REVIEW ARTICLE

Systematic review and meta-analysis of early vs late interval laparoscopic cholecystectomy following percutaneous cholecystostomy

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Abstract

Background: High risk surgical patients with acute cholecystitis are commonly treated with percutaneous cholecystostomy (PTC) drainage. The optimal timing of subsequent interval laparoscopic cholecystectomy (LC) remains unclear.

Methods: Medline, EMBASE, and Scopus were searched to identify studies published between 01/01/2000 and 31/12/2020, reporting on interval LC outcomes in patients initially treated by PTC. Early and late interval LC were defined as <30 and ≥ 30 days respectively. The Methodological Index for Nonrandomized Studies was used for quality assessment. Meta-analysis of proportions was conducted using a random-effects model.

Results: A total of 512 studies were screened, 41 met the inclusion criteria. There were 22 studies in both early and late interval LC groups, with 3 included studies reporting both early and late groups. Following quality assessment, 29 studies were included in the meta-analysis. There were no significant differences between early and late interval LC in terms of conversion rates (7.2% vs 8.3%, p = 0.854), 90-day morbidity (12.8% vs 15.9%, p = 0.496), and 90-day mortality (0.25% vs 0.32%, p = 0.704). Heterogeneity was significant (I^2>50%) in all groups.

Conclusion: Current evidence of interval LC within or beyond 30 days demonstrates no significant impact on outcomes. Patient factors, clinical experience, and hospital facilities may prove more important predictors.

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Introduction

Acute cholecystitis, an inflammatory condition of the gallbladder, is a common surgical condition that may require hospital admission and subsequent surgical management.[1,2] Presentations vary from mild and self-limiting to a life threatening disease with an approximate mortality rate of 0.6%.[1–3] Associated complications include empyema, abscess formation, haemorrhagic transformation, or perforation of the gallbladder with peritonitis.[1] The 2018 Tokyo Guidelines (TG18) provide clear guidance on the recommended management options.[4]

Early laparoscopic cholecystectomy (LC) is the recommended management option in patients deemed able to withstand surgical treatment.[4] In high-risk surgical patients with moderate and severe acute cholecystitis, the TG18 recommend the use of percutaneous transhepatic gallbladder drainage as the first alternative to surgical intervention.[4] High-risk surgical patients are those individuals presenting with associated organ dysfunction and/or significant frailty or comorbidities.[4] These can be assessed and classified using measures such as the American Society of Anaesthesiologists (ASA) or the Charleston Comorbidity Index (CCI).[4]

Previous research has highlighted the positive correlation between gallbladder distension and oedema with conversion rates,[5,6] as well as operative time and bleeding with postoperative complications.[7,8] Percutaneous Cholecystostomy (PTC) acts by providing source control, draining the gallbladder distension, and reducing the associated inflammation and oedema.[1] In a meta-analysis of 15 studies, Huang et al. compared early LC with delayed LC following PTC and found shorter operative times, reduced conversion rates, and less intraoperative bleeding in the delayed LC following PTC group.[1] In addition, the CHOCOLATE multicentre randomised clinical trial from the Netherlands provided evidence that PTC is not an optimal long term management plan with 44 out of 68 (65%) patients assigned to the PTC without planned interval LC arm experiencing major complications.[9]

The reported morbidity and mortality in high risk patients with acute cholecystitis remains high[4,10] despite PTC being the recommended management since the 2013 Tokyo Guidelines (TG13).[4] A question that remains unsolved is whether there is an optimal time period between PTC and interval LC. The TG18 have highlighted and addressed this by currently recommending that physicians need to decide regarding timing on the basis of patient factors, hospital facilities, and clinical experience.[4]

This review aims to assess the available evidence on patient outcomes in those that underwent an interval LC following PTC for acute cholecystitis, as well as compare outcomes in those with early interval LC (<30 days) and late interval LC (≥30 days). The primary outcome of interest was conversion rates and secondary outcomes included 90-day morbidity and mortality, operative time, and hospital length of stay.

Methods

Protocol and review design

The protocol was prospectively registered with PROSPERO, CRD42021228685.[11] Ethics approval was not required for this study design. A systematic review was conducted on the published literature between 1 January 2000 and 31 December 2020 using Medline, PubMed, EMBASE, and Scopus. The search strategy for Medline, PubMed and EMBASE (via Ovid) was "laparoscopic cholecystectomy AND (cholecystostomy OR (percutaneous adj4 drain*))". The same strategy but without the adj4 function was used on Scopus. The inclusion criteria included studies reporting outcomes on adults with cholecystitis that had a PTC followed by interval LC. Exclusion criteria included studies that did not report conversion rates or did not specify the time interval between PTC and LC. In studies with multiple publications from the same cohort, only the latest publication was used. Case reports, case series and non-English language studies were also excluded from this review.

Study selection and data extraction

All identified articles were screened by at least two independent reviewers following removal of duplicates. Discussion with a third author resolved any inclusion conflicts. Full text articles were retrieved for all screened results. Review articles were not included but their references were searched to identify other studies that met the inclusion criteria.

Data extraction was performed by two independent authors. Study characteristics retrieved included first author, year of publication, country of study, and study design. Cohort data retrieved included number of patients with PTC, mean or median age, percent female ratio, cohort description metric (ie. TG18, TG13, ASA, CCI), timing of interval LC, number of planned LC and open cholecystectomies (OC), conversion rates during interval LC, 90-day morbidity and mortality. Other reported outcomes also recorded included procedure time, hospital length of stay, and blood loss. There is currently no standard definition of early and late interval LC following PTC. For the purpose or this review we defined early interval LC following PTC as <30 days, and late as ≥30 days. Though other time intervals have been described previously, such as <7 and ≥ 7 days,[1] this time frame was chosen on the basis of the available evidence to allow as equal a distribution between the two groups.

Quality assessment

Assessment of study quality was performed using the Methodological Index for Nonrandomized Studies (MINORS).[12] Where study design precluded assessment of certain criteria, these were marked as not applicable (NA) and removed from the total score for overall assessment. Overall MINORS scores were calculated and classified in quartiles. Studies with a score of less than or equal to the first quartile were excluded from quantitative synthesis.

Statistical analysis

Quantitative analysis and synthesis was performed using Statistics Analysis (STATA, version 17.0).[13] Conversion rates and morbidity were analysed using a meta-analysis of proportion with a random effects model and Freeman-Tukey double arcsine transformation as described by Nyaga et al.[14] Pooled chi squared test for independence analysis was used to measure difference in mortality. Dates of publication were compared using the Mann–Whitney U test. Statistical significance was defined at $p < 0.050$. The I^2 statistic was used to evaluate heterogeneity among studies, with an I^2>50% regarded as significant heterogeneous.

Results

Literature review and study selection

A total of 921 articles were retrieved from the electronic databases. A further 12 articles were identified that complied with the inclusion criteria from the full text articles reviewed. After removal of 416 duplicates, 517 abstracts were reviewed for compliance with the inclusion criteria. Following removal of 408 non relevant abstracts, 109 full text articles were retrieved and

assessed. A total of 68 full text articles were excluded with reasoning outlined in Fig. 1. A total of 41 studies were included in the review[3,7,15–53] and are summarised in Table 1.

Study characteristics

Of these, 22 studies reported on outcomes following early interval LC,[7,15–25,36,43–45,47,49–53] and 22 studies following late interval LC.[3,25–42,45,46,48] Three studies reported and compared outcomes in both groups.[25,36,45] All included studies were cohort studies, there were no randomized trials. There were 8 prospective cohort (PC) designs and 35 retrospective cohort (RC) designs outlined in Table 1. The proportion of prospective studies was higher in the late interval LC group at 6 out of 22 studies, as opposed to 2 out of 22 studies in the early interval LC group. The year of publication also varied between the two groups. Papers reporting outcomes in late interval LC were significantly more recent, with a median publication year of 2017 (IQR 2014–2020) as opposed to 2015 (IQR 2008–2017) in the early interval LC group, $p = 0.039$.

Quality assessment

Quality assessment using MINORS was variable with scores ranging from 25 to 90%. Full scoring and marking criteria are outlined in Supplementary Table 1. The median MINOR score was 50%. The first quartile score was 42%. Of the 36 included studies, 29 studies had an overall MINORS score of >42%.[3,7,15–18,20,22,25,27,28,32–38,41,43–50,52] Only these studies were included in subsequent meta-analyses.

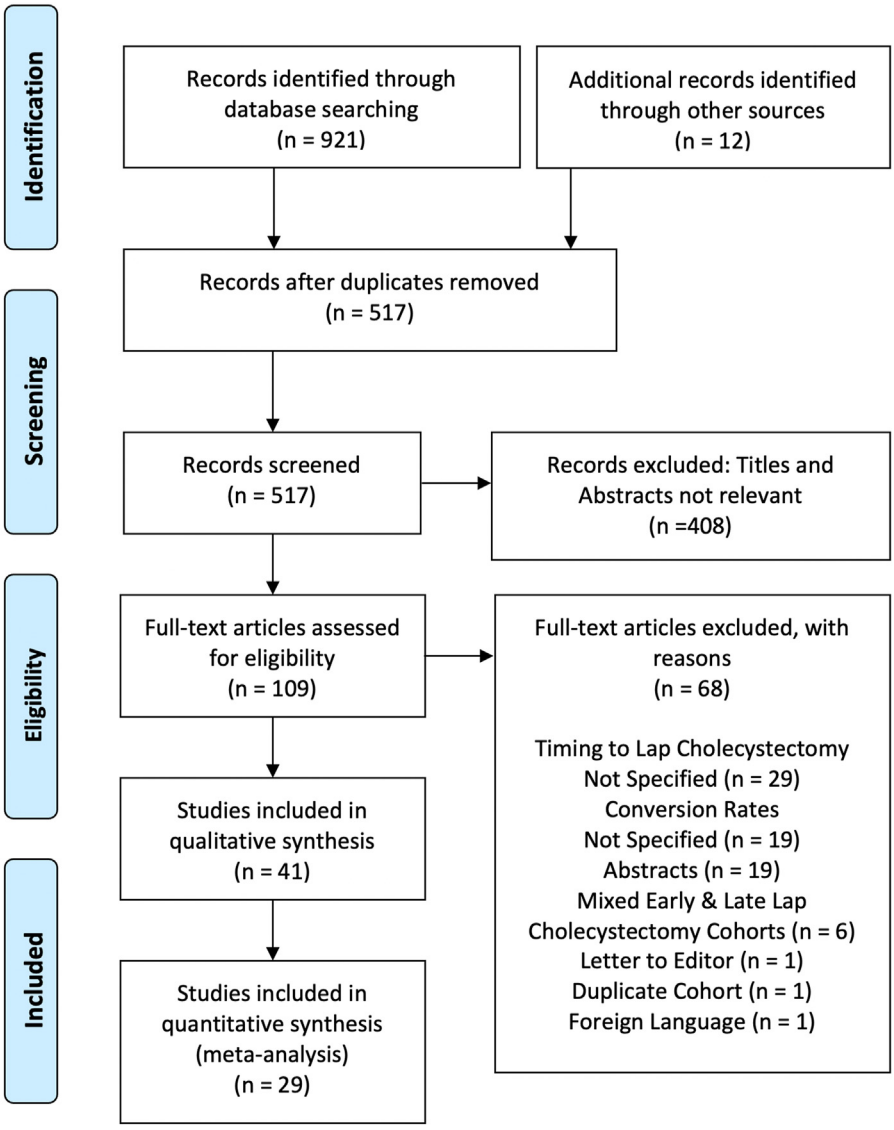

Figure 1 PRISMA flow chart of literature review

Table 1 Characteristics of included studies categorised by early and late interval cholecystectomy

Authors, Year	Country	Type of Study	No. of pts with PTC	Age	%F	Tokyo Classification or Comorbidity Score	Timing of interval LC	Planned LC	Conversion Rate n (%)	Planned OC	Mortality Morbidity n	Other
Early Interval Cholecystectomy (<30 days)												
Lee et al. 2022[43]	Korea	RC	695	66	41%	ASA ≥3 34.1%	Early 6.2 (SD 5.2)	695	11 (1.6%)	0	4 78	Subtotal Cholecystectomy 4 Mean procedure time 61.8 (SD 27.9) min Mean postoperative LOS 3.9 (SD 5.0) days
Kimura et al. 2021[44]	Japan	RC	22	76	36%	TG18 I/II/III 36%/55%/9%	Early <14 days	14	5 (35.7%)	0	0 6	Mean procedure time 117.4 (SD 10.6) min Mean postoperative LOS 19.5 (SD 7.2) days
Lyu et al. 2021[25]	China	RC	100	65	36%	TG18 I/II/III 18%/77%/5%	Early <1 week	22	2 (9%)	0	0 3	Mean procedure time 92.16 (SD 4.5) mins Mean postoperative LOS 5.2 (SD 0.70) days
				69	47%	TG18 I/II/III 27%/73%/0%	Early 1–4 weeks	30	2 (7%)	0	0 4	Mean procedure time 89.2 (SD 3.88) mins Mean postoperative LOS 5.34 (SD 0.54) days
Tomimaru et al. 2020[45]	Japan	RC	85	69	29%	TG 18 I/II/III 8%/53%/39%	Early 6 (SD 4) days	85	2 (2.4%)	0	0 6	Mean procedure time 162 (SD 61) min Mean postoperative LOS 10 (SD 8) days
Jia et al. 2018[7]	China	RC	65	62	42%	ASA 3.5 ± 0.6	Early (<5 days)	38	1 (2.6%)	0	0 2	Mean procedure time 78 ± 19 min Mean postoperative LOS 9 ± 3 days
Endo et al. 2017[36]	Japan	RC	1239	68.9	32.6%	TG13 I/II/III 19%/26%/27%	Early <30 days	456	37 (8.1%)	231	6 96	Mean procedure time 136.7 min
Inoue et al. 2017[47]	Japan	RC	67	75	38.8%	TG13 I/II/III 19.4%/62.7%/17.9%	Early <30 days	54	9 (16%)	13	0 9	25 (37%) Subtotal cholecystectomies
Jung et al. 2017[49]	Korea	RC	128	65	39%	ASA I/II/III/IV 17.2%/50.8%/31.3%/0.7%	Early Mean 8 days (Range 2–23)	128	31 (25%)	0	0 4	Mean procedure time 82 ± 40 min Mean postoperative LOS 7.3 ± 7.3 days
Zeren et al. 2017[51]	Turkey	RC	40	75.7	45%	Geriatric cohort	Early (within 72 h)	25	4 (16%)	15	4 7	
Jung et al. 2015[50]	Korea	RC	74	68	43%	ASA 2.3 ± 0.7	Early <10 days	30	10 (33%)	0	0 2	Mean procedure time 103 ± 49 min Mean postoperative LOS 7.4 ± 5.3
Yamada et al. 2015[52]	Japan	RC	46	67	28%	TG13 I/II/III 30.4%/56.6%/13.0%	Early <14 days	21	8 (38%)	0	0 NS	Median procedure time 180 min (IQR 118–240)
Borzellino et al. 2014[53]	Italy	RC	40	70	43%	NS	Early Median 3 days (IQR 2–5)	39	6 (15.4%)	1	1 12	Median procedure time 105 (IQR 75–120) mins Median postoperative LOS 3 (2–6) days
Choi et al. 2012[15]	Korea	RC	40	72.5	43%	Mean ASA 2.4	Early 5 days	40	2 (5%)	0	0 7	Mean procedure time 85 ± 28 min
Han et al. 2011[16]	Korea	RC	67	70	29%	TG13 I/II/III 14.3%/76.2%/9.5%	Early <72hr	21	0 (0%)	0	0 4	Mean procedure time 79.3 ± 25 min Mean postoperative LOS 11 ± 5 days
Kim et al. 2011[17]	Korea	RC	97	66	52%	ASA I/II/III/IV 8.2%/66%/23.7%/2.1%	Early <14 days	97	4 (4.1%)	0	0 3	Mean procedure time 120 ± 53 min Mean postoperative LOS 7 ± 4 days
Kim et al. 2009[18]	Korea	RC	73	58	40%	ASA I/II/III/IV 11%/60%/26%/3%	Early <7 days	35	5 (14%)	0	0 3	Mean procedure time 54.7 ± 25.8 min
Kim et al. 2008[19]	Korea	RC	37	66.8	65%	NS	Early 7 ± 3.5 days	37	1 (2.7%)	0	0 3	Mean procedure time 74.86 ± 35.42 min Mean postoperative LOS 3.9 ± 2.6 days
Akyürek et al. 2005[20]	Turkey	PC	70	62	67%	ASA II/III/IV 19.3%/45.2%/35.5%	Early <4 days	31	2 (6.5%)	0	0 2	
Macri et al. 2005[21]	Italy	RC	27	76	81%	ASA II/III/IV 37.1%/55.5%/7.4%	Early <8 days	25	5 (20%)	0	1 6	
Tsumura et al. 2004[22]	Japan	PC	60	65	35%	Mean ASA 2.4	Early <30 days (Range 1–26 days)	60	2 (3.3%)	0	0 7	Mean procedure time 124 (SD 51) Mean postoperative LOS 11.8 (SD 7.1) days
Chikamori et al. 2002[23]	Japan	RC	31	67	31%	NS	Early <7 days	31	1 (3%)	0	0 0	Mean procedure time 84min Mean postoperative LOS 9 ± 4 days

Table 1 (*continued*)

Authors, Year	Country	Type of Study	No. of pts with PTC	Age	%F	Tokyo Classification or Comorbidity Score	Timing of interval LC	Planned LC	Conversion Rate n (%)	Planned OC	Mortality Morbidity n	Other
Kim et al. 2000[24]	South Korea	RC	27	53	52%	NS	Early Range 4–26 days	27	4 (15%)	0	0 4	Mean postoperative LOS 6 days
Late Interval Cholecystectomy (≥30 days)												
Han et al. 2021[46]	South Korea	RC	179	72	37%	CCI ≥6 28.5%	Late 69.5 ± 89.6	179	3 (1.7%)	0	0 25	Mean procedure time 53.7 (SD 27.7) min Mean postoperative LOS 4.2 (SD 7.8) days
Hung et al. 2021[48]	Taiwan	RC	221	66	43%	TG18 II/III 88%/12%	Late 63 (46–84) days	221	13 (5.9%)	0	0 68	Mean postoperative LOS 3.88 ± 3.23 days
			123	68	45%	TG18 II/III 90%/10%	Late 74 (57–97) days	123	3 (2.4%)	0	0 36	Mean postoperative LOS 3.16 ± 2.25 days
Lyu et al. 2021[25]	China	RC	100	67	46%	TG18 I/II/III 17%/79%/4%	Late >4 weeks	48	8 (16%)	0	0 7	Mean procedure time 99.3 (SD 5.2) mins Mean postoperative LOS 4.87 (SD 0.39) days
Carti et al. 2020[26]	Turkey	RC	50	52.5	38%	TG13 Grade II	Late (4–6 weeks)	10	8 (80%)	40	0 5	Mean postoperative LOS 2.8 days
Kaura et al. 2020[42]	United States	RC	140	72	29%	TG18 I/II/III 8.6%/28.6%/62.9%	Late Median 72 days (IQR 51–109)	131	22 (16.8%)	9	0 66	
Liu et al. 2020[27]	China	RC	Transhepatic PTC 58	73.8	47%	TG18 I/II/III 8.6%/79.3%/12.1%	Late (35 ± 5 days)	58	9 (15.5%)	0	0 3	Mean procedure time 118 ± 35 min Mean postoperative LOS 14 ± 4 days
			Transperitoneal PTC 45	74.8	47%	TG18 I/II/III 85.2%/82.2%/11.1%	Late (34 ± 4 days)	45	11 (24.4%)	0	0 4	Mean procedure time 140 ± 37 min Mean postoperative LOS 18 ± 5 days
Tomimaru et al. 2020[45]	Japan	RC	86	68	35%	TG18 I/II/III 15%/49%/36%	Late 53 (SD 11) days	86	8 (9.3%)	0	0 4	Mean procedure time 160 (SD 92) min Mean postoperative LOS 8 (SD 7) days
			86	71	36%	TG18 I/II/III 12%/62%/24%	Late 148 (SD 161) days	86	2 (2.3%)	0	0 2	Mean procedure time 149 (SD 61) min Mean postoperative LOS 8 (SD 11) days
Saumoy et al. 2019[28]	International	PC	21	62	38%	Mean CCI 1.80	Late (80 ± 31 days)	17	1 (6%)	4	0 5	Mean procedure time 138 (SD 46) mins
Pal et al. 2018[29]	Pakistan	RC	65	58.5	32%	ASA I/II - 36.9% ASA III/IV - 63.1%	Late (6–8 weeks)	43	5 (11%)	0	0 2	Mean procedure time 120mins Mean postoperative LOS 5 days
El-Gendi et al. 2017[3]	Egypt	PC	75	50	60%	TG13 Grade II	Late (>6 weeks)	75	2 (2.7%)	0	0 2	Mean procedure time 38 ± 8 min Mean postoperative LOS 11 ± 6 h
Endo et al. 2017[36]	Japan	RC	1239	68.9	32.6%	TG13 I/II/III 19%/26%/27%	Late >31 days	263	21 (8.0%)	133	2 45	Mean procedure time 134 min
Kamer et al. 2017[30]	Turkey	PC	12	60	33%	ASA III/IV 58%/42%	Late Median 64.5 (Range 56–85)	12	2 (17%)	0	0 3	Median procedure time 108 (Range 45–115) mins
Tolan et al. 2017[31]	Turkey	RC	40	70.5	45%	ASA >3	Late >6 weeks	16	3 (18.8%)	0	NS NS	
Yu et al. 2017[32]	China	RC	36	73.8	55%	Geriatric cohort	Late >3 months	36	5 (13.9%)	0	0 3	Mean procedure time 78.61 ± 23.87 min Mean postoperative LOS 4.83 ± 3 days
Hu et al. 2015[33]	China	PC	35	69	34%	Mean ASA 2.2	Late (Range 6–8 weeks)	35	3 (8.6%)	0	0 2	Mean procedure time 55.6 ± 23 min Mean postoperative LOS 3 ± 1.3 days
Khasawneh et al. 2015[34]	USA	RC	245	71	37.5%	Median CCI 5 (IQR 4–6)	Late Mean 55 days (Range 42–75 days)	63	13 (21%)	8	0 21	Mean procedure time 96 (73–137 min) Mean postoperative LOS 2 (Range 1–5) days
Mizrahi et al. 2015[35]	Israel	RC	163	64	44%	Median ASA 2	Late (84 ± 5 days)	163	18 (11%)	4	2 14	Mean procedure time 142 min
Karakayali et al. 2014[37]	Turkey	PC	43	66	33%	ASA I/II 21%/79%	Late >4 weeks	43	8 (19%)	0	0 4	Mean procedure time 106 (Range 50–163) mins Mean postoperative LOS 3 days
Costi et al. 2012[38]	France	RC	12	72	42%	NS	Late (12 ± 4 weeks)	10	0 (0%)	0	0 3	Mean procedure time 91 (Range 55–215) mins Mean postoperative LOS 1.7 days

(*continued on next page*)

Table 1 (*continued*)

Authors, Year	Country	Type of Study	No. of pts with PTC	Age	%F	Tokyo Classification or Comorbidity Score	Timing of interval LC	Planned LC	Conversion Rate n (%)	Planned OC	Mortality Morbidity n	Other
Chok et al. 2010[39]	China	RC	23	83	52%	ASA II/III/IV 13%/35%/52%	Late 4–6 weeks	8	3 (37.5%)	0	NS NS	
Koebrugge et al. 2010[40]	Netherlands	RC	35	73	51%	NS	Late >2 months (Median 66 days)	12	2 (17%)	13	NS NS	
Paran et al. 2006[41]	Israel	PC	54	61	56%	NS	Late >6 weeks	25	2 (8%)	3	0 4	

Abbreviations: ASA american society of anaesthesiologists**, CCI** charleston comorbidity index**, IC** interval cholecystectomy**, IQR** interquartile range**, LC** laparoscopic cholecystectomy**, LOS** length of stay**, NS** not specified**, OC** open cholecystectomy**, PC** prospective cohort**, PTC** percutaneous cholecystostomy**, RC** retrospective cohort**, SD** standard deviation**, TG13** tokyo guidelines 2013, **TG18** tokyo guidelines 2018.

Conversion rates

All included studies reported conversion rates during interval LC following PTC. The overall conversion rate was 154 out of 2041 (7.6%) patients in the early interval LC group, and 175 out of 1808 (9.7%) patients in the late interval LC group. Fig. 2 outlines the conversion rates in the studies which were meta-analysed

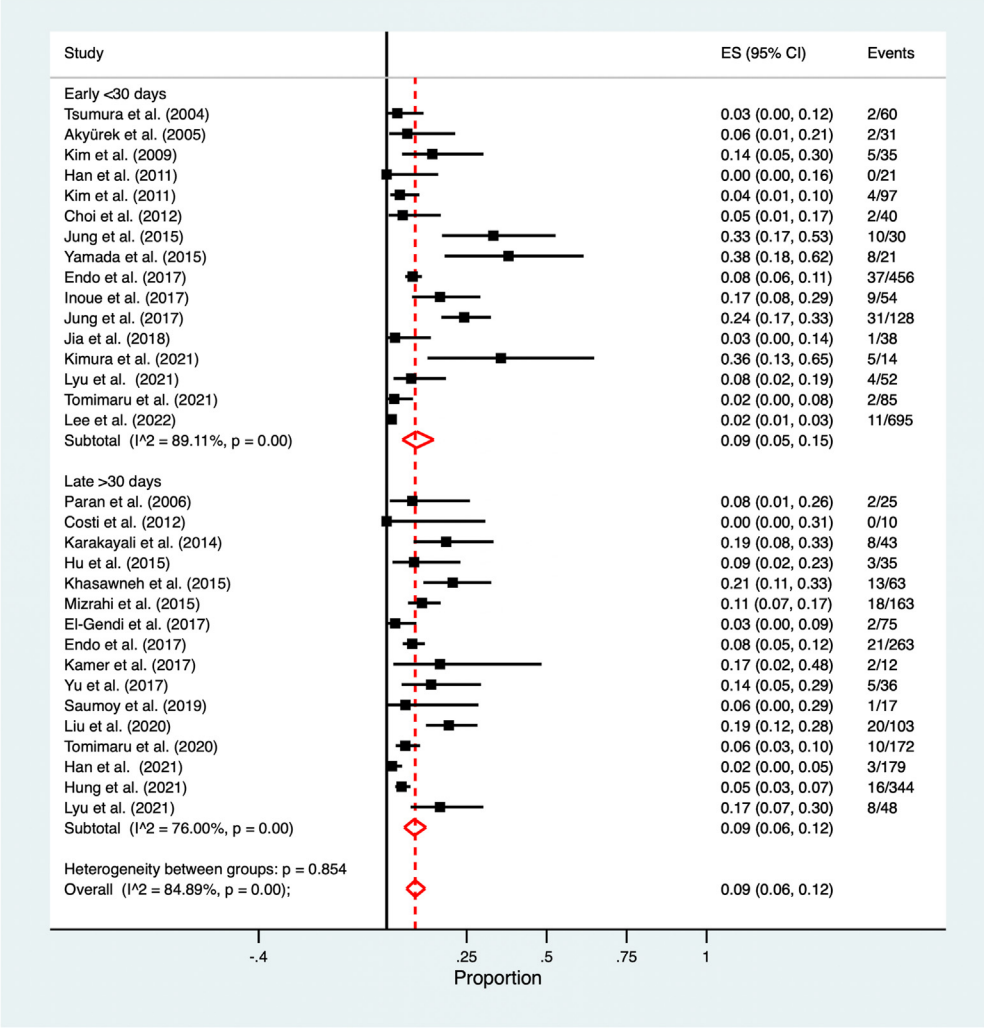

Figure 2 Forrest plot of conversion rates during early and late interval laparoscopic cholecystectomy following percutaneous cholecystostomy

following quality assessment. In this subset of papers, conversion rates were 133 out of 1857 (7.2%) patients in the early interval LC group, and 132 out of 1588 (8.3%) patients in the late interval LC group. The random effects meta-analysis of proportions confirmed no statistically significant difference in conversion rates between the two groups, p = 0.854. Heterogeneity among the studies within and between subgroups was significant (Early interval LC group I^2 = 89.1%, Late interval LC group I^2 = 76.0%, Between groups I^2 = 84.9%).

Morbidity and mortality

There were 4 studies that did not report any morbidity outcomes.[31,39,40,52] In the remaining 37 studies, the overall reported 90-day morbidity was 268 out of 2028 (13.2%) patients in the early interval LC group and 236 out of 1772 (18.4%) patients in the late interval LC group. Fig. 3 outlines morbidity rates as proportions in the studies which were meta-analysed following quality assessment. In this subset of papers, the reported 90-day morbidity was 236 out of 1844 (12.8%) patients in the early interval LC group, and 253 out of 1588 (15.9%) patients in the late interval LC group. The random effects meta-analysis of proportions confirmed no statistically significant difference in the morbidity rates of the two groups, p = 0.496. There was significant heterogeneity among the studies within and between subgroups (Early interval LC group I^2 = 78.5%, Late interval LC group I^2 = 89.5%, Between groups I^2 = 85.4%).

There were 3 studies that did not report any mortality outcomes.[31,39,40] In the remaining 33 studies, the overall reported 90-day mortality was 12 out of 2049 (0.59%) patients in the early interval LC group and 4 out of 1772 (0.23%) in the late interval LC group. The difference in mortality reduced following removal of studies with low quality assessment scores. In the subset of studies included for meta-analysis the mortality rates were 6 out of 1865 (0.32%) patients in the early interval LC group, and 4 out

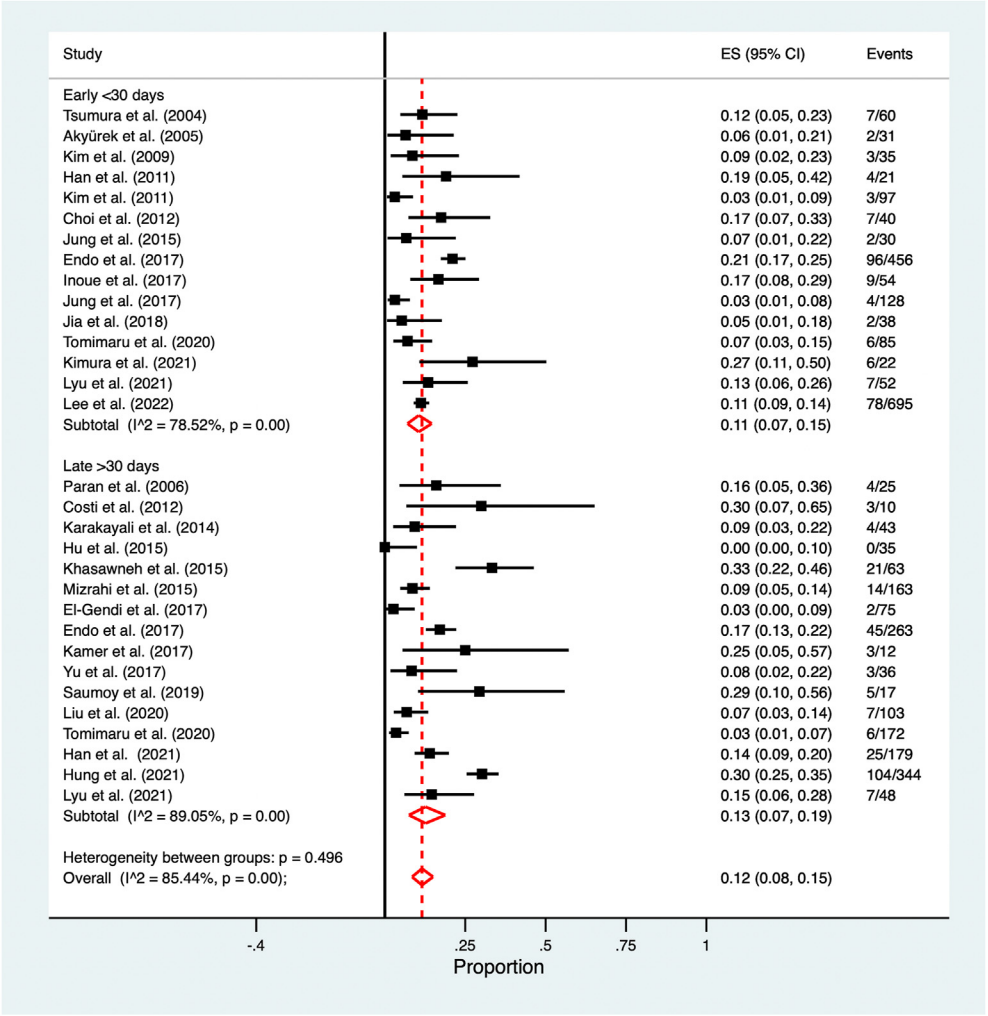

Figure 3 Forrest plot of reported 90-day morbidity rates following early and late interval laparoscopic cholecystectomy following percutaneous cholecystostomy

of 1588 (0.25%) patients in the late interval LC group. Due to most studies showing 0 frequencies, a pooled chi squared test for independence analysis was used and confirmed no significant difference between the early and later interval LC groups, $p = 0.704$.

Discussion

In this review and meta-analysis, we aimed to identify the optimal time interval for interval LC following PTC in adult patients with acute cholecystitis. Time intervals were separated into early (<30 days) and late (≥30 days) based on the intervals reported in the included literature. The current available evidence demonstrates that timing of an interval LC following PTC within or beyond 30 days does not have an impact on conversion rates as well as postoperative morbidity and mortality.

These findings are in keeping with the management guidelines published by Okamoto et al. in the TG18. They state that there is currently no consensus on the optimal timing of LC following interval PTC, and that the responsible clinician needs to make a decision based on patient factors.[4] Our meta-analysis supports that the timing of interval LC following PTC for acute cholecystitis does not seem to be a significant determinant of outcomes. Instead, patient factors, clinical experience, and hospital facilities are likely to play a bigger role.

Huang et al., in 2020, compared outcomes in those with early LC alone and those with interval LC following PTC.[1] They noted decreased intraoperative bleeding, operative times, conversion rates in the group with interval LC following PTC. The authors also divided the interval LC following PTC studies into two groups based on the time interval to LC (<7 days vs ≥ 7 days). They then compared these two subgroups with the LC without PTC studies. This showed the same results as with the overall comparison, however the ≥7 days group showed a greater difference in those outcomes. Outcomes between the <7 days and ≥7 days studies were not directly compared.

A significant limitation of the evidence base on this topic is the lack of comparative studies and randomized control trials (RCT). Only 2 of the included studies reported non-randomized cohort comparisons.[25,36] In addition, of the 36 included studies, 28 were retrospective. Patient characteristics such as their comorbidities and severity of acute cholecystitis were not uniformly reported, introducing bias that could not be controlled for. Other sources of heterogeneity include the type of PTC method used (transhepatic vs transperitoneal PTC), clinical experience of surgical teams, and variability in the hospital facilities available. The definition of early and late interval LC is also variable. There is no current consensus, with studies using cut offs at 3 days, 7 days, and 30 days. The use of the 30-day cut off in this review was used to allow for an equal distribution and comparison of the available literature.

Of note, the current review cannot comment on other timings of interval LC, such as in the use of shorter time intervals like 3 or 7 days. There are studies that have found a significant improvement in outcomes in those with interval LC at ≥3 days after PTC.[15,16] These findings could represent the need for a longer time interval required to alleviate inflammation and gallbladder oedema to allow for a less complicated LC.[1] Furthermore, we have found that studies reporting on late interval LC are significantly more likely to be more recent compared to the early interval LC studies. This could represent empirical clinical observations that favour late interval LC with increasing numbers of clinicians choosing this approach. However, this approach may be associated with additional complications and costs due to the prolonged presence of the PTC catheter, which is susceptible to mechanical blockage and/or dislocation.

This meta-analysis is the first to directly compare the impact of timing between PTC and LC. Strengths of the study include the large number of included studies as well as the implementation of the MINORS quality assessment tool to refine the studies included into the meta-analysis. The use of the methodology described by Nyaga et al.[14] allowing for the meta-analysis of proportions was vital in synthesizing these groups of mostly retrospective non-comparative cohort studies.

A RCT comparing different interval LC times would be ideal, though potentially not the most pragmatic. Patients that are deemed sufficiently high risk to undergo PTC rather than LC are currently the minority of acute cholecystitis presentations. With current evidence suggesting a limited and non-significant difference in outcomes between the early and late interval LC groups, a sufficiently powered RCT would require very large sample sizes. A potentially more pragmatic and feasible method of future comparison could be the creation of a prospectively collected multicentre database of patients that had PTC followed by interval LC. The collected information should include patient characteristics, measures of frailty and comorbidity, method of PTC insertion, time to interval LC, intraoperative and postoperative outcomes, clinical experience of performing physicians, and relevant available hospital facilities.

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Author's contributions

Conceptualisation/protocol development: GK, FG, Data Collection: MM, ZR, GK, Data Analysis: GK, FG, Manuscript writing/editing: GK, ZR, MM, FG.

Conflicts of interest

None to declare.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.hpb.2022.03.016.

