Andres Hernandez

Mini-CAT- Spring 2024

Clinical Question:

A 65-year-old female, with a medical history including hypertension and hyperlipidemia, presented to the emergency department with epigastric pain radiating to the back. The patient was diagnosed with gallstone pancreatitis. Definitive treatment involves cholecystectomy to prevent recurrence of pancreatitis. Current guidelines recommend waiting until the pancreatitis improves before initiating surgery to prevent complications due to the inflammatory state. However, the question remains whether performing surgery earlier, before the pancreatitis resolves, is more beneficial for the patient in preventing recurrence. Does early cholecystectomy associate with greater complications than later surgery for the treatment of gallstone pancreatitis?

Search Question: Clearly state the question (including outcomes or criteria to be tracked)

In adult patients diagnosed with gallstone pancreatitis, does early cholecystectomy (surgery before resolution of pancreatitis) compared to delayed cholecystectomy (surgery after the resolution of pancreatitis) result in differences in complication rates?

PICO Question:

Identify the PICO elements – this should be a revision of whichever PICO you have already begun in a previous week.

P	I	C	O
Adults with gallstone pancreatitis	Early cholecystectomy	Delayed cholecystectomy	Complication rates
Adults with pancreatitis	Immediate cholecystectomy	Late cholecystectomy	Surgical complications
Acute pancreatitis	Cholecystectomy before resolution	Cholecystectomy after resolution	Postoperative complications
Gallstone pancreatitis			

Search Strategy:

Outline the terms used, databases or other tools used, how many articles returned, and how you selected the final articles to base your CAT on. This will likewise be a revision and refinement of what you have already done.

Pubmed

"gallstone pancreatitis" AND ("early cholecystectomy" OR "immediate cholecystectomy") AND ("complication rates" OR "recurrence of pancreatitis") – 56 results

- (Published in the last 10 years) - 41 Results

Cochrane

gallstone pancreatitis AND early cholecystectomy AND complication - 4 results

- (Published in the last 10 years) -3 Results

ScienceDirect

"gallstone pancreatitis" AND ("early cholecystectomy" OR "immediate cholecystectomy") AND ("complication rates" OR "recurrence of pancreatitis") – 105 results

- (Published in the last 10 years) -69 Results

Google Scholar

"gallstone pancreatitis" AND ("early cholecystectomy" OR "immediate cholecystectomy") AND ("complication rates" OR "recurrence of pancreatitis") – 333 Results

- (Published in the last 10 years) – 237 Results

I aimed to select articles with higher levels of evidence, such as systematic reviews, meta-analyses, or randomized controlled trials (RCTs). If those were unavailable, I prioritized cohort studies next. I ensured that the articles I chose were up-to-date, no older than 10 years. My preference was for studies conducted in the United States. For studies utilizing international data, I restricted my selection to meta-analyses or systematic reviews. I conducted searches across four databases: PubMed, Cochrane, ScienceDirect, and Google Scholar. Ultimately, I chose two articles from PubMed—a meta-analysis and a randomized controlled trial—along with one systematic review from Cochrane, and another systematic review and meta-analysis from Google Scholar. Although the systematic review titled 'Early Versus Delayed Cholecystectomy for Acute Biliary Pancreatitis: A Systematic Review and Meta-Analysis' by Prasanth et al. is international, I included it in my report because it incorporates American randomized controlled studies.

Articles Chosen (3-5) for Inclusion (please copy and paste the abstract with link):

Please pay attention to whether the articles actually address your question and whether they are the highest level of evidence available. If you cannot find high quality articles, be prepared to explain the extensiveness of your search and why there aren't any better sources available.

1.Walayat S, Baig M, Puli SR. Early vs late cholecystectomy in mild gall stone pancreatitis: An updated meta-analysis and review of literature. World J Clin Cases. 2021;9(13):3038-3047. doi:10.12998/wjcc.v9.i13.3038

Abstract:

Background Gallstone pancreatitis is one of the most common causes of acute pancreatitis. Cholecystectomy remains the definitive treatment of choice to prevent recurrence. The rate of early cholecystectomies during index admission remains low due to perceived increased risk of complications.

Aim To compare outcomes including length of stay, duration of surgery, biliary complications, conversion to open cholecystectomy, intra-operative, and post-operative complications between patients who undergo cholecystectomy during index admission as compared to those who undergo cholecystectomy thereafter.

Methonds Statistical Method: Pooled proportions were calculated using both Mantel-Haenszel method (fixed effects model) and DerSimonian Laird method (random effects model).

Results Initial search identified 163 reference articles, of which 45 were selected and reviewed. Eighteen studies (n = 2651) that met the inclusion criteria were included in this analysis. Median age of patients in the late group was 43.8 years while that in the early group was 43.6. Pooled analysis showed late laparoscopic cholecystectomy group was associated with an increased length of stay by 88.96 h (95%CI: 86.31 to 91.62) as compared to early cholecystectomy group. Pooled risk difference for biliary complications was higher by 10.76% (95%CI: 8.51 to 13.01) in the late cholecystectomy group as compared to the early cholecystectomy group. Pooled analysis showed no risk difference in intraoperative complications [risk difference: 0.41%, (95%CI: -1.58 to 0.75)], postoperative complications [risk difference: 0.60%, (95%CI: -2.21 to 1.00)], or conversion to open cholecystectomy [risk difference: 1.42%, (95%CI: -0.35 to 3.21)] between early and late cholecystectomy groups. Pooled analysis showed the duration of surgery to be prolonged by 39.11 min (95%CI: 37.44 to 40.77) in the late cholecystectomy group as compared to the early group.

Conclusion In patients with mild gallstone pancreatitis early cholecystectomy leads to shorter hospital stay, shorter duration of surgery, while decreasing the risk of biliary complications. Rate of intraoperative, post-operative complications and chances of conversion to open cholecystectomy do not significantly differ whether cholecystectomy was performed early or late.

Keywords: Cholecystectomy, Gallstone pancreatitis, Acute pancreatitis, Laparoscopic cholecystectomy, Biliary colic, Open cholecystectomy

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2. Gurusamy KS, Nagendran M, Davidson BR. Early versus delayed laparoscopic cholecystectomy for acute gallstone pancreatitis. Cochrane Database of Systematic Reviews 2013, Issue 9. Art. No.: CD010326. DOI: 10.1002/14651858.CD010326.pub2. Accessed 20 April 2024.

Abstract:

Background Gallstones and alcohol account for more than 80% of acute pancreatitis. Cholecystectomy is the definitive treatment for gallstones. Laparoscopic cholecystectomy is the preferred route for performing cholecystectomy. The timing of laparoscopic cholecystectomy after an attack of acute biliary pancreatitis is controversial.

Objectives To compare the benefits and harms of early versus delayed laparoscopic cholecystectomy in people with acute biliary pancreatitis. For mild acute pancreatitis, we considered 'early' laparoscopic cholecystectomy to be laparoscopic cholecystectomy performed within three days of onset of symptoms.

We considered all laparoscopic cholecystectomies performed beyond three days of onset of symptoms as 'delayed'. For severe acute pancreatitis, we considered 'early' laparoscopic cholecystectomy as laparoscopic cholecystectomy performed within the index admission. We considered all laparoscopic cholecystectomies performed in a later admission as 'delayed'.

Search methods We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2012, issue 12), MEDLINE, EMBASE, Science Citation Index Expanded, and trial registers until January 2013.

Selection criteria We included randomised controlled trials, irrespective of language or publication status, comparing early versus delayed laparoscopic cholecystectomy for people with acute biliary pancreatitis.

Data collection and analysis Two authors independently assessed trials for inclusion and independently extracted data. We planned to analyse data with both the fixed-effect and the random-effects models using Review Manager 5 (RevMan 2011). We calculated the risk ratio (RR), or mean difference (MD) with 95% confidence intervals (CI) based on an intention-to-treat analysis.

Main results We identified one trial comparing early versus delayed laparoscopic cholecystectomy for people with mild acute pancreatitis. Fifty participants with mild acute gallstone pancreatitis were randomised either to early laparoscopic cholecystectomy (within 48 hours of admission irrespective of whether the abdominal symptoms were resolved or the laboratory values had returned to normal) (n = 25), or to delayed laparoscopic cholecystectomy (surgery after resolution of abdominal pain and after the laboratory values had returned to normal) (n = 25). This trial is at high risk of bias. There was no short-term mortality in either group. There was no significant difference between the groups in the proportion of participants who developed serious adverse events (RR 0.33; 95% CI 0.01 to 7.81). Health-related quality of life was not reported in this trial. There were no conversions to open cholecystectomy in either group. The total hospital stay was significantly shorter in the early laparoscopic cholecystectomy group than in the delayed laparoscopic cholecystectomy group (MD -2.30 days; 95% CI -4.40 to -0.20). This trial reported neither the number of work-days lost nor the costs. We did not identify any trials comparing early versus delayed laparoscopic cholecystectomy after severe acute pancreatitis.

Authors' conclusions There is no evidence of increased risk of complications after early laparoscopic cholecystectomy. Early laparoscopic cholecystectomy may shorten the total hospital stay in people with mild acute pancreatitis. If appropriate facilities and expertise are available, early laparoscopic cholecystectomy appears preferable to delayed laparoscopic cholecystectomy in those with mild acute pancreatitis. There is currently no evidence to support or refute early laparoscopic cholecystectomy for people with severe acute pancreatitis. Further randomized controlled trials at low risk of bias are necessary in people with mild acute pancreatitis and severe acute pancreatitis.

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3. Prasanth, J., Prasad, M., Mahapatra, S.J. et al. Early Versus Delayed Cholecystectomy for Acute Biliary Pancreatitis: A Systematic Review and Meta-Analysis. World J Surg 46, 1359–1375 (2022). https://doi.org/10.1007/s00268-022-06501-4

Abstract:

Background Recommendations regarding the timing of cholecystectomy for acute biliary pancreatitis (ABP) require a systematic summary of current evidence to guide clinical practice. We conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) comparing early cholecystectomy (EC) versus delayed cholecystectomy (DC) in patients with ABP.

Methods We searched databases Medline, Embase, SCOPUS, Web of Science and Cochrane CENTRAL for randomized controlled trials addressing this question. Pairs of reviewers abstracted data and assessed the risk of bias in included studies. A random-effects meta-analysis was done to study the effect of the timing of cholecystectomy on outcomes of interest in patients with ABP. GRADE methodology was used to rate the quality in the body of evidence for each outcome as high, moderate, low, or very low.

Results 11 randomized trials (1176 participants) were included. High-quality evidence from seven RCTs (867 participants) showed a statistically significant reduction in the risk for recurrent biliary events in favour of early cholecystectomy (RR 0.10, 95% CI 0.05 to 0.19, I2 = 0%). High-quality evidence from five trials was in favour of early cholecystectomy with a significant reduction in the risk 7of recurrent pancreatitis (RAP) in comparison to delayed cholecystectomy (RR 0.21, 95% CI 0.09 to 0.51, I2 = 0%).

Conclusion This review showed that EC has definite advantages over DC in terms of reducing recurrent pancreaticobiliary events and LOS following mild ABP. However, more RCTs are required to study the role of EC in patients with moderately-severe and severe ABP.

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4. Mueck, K. M., Wei, S., Pedroza, C., Bernardi, K., Jackson, M. L., Liang, M. K., Ko, T. C., Tyson, J. E., & Kao, L. S. (2019). Gallstone Pancreatitis: Admission Versus Normal Cholecystectomy-a Randomized Trial (Gallstone PANC Trial). Annals of surgery, 270(3), 519–527. https://doi.org/10.1097/SLA.0000000000003424

Abstract:

Introduction Early cholecystectomy shortly after admission for mild gallstone pancreatitis has been proposed based on observational data. We hypothesized that cholecystectomy within 24 hours of admission versus after clinical resolution of gallstone pancreatitis that is predicted to be mild results in decreased length-of-stay (LOS) without an increase in complications.

Methods Adults with predicted mild gallstone pancreatitis were randomized to cholecystectomy with cholangiogram within 24 hours of presentation (early group) versus after clinical resolution (control) based on abdominal exam and normalized laboratory values. Primary outcome was 30-day LOS including readmissions. Secondary outcomes were time to surgery, endoscopic retrograde cholangiopancreatography (ERCP) rates, and postoperative complications. Frequentist and Bayesian intention-to-treat analyses were performed.

Results Baseline characteristics were similar in the early (n = 49) and control (n = 48) groups. Early group had fewer ERCPs (15% vs 29%, P = 0.038), faster time to surgery (16 h vs 43 h, P < 0.005), and shorter 30-day LOS (50 h vs 77 h, RR 0.68 95% CI 0.65 - 0.71, P < 0.005). Complication rates were 6% in early group versus 2% in controls (P = 0.613), which included recurrence/progression of pancreatitis (2 early, 1 control) and a cystic duct stump leak (early). On Bayesian analysis, early cholecystectomy has a 99% probability of reducing 30-day LOS, 93% probability of decreasing ERCP use, and 72% probability of increasing complications.

Conclusion In patients with predicted mild gallstone pancreatitis, cholecystectomy within 24 hours of admission reduced rate of ERCPs, time to surgery, and 30-day length-of-stay. Minor complications may be increased with early cholecystectomy. Identification of patients with predicted mild gallstone pancreatitis in whom early cholecystectomy is safe warrants further investigation.

Summary of Evidence:

Author (Date)	Level of Evidence	Sample/Setting (# of subjects/ studies, cohort definition etc.)	Outcome(s) studied	Key Findings	Limitations and Bias
Walayat S, Baig M, Puli SR. (2021)	Meta-analysis	- Articles were searched in MEDLINE, PubMed, Ovid journals, Embase, Cumulative Index for Nursing and Allied Health Literature, ACP Journal Club, DARE, MEDLINE Non-Indexed Citations, OVID Healthstar, and Cochrane Central Register of Controlled Trials (CENTRAL). -Only articles in English were included performed between January 1992 to December 2019. - Initial search identified 163 reference articles based on our search criteria. After thorough screening, removal of abstracts, review papers and duplicates eighteen studies were selected and included in this analysis.	-Outcomes of early vs late cholecystectomy in patients with mild gallstone pancreatitis. -Outcomes of interest include differences in biliary complications before surgery, intraoperative complications, and post-operative complications.	-Delayed cholecystectomy is associated with an increased risk of pancreatitis, reported to be up to 14% to 31% if surgery is delayed. - Meta-analysis results show no significant difference in intraoperative and postoperative complications between early and late laparoscopic cholecystectomy. - Biliary complications were noted to be significantly higher in patients undergoing delayed cholecystectomy, by almost 10%. - Patients who underwent late cholecystectomy had a significantly longer length of hospital stay compared to those who had early cholecystectomy, with a difference of 88 hours. - findings suggest that early cholecystectomy may be preferred in patients with	- definitions of early and delayed cholecystectomy across different studies, ranging from 24 hours to 2-6 weeks post-discharge. - The median age of patients included in the studies is around 40-50 years old, which may not represent the elderly population who could be at higher risk of complications. The study did not evaluate the impact of comorbidities on outcomes, which could affect the generalizability of the findings. - Different studies used different criteria for diagnosing mild pancreatitis, reflecting variations in severity among different populations.

		-Nine studies were randomized control trials, while others were retrospective studies. - Total number of patients included in this meta-analysis was 2651. Number of patients in the early cholecystectomy group was 1336, while that in the late cholecystectomy group was 1315. Median age of patients in the early cholecystectomy group was 43.6 years while that in the late group was 43.8.		mild gallstone pancreatitis as it is safe, effective, and reduces complications associated with delayed cholecystectomy.	
Gurusamy KS, Nagendran M, Davidson BR. (2013)	Systematic Review	-451 references through the electronic searches of the Cochrane Central Register of Controlled Trials (CENTRAL) in The Cochrane Library (n = 25), MEDLINE (n = 114), EMBASE (n = 130), Science Citation Index Expanded (n = 172), and WHO ICTRP (n = 10) - Excluded 81 duplicates and	-Considered all measured outcomes up to six months after the onset of pancreatitis. -Primary outcomes that were measured are: all-cause mortality, serious adverse events (those that would increase mortality), overall quality of life (using any validated measurement	-There is no evidence indicating increased risk of complications after early laparoscopic cholecystectomy. -Early laparoscopic cholecystectomy may lead to short hospital stay. -Early cholecystectomy is preferable to delayed for individuals with mild acute pancreatitis.	-This review only includes one trial that soles compare laparoscopic cholecystectomy with delated cholecystectomy -There was an imputed standard deviation from the 95% confidence interval. The length of hospital stay may not be normally distributed.

		366 clearly irrelevant references through reading titles and abstracts. -identified one trial comparing early versus delayed laparoscopic cholecystectomy for people with mild acute pancreatitis.	scale EQ5D or SF-36). -Secondary outcomes that are measured: conversion to open cholecystectomy, total hospital stays, number of work days lost, costs.		These factors may have introduced bias.
Prasanth, J., Prasad, M., Mahapatra, S.J. et al. (2022)	Systematic Review and Meta-Analysis	- Searched databases Medline, Embase, SCOPUS, Web of Science and Cochrane CENTRAL for randomized controlled trials addressing this question. -Articles published from after 1990 till March 2021 was included. - 11 randomized trials (1176 participants) were included.	-The outcomes that are measured post-cholecystectomy: length of hospital stays (LOS), biliary colic, need for additional preoperative procedures, intraoperative complications, and post operative outcomes.	-High-quality evidence from seven most statistically significant randomized control trials involving 867 participants shows a significant reduction in the risk of recurrent biliary events favoring cholecystectomy. -There was also high-quality evidence from five trials that demonstrated significant reduction on the risk of recurrent pancreatitis with early cholecystectomy compared to delayed cholecystectomy. -Early cholecystectomy offers a clear advantage over delayed cholecystectomy	-There are inconsistences in the definitions of severity of acute pancreatitis and timing of early and delayed cholecystectomy -There is limited inclusion of moderate and severe pancreatitis in the study to make generalized finding regarding operative complication of all pancreatitis.

				in reducing recurrent pancreaticobiliary events and length of hospital stay following mild biliary pancreatitis.	
Mueck, K. M., Wei, S., Pedroza, C., Bernardi, K., Jackson, M. L., Liang, M. K., Ko, T. C., Tyson, J. E., & Kao, L. S. (2019)	Randomized Control Trial	-From June 2016 through June 2018, patients 18 or older with predicted gallstone pancreatitis who were planned to undergo cholecystectomy at Lydon Baines Johnson General Hospital in Houston, Texas were screened for eligibility. - Sample size of 100 patients consented out of the 147 originally screened. 3 patients were excluded after. -Total of 49 patients were randomized to early cholecystectomy and 48 patients were randomized to the control group. -Two patients from the control group were discharged prior to cholecystectomy	-The endpoint was a total of 30-day hospital length of stay in hours. Enough time to capture any hospital readmissions after treatment. -Secondary endpoints included ERCP rates, complications, exacerbation of pancreatitis, and conversion to open cholecystectomy.	-Early cholecystectomy group had significantly fewer ERCPs compared to the control group -The early cholecystectomy group had a significantly shorter 30-day LOS compared to the control group -The complication rates were 6% in the early cholecystectomy group versus 2% in the control group. -There is no significant differences in the overall complication rates between the two groups, although minor complications may be been increased with early cholecystectomy.	-The population consists of low socioeconomic status and racial minorities, such as Latinos that are known to present with milder disease at earlier age. -Trial did not incorporate laparoscopic common bile duct exploration -Inability to accurately predict the severity of acute pancreatitis soon after admission.

		-Patient were predominantly female, Hispanic middle aged and obese.			

Conclusion(s):
- Briefly summarize the conclusions of each article, then provide an overarching conclusion.

Walayat S, Baig M, Puli SR. (2021) Early cholecystectomy results in shorter hospital stays, shorter surgery duration, and a decreased risk of biliary complications. There are no significant differences in complication rates intraoperatively, post-operatively, of conversion to open cholecystectomy between early and late cholecystectomy groups.

Overarching conclusion: Despite similar complication rates, early cholecystectomy is a favorable approach for managing mild gallstone pancreatitis, offering benefits such as reduced hospital stay, along with a decreased risk of biliary complications.

Gurusamy KS, Nagendran M, Davidson BR. (2013) Early laparoscopic cholecystectomy does not increase the risk of complications and may shorten total hospital stay in individuals with mild acute pancreatitis. The article suggests a need for more randomized controlled trials to assess the efficacy of early cholecystectomy in both mild and severe acute pancreatitis.

Overarching conclusion: Early laparoscopic cholecystectomy shows promise by reducing hospital stay without increasing complications.

Prasanth, J., Prasad, M., Mahapatra, S.J. et al. (2022) Early cholecystectomy offers benefits over delayed cholecystectomy in reducing recurrent pancreaticobiliary events and shortening hospital stays in individuals with mild acute biliary pancreatitis.

Overarching conclusion: Early cholecystectomy is beneficial for managing mild acute biliary pancreatitis, reducing recurrent events and hospital stays. There are minimal evidence in its application in moderate and severe pancreatitis which requires the need for additional research to determine the optimal approach across the spectrum of acute biliary pancreatitis severity.

Mueck, K. M., Wei, S., Pedroza, C., Bernardi, K., Jackson, M. L., Liang, M. K., Ko, T. C., Tyson, J. E., & Kao, L. S. (2019) Cholecystectomy within 24 hours of admission significantly reduces the rate of ERCPs, time to surgery, and 30-day length of stay. However, early cholecystectomy may increase minimal complications, suggesting caution is needed in applying these results of this study.

Overarching conclusion: Early cholecystectomy reduces length of hospital stay for patients with predicted mild gallstone pancreatitis. However, there is potential for increase in complications, although not statistically significant, suggesting there is a need for more precise risk stratification tools to guide decision-making.

Clinical Bottom Line:

Please include an assessment of the following:

- Weight of the evidence – summarize the weaknesses/strengths of the articles and explain how they factored into your clinical bottom line (this may recap what you discussed in the criteria for choosing the articles)

- Magnitude of any effects

- Clinical significance (not just statistical significance)

- Any other considerations important in weighing this evidence to guide practice - If the evidence you retrieved was not enough to conclude an answer to the question, discuss what aspects still need to be explored and what the next studies will have to answer/provide (e.g. larger number, higher level of evidence, answer which sub-group benefits, etc)

Walayat S, Baig M, Puli SR. (2021) I would consider this article the strongest among the group as it is a meta-analysis that utilized recent data up to 2019. It contains data from numerous articles, with nine of them being randomized controlled trials, resulting in the inclusion of a substantial number of patients, totaling 2651 subjects. The study revealed that the late laparoscopic cholecystectomy group was associated with an increased length of stay by 88.96 hours (95%CI: 86.31 to 91.62) compared to the early cholecystectomy group. The pooled risk difference for biliary complications was higher by 10.76% (95%CI: 8.51 to 13.01) in the late cholecystectomy group. Moreover, pooled analysis showed no significant risk difference in intraoperative complications [risk difference: 0.41%, (95%CI: -1.58 to 0.75)], postoperative complications [risk difference: 0.60%, (95%CI: -2.21 to 1.00)], or conversion to open cholecystectomy [risk difference: 1.42%, (95%CI: -0.35 to 3.21)]. Additionally, the duration of surgery was prolonged by 39.11 minutes (95%CI: 37.44 to 40.77) in the late cholecystectomy group compared to the early group. However, there are some weaknesses noted in the study. The median age of patients in both early and late cholecystectomy groups was in the early forties, indicating caution should be exercised when applying these results to different patient populations. Additionally, variations in the definitions of early and delayed cholecystectomy across studies and the lack of consideration for comorbidities' impact on outcomes may limit the generalizability of the findings. Moreover, not all studies employed the same criteria for diagnosing mild pancreatitis, adding to the study's limitations. In conclusion, early cholecystectomy appears to be not only safe but also associated with shorter length of stay and duration of surgery compared to late cholecystectomy. However, caution is recommended when applying these findings clinically, especially in elderly patients and those with complications. Further research is needed to address these limitations.

Prasanth, J., Prasad, M., Mahapatra, S.J. et al. (2022) I would rate this study slightly lower than the previous one due to its source being from an international publisher, but it is still significant as it is a systematic review and meta-analysis incorporating American randomized control trials. The study contains recent research up to March 2021 and included 11 randomized control trials with 1176 patients. High-quality evidence from seven RCTs (867 participants) demonstrated a statistically significant reduction in the risk for recurrent biliary events after early cholecystectomy (RR 0.10, 95% CI 0.05 to 0.19, I2 = 0%). Similarly, high-quality evidence from

five trials indicated a significant reduction in the risk of recurrent pancreatitis after early cholecystectomy compared to delayed cholecystectomy (RR 0.21, 95% CI 0.09 to 0.51, I2 = 0%). Like the previous study, there were inconsistencies in the definitions of severity of acute pancreatitis and criteria for early or delayed cholecystectomy. Additionally, similar to the study mentioned above (Walayat, et al. 2021), there was limited inclusion of moderate and severe pancreatitis, hindering the ability to make generalized findings regarding operative complications across all subtypes of pancreatitis. This lack of high-quality data in subgroups other than mild pancreatitis makes it challenging to provide conclusive clinical recommendations for these patients, indicating the need for more randomized controlled trials. Overall, this meta-analysis has demonstrated that early cholecystectomy offers advantages in terms of reducing length of stay exclusively for patients with acute gallstone pancreatitis.

Mueck, K. M., Wei, S., Pedroza, C., Bernardi, K., Jackson, M. L., Liang, M. K., Ko, T. C., Tyson, J. E., & Kao, L. S. (2019) Of the four articles, I would rank this one third because it is a randomized control trial. It is an American study that included a total of 100 patients who consented out of 147 from June 2016 to June 2018 at Lyndon Baines Johnson General Hospital in Houston, Texas. The early group had fewer ERCPs (15% vs 29%, P = 0.038), a faster time to surgery (16 h vs 43 h, P < 0.005), and a shorter 30-day LOS (50 h vs 77 h, RR 0.68, 95% CI 0.65 - 0.71, P < 0.005). Complication rates were 6% in the early group versus 2% in controls (P = 0.613), including recurrence/progression of pancreatitis (2 early, 1 control) and a cystic duct stump leak (early). Bayesian analysis indicated a 99% probability of reducing 30-day LOS, a 93% probability of decreasing ERCP use, and a 72% probability of increasing complications with early cholecystectomy. The sample used in this study might not accurately represent the standard population, as it consisted almost entirely of individuals of low socioeconomic status and racial minorities, with the majority being Latinos who are known to present with milder disease at an earlier age than the general population. Due to these limitations, it is advisable to plan a future multi-center trial to confirm the findings and make the conclusions more generalizable to the public. Clinically, we cannot confidently apply the results from this study due to the sample not representing a general population, therefore further investigation is warranted.

Gurusamy KS, Nagendran M, Davidson BR. (2013) I would rank this study last, even below the randomized control trial by Mueck et al. (2019). While it is a systematic review, they only ended up utilizing one trial to compare early versus delayed laparoscopic cholecystectomy. Their screening process resulted in the omission of too many studies, leaving only one trial, which I found somewhat peculiar. However, given that it was a Cochrane study and Cochrane reviews are generally considered reliable, I decided to include it in this project. The single trial included fifty participants with mild acute gallstone pancreatitis who were randomized to either early laparoscopic cholecystectomy (within 48 hours of admission regardless of symptom resolution or normalization of laboratory values) (n = 25) or delayed laparoscopic cholecystectomy (surgery after resolution of abdominal pain and normalization of laboratory values) (n = 25). There was no significant difference between the groups in the proportion of participants who developed serious adverse events (RR 0.33; 95% CI 0.01 to 7.81). The hospital stay was significantly shorter in the early laparoscopic cholecystectomy group compared to the delayed group (MD -2.30 days; 95% CI -4.40 to -0.20). Clinically, there is no indication of an increase in complications following early laparoscopic cholecystectomy for mild acute pancreatitis. This

may result in a shorter hospital stay for individuals with mild acute pancreatitis, making early laparoscopic cholecystectomy a preferable option over delayed surgery for such individuals. However, there is currently insufficient evidence to either support or refute the use of early laparoscopic cholecystectomy for individuals with severe acute pancreatitis. Further randomized controlled trials with low risk of bias are needed to assess the efficacy of this approach in both mild and severe acute pancreatitis cases.

The clinical bottom-line from the four studies suggests that early cholecystectomy in patients with acute gallstone pancreatitis offers benefits although further randomly controlled trials are required to have complete confidence with the results Meta-analyses by Walayat et al. (2021) and Prasanth et al. (2022) show a reduction in length of stay and risk of recurrent biliary events and pancreatitis with early surgery. A randomized controlled trial by Mueck et al. (2019) found early cholecystectomy associated with fewer ERCPs, faster surgery, and shorter hospital stay. However, Gurusamy et al. (2013), although a systematic review limited evidence due to their reliance on a single trial, it also supports the potential benefits of early cholecystectomy in mild pancreatitis cases. Overall, early cholecystectomy may be preferable in mild cases, but further research is needed to determine its efficacy in severe cases.