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A Meta-analysis of Outcomes After Routine Aspiration of the Gallbladder During Cholecystectomy

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We conducted a meta-analysis of published literature comparing outcomes after aspirating (ASP) the gallbladder versus nonaspiration (NASP). Electronic databases were searched from January 1985 to November 2009. A meta-analysis was performed to obtain a summative outcome. Two randomized, controlled trials involving 360 patients were analyzed. A total of 180 patients were in the ASP group, and 180 were in the NASP group. There was no significant increase in operative time in the ASP group compared with the NASP group [random-effects model: standardized mean difference, −0.72; 95% confidence interval (CI), −2.16, 0.71; $z = 0.99$; $df = 1$; $P = 0.32$], but there was significant heterogeneity among trials ($Q = 42.4$; $P < 0.001$; $I^2 = 98\%$). Patients undergoing ASP were less likely to have a gallbladder perforation [random-effects model: risk ratio (RR), 0.42; 95% CI, 0.19, 0.96; $z = 2.05$; $df = 1$; $P < 0.05$], but no difference was found regarding the loss of gallstones (random-effects model: RR, 1.33; 95% CI, 0.30, 5.85; $z = 0.38$; $df = 1$; $P = 0.70$). No difference was seen for liver bed bleeding ($P = 0.43$) or overall 30-day infection rates ($P = 0.66$). After aspiration, gallbladder perforation rates may be lower. This does not appear to translate into decreased loss of gallstones or infection rates. There was no significant difference between techniques in blood loss from the liver bed. Further randomized, controlled trials and follow-up studies are required to confirm these results and to establish long-term sequelae.

Key words: Laparoscopy – Cholecystitis – Gallbladder diseases – Gallbladder – Aspiration – Cholecystectomy, Laparoscopic

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Originally described in 1985,[1] laparoscopic cholecystectomy (LC) has progressed from intermittent to routine use, with a push toward day surgery.[2] Although there are well-known advantages of minimally invasive work,[3,4] techniques aimed at safer procedures are continuously proposed.[5] One area of focus has been on preventing conversion to an open operation due to bile duct injury.[6] Previously, authors had advocated conversion for iatrogenic gallbladder perforation,[7] although current practice is to wash out the peritoneal cavity and retrieve spilled stones.[6]

Gallbladder perforation may occur in up to 50% of LCs, and spilled gallstones and bile leakage may occur in 10% to 40%.[8] It is unclear as to the exact short- and long-term sequelae of these intraoperative complications. However, retained intraperitoneal stones may act as a nidus for infection,[9] and bile spillage can cause chemical peritonitis, leading to systemic and local infection,[10,11] intraperitoneal abscesses,[12] fistulae,[13,14] adhesions,[15] and small-bowel obstruction.[16]

One method suggested to reduce gallbladder perforation and subsequent complications is aspiration (ASP) of the gallbladder. With a subsequent reduction in volume and wall tension, gallbladder perforation may occur less frequently.[17] The objective of this study is to meta-analyze the published literature comparing the ASP versus nonaspiration (NASP) of the gallbladder during LC.

Methods

All randomized, controlled studies investigating ASP versus NASP of the gallbladder during LC in adult patients between January 1985 and January 2010 were identified. We searched Medline, Embase, and CINAHL, available through the National Library of Health website, and the Cochrane library and PubMed databases available online. The text words ''minimally invasive,'' ''keyhole surgery,'' and ''aspiration'' were used in combination with the medical subject headings ''laparoscopy,'' ''cholecystitis,'' ''gallbladder,'' ''gallbladder diseases,'' and ''cholecystectomy, laparoscopic.'' Irrelevant articles, reviews, and meta-analyses evident from the titles and abstracts were excluded. Relevant articles referenced in these publications were obtained, and the ''related article'' function was used to widen the results. No language restriction was applied. All abstracts, comparative studies, nonrandomized trials, and citations were searched comprehensively. A flow chart of the literature search according to PRISMA guidelines[18] is shown in Fig. 1. A total of 265 articles were screened for relevance. On further scrutiny, only 2 randomized, controlled trials were found to have useful data for this meta-analysis.

Each article was critically reviewed by 2 researchers using a double-extraction method for eligibility in our review (Table 1). This was performed independently, and any conflict was resolved prior to final analysis. A third researcher confirmed the data extraction.

Outcome variables were chosen based on whether the included articles reported results.

Operation time was only defined by one of the trials as the time taken from insufflation to pulling out the trocars.[17]

Statistical analyses were performed using Review Manager 5.0.23 (RevMan, Cochrane Collaboration, Copenhagen, Denmark).[19] A value of $P < 0.05$ was chosen as the significance level for outcome measures. For continuous data (operation time), the inverse-variance method was used for the combination of standardized mean differences (SMDs). Binary data (gallbladder perforation, loss of gallstones, liver bed bleeding, and 30-day morbidity) were summarized as risk ratios (RRs) and combined using the Mantel-Haenszel method. In each case, a heterogeneity test was carried out to see whether the fixed-effects model was appropriate. In a sensitivity analysis, 1 was added to each cell frequency for trials in which no event occurred, according to the method recommended by Deeks *et al*.[20] Where standard deviations were not reported, these were estimated either from ranges or *P* values. Forest plots were used for the graphic display.

Results

Two randomized, controlled trials[17,21] comparing ASP to NASP of the gallbladder during cholecystectomy were retrieved from the electronic databases and included in our study according to our inclusion criteria (Table 1). One article[22] was excluded (Table 2). Characteristics of each trial are given in Table 3. There were 180 patients in the ASP group and 180 in the NASP group. The outcome variables extracted are shown in Table 4. The methodologic quality of included trials is explained comprehensively in Table 5.[23,24]

Operative time

Two studies[17,21] contributed to a summative outcome. There was significant heterogeneity among

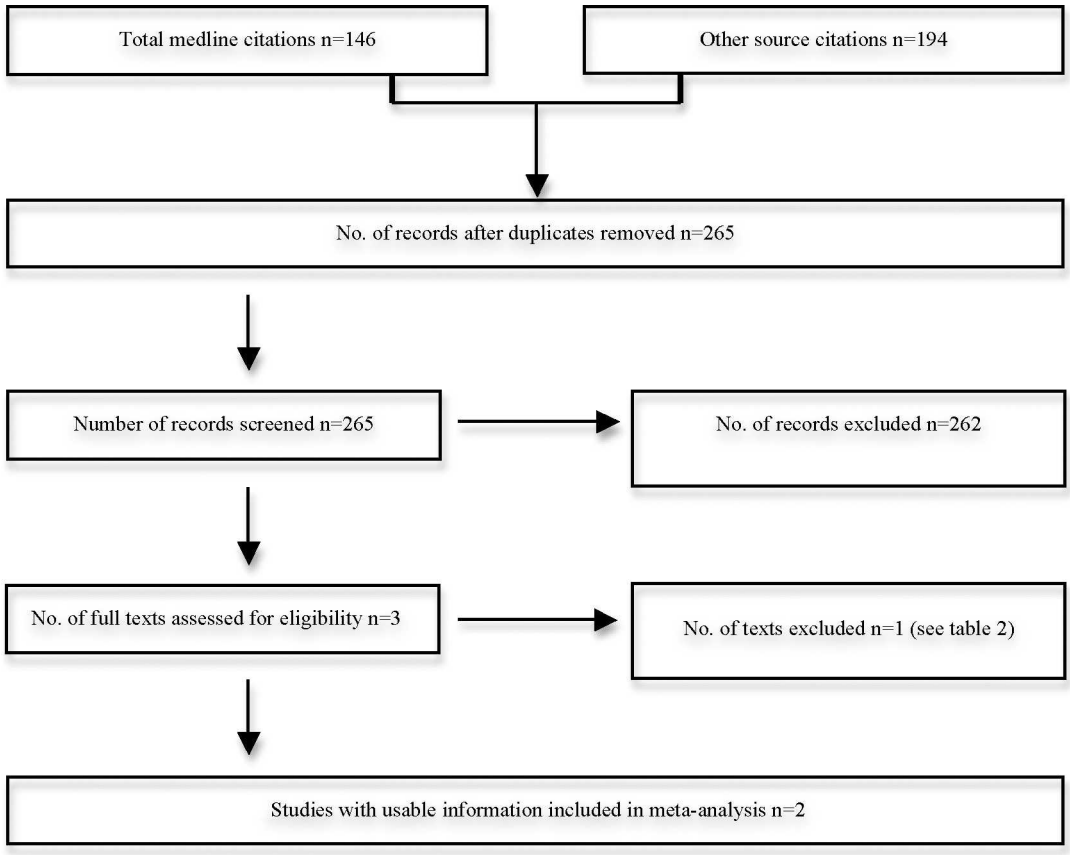

Fig. 1 Search strategy of electronic databases.

trials ($Q = 42.40$; $df = 1$; $P < 0.00001$; $I^2 = 98$); therefore, the fixed-effects model was inappropriate. There was no difference in operative time [random-effects model: SMD, −0.72; 95% confidence interval (CI), −2.16, 0.71; $z = 0.99$; $P = 0.32$; Fig. 2].

Gallbladder perforation

Two trials[17,21] discussed gallbladder perforation. There was no significant heterogeneity among trials ($Q = 2.71$; $df = 1$; $P = 0.10$; $I^2 = 63$). Gallbladders were less likely to perforate after ASP (fixed-effects model: RR, 0.43; 95% CI, 0.26, 0.69; $z = 3.48$; $P < 0.001$; Fig. 3).

Loss of gallstones

There was no significant heterogeneity ($Q = 0.06$; $df = 1$; $P = 0.81$; $I^2 = 0$) among 2 trials.[17,21] There was no increased loss of gallstones in the NASP group compared with the ASP group (fixed-effects model: RR, 1.33; 95% CI, 0.30, 5.85; $z = 0.38$; $P = 0.70$; Fig. 4).

Liver bed bleeding

Two trials[17,21] investigated liver bed bleeding, and no significant heterogeneity existed between trials ($Q = 0.06$; $df = 1$; $P = 0.81$; $I^2 = 0$). No significant

Table 1 Inclusion criteria

All studies comparing aspiration with non-aspiration of gallbladder during cholecystectomy.
All randomized controlled trials
All elective cases
Trials on adult patients of any sex.
Trials in all languages

Table 2 Excluded trials

Trial	Reason for exclusion
Khandelwal et al 2003	Meta-analysis including partial posterior and complete posterior wraps

Table 3 Characteristics of randomized controlled trials

Trial	Year	Type	N	Country	Patient Characteristics	Surgical Characteristics
Ezer et al	2008	Asp	80	Turkey	Symptomatic gallbladder stones without cholecystitis. American Society of Anesthesiology score 1 or 2. Elective cases. Ultrasonographically proven cholelithiasis. Conversions to open surgery, refusals and previous upper abdominal operations excluded.	6 surgeons. 4 ports. 0° camera. Sharp dissection and electrocautery used. 200 ml saline used to wash liver bed. Aspiration performed before dissection.
		N.Asp	80			
Calik et al	2007	Asp	100	Turkey	Symptomatic gallstone disease. Ultrasonic assessment of gallbladder thickness. Acute abdominal complaints and fever, leukocytosis, elevated liver function tests or serum amylase excluded Acute, subacute cholecystitis or choledocholithiasis excluded American Society of Anesthesiology score 2 or 3.	1 surgeon. 4 ports. 0° camera. Blunt dissection and electrocautery on scissors. Aspiration performed before the dissection of Calot's triangle.
		N.Asp	100			

Table 4 Outcome variables of studies

Trial	Year	Type	N	Operative Time	Perforation	Loss of gallstones	Liver bed bleeding	30 day Infection
Ezer et al	2008	Asp	80	55.94 ± 14.54	13	3	17	1/74
		N.Asp	80	55.88 ± 14.83	21	2	12	0/74
Calik et al	2007	Asp	100	46.70 ± 15.93	7	0	0	0
		N.Asp	100	60.75 ± 22.09	26	1	1	2

Table 5 Modified Quality Score for randomized controlled trials (Jadad et al[24] and Chalmers et al[23])

Quality variables	Ezer et al	Calik et al
Was the study described as randomized such as using the words randomly, random, and randomization? [0,1]	1	1
Was randomization described and appropriate? [-1,0,1]	1	0
Was the study described as double blind? [0,1]	0	0
Was method of blinding appropriate? [-1,0,1]	0	0
Was there a description of withdrawals and dropouts? [0,1]	0	1
Inclusion Criteria	1	1
Exclusion Criteria	1	1
Study Period Given	1	1
Appropriate statistical analysis	1	1
Hard End Points	1	1
Sample size calculation	1	0
Baseline comparable	1	1
Any missing post op data	0	1
Allocation concealment	0	0
Analysis by intention to treat	0	0
Score	9	9
Score Max 15. Poor = -1-5 Fair = 6-10 Good = 11-15		

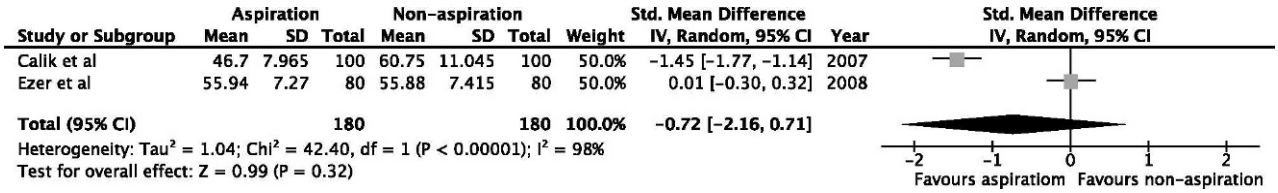

Fig. 2 Operative time.

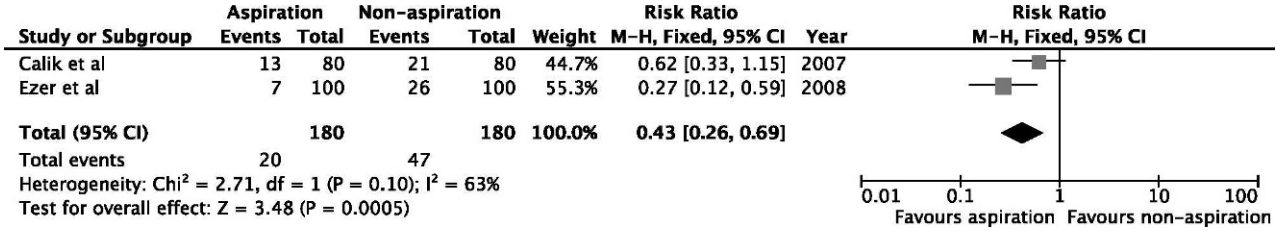

Fig. 3 Gallbladder perforation.

difference was highlighted (fixed-effects model: RR, 1.38; 95% CI, 0.72, 2.66; $z = 0.98$; $P = 0.33$; Fig. 5).

Thirty-day infection

Two studies[17,21] reported on 30-day infection. There was no significant heterogeneity among trials ($Q = 0.14$; $df = 1$; $P = 0.71$; $I^2 = 0$). No significant difference was highlighted between the 2 techniques (fixed-effects model: RR, 0.67; 95% CI, 0.11, 3.94; $z = 0.45$; $P = 0.65$; Fig. 6).

Discussion

Advocates of gallbladder ASP suggest the decrease in tension of the gallbladder wall may decrease perforation rates.[25] As the volume decreases the liver bed may open, making the dissection easier, with theoretically less bleeding.[17] The aforementioned proposals may also decrease operative time.

This meta-analysis shows that gallbladder perforation is less likely to occur after ASP. This is consistent with one study[17] and would be in keeping with the assertion that hydrops of the gallbladder is a principal cause of perforation.[25] Calik *et al*[21] showed no difference in perforation rates. This finding may be due to the inclusion of fewer overfilled gallbladders.

This meta-analysis showed no significant difference in operative time, liver bed bleeding, gallstone spillage, or 30-day infection rates.

Operative time was significantly shorter according to Calik *et al*,[21] suggesting that even with time taken to aspirate the gallbladder, the procedure is quicker to perform. This is countered by Ezer *et al*,[17] who showed that there was no statistical significance; however, they also examined dissection time, which was slightly less in the ASP group, albeit nonsignificant. The lack of significant difference may also be confounded by the lack of overfilled gallbladders seen at time of operation.[25] Our summative outcome would suggest that although ASP decreases dissection time, the additional time taken to aspirate the gallbladder may cancel out any advantage gained.

Liver bed bleeding was not clearly defined by either of the constituent papers. In one paper it is defined as the use of electrocautery[17]; however, no attempt was made to quantify the amount. The other article only comments on hemostasis being achieved

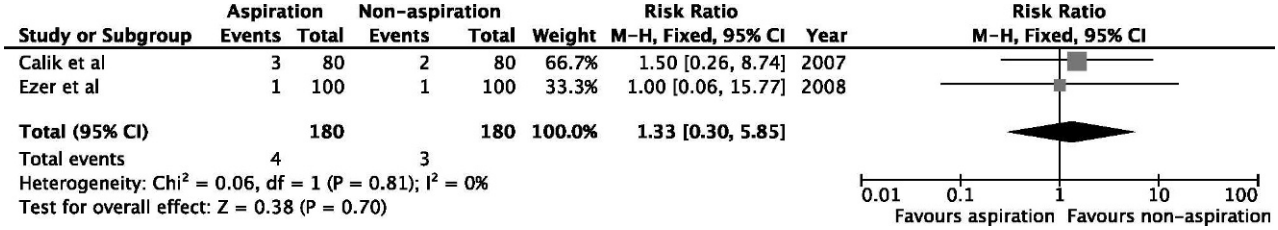

Fig. 4 Loss of gallstones.

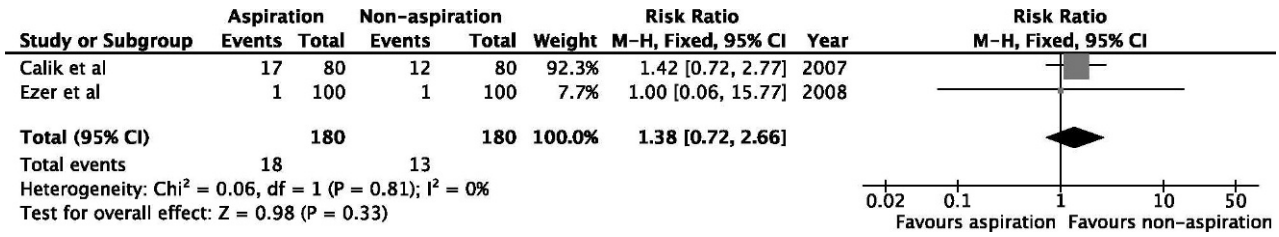

Fig. 5 Liver bed bleeding.

after one case of gallbladder avulsion and does not quantify the amount.[21] In both studies, no significant difference was found between ASP and NASP. Our paper corroborates these findings. It may be that other factors, such as the use of monopolar diathermy,[26] use of hydrodissection,[27] use of collagens,[28] and comorbidities such as cirrhosis,[29] are more important than gallbladder ASP in the prevention of liver bed bleeding.

Although ASP led to fewer gallbladder perforations, this did not translate into loss of more gallstones. This may be related to the size of the perforation and the size and number of contained gallstones. No clear definition was given for gallstones. It is also unclear whether biliary sludge (although considered a different entity than stones[30]) was included in this variable. We were unable to meta-analyze bile leakage because of different methods of reporting. Calik *et al*[21] reported number of instances of bile leakage without quantification and found no significant difference. Ezer *et al*[17] showed that although the amount of bile *leaked* was less in the ASP group, the difference was not significant. Because gallstone loss and bile leakage have been linked to infection rates,[10,11] the lack of difference found above is consistent with our finding of no significant difference in infection rates.

Limitations of our meta-analysis include a lack of clear definitions in individual studies relating to gallstone loss, liver bed bleeding, and diagnostic criteria for infections. Furthermore, the size of the gallbladder perforation, which may affect whether spillage occurred, was not mentioned. The limited number of trials also makes specific conclusions that are challenging to make. For most of our variables, heterogeneity was not significant except in operative time. This may relate to the number of surgeons involved. Calik *et al*[21] included only 1 surgeon, whereas Ezer *et al*[17] had 6 different surgeons operating.

In summary, even though there appears to be no immediate morbidity as a result of gallbladder perforation, only 2 complications were examined. Short- and long-term follow-up of these patients is needed before more robust conclusions can be made. Intuitively, gallbladder perforation gives rise to potentially more bile leakage or gallstone spillage. Given that there is a wealth of literature warning against these events,[9–16] it may still be prudent to consider ASP of the gallbladder in certain circumstances, such as in the elderly,[13] hydropic gallbladders,[25] infected bile, or pigment stones,[31] during the surgeon's learning curve,[5] or circumstances involving those who may have an inherent increased chance of developing infections or abscesses, such as the immunocompromised.

Conclusion

Aspiration of the gallbladder is safe and does not appear to add additional time to the procedure. After aspiration, gallbladder perforation rates may be lower. This does not appear to translate into decreased loss of gallstones or infection rates. There was no significant difference between techniques in blood loss from the liver bed. Further randomized, controlled trials and follow-up studies are required to confirm these results and to establish long-term sequelae.

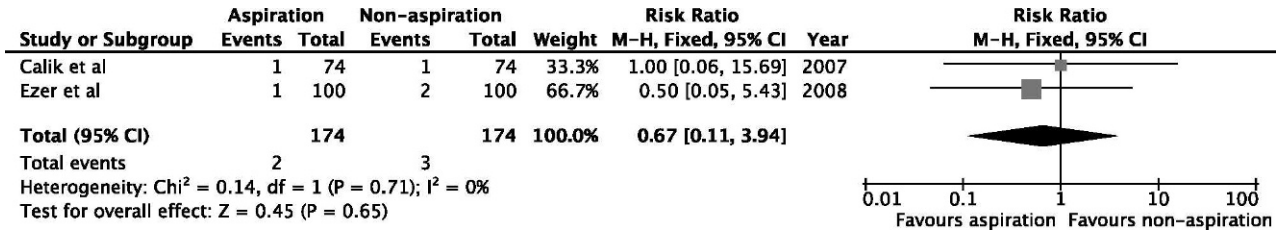

Fig. 6 Thirty-day infection rates.

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