laparoscopic or open LLS due to benign or malignant liver disease.

2. Methods

This study was approved by the Institutional Ethics Committee and conducted in compliance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and AMSTAR (Assessing the methodological quality of systematic reviews) Guidelines. This research protocol was registered in the International Prospective Register of Systematic Reviews (http://www.crd.york.ac.uk/PROSPERO).

2.1. Literature search

Medline, EMBASE, Cochrane Library Central and Scielo/LILACS (Scientific Library Electronic Online/Latin American and Caribbean Health Sciences Literature) databases and the grey literature were systematically and independently searched by 2 authors. Databases were searched for RCTs and observational studies comparing perioperative outcomes of patients submitted to laparoscopic or open LLS. The search was limited to human subjects and included prospective and retrospective studies, regardless of language, date of publication or publication status. Retrieved references were cross-checked manually for additional studies. The last search was performed on December 31st, 2017.

Search strategies consisted of different combinations of Medical Subject Headings (MeSH) and search terms per database, as follows: Medline - ((((((hepatectomy OR liver resection OR sectionectomy OR segmentectomy))) AND ((laparoscop*) OR (Hand Assisted OR Hand-Assisted) OR (video) OR (hybrid)))) AND ((therapy/broad[filter] OR comparative study OR epidemiologic methods))); EMBASE - similar search terms and the “comparative clinical studies” filter; Cochrane and Scielo/LILACS - search terms only (i.e, no additional filters).

2.2. Study selection

Eligibility screening and article selection were performed independently by two reviewers. Titles and abstracts were screened first and duplicate or irrelevant studies excluded; full-text versions of potentially eligible articles were then obtained. The following inclusion criteria were used: (1) RCTs and prospective or retrospective studies comparing perioperative outcomes of open and laparoscopic LLS, regardless of sample size; (2) Studies with patients submitted to pure, hand-assisted and hybrid laparoscopic procedures (laparoscopic group); (3) If the same patients were included in more than one study, the most recent or the one of higher quality was selected.

Exclusion criteria were as follows: (1) Non-comparative studies, review articles, letters and case reports; (2) Studies comparing robotic surgery or single-port resections: (3) Studies including patients submitted to LLS for living donation; (4) Studies with missing values or data for calculation of mean and standard deviation (SD); (5) Studies unavailable in full-text.

Disagreements on eligibility of specific studies for final inclusion were resolved by consensus.

2.3. Data extraction

Full text, tables and figures of selected studies were independently assessed by two researchers for data extraction. The following data were collected: (1) Name of first author and year of publication; (2) Study type; (3) Laparoscopic approach – pure, hand-assisted or hybrid; (4) Number of patients per arm; (5) Perioperative outcomes - conversion rates, operative time, estimated blood loss, transfusion rates, length of in-hospital stay, reoperation rates, overall morbidity and specific complications (cardiac, pulmonary, biliary or wound-related), and perioperative mortality within 90 days of surgery.

2.4. Level of evidence and quality assessment

Level of evidence assessment was based on the 2011 Oxford Scale [20]. The Cochrane Collaboration tool [21] was used to assess the risk of bias in RCTs; this tool grades random sequence allocation, allocation concealment, blinding of participants, blinding of outcome assessment, incomplete outcome data, selective reporting and other biases. The Newcastle-Ottawa Scale (NOS) was used for quality assessment of observational studies [22]. Studies scoring 6 stars or higher were considered of sufficient quality for inclusion in the quantitative analysis.

2.5. Statistical analysis

Meta-analysis was performed using software (Review Manager, version 5.3; Copenhagen: The Nordic Cochrane Center, The Cochrane Collaboration, 2014). Continuous variables were expressed as mean ± SD. Whenever continuous data were expressed as medians and ranges, means and SDs were calculated as described by Hozo et al. [23]. The mean difference (MD) or the risk difference (RD) were used as a summary measures for continuous and dichotomous data respectively; a 95% confidence interval (CI) was reported in both cases.

Study heterogeneity was assessed using chi-square and I^2 statistic (I^2 values of 0–25%, 26–50% and ≥51% equal low, moderate and high heterogeneity respectively). Causes of statistical heterogeneity were investigated using sensitivity analysis based on exclusion of specific studies. The fixed effects or the random effects model was used for outcomes with low to moderate heterogeneity (0–50%) and high heterogeneity respectively. The funnel plot was used to assess publication bias; sensitivity analysis excluding outliers was performed whenever risk of bias was identified.

Whenever possible, subgroup (RCT or observational study) analysis was performed. Individual analysis of patients submitted to pure laparoscopic LLS was also carried out. The level of significance was set at 5% ($P < 0.05$).

3. Results

A total of 2838 potentially relevant articles were retrieved from the primary literature search. Of these, 23 studies (21 non-randomized trials and 2 RCTs) published between 2002 and 2017 met the selection criteria and were included in the qualitative synthesis (Fig. 1). All 23 articles were included in the meta-analysis following quality assessment

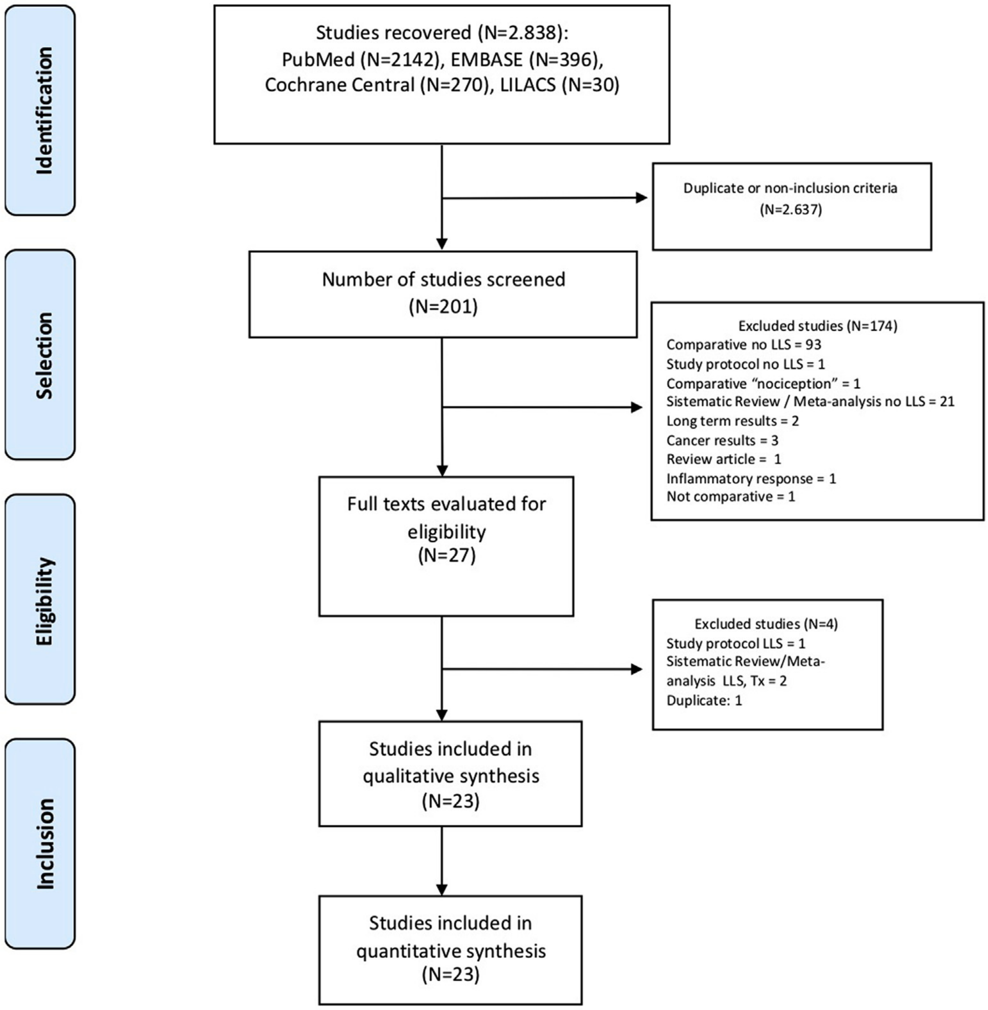

Fig. 1. Flowchart showing search strategy and study selection.

(Table 1).

3.1. Conversion rate

Pooled data analysis revealed a conversion rate of 7.4%, while separate analysis of observational studies and RCTs revealed conversion rates of 8.6% and 4% respectively.

3.2. Operative time

Mean operative time was reported in 21 studies (1138 patients); pooled analysis failed to detect significant differences between open and laparoscopic approaches (MD = 5.43 min; 95% CI = −13.06, 23.91; P = 0.57; I^2 = 97%). Likewise, operative time did not differ significantly between randomized and non-randomized studies (Fig. 2).

3.3. Estimated blood loss

Estimated blood loss was assessed in 19 studies (1032 patients). Pooled data analysis revealed significantly less blood loss in the laparoscopic group (MD = - 109.09 ml; 95% CI = - 116.00, - 102.19; P < 0.00001), with high levels of heterogeneity between studies (I^2 = 92%).

Sensitivity analysis based on the funnel plot method detected seven outliers (Aldrighetti 2007; Robles Campos 2008; Stoot 2012; Hilal 2013; Hirokawa 2013; Peng 2017; Hung-Lun-Hing 2017 – observational study). Statistical heterogeneity dropped to 32% and blood loss remained significantly less in the laparoscopic group following exclusion of outliers (MD = −119.81 ml; 95% CI: 127.90, −111.72; P < 0.00001; 618 patients; Figs. 3a and 4).

3.4. Transfusion rates

Blood transfusion rate data were reported in 17 non-randomized studies (3174 patients), with significant differences in favor of laparoscopic LLS (RD = - 0.07; 95% CI = - 0.09, - 0.05; P < 0.00001; I^2 = 58%).

Funnel plot analysis revealed potential biases in 2 studies (Stoot 2012; Bell 2014); however, blood transfusion rates remained significantly lower in patients submitted to laparoscopic compared to open LLS (4.1% and 10.1% respectively) following exclusion of these studies (RD = - 0.06; 95% CI = - 0.08, - 0.05; P < 0.00001; N = 2968; Figs. 3b and 5), with low levels of heterogeneity between studies (I^2 = 13%).

3.5. Morbidity

Overall morbidity was reported in 20 studies. Analysis of data of 3331 patients revealed lower complication rates in laparoscopic compared to open LLS (RD = - 0.04; 95% CI = - 0.07, - 0.01; P = 0.02; I^2 = 26%).

Funnel plot analysis detected 1 outlier (Shin 2015). Outlier

Table 1
Summary of studies included in the meta-analysis. CRBT-RCT: Cochrane Risk of Bias Tool for Randomized Controlled Trials; RCT: Randomized Controlled Trial; HALR: Hand-assisted liver resection.

								Number of patients	
Author	Country	Year	Study	Level of evidence*	CRBT - RCT	NOS	Comparison	Open	Laparoscopic
Lesurtel M [24]	France	2002	Observational	3	–	9	Lap vs. Open	20	18
Tang CN [25]	China	2005	Observational	4	–	8	HALR vs. Open	7	10
Aldrighetti L [26]	Italy	2007	Observational	4	–	9	Lap vs. Open	20	20
Robles Campos R [27]	Spain	2008	Observational	3	–	8	Lap vs. Open	10	10
Cai XJ [28]	China	2008	Observational	3	–	9	Lap vs. Open	3	3
Vanounou T [29]	USA	2009	Observational	3	–	8	Lap + HALR vs. Open	29	44
Endo Y [30]	Japan	2009	Observational	4	–	8	Hybrid vs. Open	11	10
Carswell KA [31]	United Kingdom	2009	Observational	4	–	8	Lap vs. Open	10	10
Nanashima A [32]	Japan	2009	Observational	4	–	7	Hybrid vs. Open	5	3
Lee KF [33]	China	2011	Observational	4	–	8	Lap vs. Open	10	18
Stoot JHMB [16]	Netherlands	2012	Observational	3	–	8	Lap + HALS vs. Open	90	30
Dokmak S [34]	France	2013	Observational	4	–	8	Lap + HALR vs. Open	31	31
Hilal MA [35]	United Kindon	2013	Observational	4	–	8	Lap vs. Open	19	46
Hirokawa F [36]	Japan	2014	Observational	3	–	8	Lap vs. Open	34	24
Bell R [37]	United Kindon	2014	Observational	3	–	8	Lap vs. Open	43	43
Zhang Y [38]	China	2015	Observational	3	–	8	Lap vs. Open	20	30
Cheung TT [39]	China	2015	Observational	3	–	9	Lap vs. Open	29	24
Shin YC [40]	South Korea	2015	Observational	3	–	8	Lap vs. Open	30	33
Goh BKP [41]	Singapore	2016	Observational	4	–	8	Lap vs. Open	114	42
Goutte N [17]	France	2016	Observational	3	–	9	Lap vs. Open	1572	626
Ding G [18]	China	2015	RCT	1	Low risk	–	Lap vs. Open	49	49
Wong-Lun-Hing EM** [19]	Netherlands	2017	RCT	1	Low risk	–	Lap vs. Open	11	13
Wong-Lun-Hing EM** [19]	Netherlands	2017	Observational	3	–	9	Lap vs. Open	13	54
Peng L [42]	China	2017	Observational	4	–	9	Lap vs. Open	23	21

* According to Oxford Level of Evidence 2011.
**ORANGE II Trial divided in RCTs and observational studies for analysis.

exclusion led to a marginal decrease in the risk of perioperative complications (21.4% and 27.5%, laparoscopic and open LLS respectively; RD = - 0.03; 95% CI = - 0.06, - 0.00; P = 0.05; I^2 = 0%). Morbidity rates did not differ significantly between groups following separate analysis of RCTs and observational studies (Figs. 3c and 6).

Specific perioperative complication rates did not differ significantly between laparoscopic and open LLS. Specific complication rates were as follows: Postoperative biliary fistula (0.7% and 3.1%, laparoscopic and open LLS respectively; RD = - 0.02; 95% CI = - 0.05, 0.01; P =0 .17; I^2 = 0%; 9 studies; N = 528); cardiac complications (RD = - 0.02; 95% CI = - 0.06, 0.02; P = 0.28; I^2 = 0%; 8 studies; N = 418); pulmonary complications (RD = - 0.00; 95% CI = - 0.04, 0.03; P = 0.76; I^2 = 0%; 12 studies; N = 2791); wound-related complications (RD = - 0.01; 95% CI = - 0.01, 0.00; P = 0.22; I^2 = 36%; 10 studies; N = 2696).

3.6. Reoperation

Need for reoperation was assessed in 7 non-randomized studies (437 patients). Reoperation rates were similar regardless of surgical approach (0.5 and 1.8%, laparoscopic and open LLS respectively), with homogeneity between studies (RD = - 0.00; 95% CI = - 0.04, 0.03; P =0 .76; I^2 = 0%).

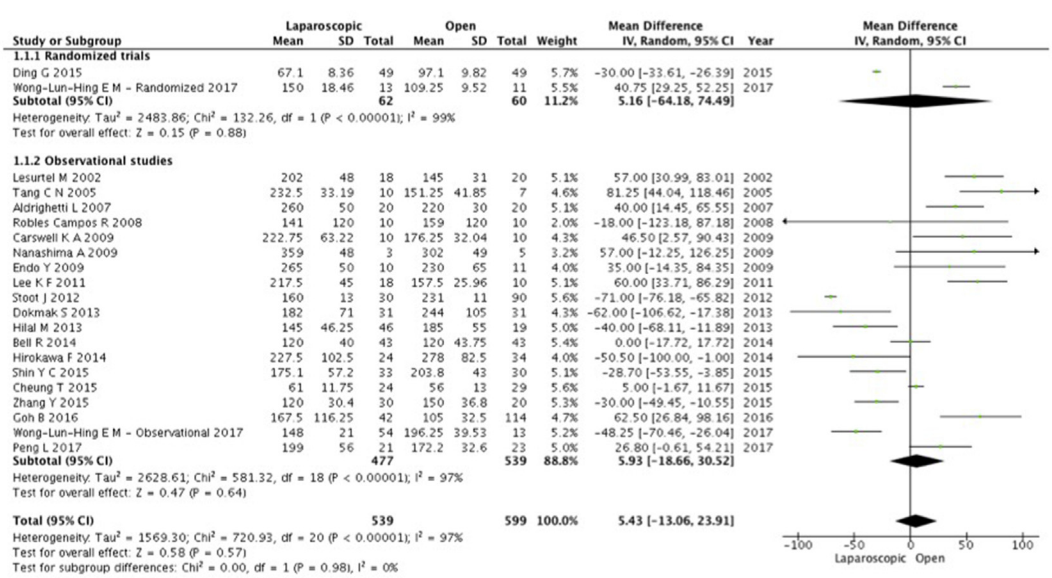

Fig. 2. Forest plot depicting operative time.

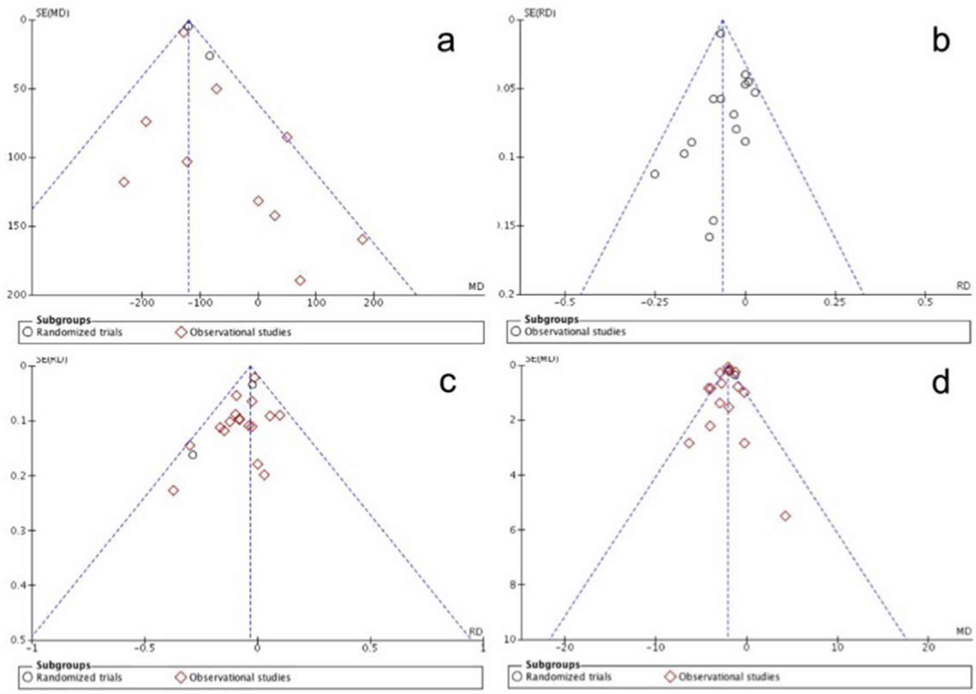

Fig. 3. Funnel plot after exclusion of outliers (a) estimated blood loss, (b) transfusion rates, (c) overall morbidity, (d) length of in-hospital stay.

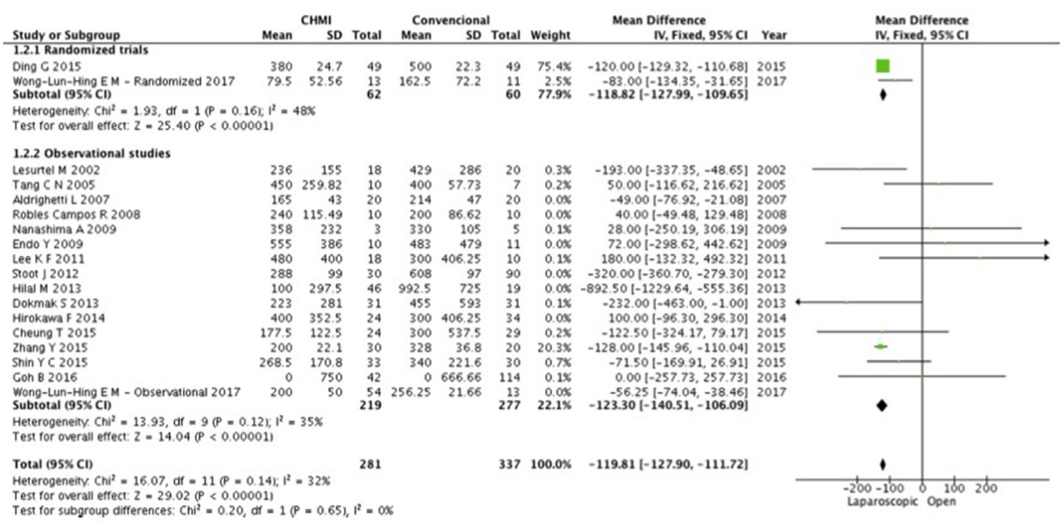

Fig. 4. Forest plot depicting estimated blood loss after exclusion of outliers.

3.7. Length of in-hospital stay

Length of in-hospital of stay was reported in 22 articles (3336 patients). Overall, length of in-hospital stay of patients submitted to laparoscopic resection was 2 days shorter (MD = - 1.95 days; 95% CI = - 2.08, - 1.83; $P < 0.00001$; $I^2 = 87\%$]. This finding was limited to non-randomized studies (MD = - 2.11 days; 95% CI = - 2.24, - 1.98); $P < 0.00001$), with no significant differences found in RCTs (MD = - 0.56 days; 95% CI = - 0.95, 0.18; P = 0.16).

Sensitivity analysis revealed 5 outliers (Robles Campos 2008; Endo 2009; Dokmak 2013; Zhang 2015; Wong-Lun-Hing 2017 - RCT). Length of in-hospital stay remained shorter in the laparoscopic group following exclusion of outliers (MD = - 2.02 days; 95% CI = - 2.15, - 1.89; $P < 0.00001$; $I^2 = 77\%$; 3160 patients). Findings of RCTs and observational studies were similar (Figs. 3d and 7).

3.8. Perioperative mortality

Perioperative mortality rates following laparoscopic and open LLS corresponded to 0.3% and 1.5% respectively (21 studies; 3332 patients). Pooled data analysis revealed marginal differences in favor of laparoscopic LLS (RD = - 0.01, 95% CI = - 0.02, 0.00, P = 0.01; $I^2 = 0\%$; Fig. 8). Separate analysis of non-randomized studies yielded similar results (RD = - 0.01; 95% CI = - 0.02,–0.00; P = 0.01; $I^2 = 0\%$), whereas no differences were observed in RCTs.

3.9. Pure laparoscopic LLS

Six studies were excluded from this analysis (Tang 2005, Vanounou 2009, Endo 2009, Nanashima 2009, Stoot 2012 and Dokmak 2013). Our findings were similar to previous analyses including other minimally invasive techniques. Pure laparoscopic LLS was associated with

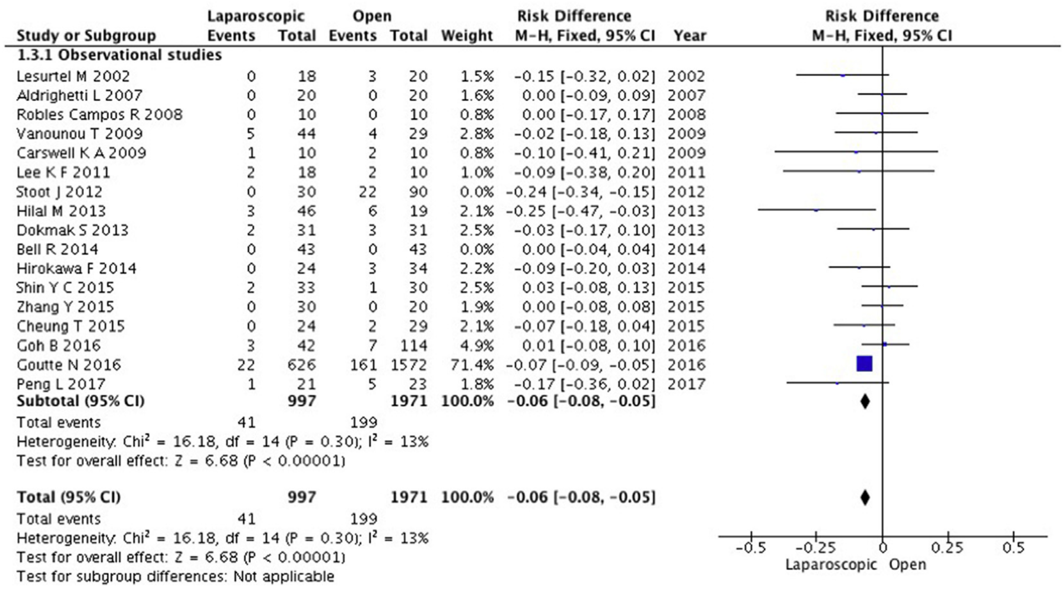

Fig. 5. Forest plot depicting blood transfusion rates after exclusion of outliers.

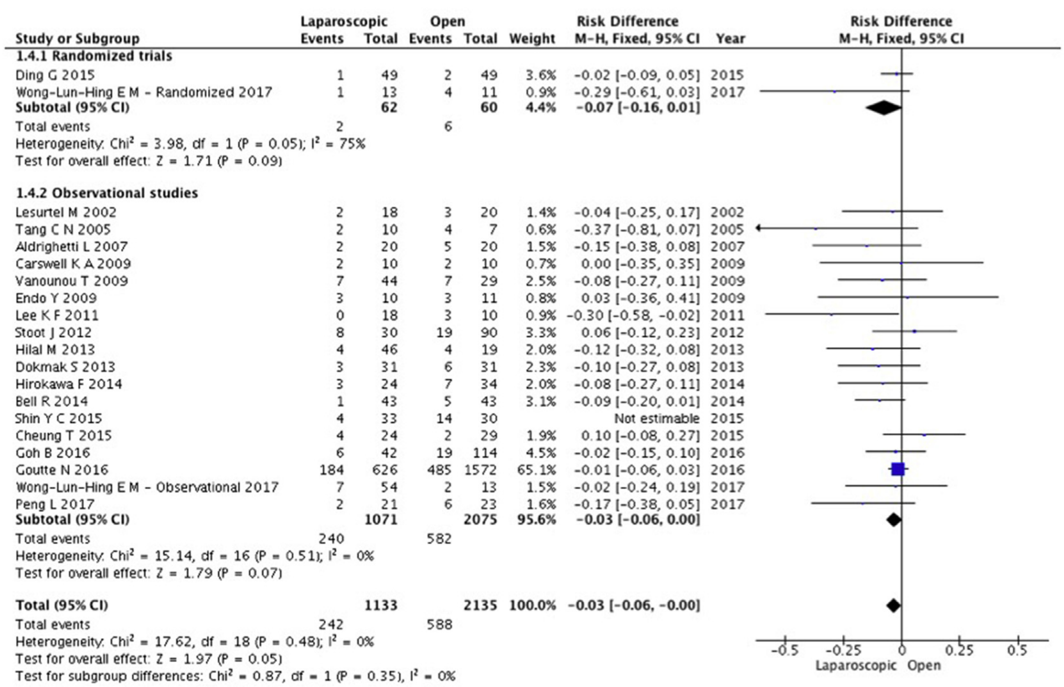

Fig. 6. Forest plot depicting overall morbidity after exclusion of outliers.

less blood loss (MD = - 120.74 ml, 95% CI = - 128.85, - 112.63, $P < 0.00001$, $I^2 = 73\%$, N = 575], lower transfusion rates (RD = - 0.07, 95% CI = - 0.09, - 0.05, $P < 0.00001$, $I^2 = 25\%$, N = 2833] and shorter length of in-hospital stay (RD = - 1.86, 95% CI = - 2.08, - 1.65, $P < 0.00001$, $I^2 = 76\%$, N = 2994). As in the previous analysis, marginal decrease in morbidity and perioperative mortality rates was noted. Operative time, incidence of biliary fistula and cardiac or pulmonary complication rates did not differ significantly (supplementary material).

4. Discussion

Laparoscopic liver resections have enjoyed increasing acceptance for treatment of benign and malignant liver lesions over the last two decades. However, in spite of advances in laparoscopic liver surgery, recent population-based studies have shown that less than 15% of liver resections are currently performed using minimally invasive techniques in countries such as France and the United States [43,44].

Of anatomical liver resection procedures, LLS is thought to be the best suited for the laparoscopic approach due to favorable anatomical features and ease of control of pedicle and veins using laparoscopic staplers, with no need for extensive dissection [12–14]. These characteristics justify the increasing popularity of laparoscopic LLS worldwide. LLS was the laparoscopic procedure most commonly performed in a survey of 27 specialized centers, accounting for 61.8% of LLSs [45]. In a recent review of the French experience [46], laparoscopic LLS was the only procedure to increase in numbers between 2007 and 2011 (from 22% in 32%).

Laparoscopic LLS is categorized as an intermediate difficulty procedure according to the difficulty scoring system proposed by Ban et al.

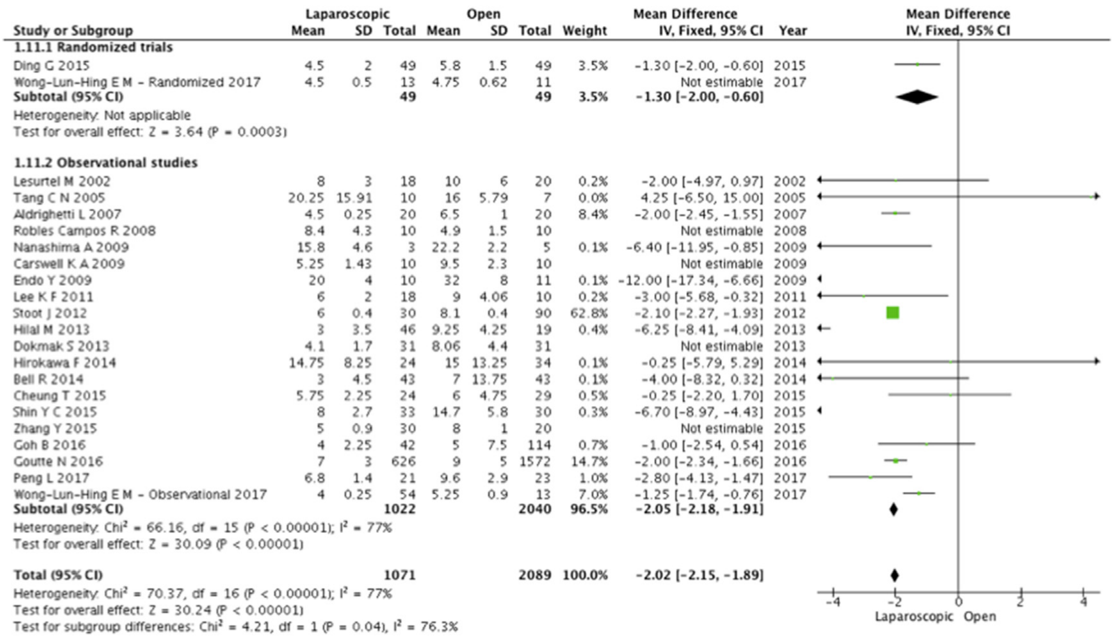

Fig. 7. Forest plot depicting hospital length of stay after exclusion of outliers.

[47], and therefore constitutes an attractive training platform. Laparoscopic LLS is a fully standardized procedure associated with short learning curve. According to Ratti et al. [15], the estimated learning curve for laparoscopic LLS is approximately 15 cases. In contrast, the learning curve for major resections is considerably longer, ranging from 45 to 75 cases [48–50]. Moreover, Hasegawa et al. [51] have shown that laparoscopic LLS is highly reproducible and easy to teach to less experienced surgeons. The best candidates for laparoscopic LLS are patients with tumors smaller than 10 cm confined to the liver and with no vascular invasion. Laparoscopic LLS is also the current routine procedure for living donors in specialized centers [12,33–35].

According to the 2nd International Consensus Conference on Laparoscopic Liver Resections held in Morioka in 2014 [52], laparoscopic LLS should be considered a standard practice. Still, evidence supporting this procedure are derived from retrospective, single center studies with small numbers of patients [24–26,31,36].

In a previous meta-analysis published by Rao et al. [13] laparoscopic LLS was associated with lower complication rates and shorter length of in-hospital stay, but longer operative time compared to open procedures. However, that review was limited to 7 studies and 245 patients and included patients submitted to laparoscopic living donation. After the first meta-analysis, 16 related studies have been published, including population-based studies [17] and 2 RCTs [18,19]. The first RCT included exclusively patients with intrahepatic lithiasis

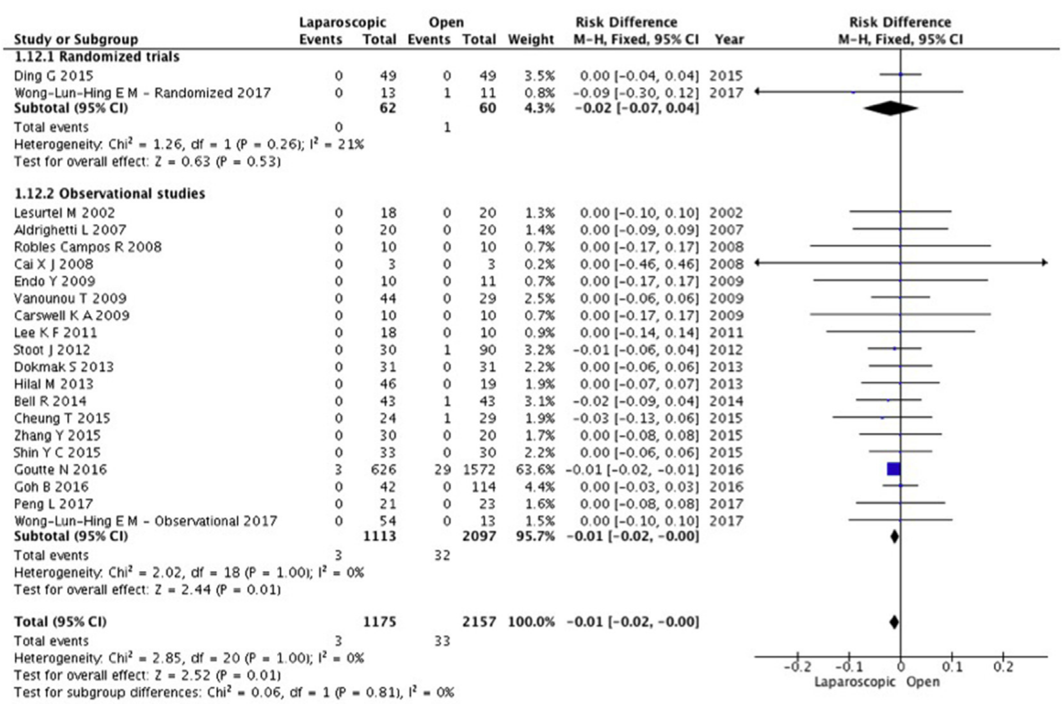

Fig. 8. Forest plot depicting perioperative mortality.

[18] while the second (ORANGE II trial) failed to randomize patients over a 4-year period and was discontinued due to insufficient numbers of patients. This suggests that, although advisable, prospective studies are not feasible [19]. Therefore, systematic reviews and meta-analyses constitute useful tools for current evidence assessment.

This systematic review was limited to patients submitted to liver resection due to benign or malignant disease and is the most comprehensive review on the topic to date, including 23 studies and 3415 patients. Separate analysis of randomized and observational studies was also performed.

Different from a previous meta-analysis reporting shorter operative time in open LLS [13], findings of this study revealed similar operative time regardless of surgical approach. This discrepancy may have reflected the low number of studies included in the first meta-analysis [13], most of which described early experience with laparoscopic liver resections. In recent observational studies and RCTs, laparoscopic LLS has been associated with similar or shorter operative time compared to open liver resection [18,33,34,36,39]. In fact, operative time decreases when the learning curve is overcome, reflecting standardization of surgical procedure steps. Also, widespread use of laparoscopic staplers and improvement in energy devices have made laparoscopic LLS easier and faster [14,53].

Reduced blood loss in patients submitted to laparoscopic LLS is in keeping with findings of several observational studies [24,35,36] and the two existing RCTs [18,19]. However, clinical impact of blood transfusion has been less frequently investigated. This analysis included more than 2900 patients and revealed significant difference in transfusion rates favoring the minimally invasive approach (4.1% and 10.1%; laparoscopic and open LLS respectively), with low heterogeneity between studies, while a previous meta-analysis [13] failed to detect differences in estimated blood loss and transfusion rates. Magnified vision offered by laparoscopy and resulting precise and meticulous dissection, effects of positive pneumoperitoneum on venous blood loss and the systematic use of devices such as vascular staplers for Glissonian pedicle and left hepatic vein control may explain the reduced blood loss in patients undergoing minimally invasive LLS.

The minimally invasive approach was associated with marginally lower perioperative morbidity rates in this analysis, with an absolute reduction of 3%. Similar trends in favor of laparoscopy have been reported in observational studies. Importantly, similar or lower morbidity rates were documented in patients submitted to laparoscopic LLS in all comparative studies.

Reduced length of in-hospital stay has been reported in most studies to date [18,29,34,36]. Pooled data analysis in our study revealed that patients undergoing laparoscopic surgery stayed 2 days less in. This finding may have reflected less blood loss, fewer postoperative complications and particularly less postoperative pain [30,54,55].

Reported perioperative mortality rates were low (0.3% and 1.5%; laparoscopic and open group respectively). Interestingly, a trend towards lower mortality was observed in patients submitted to laparoscopic surgery, with absolute risk reduction of 1%. This finding should be interpreted with caution given the questionable clinical relevance. Most individual-based studies failed to detect mortality differences between laparoscopic and open LLS. However, significant lower 90-day mortality rates (1.3% vs. 5.8% for open LLS, $P = .006$) in patients undergoing laparoscopic LLS for primary liver malignancy were reported in a recent population-based study after adjustment for confounding [17].

Albeit encouraging, findings this study must be interpreted with caution due to several limitations. Firstly, most studies included in the analysis were retrospective, therefore patient selection may have been biased. Secondly, standards differed between studies, depending on surgical expertise and technology employed. Finally, despite the low risk of bias in RCTs [18,19], the number of patients per arm was small. Given pure laparoscopy is the gold standard approach for LLS, the inclusion of studies involving hand-assisted and hybrid techniques is yet another potential reason for criticism. However, subgroup analysis exclusively with patients undergoing pure laparoscopic LLS was performed and the results were similar to those of analyses including other minimally invasive techniques. Indeed, according to recent studies from our group, hybrid resections offer similar benefits to pure laparoscopic surgery [56,57].

In conclusion, current evidence supports the adoption of the laparoscopic minimally invasive approach as the gold standard for LLS. This meta-analysis of randomized and non-randomized studies revealed that laparoscopic LLS is a safe and feasible procedure, and is associated with reduced blood loss, lower transfusion rates and shorter length of in-hospital stay. Further well-designed studies are warranted to determine the actual benefits of laparoscopic LLS regarding perioperative morbidity and mortality.

Disclosures

None of the authors involved has a conflict of interest.

Conflicts of interest

There is no conflict of interest of the author.

Funding

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Ethical approval

The research protocol of this systematic review and meta-analysis was approved by the Ethics Committee for Analysis of Research Projects of University of São Paulo Medical School and was registered by the research protocol number 0028/17.

Research registration unique identifying number (UIN)

The research protocol of this systematic review and meta-analysis was registered in the International Prospective Register of Systematic Review (http://www.crd.york.ac.uk/PROSPERO/) under the number: CRD42017056062, http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42017056062.

Author contribution

Please specify the contribution of each author to the paper, e.g. study design, data collections, data analysis, writing. Others, who have contributed in other ways should be listed as contributors.

1) Rodrigo Luiz Macacari: study design, data collection, data analysis and writing.

2) Fabrico Ferreira Coelho: study design, data collection, data analysis and writing.

3) Wanderley Marques Bernardo: study design.

4) Jaime Artur Pirola Kruger: contributor.

5) Vagner Birk Jeismann: contributor.

6) Giltron Marques Fonseca: contributor.

7) Danielle Menezes Cesconetto: contributor.

8) Ivan Cecconello: contributor.

9) Paulo Herman: contributor.

Guarantor

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Appendix A. Supplementary data

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