Laparoscopic and open liver resection – a literature review with meta-analysis

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Abstract

Introduction: In recent years laparoscopic approach to liver resections has gained important attention from surgeons worldwide. The aim of this review was to compare the results of laparoscopic and open liver resections.
Material and methods: We have performed a search in Medline, Embase and the Cochrane Library databases. Studies comparing laparoscopic and open liver resections were included.
Results: No randomized clinical trial were identified. In the 16 observational studies included in the analysis there were 927 laparoscopic and 1049 open liver resections. The laparoscopy group had lower blood loss (MD = 244.93 ml, $p < 0.00001$), lower odds of transfusion (OR = 0.35, $p = 0.0002$), lower odds of positive margins on pathology report (OR = 0.22, $p < 0.00001$), lower odds of readmission (OR = 0.36, $p = 0.04$), lower odds of pulmonary (OR = 0.38, $p = 0.003$) and cardiac complications (OR = 0.30, $p = 0.02$) and lower odds of postoperative liver failure (OR = 0.24, $p = 0.001$), but in many cases the results were based on a low number of events reported in included studies.
Conclusions: Laparoscopic resection of liver yields complications rates comparable to open resection, but the results are based on low quality evidence from nonrandomised studies.

Key words: hepatectomy, surgery, meta-analysis.

Introduction

With the advent of minimally invasive surgical techniques the interest in laparoscopic resection of the liver increased significantly [1]. Following the initial report on the applicability of laparoscopy in liver surgery in 1993, several authors reported their experience [2]. The first published series dealt with relatively simple liver resections, which left major liver resection for the traditional, open approach [3]. However, with growing experience more surgeons started to perform all types of liver surgery laparoscopically [4]. Unfortunately, the scientific evidence supporting this approach is scarce [5]. In this review we have looked at the available data comparing open and laparoscopic approaches to liver resection.

Material and methods

Literature search strategies

A literature search was conducted using Medline, Embase and the Cochrane Library from the inception to February 2014. Search terms were "liver" AND "laparoscopy". All papers with English abstracts were evaluated by two authors (ALK and WMW). Relevant journals that were not well abstracted were hand-searched for full text articles and retrieved as appropriate. Overlapping search results from different databases were excluded.

Inclusion criteria and definitions

Articles were included if the English abstract contained information on comparison of the frequency of complications of open and laparoscopic liver resection, regardless of the underlying disease or study design. Randomized clinical trials, clinical controlled trials and observational studies with a control group were all considered eligible for this review.

We excluded studies evaluating techniques other than conventional laparoscopy (i.e. hand-assisted laparoscopy, robotic surgery), studies on pyogenic abscess, hydatid cyst, cystic disease and hepatolithiasis management and studies evaluating living donor hepatectomy. In order to limit our review to studies performed by highly experienced teams, we also excluded all observational studies with less than 30 patients in any of the study arms. The odds of postoperative surgical and general complications as well as oncologic results (if applicable) were compared between open and laparoscopy groups.

Statistical analysis

Binary data (odds ratio) on complications were pooled using the Mantel-Haenszel method fixed or random effect model (in the case of unexplained moderate heterogeneity) or Peto fixed methods (in the case of event rates below 1%) [6–8]. Continuous data (means with SD) were pooled using inverse variance random effects models and in cases of missing SD they were calculated (whenever possible) using the range rule. The meta-analysis was performed using the Review Manager (RevMan) computer program, version 5.2 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2012).

The main results are presented in the form of forest plots. For each study odds ratios with 95% CI are presented. The horizontal line represents 95% CI and the effects estimates are presented as black squares. The size of those squares represents the weight that the study has in the overall effect estimate. The pooled odds ratio with its 95% CI is displayed as a diamond at the bottom of the figure. For each meta-analysis the number of studies for which results for reported outcomes were available is summarized in Table I.

Table I. Results of meta-analyses with number of included studies and patients with events*

Endpoint	No. of studies	No. of patients with events lap/open	Result (odds ratio)/mean difference (95% CI)	Heterogeneity (%)
Blood loss [ml]	7	NA	–244.93 (–300.37, –189.5)	25
Blood transfusion	12	43/155	0.35 (0.2, 0.61)	43
Postoperative bleeding	4	1/9	0.33 (0.08, 1.33)	0
Operative time [min]	7	NA	–3.75 (–16.56, 9.07)	25
Positive resection margin	8	11/72	0.22 (0.12, 0.43)	0
Bile leak	9	8/16	0.51 (0.22, 1.22)	40
Intraabdominal abscess formation	5	5/9	1.00 (0.32, 3.16)	0
Postoperative ascites	8	8/25	0.39 (0.14, 1.07)	19
Reoperations	2	2/4	0.77 (0.14, 4.11)	0
Local recurrence	5	56/92	0.89 (0.58, 1.37)	0
Readmissions	3	4/13	0.36 (0.13, 0.97)	0
Pulmonary complications	11	11/49	0.38 (0.2, 0.72)	0
Cardiac complications	6	2/16	0.30 (0.11, 0.83)	0
Risk of liver failure	6	5/26	0.24 (0.10, 0.58)	0

**Since the results for some complications in the Belli study were only reported for the laparoscopy group, the study was excluded from the analysis of the following complications: ascites, postoperative bleeding, pulmonary and cardiac complications, bile leak, intraabdominal abscess.*

Heterogeneity between the studies was calculated using the I^2 test, and it was defined as low if I^2 was below 30%, moderate if I^2 was up to 50%, and substantial if I^2 was above 50% [9]. Heterogeneity between the studies was explored. In case of substantial heterogeneity study results were not pooled.

Results

The first search resulted in 489 abstracts. All were revised by two authors (ALK and WMW) for the inclusion criteria. At this stage 416 abstracts were rejected. The remaining 73 studies were retrieved and evaluated in full text versions. At this stage studies were excluded because they were: studies evaluating techniques other than laparoscopy (6) or only laparoscopy with no comparison to open technique (2), studies evaluating synchronous liver and colon resections (2), hydatid cyst resections (3), pyogenic abscess management (2), liver cyst (2), living donor hepatectomies (3), meta-analysis (4), hepatolithiasis resections (3) and one study protocol. A further 31 studies were excluded because in one of the study arms there were less than 30 patients.

Sixteen studies were included in the final analysis [1, 10–24]. Three of the included studies were prospective and 13 were retrospective cohort studies. The flow chart is presented in Figure 1.

Description of included studies

Study quality was assessed using the Newcastle-Ottawa Scale part for cohort studies [25]. Three major domains were evaluated: selection of the study groups, comparability and assessment of the outcome. The maximum score that could be achieved was 9 stars. Two authors (MMB and JWM) independently assessed scale components for each study. All of the differences between authors were resolved by discussion until a consensus was reached. Table II presents the characteristics of the selected studies.

Results of the quality evaluation showed that two out of 16 studies were of good quality in all domains, 11 studies were of good quality in two domains and eight studies were of poor quality in one domain [26].

The basic characteristics of patients included in the reviewed studies are presented in Table III.

Blood loss

The difference in the mean intraoperative blood loss was evaluated in seven studies. The blood loss was significantly lower in the laparoscopy group (MD = –244.93 ml (–300.37, –189.5), p < 0.00001). Heterogeneity between the studies was low (I^2 = 25%).

The study by Hu *et al.* was analyzed separately as they reported blood loss in grams instead of ml (40.00 g (20.35, 59.65)) [16].

Blood transfusion

Twelve studies provided data on perioperative blood transfusion for meta-analysis. The odds of blood transfusion was lower in the laparoscopy group (OR = 0.35, 95% CI: 0.20–0.61, p = 0.0002). The forest plot of odds ratio of perioperative blood transfusion is presented in Figure 2.

Positive resection margin

The odds of leaving a positive margin on pathology examination after liver resection was

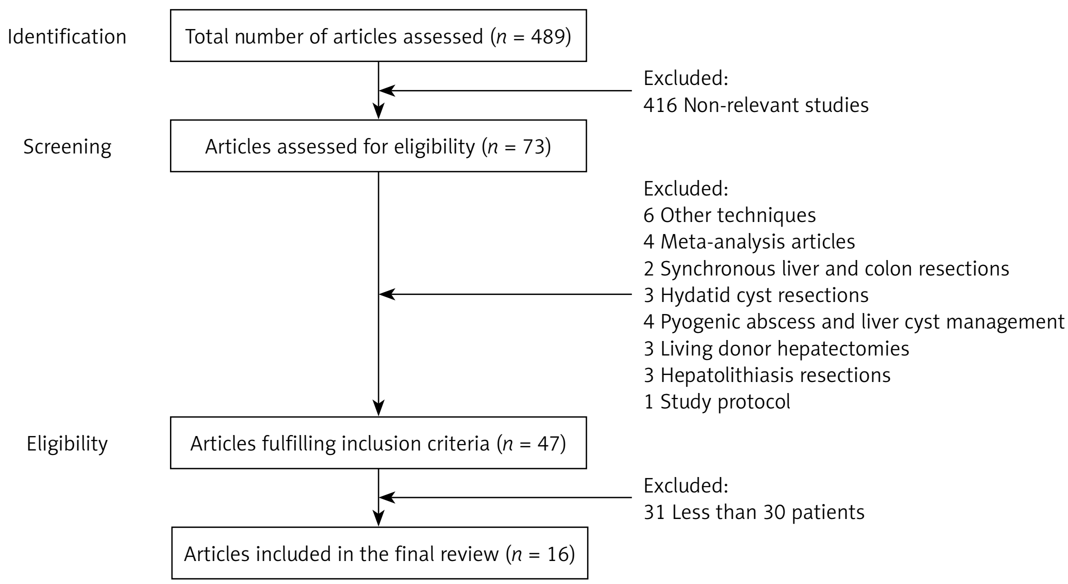

Figure 1. Flow chart of the study

Table II. Summary of the Newcastle-Ottawa quality assessment scale

Study	Year	Quality of selection	Quality of comparability	Quality of outcome	Total stars (*)
Abu Hilal *et al.* [17]	2011	3	2	1	6
Belli *et al.* [19]	2009	2	0	2	4
Bhojani *et al.* [15]	2012	2	2	1	5
Cai *et al.* [21]	2008	2	2	2	6
Cannon *et al.* [13]	2012	3	2	2	7
Castaing *et al.* [20]	2009	2	2	2	6
Cheung *et al.* [10]	2013	3	1	2	6
Guerron *et al.* [11]	2013	3	1	2	6
Hu *et al.* [16]	2011	3	0	2	5
Ito *et al.* [18]	2009	2	2	2	6
Koffron *et al.* [22]	2007	3	2	1	6
Morino *et al.* [23]	2003	2	2	1	5
Slim *et al.* [14]	2012	2	2	2	6
Topal *et al.* [24]	2008	3	2	1	6
Tranchart *et al.* [12]	2013	3	2	1	6
Tranchart *et al.* [1]	2010	3	2	2	7

Assessment of methodological quality with the Newcastle-Ottawa Scale. The maximum possible score was 9 (4 for selection, 2* for comparability and 3* for outcome).*

Table III. Basic patients' characteristics

Paramenter	Lap	Open
No. of patients	1010	1122
Age, median [years]	From 46 to 66	From 48 to 66
Males	From 35% to 77%	From 37.0% to 84.0%
HBV infection[a]	From 4.0% to 81.0%	From 0.0% to 77.0%
Cirrhosis[b]	From 0.0% to 83.0%	From 0.0% to 81.0%
Conversion rate	From 3% to 14%	–

[a]Based on the data from 4 studies reporting the rate of HBV infection, [b]based on the data from 14 studies reporting the rate of cirrhosis.

evaluated in eight studies. The odds of a positive margin was significantly lower in the laparoscopy group: OR = 0.22, 95% CI: 0.12–0.43, p < 0.00001). The forest plot of probability of a positive margin on pathology examination is presented in Figure 3.

Readmissions

Readmissions defined as admission of a patient discharged 30 days or less postoperatively were reported in three studies. The odds of readmission were lower in the laparoscopy group (OR = 0.36, 95% CI: 0.13–0.97, p = 0.04).

Pulmonary complications

Eleven studies provided data on pulmonary complications for meta-analysis. The odds of pulmonary complications were significantly lower in the laparoscopy group (OR = 0.38, 95% CI: 0.20–0.72, p = 0.003).

The forest plot of probability of perioperative pulmonary complications is presented in Figure 4.

Cardiac complications

Six studies provided data on cardiac complications for meta-analysis. The odds of cardiac complications were significantly lower in the laparoscopy group (OR = 0.30, 95% CI: 0.11–0.83, p = 0.02).

Risk of liver failure

Six studies provided data which could be used in the meta-analysis of the odds of postoperative liver failure. The odds were lower for the laparoscopy group (OR = 0.24, 95% CI: 0.10–0.58, p = 0.001). The forest plot of risk of liver failure is presented in Figure 5.

Mortality

Four perioperative deaths occurred in the laparoscopic group and 18 deaths in the open group. The number of deaths was low; six studies reported no deaths, six studies reported single deaths

Study or subgroup	Lap Events	Lap Total	Open Events	Open Total	Weight (%)	Odds ratio M-H, random, 95% CI
1.13.1 Perioperative blood transfusion						
Abu Hilal 2011	8	36	7	34	11	1.10 (0.35–3.46)
Belli 2009	6	54	32	125	13.1	0.36 (0.14–0.93)
Cannon 2012	5	35	30	140	12.1	0.61 (0.22–1.71)
Castaing 2009	9	60	22	60	13.7	0.30 (0.13–0.74)
Cheung 2013	0	32	3	64	2.9	0.27 (0.01–5.39)
Guerron 2013	2	40	8	40	7.4	0.21 (0.04–1.06)
Ito 2009	1	65	19	65	5.4	0.04 (0.00–0.29)
Koffron 2007	0	241	8	100	3.1	0.02 (0.00–0.39)
Morino 2003	4	30	2	30	6.6	2.15 (0.36–12.76)
Slim 2012	2	46	8	46	7.5	0.22 (0.04–1.08)
Tranchart 2010	4	42	7	42	9.6	0.53 (0.14–1.95)
Tranchart 2013	2	52	9	52	7.6	0.19 (0.04–0.93)
Subtotal (95% CI)		**733**		**798**	**100**	**0.35 (0.20–0.61)**
Total events	43		155			
Heterogeneity: $\tau^2 = 0.37$; $\chi^2 = 19.30$, d*f* = 11 ($p = 0.06$); $I^2 = 43\%$						
Test for overall effect: $Z = 3.73$ ($p = 0.0002$)						
1.13.2 Postoperative blood transfusion						
Bhojani 2012	11	57	10	114	100.0	2.49 (0.99–6.27)
Subtotal (95% CI)		**57**		**114**	**100.0**	**2.49 (0.99–6.27)**
Total events	11		10			
Heterogeneity: not applicable						
Test for overall effect: $Z = 1.93$ ($p = 0.05$)						
1.13.3 Intraoperative blood transfusion						
Bhojani 2012	7	57	12	114	100.0	1.19 (0.44–3.21)
Subtotal (95% CI)		57		114	100.0	1.19 (0.44–3.21)
Total events	7		12			
Heterogeneity: not applicable						
Test for overall effect: $Z = 0.34$ ($p = 0.73$)						
Test for subqroup differences: $\chi^2 = 14.33$, d*f* = 2 ($p = 0.0008$), $I^2 = 86.0\%$						

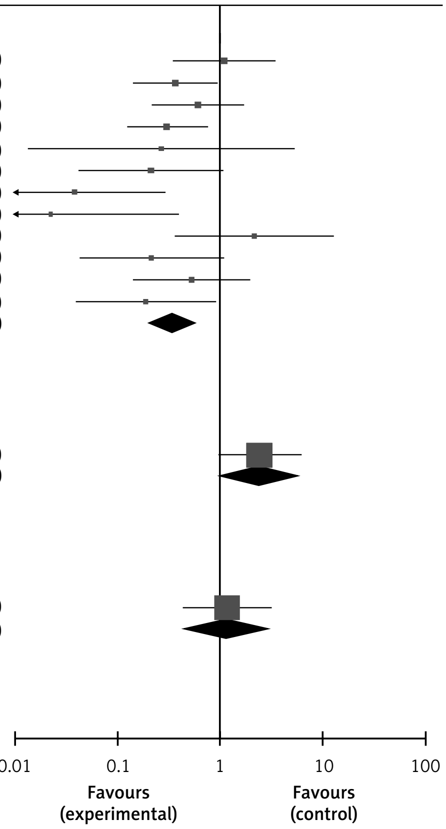

Figure 2. Forest plot of the probability of blood transfusion

Study or subgroup	Lap Events	Lap Total	Open Events	Open Total	Weight (%)	Odds ratio M-H, fixed, 95% CI
Abu Hilal 2011	2	36	7	34	13.8	0.23 (0.04–1.18)
Belli 2009	0	54	8	125	10.4	0.13 (0.01–2.24)
Bhojani 2012	1	57	4	114	5.3	0.49 (0.05–4.50)
Cai 2008	0	31	0	31		Not estimable
Cannon 2012	1	35	26	140	20.5	0.13 (0.02–0.99)
Castaing 2009	5	60	17	60	31.7	0.23 (0.08–0.67)
Cheung 2013	1	32	4	64	5.2	0.48 (0.05–4.52)
Guerron 2013	0	40	0	40		Not estimable
Ito 2009	0	65	0	65		Not estimable
Koffron 2007	0	241	0	100		Not estimable
Morino 2003	0	30	1	30	3.0	0.32 (0.01–8.24)
Topal 2008	1	76	5	76	10.0	0.19 (0.02–1.66)
Tranchart 2010	0	42	0	42		Not estimable
Tranchart 2013	0	52	0	52		Not estimable
Total (95% CI)		**851**		**973**	**100.0**	**0.22 (0.12–0.43)**
Total events	11		72			
Heterogeneity: $\chi^2 = 1.45$, d*f* = 7 ($p = 0.98$); $I^2 = 0\%$						
Test for overall effect: $Z = 4.45$ ($p < 0.00001$)						

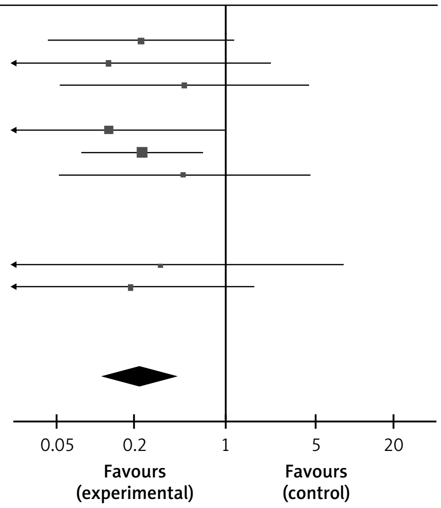

Figure 3. Forest plot of the probability of positive margin on pathology report

in one or both groups, and four studies reported more than one death.

Length of stay

Data on the length of stay were available for fourteen studies. There was no difference in the length of stay between the study groups, but there was substantial heterogeneity between the studies, so their results were not pooled. The mean differences reported in the studies varied from –0.8 days (–1.66, 0.06) to –7.0 days (–8.37, –5.63) and median values varied between –1.0 day (–4.39, 2.39) and –4.0 days (–7.95, –0.05).

Study or subgroup	Lap		Open		Weight	Odds ratio
	Events	Total	Events	Total	(%)	M-H, random, 95% CI
Abu Hilal 2011	1	36	1	34	5.4	0.94 (0.06–15.70)
Bhojani 2012	3	57	4	114	18.2	1.53 (0.33–7.07)
Cai 2008	0	31	1	31	4.1	0.32 (0.01–8.23)
Cannon 2012	1	35	10	140	9.8	0.38 (0.05–3.09)
Castaing 2009	0	60	0	60		Not estimable
Cheung 2013	1	32	9	64	9.6	0.20 (0.02–1.63)
Guerron 2013	1	40	5	40	8.9	0.18 (0.02–1.61)
Hu 2011	0	30	0	30		Not estimable
Ito 2009	0	65	3	65	4.8	0.14 (0.01–2.69)
Koffron 2007	0	241	0	100		Not estimable
Morino 2003	0	30	2	30	4.5	0.19 (0.01–4.06)
Slim 2012	3	46	8	46	21.9	0.33 (0.08–1.34)
Topal 2008	0	76	0	76		Not estimable
Tranchart 2010	1	42	3	42	8.0	0.32 (0.03–3.18)
Tranchart 2013	0	52	3	52	4.8	0.13 (0.01–2.67)
Total (95% CI)		**873**		**924**	**100.0**	**0.38 (0.20–0.72)**
Total events	11		49			

Heterogeneity: $\tau^2 = 0.00$, $\chi^2 = 5.65$, $df = 10$ ($p = 0.84$); $I^2 = 0\%$
Test for overall effect: $Z = 2.93$ ($p = 0.003$)

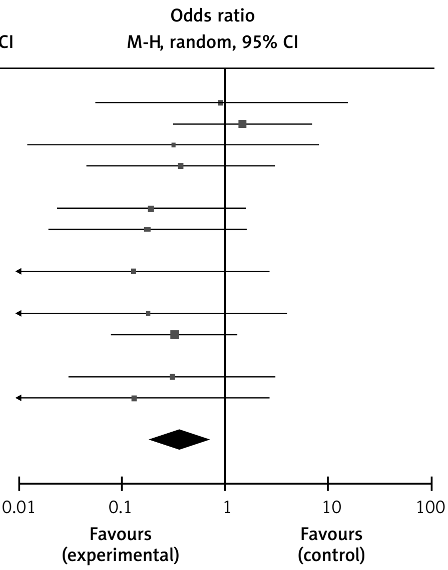

Figure 4. Forest plot of the risk of pulmonary complications

Study or subgroup	Lap		Open		Weight	Odds ratio
	Events	Total	Events	Total	(%)	M-H, fixed, 95% CI
Abu Hilal 2011	0	36	1	34	6.0	0.31 (0.01–7.77)
Belli 2009	0	54	0	125		Not estimable
Bhojani 2012	0	57	0	114		Not estimable
Cai 2008	0	31	1	31	5.8	0.32 (0.01–8.23)
Cannon 2012	0	35	2	140	3.9	0.78 (0.04–16.62)
Castaing 2009	0	60	0	60		Not estimable
Cheung 2013	0	32	0	64		Not estimable
Guerron 2013	0	40	0	40		Not estimable
Hu 2011	0	30	0	30		Not estimable
Ito 2009	0	65	0	65		Not estimable
Koffron 2007	0	241	0	100		Not estimable
Morino 2003	0	30	0	30		Not estimable
Slim 2012	2	46	6	46	22.5	0.30 (0.06–1.59)
Topal 2008	0	76	0	76		Not estimable
Tranchart 2010	3	42	10	42	36.5	0.25 (0.06–0.97)
Tranchart 2013	0	52	6	52	25.3	0.07 (0.00–1.24)
Total (95% CI)		**873**		**924**	**100.0**	**0.24 (0.10–0.58)**
Total events	5		26			

Heterogeneity: $\chi^2 = 1.41$, $df = 5$ ($p = 0.92$); $I^2 = 0\%$
Test for overall effect: $Z = 3.22$ ($p = 0.001$)

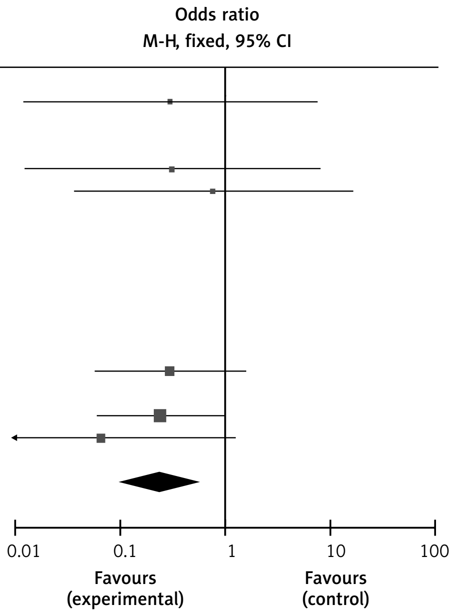

Figure 5. Forest plot of the risk of liver failure

There was no difference between the groups in the odds of: postoperative bleeding (OR = 0.33, 95% CI: 0.08–1.33, p = 0.12), operative time (MD = –3.75 min (–16.56, 9.07), p = 0.57), bile leak (OR = 0.51, 95% CI: 0.22–1.22, p = 0.13), intraabdominal abscess formation (OR = 1, 95% CI: 0.32–3.16, p = 1.00), postoperative ascites (OR = 0.39, 95% CI: 0.14–1.07, p = 0.07), 30 days reoperation rate (OR = 0.77, 95% CI: 0.14–4.11, p = 0.76), or local recurrence (OR = 0.89, 95% CI: 0.58–1.37, p = 0.60), however in many case numbers of events reported in the studies were low.

Discussion

In the recent decades we have witnessed an important rise in the indications for curative liver resections [27]. At the same time, with the advent of minimally invasive techniques, liver resection is performed by many surgeons laparoscopically [4, 28]. However, we do not have results of any randomized clinical trial directly comparing these two approaches. Results of the two ongoing trials are expected [5]. Current evidence is based on case-series and cohort studies.

At the beginning of the liver laparoscopy learning curve, the surgeons tend to choose less technically demanding resections for laparoscopy. However, the current cumulative experience in liver laparoscopy has risen to the point that we need to have a higher level of evidence to decide whether laparoscopic liver resection is equal to the open approach. According to the 2015 Morioka statement, the indication for laparoscopic liver resections depends on the technical expertise of the surgeon [29].

In the current review we have looked for papers comparing laparoscopy with the open approach to liver resection performed by highly experienced teams with at least 30 patients in each study arm. Such centers represent the best platform to compare the technique, as they have important experience in both open liver surgery and liver laparoscopy [20]. The current review has some important limitations. It was limited to English abstracts, and there were only two key words used as search terms. This approach may have resulted in missing some studies. In addition, we have not found any randomized trial, only three studies were prospective, and a significant number of studies (31) were excluded based on the number of participating patients. Also, the overall quality of the included studies was poor, with only two studies evaluated as having good quality in all domains. Furthermore, most studies did not provide definition for the outcomes reported. For several of analysed outcomes the numbers of events were low and in several studies no events were reported.

Ten studies did not report any events for the liver failure, so the effect of the surgical approach on that was also not estimable. The pooled odds ratio of postoperative liver failure for patients undergoing laparoscopic resections was significantly lower than for open resections, but this was based on small number of events reported in six studies. These are interesting findings, and one of the explanations for this phenomenon is selection bias. Even in experienced centers the surgeons tend to choose fitter patients for a technique still considered as a novelty [17]. This bias could have been eliminated by a prospective randomized trial comparing open and laparoscopic liver resections. However, as stated before, we have failed to find such a study in our review. Also, the number of the available studies is too small to perform a meta-analysis of only one type of liver resection.

Contrary to the findings on postoperative liver failure, ascites has been found with similar frequency in both groups. In the pooled studies the laparoscopy group had lower intraoperative blood loss and required less blood transfusion. This finding may be explained by an augmented surgical view offered by modern high definition laparoscopy optics, as well as meticulous surgical technique [24]. However, one study (Hu) which reported blood loss in grams showed the opposite effect in blood loss, while another study (Bhojani) which reported intra- and postoperative transfusions separately did not find a significant difference between the groups [15, 16].

The laparoscopy patients less frequently suffered from pulmonary and cardiac complications (low number of events reported in six studies). There was no difference in the frequency of intraabdominal abscess formation between the groups (low number of events reported in five studies), and the odds of postoperative bile leak and bleeding were similar in both study groups; however, the number of events was low, and most studies did not report any events, so they had no influence on the results of the meta-analysis.

The odds of a positive resection margin on pathology examination after liver resection for malignancy were lower in the laparoscopy group. Probably patient selection bias can also play a role here, as bigger tumors and/or more technically demanding cases were more frequently scheduled for open surgery. However, local recurrence rates were found to be similar in both laparoscopy and open surgery groups.

Surprisingly, operative time was similar for both groups. This probably reflects our inclusion criteria, which favored papers with at least 30 patients in each study arm. That approach eliminated papers from centers with a low laparoscopy case load. The risk of readmission was lower for the laparoscopy group, this result was based on such events reported in only 3 studies, but the risk of reoperation did not differ between the groups this was based on such events reported in only 2 studies. And finally, the length of stay in most studies was shorter in laparoscopy groups, but substantial heterogeneity precluded us from pooling the results of those studies.

In conclusion, the results of this review with meta-analysis of available data should be interpreted with caution. We have not found any randomized clinical trial on the subject. Included studies were observational, of low quality, most likely with high risk of selection bias and heterogeneous. However, the pooled results showed that the laparoscopic approach to liver resection may be at least equally safe for patients as the open technique in experienced centers.

Conflict of interest

The authors declare no conflict of interest.

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