



Fundus-first laparoscopic cholecystectomy for complex gallbladders: A systematic review

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ABSTRACT

Background: Retrograde ‘fundus-first’ cholecystectomy (FF) signifies the dissection that starts from the fundus of the gallbladder to the infundibulum in case structures of Calot’s triangle cannot be identified. Although feasible in laparoscopic cholecystectomy (LC), FF remains an underutilized approach in difficult cases. We aimed to systematically review the fundus-first laparoscopic cholecystectomy (FFLC) and to evidence-base its advantages and feasibility.

Methods: A systematic review was performed in compliance with PRISMA guidelines. A literature search was performed using PubMed/MEDLINE, ScienceDirect and Cochrane-Library for articles published from 2001 to 2021. Search keywords included ‘retrograde cholecystectomy’, ‘fundus-first cholecystectomy’ and ‘fundus-down cholecystectomy’. Quality assessments were applied using the Medical Education Research Quality Instrument (MERSQI) scores. Also, evidence levels were employed using GRADE. The protocol was registered with PROSPERO register (CRD42021227518).

Results: Altogether 9393 citations were identified and reviewed for this study. A final 23 studies were included, with a total of 7973 cholecystectomies comprising 3020 with FF approach. The endpoints were operative time, duration of postoperative hospital-stay and intraoperative and postoperative complications, as well as rate of conversion to open surgery. MERSQI mean score was 10.2 (SD= 1.85). The FF dissection was evidenced to be a superior technique when compared to conventional antegrade dissection as regards duration of operation, pain, nausea, conversion to open surgery and duration of sick leave. Furthermore, FF was found to be appropriate for difficult LC

Conclusion: The fundus-first laparoscopic cholecystectomy was associated with a shorter operating time, decrease in pain and nausea scores and reduced incidence of conversion to open cholecystectomy. Ultrasonic dissection was favoured in the retrograde dissection compared to that with electrocautery.

Introduction

Gallstone disease affects 10–15% of the adult population in the UK, with the majority being asymptomatic [1]. Laparoscopic cholecystectomy (LC) remains the gold standard in surgical management of symptomatic gallbladder diseases. The indications include, but are not limited to, symptomatic cholelithiasis, cholecystitis, common bile-duct stones and biliary dyskinesia [2]. Serious complications can occur even during a routine cholecystectomy [3]. Namely, difficulty in identifying key anatomical structures at Calot’s triangle, secondary to severe adhesions and fibrosis, enhances the surgical risk and constitutes the most common reason for conversion to open cholecystectomy [4]. Furthermore,

conversion of technique is associated with a significantly higher postoperative complication rate [5].

However, several advanced approaches in management of complex gallbladders, such as cholecystostomy, subtotal or partial cholecystectomy and retrograde ‘fundus-first’ approach have been described in the literature with the aim of decreasing the conversion rate to open surgery and to minimize the intraoperative and postoperative complications [5–8]. Then again, a completion procedure may be required after a subtotal cholecystectomy or cholecystostomy [9,10].

In the fundus-first (FF) approach, the dissection starts from the fundus of the gallbladder to the infundibulum, with the aim of giving the operating surgeon an easier task in identifying the structures within Calot’s

Abbreviations: FF, Fundus-first; LC, Laparoscopic cholecystectomy; FFLC, Fundus-first laparoscopic cholecystectomy; UD, Ultrasonic dissection; CED, Conventional electrocautery dissection; CLC, Conventional laparoscopic cholecystectomy; CBD, Common bile duct; LPC, Laparoscopic partial-cholecystectomy; SILC, Single incision laparoscopic cholecystectomy; RD, Retrograde dissection; IOC, Intra-operative cholangiography.

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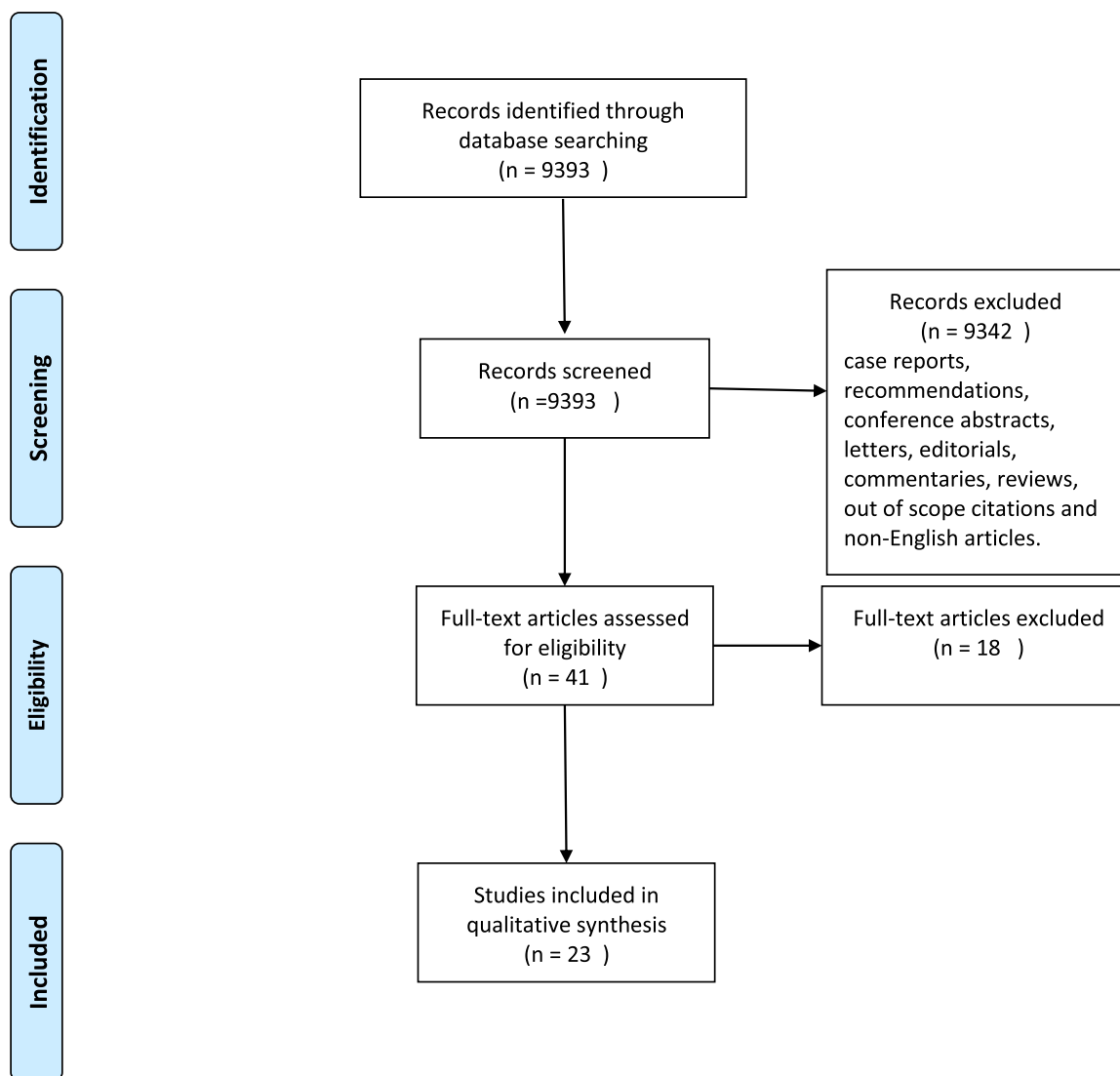


Fig. 1.

triangle [11] when anterograde cholecystectomy with conventional dissection is technically difficult. Although frequently used in open cholecystectomy, it remains an underutilized approach in laparoscopic cholecystectomy [12].

The aim of this study was to systematically review the fundus-first laparoscopic cholecystectomy (FFLC) and to evaluate its safety and feasibility mainly in patients with difficult gallbladders. Our rationale was to answer the following research questions:

- 1 Does retrograde FFLC differ from conventional anterograde laparoscopic cholecystectomy as regards duration of operation time?
- 2 Does retrograde FF differ from conventional laparoscopic cholecystectomy as regards rate of conversion to open surgery?
- 3 Is there a difference between FFLC with ultrasonic and electrocautery dissection, respectively as regards patient's post-surgery discomfort?

Methods

Protocol

The research protocol was registered with PROSPERO register for systematic reviews (CRD42021227518).

A systematic review was performed in compliance with the PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analysis) guideline [13].

Search strategy

A literature search was carried out by means of PubMed, ScienceDirect and the Cochrane Library for articles published from 2001 to 2021 (Fig. 1). Articles in the English language were included. Search-keywords included 'retrograde cholecystectomy', 'fundus-first cholecystectomy', 'fundus-down cholecystectomy'.

Inclusion and exclusion criteria

Only publications related to retrograde fundus-first cholecystectomy were included in this study. Conference abstracts, letters, editorials, commentaries, protocols, reviews and non-English publications were excluded.

Procedure

The procedure for developing a systematic review comprised two authors' inspection of titles, abstracts, and full-text papers, which were

systematically reviewed against the inclusion and exclusion criteria. The detailed literature search was independently performed. The final list of citations was completed by two authors. Search items were studied from the nature of the article, date of publication, and aim as well as main findings in relation to the fundus-first laparoscopic cholecystectomy (FFLC).

Grading and synthesis

The retrieved citations were read in full text for further assessment for eligibility. Quality assessments of studies were applied using The Medical Education Research Study Quality Instrument (MERSQI) [14]. The MERSQI contains 10 items that reflect 6 domains of study quality including study design, sampling, type of data, validity, data analysis, and outcomes. MERSQI produces a maximum score of 18 with a potential range from 5 to 18. The maximum score for each domain is 3. Insufficient quality was applied when 5–7 scores given, 8–9 scores indicated low quality, 10–11 scores denoted moderate quality and those citations with ≥ 12 scores signified high-quality. The quality assessments and evidence grading were performed following the protocol of The Grading of Recommendations Assessment Development and Evaluation Working Group (GRADE) [15]. The assessments included four grades of evidence:

Evidence grade 1: strong scientific evidence based on at least 2 studies with high evidential value or a systematic review/meta-analysis with high evidential value

Evidence grade 2: moderate scientific basis: A study with high evidential value and at least 2 studies with moderate scientific evidence: A study with high evidential value or at least 2 studies with moderate evidence value

Evidence grade 3: low scientific evidence: A study with high evidential value or at least 2 studies with moderate evidence value

Evidence grade 4: insufficient scientific evidence: 1 study with moderate evidence and/or at least 2 studies with low evidential value

Risk of bias within and across studies

We assessed the risk of bias in a blind manner; and the assessments were completed by the two authors, independently. If the assessment scores did not agree, we calculated the mean score of the given scores between the two evaluators. We controlled for accumulated risk of bias by calculating and grading the body of evidence of the findings according to GRADE recommendations.

Results

Study selection and characteristics

The results of the present search provided a total of 9393 studies (Fig. 1). After screening of titles and abstracts, two authors inspected the remaining full texts and applied the inclusion and exclusion criteria. The 23 citations defended their place in this review. The final list of citations was studied from the type of the articles, date of publication, aims, main findings, quality scores and evidence level (Table 1) [16–38].

For the currently included citations, the quality mean score was 10.2 (SD 1,85) and the scores ranged from 8 to 15 scores. Five citations got high quality, eleven moderate and seven low quality scores.

Synthesis of results of individual studies

A total of 7973 procedures including 3020 with FF approach have been studied. The endpoints were different across the studies. These included: Operative time, hospital stay, intraoperative complications including total blood loss, common bile duct injury, perforation of the gallbladder, rate of conversion to open surgery and intravenous fluid given, as well as whether a cholangiography was performed. In addition to secondary outcome measures such as postoperative complications in forms of pain, postoperative nausea, vomiting, postoperative

bile leaks through the subcostal drain, periumbilical port infections, or hematomas, were reported. For the included 23 citations, the MERSQI quality assessment resulted in 5 high quality, 11 moderate, 7 low quality studies; no citation with insufficient quality emerged from the included citations (Tables 1 and 2).

Results of individual studies

Five citations reached high quality through MERSQI ratings and our three null hypotheses were rejected based on the evidence-based findings (Table 2).

- Does retrograde FF differ from conventional anterograde laparoscopic cholecystectomy as regards operation time?

Saeed et al. (2020):

This citation included a randomized control trial in which 41 FF dissection versus 41 conventional dissection with electrocautery in LC were compared. Mean duration of surgery in the FF group was 46.44 ± 6.71 min. and in the CLC group the mean duration of surgery was 57.61 ± 13.31 min. Thus, mean duration of surgery in the FF group was statistically shorter, ($p < 0.001$). In addition, in the FF group 3 (7.3%) cases had overnight stays while in the latter group 15 (36.6%) cases had overnight stays, the frequency of overnight stay was statistically smaller in the FF group as compared to the CLC group ($p < 0.05$).

Cengiz et al. (2010):

The aim of this study was to measure the outcome with the FF method using ultrasonic dissection among 243 patients, out of these 73 had FF dissection with ultrasonic, 81 using electrocautery and 79 had conventional with electrocautery. The FF approach had a shorter operating time with ultrasonic dissection (58 min) compared to electrocautery (74 min; $p = 0.002$). In addition, the FF using ultrasonic dissection compared to electrocautery or the conventional method produced less blood loss (12 vs. 53 or 36 ml; $p < 0.001$) and fewer gallbladder perforations (26% vs. 46% or 49%; $p = 0.005$). Also, the pain and nausea scores at 4 and 6 h were lower, and the sick leave was shorter (6.1 vs. 9.4 and 9 days, respectively; $p < 0.001$).

Cengiz et al. (2005):

In this study, out of 80 patients, 43 had ultrasonic fundus-first (FF) dissections and were compared to 37 with conventional electrocautery dissection. FF ultrasonic dissection was associated with a shorter duration of operation ($M = 46$ vs 61 min) and fewer overnight hospital stays (2 vs 8 stays).

- Does retrograde FF differ from conventional anterograde laparoscopic cholecystectomy as regards rate of conversion to open surgery?

Tuveri et al. (2009):

The researchers performed a retrospective analysis of 194 obese patients that underwent LC between 1994 and December 2007. LC was performed in 113 (58.2%) patients with obesity type I, and 55 (28.3%) in patients with obesity type II, as well as 26 (13.5%) in patients with obesity type III. None of the differences among obese groups treated with the two techniques (FF and CLC) were statistically significant, with the exception of the shorter operative times in type 3 obese patients treated with the FF. Consequently, there was a significant reduction in the operative time in type III obese patients with no requirement for open conversions and a 100% success rate amongst all patients. Obese people subject to c CLC technique had a conversion rate of 4% out of 124 patients. Of 70 obese patients subject to FFLC no conversion to open surgery occurred.

Gupta et al. (2004):

Between a total of 145 patients, 45 had FFLC and 100 had CLC, the time taken during surgery on noninflammatory cases was 50.2 ± 11.4 min. and 60.95 ± 18.1 min. for the CLC and FFLC group, respectively. The same procedures performed on the severely inflamed group took 104.8 ± 18.6 min. and 89.8 ± 14.05 min., respectively. The results are significant ($p < 0.05$). None of the patients who underwent the

Table 1
Tabular analysis of the included citations.

AUTHOR (YEAR)	JOURNAL	TYPE OF STUDY	OBJECTIVE	PATIENTS N	FINDINGS	MERSQI SCORES ¹	QUALITY OF STUDY
Raj et al. (2001)	Journal of Laparo-endoscopic & Advanced Surgical Techniques	Cohort study	To present a technique for fundus-first laparoscopic cholecystectomy (FFLC) that is safe and utilizes instruments familiar to the surgeon performing conventional laparoscopic cholecystectomy (CLC).	Altogether 50 with FFLC	The fundus-down technique of LC may lower the incidence of common bile duct (CBD) injury.	8	Low
Mahmud et al. (2002)	Surgical endoscopy	Cohort study	To evaluate the indications and safety aspects of FF dissection and assess its effect on the conversion rate.	Altogether 710 patients with LC FFLC: 35	FFLC is a feasible, safe option for cases with difficult cystic pedicle and it leads to a reduced conversion rate.	9	Low
Gupta et al. (2004)	Journal of the Society of Laparo-endoscopic Surgeons	Cohort study	To compare CLC with the FF procedure and to evaluate whether FF technique can prevent conversion in difficult cases.	Altogether 145 patients with: FFLC=45 CLC=100	The FF technique leads to a reduced conversion rate when compared to CLC.	10	Moderate
Ichihara et al. (2004)	Hepato-gastro-enterology Journal	Cohort study	To evaluate the outcome of LC with taping of the cystic duct and resection via the fundus-first approach.	Altogether 505 patients with: FFLC: 500 Open conversion: 5	FFLC was successfully performed in 500 out of 505 patients with no postoperative death. Mean time of surgery: 52,7 min. Five patients were subject to open surgery because of colecystoduodenal fistula, concurrent cancer and liver laceration. Complications: 12 wound infections; 2 CBD stone. The dome-down FF approach seems promising especially in cases of acute inflammation and in fibrosis or contraction of triangle of Calot. The technique was easy to learn with a short learning curve, and it is therefore recommended that laparoscopic surgeons acquire this technique for the use in "the difficult gallbladder".	10	Moderate
Rosenberg et al. (2004)	Scandinavian Journal of Surgery	Cohort study	To describe a new technique using the dome-down (fundus-first) approach combined with laparoscopic FFLC ultrasonic dissection (UD).	Altogether 20 patients with FFLC	The dome-down FF approach seems promising especially in cases of acute inflammation and in fibrosis or contraction of triangle of Calot. The technique was easy to learn with a short learning curve, and it is therefore recommended that laparoscopic surgeons acquire this technique for the use in "the difficult gallbladder".	11	Moderate
Cengiz et al. (2005)	The British journal of surgery	Rando-mised clinical trial	To compare ultrasonic FF dissection and electro-cautery dissection starting at the triangle of Calot in patients undergoing laparoscopic cholecystectomy.	Altogether 80 patients with FF dissection with ultrasonic shears=43 CLC from triangle of Calot by electrocautery dissection=37	Ultrasonic fundus-first (FF) dissection provided a shorter duration of operation, fewer over-night hospital stays, lower pain scores, less nausea and a shorter period of sick leave compared with those subjected to electrocautery from the triangle of Calot. Out of the ultrasonic FF group 3 cases were converted and out of the CLC-group 4 cases were converted to open surgery.	12	High
Wang et al. (2006)	Journal of laparo-endoscopic & advanced surgical techniques	Cohort study	To evaluate whether FFLC could lower the conversion rate in geriatric patients with acute cholecystitis	Altogether 125 patients: FFLC: 112 Open conversion: 13	FFLC is a safe and effective technique for elderly patients with acute cholecystitis.	10	Moderate
Neri et al. (2007)	Journal of the Society of Laparo-endoscopic Surgeons	Cohort study	To evaluate the usefulness of antegrade dissection for obtaining a lower risk of common biliary duct injuries and to show an easier and more time-sparing technique than the traditional one. Antegrade dissection was described as incision of the visceral peritoneum from the infundibulum away from Calot's triangle along the gallbladder bed up to the fundus; then the dissection continues from the fundus up to the infundibulum.	Altogether 246: Antegrade dissection 127 Retrograde dissection 119	Gallbladder antegrade dissection is an easy, safe, and time-sparing technique	8.5	Low

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Table 1 (continued)

AUTHOR (YEAR)	JOURNAL	TYPE OF STUDY	OBJECTIVE	PATIENTS N	FINDINGS	MERSQI SCORES ¹	QUALITY OF STUDY
Tuveri et al. (2008)	Journal of laparo-endoscopic & advanced surgical techniques	Retro-spective cohort study	To highlight the limits and advantages of FFLC, in order to evaluate whether the potential complications are counterbalanced by the expected reduction of the conversion rate.	Altogether 1965 patients: FFLC was used for 29.	The FFLC was performed in 29 cases and was successful in 23 patients. Median operating time for the FFLC was 65 min (40–170 min). In 6 patients FFLC was converted to open operation. Intraoperative cholangio- graphy (IOC) was performed successfully in 17 cases. CBD stones were found in 6 cases. Minor complications occurred in 6 patients. No CBD injuries occurred. Two cases of residual CBD stones were treated postoperatively. Mortality rate was nil. - The FLC remains a safe option when dealing with difficult anatomy at the Calot's triangle and a scarred porta hepatis, but its use needs a good surgical judgment. A high incidence of CBD stones and the high failure rates in performing an IOC represent the most limiting factors.	10.5	Moderate
Kelly (2009)	BMC surgery	Pro-spective cohort study	To investigate the possible feasibility of FF laparoscopic cholecystectomy.	Altogether 1041; FFLC: 11/1041	FFLC is an achievable, alternative technique in difficult laparoscopic cholecystectomy.	8	Low
Tuveri et al. (2009)	Journal of laparo-endoscopic & advanced surgical techniques	Retro-spective cohort study	To analyze results of LC performed in patients with types I-III of obesity by the traditional technique versus the FF technique.	Altogether 194 patients: FFLC= 70 Traditional LC= 124	LC was performed in 113 patients with obesity type I, 55 patients with type II, and 26 patients with type III with no significant difference with the exception of the shorter operative times in type III patients treated with the FFLC. The Md operating time was 90 min for traditional LC and 65 (range, 45–130) for FFLC ($P < 0.05$) with no conversion to open surgery. FFLC can safely support the traditional LC in the treatment of obese patients, yielding a complication rate comparable with traditional technique. It reduced the operative time in type III patients, simplifying the intraabdominal manoeuvres and the gallbladder dissection.	12.5	High
Lirici et al. (2010)	Minimally Invasive Therapy & Allied Technologies	Pro-spective non-rando-mised cohort study	To evaluate whether the FF approach (anterograde) combined with ultrasonic dissection (UD) reduces the risk of conversion and bile-duct injury in difficult chole-cystectomies. Further, to evaluate the use of a preoperative scoring system that predicts the difficulty of LC, and to decide clinical relevance of an intraoperative assessment based on the Nassar scale.	Altogether 237 patients: 122 retro-grade LCs for complex gall stones (acute cholecystitis, severe chronic cholecystitis), with no pre-operative risk-rating of difficult LC.	The FF approach reduced the need forIOC, shortened operating time, lowered incidence of bile duct complications and reduced incidence of conversion compared to the conventional method. The FF approach and UD may be advised in difficult cases. Complicated gallbladder necessitates a careful management of the entire treatment process. The use of surgical risk-prediction scores and an objective establishment of the degree of difficulty for LCs are the foundations for correct surgical planning. From this perspective, the FF approach to LC, along with UD is a safe method.	11	Moderate
Huang et al. (2010)	Surgical Endoscopy	Cohort study	To compare the efficacy and complications between FF and (CLC) in treating contracted gallbladders with gallstones.	Altogether 64 patients: FFLC 33 CLC 31	FF is associated with lower conversion and complication rates and shorter postoperative hospital stay as compared with CLC when used to treat patients with contracted gallbladders and gallstones.	11	Moderate

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Table 1 (continued)

AUTHOR (YEAR)	JOURNAL	TYPE OF STUDY	OBJECTIVE	PATIENTS N	FINDINGS	MERSQI SCORES ¹	QUALITY OF STUDY
Cengiz et al. (2010)	Surgical Endoscopy	Multicentred randomised trial	To study the outcome with the fundus-first method using ultrasonic dissection (FFUD)	Altogether 243 patients FFUD =73 FF using electrocautery:81 Conventional with electrocautery LC: 79	The FFUD had a shorter operating time (58 min) than with electrocautery (74 min). The FFUD compared with electrocautery or the conventional method produced less blood loss and fewer gallbladder perforations (26% vs. 46% or 49%). Also, the pain and nausea scores at 4 and 6 h were lower, and the sick leave was shorter (6.1 vs. 9.4 and 9 days, respectively).	15	High
Cui et al. (2011)	Surgical endoscopy	Cohort study	To assess the feasibility and safety of single incision LC (SILC) using a modified FF approach.	Altogether 16 patients	SILC using a FF approach is technically doable.	8	Low
Patel et al. (2011)	Surgical endoscopy	Pro-spective cohort study	To evaluate the feasibility of fundus-first trans-umbilical single-incision laparoscopic cholecystectomy (SILC) with a cholangiogram.	Altogether 20 patients	The FF approach provided better retraction and was significantly easier to perform than an antegrade cholecystectomy when carried out solely via a single port.	10	Moderate
Strasberg et al. (2012)	HPB	Cohort study	To explain the mechanisms of vasculobiliary injuries through analysis of clinical records of patients.	Altogether 8 patients	Extreme vasculobiliary injuries tend to occur when FF cholecystectomy is performed in the presence of severe inflammation.	8	Low
Tempé et al. (2013)	Surgical Endoscopy	Rando-mised trial	To compare the costs with an ultrasonic fundus-first technique to the costs with a CLC using electrocautery.	Altogether 80 patients FF:40	The direct and indirect cost was lower with the ultrasonic FF technique. CLC was associated with both a longer duration of operation and hospitalization.	8.5	Low
Mattila et al. (2015)	Surgical Endoscopy	Randomised trial	To examine the impact of fundus-first laparoscopic cholecystectomy (FFLC) using ultrasonic dissection and CLC using diathermy hook dissection on operative time, same-day discharge and intra-operative complications.	Altogether 169 patients FF with ultrasonic scissors:88 Standard LC with diathermy hook:79	FFLC with ultrasonic dissection resulted in similar operative time, blood loss and postoperative recovery profile compared to CLC diathermy hook dissection.	13	High
Yamamoto et al. (2016)	Journal of Laparo-endoscopic & Advanced Surgical Technique	Cohort study	To evaluate the clinical outcome of a SILC via a teres hanging technique combined with fundus-first, dome-down separation.	Altogether 18 patients SILC	This novel procedure was successfully completed in all cases with no intraoperative complications.	8	Low
Sormaz et al. (2018)	Turkish journal of trauma and emergency surgery	Cohort study	To evaluate the effect of conversion from retrograde dissection (RD) to fundus-first technique (FF) or laparoscopic partial-cholecystectomy (LPC) on complication rates, operation time, and duration of hospitalization. FF was defined as antegrade dissection. Retrograde used for separation of gallbladder from liver bed.	Altogether 210 patients with LC: 197 completed with RD. FF in 13 patients out of which 6 needed LPC	In difficult cholecystectomies, safer options such as the FF technique may decrease conversion rates to open surgery and contribute to accomplishing the laparoscopic intervention safely. . Three postoperative complications occurred in the RD group and two in the LPC group. No major intraoperative complications or perioperative mortality happened in any patients.	9.5	Low
Cengiz et al. (2019)	Scientific Reports	Cohort study	To study the feasibility and safety profile when offering fundus-first (FF) as standard technique in cholecystectomy.	Altogether 1745 patients: 1425 FFLC and 320 conventional	The FF technique was associated with lower rates of bile duct injuries and shorter operation time in cholecystectomy. It was found that a conventional technique starting dissection at the triangle of Calot was a significant risk factor for a CBD injury.	10.5	Moderate
Saeed et al. (2020)	Pakistan journal of medical and health sciences	Randomised controlled trial	To compare the outcome of FF dissection versus conventional dissection with electrocautery in LC in terms of operative time and overnight hospital stay.	Altogether 82 patients FFLC: 41 CLC: 41	FFLC resulted in reduced surgery time and frequency of overnight stay compared to CLC.	12.5	High

¹ 5–7 indicate insufficient quality; 8–9 scores are of low quality, 10–11 are of moderate quality and those with 12–15 scores represented high-quality studies.

Table 2
Citations along with MERSQI scores and null hypotheses

CITATIONS	NULL HYPOTHESES	MERSQI SCORES	QUALITY ESTIMATION (EVIDENCE GRADE)
First null hypothesis	There is no difference between laparoscopic cholecystectomy and fundus-first (FF) as regards duration of operation	Scores (n)	Quality
Cengiz et al. (2010)	FF ultrasonic dissection (FFUD) provided a shorter duration of operation compared to the conventional electrocautery dissection (CED) technique.	15,0	HIGH (1)
Saeed et al. (2020)	Mean duration of surgery in FFLC group was shorter than that in the CED group.	12,5	HIGH (1)
Second null hypothesis	There is no difference between laparoscopic cholecystectomy, conventional dissection and fundus-first in difficult gallbladder as regards conversion rate to open surgery		
Tuveri et al. (2009)	Obese people subject to CED technique had a conversion rate of 4% out of 124 patients. Of 70 obese patients subject to FFLC no conversion to open surgery occurred.	12,5	HIGH (1)
Gupta et al. (2004)	The FF technique leads to a reduced conversion rate when compared to conventional LC.	10	MODERATE (2)
Tuveri et al. (2008)	FFLC contributed significantly to a substantial reduction of the conversion rate in patients who otherwise were candidates for conversions of the laparoscopic procedure due to an undistinguishable anatomy.	10,5	MODERATE (2)
Huang et al. (2010)	The conversion rate and complication rate were 0% and 3.00% for FF technique, and 32.3% vs 22.6% for conventional technique.	11,0	MODERATE (2)
Third null hypothesis	There is no difference between laparoscopic cholecystectomy fundus-first ultrasonic dissection (FFUD) and conventional electrocautery dissection (CED) as regards patient's pain, nausea and duration of sick leave		
Cengiz et al. (2005)	FFUD resulted in lower pain scores, less nausea and a shorter sick leave compared to the CED technique.	12,0	HIGH (1)
Cengiz et al. (2010)	FFUD resulted in less pain, less nausea and shorter sick leave compared to the CED. technique.	15,0	HIGH (1)

fundus-first method required conversion either to the cystic duct method or to an open procedure. However, 27 patients in the CLC group required conversion to the FFLC method. Of these, 3 were further converted to an open procedure. One patient had a small duodenal perforation during the procedure and had dense adhesions. She was opened and cholecystectomy along with repair of duodenal perforation was performed. The other 2 were converted due to dense adhesions. The FF technique led to a reduced conversion rate when compared to CLC.

Tuveri et al. (2008):

In a total of 1965, FFLC was studied in 29 patients. The FFLC technique contributed significantly to a substantial reduction of the conversion rate in patients who otherwise were candidates for conversions of the laparoscopic procedure due to difficult anatomy at the Calot's triangle. Nevertheless, the technique's adoption needs a good surgical judgment. Considering the high incidence of CBD stones in the researchers' series, the high failure rates in performing an intraoperative cholangiogram represent the most important limiting factor.

Huang et al. (2010):

Among 64 patients, 33 had FFLC and 31 had CLC. The researchers found that average postoperative hospital stay for FF technique was 5 ± 3 days, and 7 ± 3 days for conventional technique ($p < 0.003$). The conversion rate and complication rate were 0% (0/33) and 3.00% (1/33) for FF, and 32.3% (10/31) and 22.6% (7/31) for conventional technique ($p < 0.001$ and 0.02 respectively). In the subgroup analysis, FF LC seemed to lower the bile duct injury rate from 2/31 (6.5%) to 0/33 (0%) compared with 6/1 (0.4%) ($p = 0.01$ between 6.5% and 0.4% vs. $p = 1.00$ between 0% and 0.4%). The conversion and complication rates were 0% and 3.00% for FF technique, and 32.3% vs 22.6% for conventional technique.

- *Is there a difference between FF laparoscopic cholecystectomy with ultrasonic and electrocautery dissection, respectively as regards patient's pain, nausea and duration of sick leave?*

Cengiz et al. (2005):

Ultrasonic fundus-first (FF) dissection provided a shorter duration of operation, fewer over-night hospital stays, lower pain scores, less nausea and a shorter period of sick leave compared with patients subject to electrocautery from the triangle of Calot. Out of the ultrasonic FF group 3 cases were converted and out of the CLC-group 4 cases were converted to open surgery. The FF dissection was independently associated with less pain after 1, 4 and 24 h, and less nausea after 2, 4 and 24 h as regis-

tered on a visual analogue scale. FF was also an independent predictor of same-day discharge from hospital and of short sick leave (M 5,5 vs 9,3 days).

Cengiz et al. (2010):

The FF method using ultrasonic dissection (UD) provided a shorter surgery time (58 min.) than with electrocautery (74 min.). The FFUD compared with electrocautery or the conventional method produced less blood loss and fewer gallbladder perforations (26% vs. 46 and 49%). Also, the pain and nausea scores at 4 and 6 h were lower, and the sick leave was shorter (6.1 vs. 9.4 and 9 days, respectively). In sum, the FF ultrasonic dissection resulted in less pain, less nausea and shorter sick leave compared to the conventional electrocautery dissection technique.

Risk of bias across studies

The MERSQI was designed to evaluate the methodological quality of medical education research [14]. MERSQI has been demonstrated to be a reliable and valid instrument for measuring methodological quality in medical research and consequently, we applied it in our systematic review. In order to decrease the risk of bias within studies in our review of citations over 20 years, we excluded recommendations, case reports, as well as review studies to avoid bias and duplications of citations. In addition, the quality levels based on the scored citations were applied. We filled the GRADE's criteria for consideration of an individual study's risk of bias to estimate the citation's suitability to contribute to the body of evidence of the findings in this systematic review.

In sum, the positive outcome of the FF approach for difficult LC was supported with 4 high quality and 3 moderate quality studies, comprising decrease in the operative time, shorter sick leave, as well as intra- and post-operative complications.

Discussion

The current standard for cholecystectomy is through a laparoscopic approach with initial dissection of the Calot's triangle followed by fundus dissection. The fundus-first approach was initially proposed by French surgeons in the late 1980's. Since then, it has become a possible alternative technique reserved for cases with limited ability to dissect at Calot's triangle [11]. By initiating the dissection at the fundus, the retrograde method allows the surgeon to clearly identify the cystic duct and cystic artery prior to ligation [11,25,39]. To our knowledge this is

the first review whose aim was to solely study the FFLC approach as a standardized technique for difficult gallbladders.

Indications for the FF approach included dense adhesions, impacted stones in Hartmann's pouch, short dilated cystic duct, Mirizzi syndrome and contracted burned-out gallbladder [17,24]. The FF approach was also indicated in the presence of marked induration and thickening around the junction of the common and cystic duct as well as when clear exposure of the cystic duct and the common bile duct could not be safely achieved [18].

Then again, a decision for conversion to open cholecystectomy or abandoning the operation may be an instant safe option necessary in difficult cases. In other words, such difficult conditions include the inability to identify the gallbladder and the failure to recognize the biliary anatomy due to the presence of dense adhesions or anatomical anomalies [40]. Experts in the field have recommended that FF or partial cholecystectomy can be safe alternative techniques when it is not possible to achieve the critical view of safety with the aim to decrease the risks related to difficult cases in order to avoid bile duct injuries [41].

A subtotal approach can be associated with longer duration of hospitalization, higher rates of surgical site infection and a greater necessity for secondary interventions such as postoperative endoscopic retrograde cholangiopancreatography, percutaneous drainage and interval completion cholecystectomy [42]. Although partial or subtotal cholecystectomy can be performed with a retrograde technique, we focused in our review on the FF total cholecystectomy as an alternative technique for difficult gallbladders in order to avoid complications of subtotal approach and to prevent the future possible need for completion procedures.

In complex cases to better identify the biliary anatomy, intra-operative cholangiogram has been used, along with other imaging techniques such as fluorescence cholangiography and intra-operative ultrasonography [43]. The main limitations of these imaging techniques include the high costs and limited availability; increased operating time, exposure of radiation to both patient and theater staff and false positive results leading to unnecessary common bile duct exploration [44]. In contrast, FF is mostly performed without a need for intraoperative imaging [27].

Also, it has been cautioned against the FF approach, while adverse events have been described such as dislodgement of gallbladder stones into the common bile duct, excessive bleeding from the cystic artery prior to ligation and traction distortion [39]. In severely inflamed gallbladders extreme vascular-biliary injuries have occurred in open cholecystectomy when the FF approach had been attempted [32]. Therefore, the FF technique requires good surgical judgment and must be performed by experienced laparoscopic surgeons [24].

It has been shown that ultrasonic dissection of the gallbladder causes less thermal injury to the surrounding tissues than hook diathermy [45]. Furthermore, a FFLC combined with UD was reported to minimize the rate of conversion and biliary injuries in difficult cases [27]. Similarly, also ultrasonic FF dissection has been set up against with conventional LC via electrocautery at Calot's triangle; it was found that the ultrasonic FF dissection was quicker, leads to fewer overnight hospital stays, caused less nausea and post-operative pain with fewer direct and indirect hospital costs [21,29,33].

Conclusion

The present review included citations revealing fundus-first laparoscopic cholecystectomy as a feasible technique. This technique was associated with a shorter operation time and short-term sick leave. The fundus-first approach yielded fewer pain and nausea scores and reduced incidence of conversion to open cholecystectomy. Ultrasonic dissection was favoured in the fundus-first dissection compared to that with electrocautery.

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Ethical standard

The authors declare no conflict of interests.

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