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Radiological and biochemical predictors of spontaneous common bile duct stone passage prior to endoscopic retrograde cholangiopancreatography: a systematic review and meta-analysis

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Abstract

Background Spontaneous passage of common bile duct (CBD) stones is the absence of CBD stones at the time of endoscopic retrograde cholangiopancreatography (ERCP), after prior radiological confirmation of choledocholithiasis. This phenomenon is clinically important for optimizing the triaging of patients to avoid unnecessary procedures. Identifying preprocedural predictive variables that may be associated with stone clearance can improve patient selection and ERCP timing. Our objective was to estimate the pooled rate of spontaneous CBD stone passage and identify the preprocedural predictors of stone absence at ERCP in patients with radiologically confirmed choledocholithiasis.

Methods A systematic review and meta-analysis were conducted in accordance with PRISMA guidelines. A comprehensive search of PubMed, Embase and Scopus was performed for studies published between January 2015 and December 2025. Eligible studies included adults with radiologically confirmed choledocholithiasis and subsequent ERCP.

Results Eight cohort studies (n=3526 patients) met the inclusion criteria. The pooled rate of spontaneous CBD stone passage was 16% (95% confidence interval [CI] 12-22%). Statistically significant predictors of spontaneous passage were stone diameter ≤5 mm (pooled unadjusted odds ratio [OR] 5.01, 95%CI 3.35-7.50), smaller CBD diameter (pooled mean difference -2.05 mm, 95%CI -3.28 to -0.83), and normalizing or lowering alkaline phosphatase (pooled mean difference -67.99 U/L, 95%CI -97.36 to -38.61).

Conclusions Overall, approximately 1 in 6 patients with pre-ERCP radiologically confirmed CBD stones are stone-free at ERCP. Pre-ERCP imaging and biochemical markers may help triage appropriate candidates for endoscopic intervention, with which conservative management can be safely implemented to reduce the number of unnecessary ERCPs.

Keywords Choledocholithiasis, common bile duct, endoscopic retrograde cholangiopancreatography, cholangitis

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Conflict of Interest: The authors acknowledge the inclusion of JG's previous original research on spontaneous stone passage in the meta-analysis. No data analysis beyond that included in the published study was performed, and bias analysis was performed independently by AL to minimize bias
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Introduction

Common bile duct (CBD) stones are a frequent complication of gallstone disease and a major cause of biliary obstruction. The standard treatment pathway following confirmed CBD stones is endoscopic retrograde cholangiopancreatography (ERCP) for stone extraction. However, ERCP carries substantial risk, with a 6-16% overall complication rate, and a 0.3-1.0% procedure-related mortality [1-5]. The most frequent major adverse event is post-ERCP pancreatitis, occurring in 10% of patients [6]. Perforation, despite its rarity, carries a mortality of up to 20% [7]. Given these significant risks, avoiding unnecessary ERCPs is a priority.

Spontaneous migration of CBD stones through an intact papilla is a well-documented process. Spontaneous passage is defined as the radiological confirmation of choledocholithiasis with no stone identified at the time of ERCP. In view of the risks, there is clinical interest in identifying patients who may not require a therapeutic ERCP, with a view to optimizing patient selection and improving clinical efficiency.

The preprocedural variables that may contribute to spontaneous CBD stone clearance can be broadly divided into radiological and biochemical. Stone size on radiological imaging has emerged as the most consistently reported factor, with smaller stones proving more likely to pass through the papilla spontaneously. The number of stones may also prove relevant, with solitary stones hypothesized to have greater chances of passing relative to multiple stones or stone fragments. Other radiological variables that may influence the passage include the stone location (distal vs. non-distal CBD) and the CBD diameter, while stones located just proximal to the ampulla may have greater chances of passing more readily.

Regarding clinical and biochemical factors, we may see patients with mild symptoms, mildly elevated liver function tests (LFTs) and low inflammatory markers, thereby representing a population where rapid clinical improvement with antibiotics may suffice as initial management. Biochemical markers have been previously evaluated as surrogate predictors. Lower LFT patterns (including bilirubin, alkaline phosphatase [ALP], gamma glutamyl transferase [GGT], aspartate aminotransferase [AST], and alanine aminotransferase [ALT]) following initial spikes may suggest stone migration, compared to persistent elevation or increase indicating ongoing anatomical obstruction and ongoing hepatocellular injury [8].

Limited systematic reviews and meta-analyses have investigated spontaneous passage of CBD stones. These include a study by Arabpour *et al*, who reported that a substantial proportion of patients with radiologically confirmed choledocholithiasis were stone-free at the time of ERCP [9]. That review identified stone size and bile duct diameter as significant predictors of spontaneous passage. However, since its publication, additional cohort studies have emerged, incorporating more detailed biochemical variables and multivariable analytical models. To date, no meta-analysis has quantitatively synthesized the biochemical predictors of spontaneous CBD stone passage, representing an important gap in the literature.

Thus, despite the above insights, predicting spontaneous stone passage in real time remains challenging. As a result, many patients with imaging evidence of CBD stones undergo ERCP only to find no stone present, making the intervention unnecessary. The decision to proceed to ERCP vs. a conservative watch-and-wait approach (with repeat imaging to confirm stone clearance) depends on accurately assessing the probability of spontaneous passage. To inform such decisions, we performed a meta-analysis focusing on selected studies of patients with radiologically confirmed choledocholithiasis. Our objectives were: 1) to quantify the rate of spontaneous CBD stone passage; and 2) to determine predictive factors associated with spontaneous CBD stone passage, with the goal of avoiding unnecessary ERCP and preventing exposure to invasive procedural risks.

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Materials and methods

Search strategy

This meta-analysis was performed in accordance with Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines and registered with PROSPERO (CRD420251108251) [10,11].

A comprehensive literature search was conducted in PubMed, Embase, and Scopus from January 2015 to December 2025. The electronic search strategy combined terms relating to CBD stones with terms relating to ERCP. These were further combined with terms describing stone detection or absence following ERCP, including radiological confirmation and biliary imaging. Searches were last run on December 1 2025, and database-specific syntax was used. The full search strategies for each database are provided in Supplementary Table 1.

Data extraction and study selection

Records retrieved from PubMed, Embase and Scopus were exported, and were then imported into Rayyan, where duplicate records were identified and removed prior to screening. Following de-duplication, titles and abstracts were independently screened by 2 reviewers. Full-text articles were subsequently assessed for eligibility, with any disagreements resolved by consensus.

We included retrospective cohort studies that met the following inclusion criteria: (a) radiological evidence of CBD stones demonstrated on pre-ERCP imaging, including ultrasonography (US), magnetic resonance cholangiopancreatography (MRCP), endoscopic ultrasound (EUS), or computed tomography (CT) cholangiography; (b) a subsequent ERCP performed to determine the presence or absence of CBD stones; and (c) reporting of imaging and/or biochemical variables prior to ERCP that allowed for comparison between patients with spontaneous stone passage and those in whom stones persisted at ERCP. We excluded studies involving pediatric patients or those lacking follow-up ERCP confirmation of stone status. Case reports, conference abstracts, posters, review articles, letters, expert commentaries, and studies for which full-text manuscripts or original data were unavailable were excluded. Only English-language articles were included. The included studies and selection process are illustrated in the PRISMA flow diagram (Fig. 1).

Following study selection, bibliographic information, including title, authors, year of publication, journal, abstract, and database source, were extracted for each eligible study. Study-level and patient-level data were extracted where

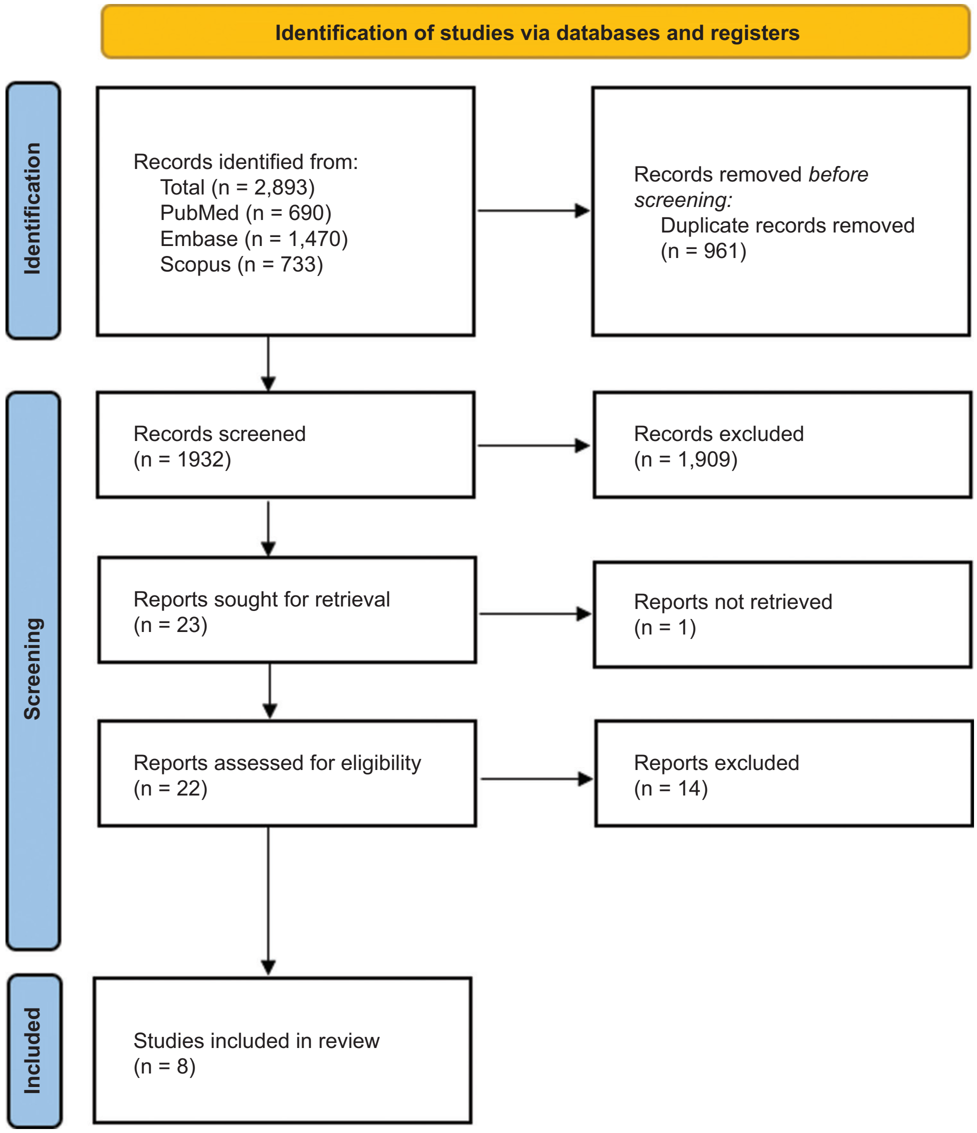

Figure 1 PRISMA flow diagram of study selection for meta-analysis on spontaneous common bile duct stone passage prior to endoscopic retrograde cholangiopancreatography

available, including study design, clinical setting, sample size, patient demographics, stone characteristics (size, number, and location), CBD diameter and relevant biochemical parameters.

The primary outcome was the rate of spontaneous CBD stone passage prior to ERCP, defined as the proportion of patients with radiologically confirmed CBD stones on pre-ERCP imaging who had no stone identified at subsequent ERCP. Secondary outcomes included pre-ERCP imaging findings and biochemical factors associated with spontaneous CBD stone passage.

Statistical analysis

All statistical analyses were performed using RStudio (R version 4.5.2) with the meta package. Variables were selected *a priori*, based on clinical relevance and availability across studies, and were included in the meta-analysis when reported by at least 3 studies. The pooled rate of spontaneous CBD stone passage was estimated using a random-effects meta-analysis of proportions with logit transformation, and the DerSimonian-Laird estimator for between-study variance [12]. For dichotomous predictors, pooled odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using the Mantel-Haenszel method. For continuous outcomes, pooled mean differences (MDs) with 95%CIs were calculated using the inverse variance method [13]. When continuous data were reported as medians with interquartile ranges, means and standard deviations were estimated to enable inclusion in quantitative synthesis [14].

Stone size was dichotomized as ≤5 vs. >5 mm, representing the most consistently reported threshold across included studies. This included additional data provided by 1 corresponding author of the included studies, which were used solely for the purposes of standardized data extraction and quantitative synthesis. Studies reporting alternative but closely related cutoffs (e.g., <5 vs. ≥5 mm or <6 vs. ≥6 mm) were treated as equivalent for pooling, as these thresholds reflect minor methodological variation and were considered clinically comparable.

Statistical heterogeneity was assessed using Cochran's Q test and quantified with the I^2 statistic. Random-effects models were preferentially interpreted, given the anticipated clinical and methodological heterogeneity. Statistical significance was defined as a 2-sided P-value <0.05. Forest plots were generated to visually summarize all pooled analyses [13]. Sensitivity analyses were conducted by comparing fixed-effect and random-effect models to evaluate the robustness of pooled estimates.

Assessment of risk of bias and certainty of evidence

Risk of bias was assessed using the Risk of Bias In Non-randomized Studies of Interventions (ROBINS-I) tool [15]. Given that this meta-analysis evaluated predictors of spontaneous CBD stone passage, rather than the effects of assigned interventions, the ROBINS-I framework was applied in an adapted manner, treating predictor variables as exposures and spontaneous CBD stone passage prior to ERCP as the outcome. Each study was assessed across the 7 ROBINS-I domains by 2 independent reviewers, any discrepancies were resolved by consensus.

Publication bias was assessed using funnel plots and/or statistical tests for small-study effects, in accordance with Cochrane Handbook guidance [13].

The certainty of evidence for each outcome was assessed using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach with the GRADEpro GDT (Guideline Development Tool). As all included studies were observational cohort studies, the certainty of evidence was initially rated as low, and was downgraded where appropriate, based on risk of bias, inconsistency, indirectness, imprecision, and publication bias [16].

Results

Study characteristics

A total of 8 studies (n=3526) met the inclusion criteria for this meta-analysis. Table 1 presents a summary of the included studies and associated patient demographics. All studies included were retrospective cohort analyses published between 2015 and 2025. Each study explicitly included patients with radiologically confirmed choledocholithiasis who underwent subsequent ERCP. Six studies were single-center-based, and 2 were multicenter. Mean patient age ranged from 60-75 years across studies, with a slight female predominance (around 53%).

Spontaneous stone passage rate

Across all 8 included studies, 498 of 3526 patients (approximately 14%) experienced spontaneous CBD stone passage before ERCP. In other words, approximately 1 in 7 patients with confirmed CBD stones no longer had a stone at ERCP, thus risking undergoing unnecessary ERCP. The pooled estimate using a random-effects model was 16% (95%CI 12-22%) (Fig. 2). However, substantial heterogeneity was observed (I^2=94.0%), indicating considerable variability between studies.

Stone size was the only variable consistently reported across studies, and was therefore selected as the primary predictor for quantitative synthesis. Several secondary predictors were identified in studies, both radiological and biochemical. These included stone location, CBD diameter and LFTs.

Stone size

Stone size proved to be the key predictor of spontaneous stone passage. All 8 studies included in this meta-analysis confirmed this by demonstrating a statistically significantly higher rate of spontaneous stone passage in those with a smaller CBD stone diameter. Five studies reported data comparing spontaneous passage of CBD stones in patients with stones ≤5 vs. >5 mm. A meta-analysis (Fig. 3) of raw dichotomous data (n=3069) demonstrated that stones ≤5 mm were associated with significantly higher odds of spontaneous passage (OR 5.01, 95%CI 3.35-7.50, P<0.001), with low heterogeneity (I^2=17.3%). A separate meta-analysis of continuous data from 4 studies (n=802) comparing mean stone diameter between the spontaneous passage and non-spontaneous passage groups (Supplementary Fig. 1) yielded a consistent association between smaller stone diameter and spontaneous passage (MD -2.80 mm, 95%CI -3.43 to -2.17, P<0.001), with low heterogeneity (I^2=26.7%), supporting the previously established association.

CBD diameter

CBD diameter has previously been proposed as a potential marker of duct obstruction. Four studies reported CBD diameter stratified by spontaneous stone passage status. The mean diameters in the spontaneous passage group ranged from 8.04-9.75 mm, while in the retained group, they ranged from 9.5-12.4 mm. A meta-analysis of continuous data (n=1455) showed that those who passed the stone spontaneously had significantly smaller CBD diameters than those who did not, with a mean difference of -2.05 mm (95%CI -3.28 to -0.83, P=0.001), although heterogeneity was substantial (I^2=69%) (Supplementary Fig. 2).

Stone location

Three studies evaluated the association between CBD stone location (proximal vs. distal) and spontaneous passage.

Table 1 Demographic and clinical summary of included studies

Author (year) [ref.]	Design	Country	Exclusion criteria (summary)	Total Population (M/F)	Age	Imaging Modalities	Cholecystectomy Status	Stone Passage (Rate)
Andreozzi (2022) [18]	Retrospective, multicentre	Italy & Greece	Not naive papilla, presence of any CBD strictures, severe cholangitis, unsuccessful biliary cannulation	1016 (440/576)	69.9±16.5	MRCP, CT, US, EUS	History of cholecystectomy reported (165/1016; 16.2%)	17.6% (179/1016)
Correia (2025) [19]	Retrospective, single-centre	Portugal	Not naive papilla (i.e. with previous ERCP), altered biliopancreatic anatomy (Billroth I or II and Roux-Y)	334 (131/203)	71.4±17.4	MRCP, CT, US	NR	23.4% (78/334)
Graham (2025) [25]	Retrospective, single-centre	United Kingdom	Previous ERCP procedures, previous biliary stenting, altered biliary anatomy, post-cholecystectomy, previous sphincterotomy, diagnosed strictures, any evidence of malignant obstruction	381 (168/213)	68±17	MRCP, CT, US, Tubogram, EUS	Cholecystectomy patients were excluded	18.1% (69/381)
Inan (2024) [21]	Retrospective, single-centre	Turkey	Prior ERCP, other ERCP indication, altered anatomy, <18, pancreaticobiliary anomalies, transfers delaying assessment, poor MRCP quality, unsuccessful cannulation	236 (109/127)	60.3±17.52	MRCP	History of cholecystectomy reported (47/236; 19.9%)	11.0% (26/236)
Khoury (2019) [22]	Retrospective, single-centre	Israel	Primary liver or bile duct disease (including cirrhosis, primary sclerosing cholangitis, hepatitis); all liver transplant and hepatobiliary oncological patients	71 (41/30)	65.9±18.9	MRCP	NR	18.3% (13/71)
Kucuk (2023) [23]	Retrospective, single-centre	Turkey	Malignancy, GI resection, prior ERCP, <18 years-old, chronic hepatobiliary disease, bile duct strictures; + conditions altering inflammatory indices	132 (72/60)	65.1	MRCP	History of cholecystectomy reported (30/132; 22.7%)	27.3% (36/132)
Saito (2023) [20]	Retrospective, multi-centre	Japan	Patients without naive major duodenal papillae; unsuccessful biliary cannulation; inadequate cholangiography to confirm CBDSs; Roux-en-Y or Billroth-II reconstruction	1260 (662/598)	74.9±13.9	MRCP, CT, US, EUS	History of cholecystectomy reported (132/1260; 10.5%)	6.2% (78/1260)
Sanguanlosit (2020) [24]	Retrospective, single-centre	Thailand	Patients who did not receive ultrasound, CT scan or MRI before ERCP and the cause of cholangitis was not from CBD stones	96 (39/57)	63.5±18.3	MRCP, CT, US	NR	19.8% (19/96)

Table summarizing the design, population, exclusion criteria, imaging modalities, cholecystectomy status, and reported rates of spontaneous CBD stone passage across the 8 included studies. Age is reported as mean±standard deviation unless otherwise stated. Imaging modalities refer to the diagnostic modality used to identify choledocholithiasis prior to ERCP, with several studies employing more than 1 modality. Cholecystectomy status was not explicitly reported or stratified and is indicated as not reported

**NR, not reported; MRCP, magnetic resonance cholangiopancreatography; CT, computed tomography; US, ultrasound; EUS, endoscopic ultrasound*

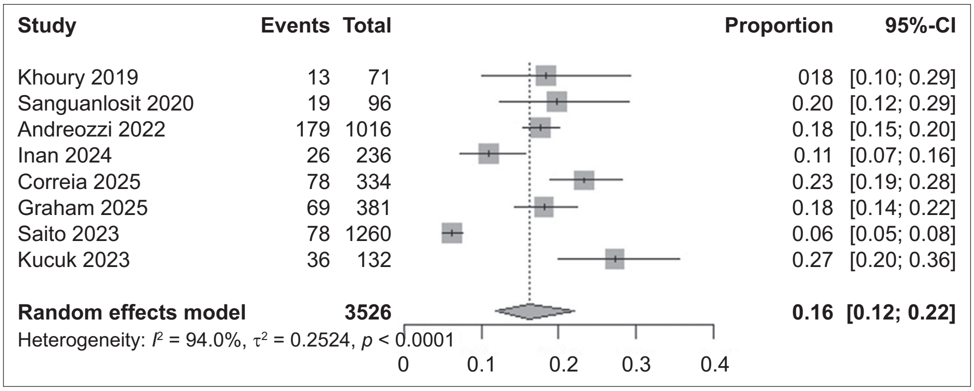

Figure 2 Forest plot of spontaneous common bile duct stone passage rates across included studies [18-25]
CI, confidence interval

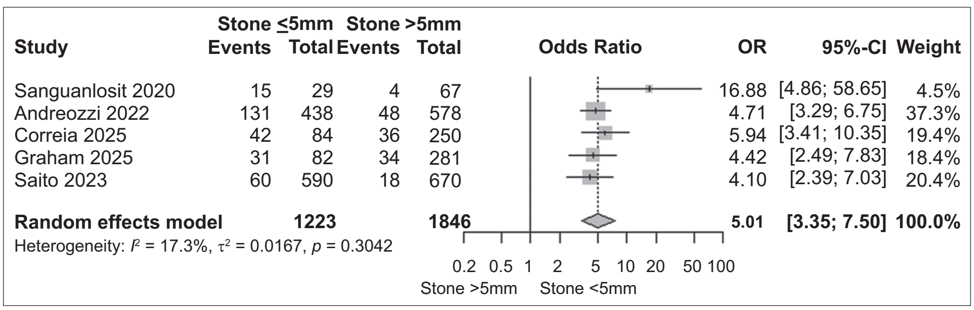

Figure 3 Forest plot of pooled unadjusted odds ratio for spontaneous common bile duct stone passage in patients with stone size ≤5 vs. >5 mm [18-20, 24,25]
OR, odds ratio; CI, confidence interval

A meta-analysis of dichotomous data (n=403) showed that distal stones were associated with higher odds of spontaneous passage compared to non-distal stones (OR 2.32, 95%CI 0.64-8.38), although this was not statistically significant (P=0.1992), heterogeneity was moderate (I^2=37.6%) (Supplementary Fig. 3).

Biochemical markers

ALT, AST and bilirubin were pooled from 4 studies (n=535) and ALP from 5 studies (n=853). A meta-analysis of continuous data showed a trend toward lower ALT levels, with a pooled mean difference of -21.18 U/L; however, the difference was not statistically significant (95%CI -82.45 to 40.09, P=0.2338) (Supplementary Fig. 4). The result was similar for the AST pooled mean difference of -20.83 U/L, showing a non-statistically significant finding (95%CI -47.46 to 5.80; P>0.05) (Supplementary Fig. 5). Although bilirubin levels appeared slightly lower in patients with spontaneous passage, the pooled mean difference of -0.21 mg/dL (95%CI -0.88 to 0.46, P=0.3340) was not statistically significant (Supplementary Fig. 6). A random-effects meta-analysis of 5 studies showed that ALP levels were significantly lower in the spontaneous stone passage group compared with the retained stone group, with a mean difference of -67.99 U/L (95%CI -97.36 to -38.61, P<0.001). Low heterogeneity was observed (I^2=15.1%) (Supplementary Fig. 7).

Sensitivity analysis

Sensitivity analyses using a fixed-effect model yielded results consistent in direction and magnitude with the primary random-effects analyses, with no change in statistical significance.

Risk of bias and quality of evidence

Overall, the risk of bias across included studies ranged from moderate to serious, with confounding representing the main source of bias. Two studies were judged to be at serious risk of bias, primarily due to inadequate control of confounding, including limited or absent multivariable adjustment and small outcome event counts. The remaining studies were assessed as having a moderate risk of bias, although residual confounding was unavoidable given the retrospective observational design.

Risk of bias assessments are summarized in Supplementary Table 2, with domain-level justifications provided in Supplementary Table 3 and a visual overview shown in Supplementary Fig. 8.

Publication bias could not be formally assessed because the analysis included only 8 studies. Funnel plot assessment and statistical tests for small-study effects were therefore not performed, in accordance with Cochrane Handbook guidance, as these methods are unreliable when fewer than 10 studies are included [13].

Using the GRADE approach, the certainty of evidence was very low across all outcomes, including pooled spontaneous passage rates and predictors for spontaneous stone passage (stone size, stone location, CBD size, biochemical predictors). Certainty was most frequently downgraded for risk of bias, reflecting residual confounding inherent to the observational study designs. Additional downgrading occurred for inconsistency where substantial heterogeneity was present, and for imprecision where confidence intervals were wide or crossed the null effect. Details of the GRADE certainty assessments for each outcome are provided in Supplementary Table 4.

Discussion

Across the included studies, stone size was consistently identified as the dominant determinant of spontaneous CBD stone passage. Smaller stones, most commonly defined by the threshold of 5 mm, were repeatedly identified as independent predictors of spontaneous passage, even after adjustment for clinical, biochemical and radiological variables. This finding aligns with the pooled analyses in the present study, and reinforces the biological plausibility that smaller stones are more likely to migrate without intervention.

This systematic review and meta-analysis found approximately 16% of patients with radiologically confirmed choledocholithiasis to have no stone at the time of ERCP, indicating spontaneous passage prior to endoscopic intervention. This result confirms that spontaneous clearance of CBD stones is a relevant and significant phenomenon that should be considered in the clinical setting. Regarding pre-ERCP radiological factors, our meta-analysis identified stone size as the most significant and consistent predictor of stone passage, aligning with the individual studies' findings. CBD diameter was another significant radiological predictive factor that we identified. Patients with a relatively narrower CBD had greater chances of spontaneous stone clearance prior to ERCP. A narrower duct probably reflects that a stone is not causing prolonged or severe obstruction and therefore correlates with an increased chance of spontaneous passage.

Regarding biochemical markers, this meta-analysis investigated ALT, AST, ALP and bilirubin as preprocedural liver markers. ALP was the only marker to demonstrate a statistically significant association with spontaneous stone passage. This suggests that transient obstruction leads to significantly lower ALP levels compared with retained stone groups, suggesting a picture of longer cholestatic injury.

The previous literature has described the concept of spontaneous passage rates of CBD stones ranging widely, though studies were often based on heterogeneously selected patient populations and varying definitions of confirmation. Earlier work by Tranter and Thompson reported spontaneous passage of bile duct stones, and how it relates to clinical presentation pre-cholecystectomy and at the time of operation, and introduced the concept of investigating variables that may be associated with this phenomenon [17]. Our meta-analysis across 8 studies and 3526 patients provides a more robust estimate of passage rate (16%) and supports the predictive utility of stone size, CBD diameter and LFT trends. Our findings align with those of Arabpour *et al*, confirming that spontaneous CBD stone passage occurs in approximately 1 in 6 patients, and that smaller stone size and narrower CBD diameter are key radiological predictors [9]. However, in contrast to Arabpour *et al*, we were able to quantitatively analyze biochemical predictors and demonstrate that lower ALP levels are independently associated with spontaneous stone passage. Although there was no explicit consideration of the impact of cholecystectomy and primary bile duct stone formations, the findings of LFT trend criteria set our work apart from the prior generalized analyses of ERCP outcomes.

The clinical implications of these findings are a step into developing a more nuanced and measurable approach to patient selection for ERCP. If all patients with CBD stones undergo an ERCP, the total number of patients with complications will increase, despite the same overall ERCP complication rate. Using predefined predictors can guide clinicians into estimating the clinical necessity of performing ERCP. In patients with a smaller CBD stone and a smaller CBD diameter on imaging, together with declining LFTs, the chance of spontaneous passage is relatively higher. The studies analyzed made their own suggestions about reducing unnecessary ERCP numbers. Andreozzi *et al* suggested stones ≤5 mm do not require immediate removal, while Correia *et al* recommended EUS evaluation prior to ERCP intervention, as a precursor to assess for stone passage [18,19]. Building on this, Saito *et al* similarly advocated preliminary EUS immediately before ERCP to avoid unnecessary ERCP, especially in patients with solitary, small stones (<6 mm), and in those who are asymptomatic (where imaging-to-ERCP intervals may be longer) [20]. İnan *et al* and Khoury *et al* suggested considering repeat radiological assessment together with close follow-up when there is doubt that a small stone has already passed; however, they did not specify an imaging technique [21-22]. Küçük *et al* proposed that low inflammatory markers should be used to guide the possibility of migrated stones [23]. This concept of triaging medium-risk patients may be helpful for patients with clinical and radiological indications (e.g., smaller stone, smaller CBD, improving biochemistry).

In the individual studies, statistically significant findings beyond those included in our meta-analysis were identified in their multivariate analysis. Khoury *et al* found that lower peak bilirubin level and distal stone location were independently associated with spontaneous passage, with a multivariate analysis showing that GGT was also significantly lower in patients with stone clearance [22]. As mentioned, Correia *et al* identified 3 independent predictors in a multivariate model: 1) stone diameter ≤5 mm; 2) absence of clinical cholangitis; and 3) bilirubin ≤2 mg/dL at the time of ERCP [19]. Cholangitis was not included in our pooled data analyses given the incomplete data across studies; however, it is important to consider these findings. Sanguanlosit *et al* identified that single, small stones (cutoff 4.8 mm) were associated with significantly greater odds of spontaneous passage compared to multiple, larger stones [24]. İnan *et al* found only stone size to be significant in their multivariate analysis [21]. Küçük *et al* identified lower inflammatory markers, in particular reduced C-reactive protein-based indices, as independent predictors of stone migration [23]. Graham *et al*. (2025) found that higher ALP levels at time of imaging and ERCP were statistically significant in univariate modelling, however did not retain predictive value in multivariate analysis [25].

Predictive modeling is one of the next steps for triaging patients for ERCP; however, there is no consensus. Prospective trials are therefore required to investigate findings, to test variables, and consider serial imaging as an alternative approach to ERCP intervention.

The findings from this meta-analysis, we believe, align well with those of Correia *et al* [19]. Suggestions include the relevance of performing EUS prior to ERCP to risk-stratify patients in order to avoid unnecessary ERCP (in those where spontaneous stone passage has occurred). The impact of same-session EUS for bile duct stones has been investigated [26]. We therefore believe that a 3-tier approach should be considered when managing patients with radiologically confirmed bile duct stones. To summarize, the most significant pre-ERCP predictors of spontaneous stone passage from our meta-analysis are smaller stone size (≤5 mm), smaller CBD diameter (-2.05 mm), and declining ALP levels (-67.99 U/L).

Based on pre-procedural biochemical and radiological predictors, patients with confirmed choledocholithiasis can be stratified into 3 risk categories reflecting the likelihood of spontaneous CBD stone passage prior to ERCP.

Group 1: High likelihood of spontaneous stone passage

- Typical features: Small stone size on imaging, absence or minimal CBD dilatation, normalizing/declining ALP levels.
- Recommended management: conservative approach to avoid ERCP unless clinical deterioration.
- Rationale: ERCP in this group risks unnecessary invasive intervention in patients with a high probability of stone clearance.

Group 2: Intermediate likelihood of spontaneous stone passage

- Typical features: Borderline stone size, modest CBD dilatation, partial/stagnant intermediate ALP levels.
- Recommended management: Consider same-session EUS immediately before ERCP.
- Rationale: This strategy balances the avoidance of unnecessary ERCP against the risk of missing retained stones, optimizing patient safety and resource utilization.

Group 3: Low likelihood of spontaneous stone passage

- Typical features: Large stone size, significant CBD dilatation, persistent elevation/ongoing increasing ALP levels.
- Recommended management: No repeat pre-procedural imaging indicated, proceed with ERCP.
- Rationale: The probability of retained stones is high, and delaying intervention may increase the risk of complications.

This meta-analysis has several limitations. The variability of diagnostic imaging modality was not standardized in this analysis, and the use of CT and ultrasound, both associated with elevated false positive rates for CBD stones, may have influenced the study's estimates [27,28]. Another limitation is the inclusion of patients with prior cholecystectomy and altered biliary anatomy. 212 patients had previously undergone cholecystectomy and subgroup-level data were not available for us to exclude these individuals [18,21]. The inclusion of post-cholecystectomy patients introduces potential heterogeneity into our results, as patients without a gallbladder may differ in stone composition, CBD diameter and dilatation [29]. Third, biochemical predictors were inconsistently reported thereby limiting the pooled analysis. Correia *et al* identified a pre-ERCP bilirubin <2 mg/dl as an independent predictor of spontaneous passage, a finding which was unfortunately not included in the analysis due to the absence of reported standard deviation or dispersion data [19]. Fourth, all included studies were retrospective observational cohorts, which are subject to selection bias. We only included patients in the analysis who underwent ERCP as a confirmed endpoint for our primary outcome, excluding the cohorts where patients were treated conservatively. Imaging-to-ERCP interval times likely influenced these results, despite us attempting to account for heterogeneity with a random-effects model (I^2=~94%). Finally, the relatively small number of included studies and sample size limited subgroup analyses and assessment of publication bias, and some pooled estimates were derived from unadjusted or converted data, which may reduce precision. Overall, the retrospective study design, high risk of bias, methodological heterogeneity, and very-low GRADE criteria across all outcomes means that the findings and implications of this study should be treated as low certainty.

In conclusion, approximately 16% of patients in the included studies underwent an ERCP unnecessarily, as spontaneous passage of CBD stones had already occurred. Future research should focus on identifying the characteristics of this cohort of patients and developing clinical prediction tools to help avoid unnecessary ERCP procedures. Smaller stone size, smaller CBD diameter, and lower or improving ALP levels were associated with a higher likelihood of spontaneous stone passage. These results encourage ongoing development of strategies and alternatives in medium-risk patients. Adopting standardized guides could spare many patients an invasive procedure and risk of complications. Our findings hopefully provide a foundation for evidence-based decision-making in the management of choledocholithiasis.

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Summary Box

What is already known:

- Spontaneous passage of common bile duct (CBD) stones is a recognized phenomenon, with some patients having no stones at endoscopic retrograde cholangiopancreatography (ERCP) despite prior radiological confirmation
- ERCP carries significant risks, including pancreatitis, perforation, and anesthetic risks, making avoidance of unnecessary procedures clinically important
- Smaller stone size and bile duct diameter have been suggested as key predictors of spontaneous stone passage in previous studies

What the new findings are:

- Approximately 16% of patients with radiologically confirmed CBD stones have spontaneous stone passage prior to ERCP
- Stone diameter ≤5mm is the strongest predictor of spontaneous passage (pooled unadjusted odd ratio 5.01, 95% confidence interval 3.35-7.50)
- Smaller CBD diameter is significantly associated with increased likelihood of spontaneous clearance
- Lower or declining alkaline phosphatase is the only biochemical marker significantly associated with spontaneous stone passage

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Supplementary material

Supplementary Table 1 Full electronic search strategies used for each database

Database	Search string
PubMed	(“Choledocholithiasis”[MeSH] OR choledocholithiasis[tiab] OR “common bile duct stone*”[tiab] OR “bile duct stone*”[tiab] OR “CBD stone*”[tiab]) AND (“Cholangiopancreatography, Endoscopic Retrograde”[MeSH] OR ERCP[tiab] OR “endoscopic retrograde”[tiab]) AND (detect*[tiab] OR predict*[tiab] OR spontaneous[tiab] OR migration[tiab] OR passage[tiab] OR clearance[tiab] OR negative[tiab]) AND (“Diagnostic Imaging”[MeSH] OR radiolog*[tiab] OR imaging[tiab] OR ultrasound[tiab] OR ultrasonograph*[tiab] OR MRCP[tiab])
Embase	(‘choledocholithiasis’/exp OR choledocholithiasis OR ‘bile duct stone*’ OR ‘common bile duct stone*’ OR ‘cbd stone*’) AND (‘ercp’/exp OR ercp OR ‘endoscopic retrograde’) AND (detect* OR predict* OR spontaneous OR ‘migration’/exp OR migration OR passage OR ‘clearance’/exp OR clearance OR negative) AND (radiolog* OR ‘imaging’/exp OR imaging OR ‘ultrasound’/exp OR ultrasound OR ultrasonograph* OR mrcp)
Scopus	(TITLE-ABS-KEY (choledocholithiasis) OR TITLE-ABS-KEY (bile AND duct AND stone) OR TITLE-ABS-KEY (cbd AND stone)) AND (TITLE-ABS-KEY (ercp) OR TITLE-ABS-KEY (endoscopic AND retrograde)) AND (TITLE-ABS-KEY (detect*) OR TITLE-ABS-KEY (predict*) OR TITLE-ABS-KEY (spontaneous) OR TITLE-ABS-KEY (migration) OR TITLE-ABS-KEY (passage) OR TITLE-ABS-KEY (clearance) OR TITLE-ABS-KEY (negative)) AND (TITLE-ABS-KEY (radiolog*) OR TITLE-ABS-KEY (imaging) OR TITLE-ABS-KEY (mrcp) OR TITLE-ABS-KEY (ultrasound))

Supplementary Table 2 Risk of bias assessment of included studies using the ROBINS-I (2016) tool

Study [ref.]	Confounding	Selection of participants	Classification of exposure	Deviations from intended exposure	Missing data	Outcome measurement	Selective reporting	Overall risk of bias
Khoury 2019 [22]	Serious	Moderate	Moderate	Low	Moderate	Low	Moderate	Serious
Sanguanlosit 2020 [24]	Moderate	Moderate	Moderate	Low	Moderate	Low	Moderate	Moderate
Andreozzi 2022 [18]	Moderate	Moderate	Moderate	Low	Moderate	Low	Moderate	Moderate
Inan 2024 [21]	Moderate	Moderate	Moderate	Low	Moderate	Low	Moderate	Moderate
Correia 2025 [19]	Moderate	Moderate	Moderate	Low	Moderate	Low	Moderate	Moderate
Graham 2025 [25]	Moderate	Moderate	Moderate	Low	Moderate	Low	Moderate	Moderate
Saito 2023 [20]	Moderate	Moderate	Moderate	Low	Moderate	Low	Moderate	Moderate
Küçük 2023 [23]	Serious	Moderate	Low	Low	Moderate	Low	Moderate	Serious

Supplementary Table 3 Domain-level justification for ROBINS-I (2016) risk of bias judgements

Study [ref.]	Bias due to confounding	Bias in selection of participants	Bias in classification of intervention (exposure)	Bias due to deviations from intended interventions	Bias due to missing outcome data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall risk of bias
Khoury 2019 [22]	Serious	Moderate	Moderate	Low	Moderate	Low	Moderate	**Serious**
Justification	Key confounders (e.g., stone size, CBD diameter, biochemical markers) were reported but no multivariable adjustment was performed. Residual confounding is therefore likely.	Participants were identified retrospectively from clinical records; inclusion depended on undergoing ERCP, which may be related to prognosis.	Exposure status (spontaneous passage vs no passage) was defined based on imaging and ERCP findings, but timing relative to imaging was not always explicit.	No evidence that post-classification management differed between groups in a way likely to affect outcome classification.	Some patients lacked complete paired imaging/ERCP data, and no sensitivity analyses for missing data were reported.	Outcome ascertainment relied on objective imaging and ERCP findings, with low risk of differential misclassification.	No pre-specified analysis plan was reported, raising the possibility of selective reporting.	Multiple domains at moderate/ serious risk, driven mainly by confounding and selection mechanisms.
Sangunlosit 2020 [24]	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
Justification	Major confounders were partially addressed descriptively, but adjustment was limited. Some residual confounding cannot be excluded.	Retrospective cohort design with inclusion based on ERCP referral introduces potential selection related to disease severity.	Classification of spontaneous passage was clearly defined using ERCP findings.	Management following exposure classification reflected routine care.	Outcome data were largely complete with minimal attrition.	Objective outcome assessment using ERCP minimises measurement bias.	Absence of a registered protocol means selective reporting cannot be ruled out.	Overall risk judged moderate due to residual confounding and reporting uncertainty.
Andreozzi 2022 [18]	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
Justification	Important confounders were measured but not fully adjusted for in multivariable models.	Selection restricted to patients undergoing ERCP may be related to predictors of stone persistence.	Exposure classification was based on clear radiological and procedural criteria.	No deviations from intended clinical pathways were apparent.	Missing outcome data were minimal.	Outcomes were assessed using standard imaging and ERCP reports.	No protocol available to confirm pre-specification of analyses.	Moderate overall risk driven by confounding and selection processes.
Inan 2024 [21]	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
Justification	Confounders were reported but analyses were largely unadjusted, leaving potential residual confounding.	Retrospective identification of participants based on ERCP introduces possible selection bias.	Exposure status was clearly defined using objective criteria.	Clinical management was consistent across groups.	Outcome data completeness was high.	Measurement relied on objective diagnostic findings.	Selective reporting cannot be excluded due to lack of protocol.	Overall moderate risk of bias.

(Contd...)

Supplementary Table 3 *(Contined)*

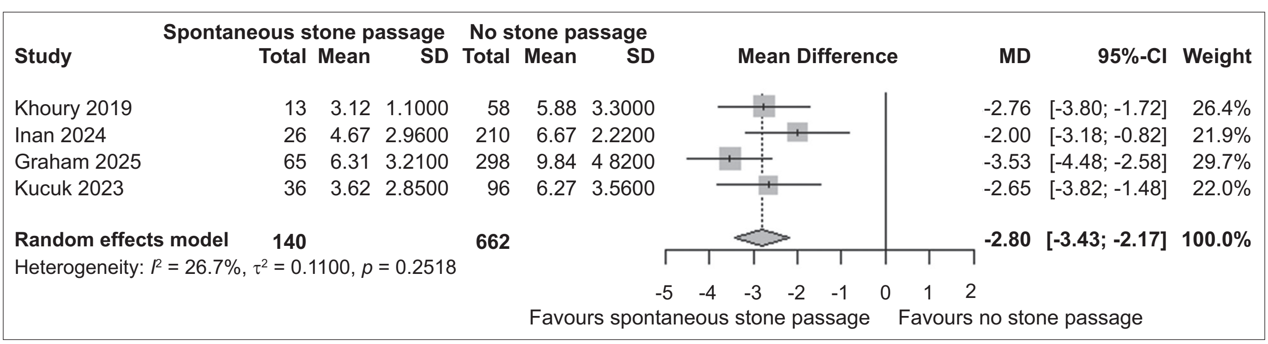
Study [ref.]	Bias due to confounding	Bias in selection of participants	Bias in classification of intervention (exposure)	Bias due to deviations from intended interventions	Bias due to missing outcome data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall risk of bias
Correia 2025 [19]	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
Justification	Partial control of confounding variables without full adjustment.	Inclusion depended on ERCP referral, which may be associated with disease severity.	Clear definition of exposure using imaging and ERCP.	No evidence of differential deviations from intended care.	Minimal missing data.	Objective outcome assessment.	Unclear whether analyses were pre-specified.	Moderate risk overall.
Graham 2025 [25]	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
Justification	Key prognostic factors were measured but not comprehensively adjusted for.	Retrospective cohort with potential selection linked to clinical decision-making for ERCP.	Exposure classification was well defined.	Standard clinical management followed.	Outcome data largely complete.	Objective outcome measurement.	No published protocol to exclude selective reporting.	Overall moderate risk.
Saito 2023 [20]	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
Justification	Limited adjustment for confounders despite their availability.	Selection based on ERCP performance may introduce bias.	Clear exposure definition.	No meaningful deviations from intended interventions.	Missing data unlikely to influence results.	Reliable outcome measurement.	Reporting bias cannot be excluded.	Moderate overall risk.
Küçük 2023 [23]	Serious	Serious	Low	Low	Low	Low	Moderate	Serious
Justification	No adequate adjustment for major confounders; strong potential for residual confounding.	Participant inclusion was highly selected and likely related to both predictors and outcome.	Exposure classification was clear.	Post-classification care appeared routine.	Outcome data were complete.	Objective outcome assessment.	No pre-specified analysis plan reported.	Serious risk driven by confounding and participant selection.

**CBD, common bile duct; ERCP, endoscopic retrograde cholangiopancreatography*

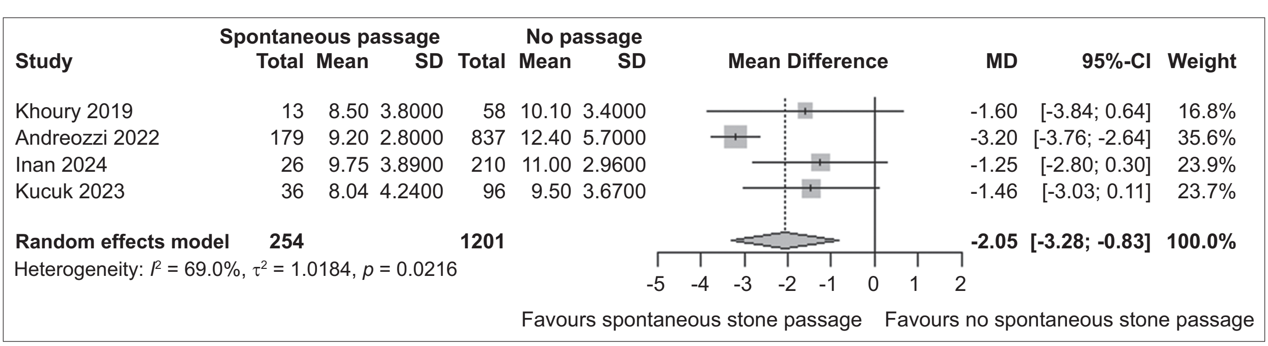
Supplementary Table 4 GRADE assessment of certainty of evidence for predictors of spontaneous common bile duct stone passage [18-25]

Outcome	No. of studies	Participants	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty (GRADE)
Spontaneous CBD stone passage rate	8	3,526	Serious†	Serious‡	Not serious	Serious§	Not assessed	⊕◯◯◯ Very low
Stone size ≤5 mm vs >5 mm	5	3,069	Serious†	Not serious	Not serious	Not serious	Not assessed	⊕◯◯◯ Very low
Mean stone diameter (mm)	4	802	Serious†	Not serious	Not serious	Not serious	Not assessed	⊕◯◯◯ Very low
Stone location (distal vs non-distal)	3	403	Serious†	Not serious	Not serious	Serious§	Not assessed	⊕◯◯◯ Very low
CBD diameter (mm)	4	1,455	Serious†	Serious‡	Not serious	Not serious	Not assessed	⊕◯◯◯ Very low
ALT (U/L)	4	535	Serious†	Not serious	Not serious	Serious§	Not assessed	⊕◯◯◯ Very low
AST (U/L)	4	535	Serious†	Not serious	Not serious	Serious§	Not assessed	⊕◯◯◯ Very low
Bilirubin (mg/dL)	4	535	Serious†	Not serious	Not serious	Serious§	Not assessed	⊕◯◯◯ Very low
ALP (U/L)	5	853	Serious†	Not serious	Not serious	Not serious	Not assessed	⊕◯◯◯ Very low

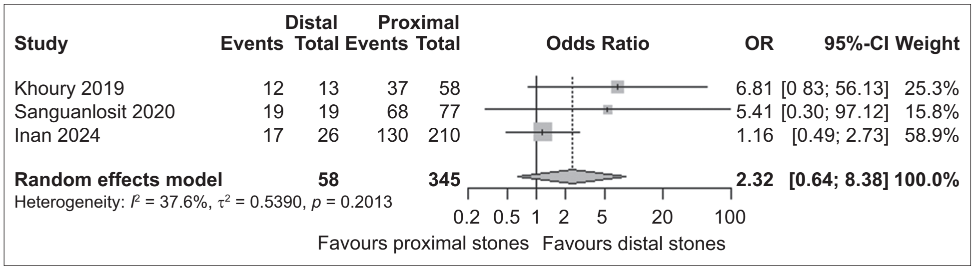
† Downgraded 1 level due to risk of bias across the contributing retrospective cohorts, primarily due to residual confounding
‡ Downgraded 1 level due to substantial unexplained heterogeneity (I^2>60%)
§ Downgraded 1 level due to imprecision, as confidence intervals included both no effect and clinically important effects
Publication bias was not formally assessed because fewer than 10 studies were available
CBD, common bile duct stone; ALT, alanine transferase; AST, aspartate transferase; ALP, alkaline phosphatase



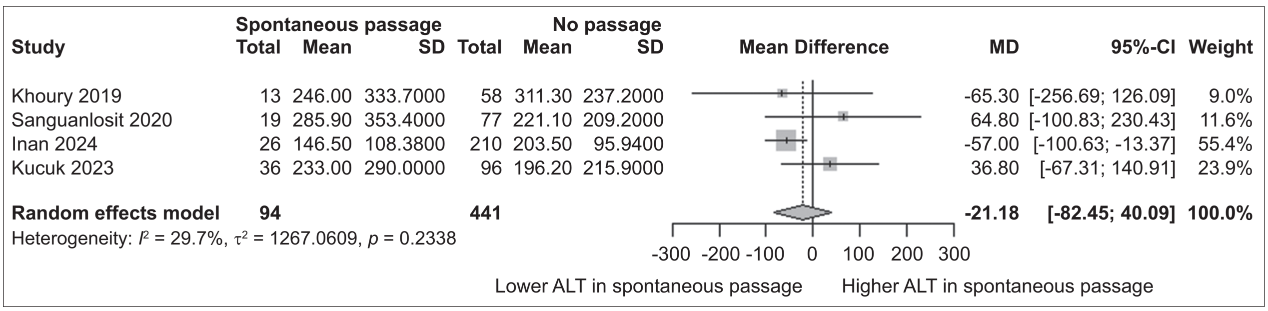
Supplementary Figure 1 Mean difference in common bile duct (CBD) stone diameter between patients with and without spontaneous common bile duct stone passage [21-23,25]
SD, standard deviation; MD, mean difference; CI, confidence interval



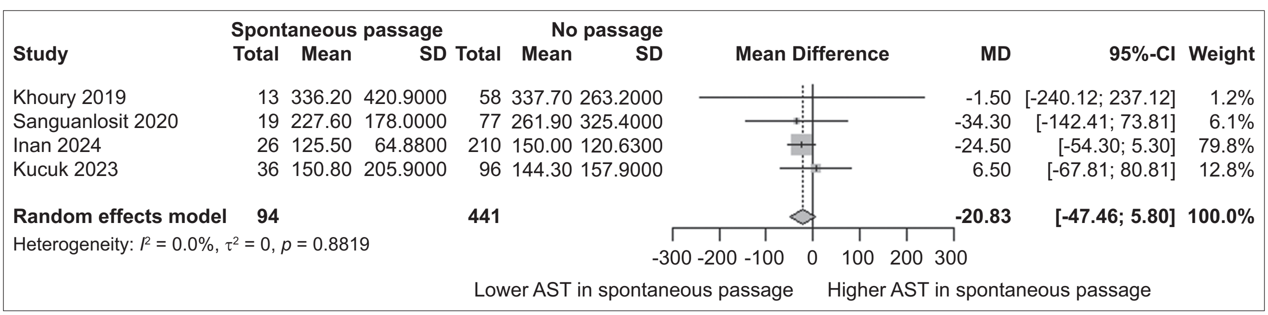
Supplementary Figure 2 Mean difference in common bile duct diameter between patients with and without spontaneous common bile duct stone passage [18,21-23]
SD, standard deviation; MD, mean difference; CI, confidence interval



Supplementary Figure 3 Association between stone location (distal vs proximal) and spontaneous common bile duct stone passage [21,22,24]
OR, odds ratio; CI, confidence interval

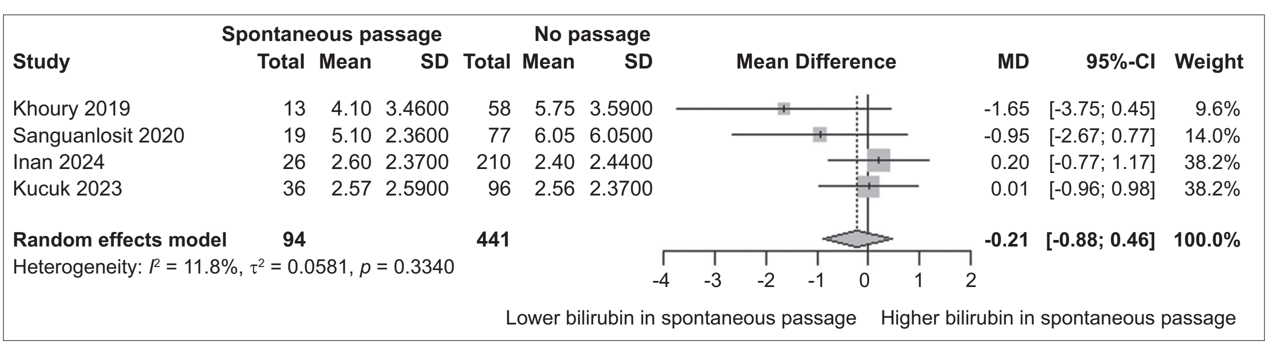


Supplementary Figure 4 Difference in alanine transaminase (ALT) levels between patients with and without spontaneous common bile duct stone passage [21-24]
SD, standard deviation; MD, mean difference; CI, confidence interval; ALT, alanine transaminase

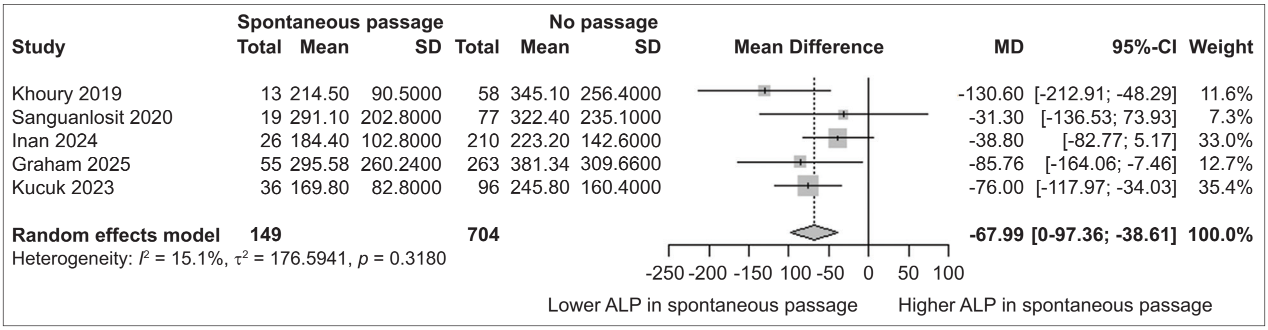


Supplementary Figure 5 Difference in AST level between patients with and without spontaneous common bile duct stone passage [21-24]

MD, mean difference; SD, standard deviation; CI, confidence interval; AST, aspartate transaminase

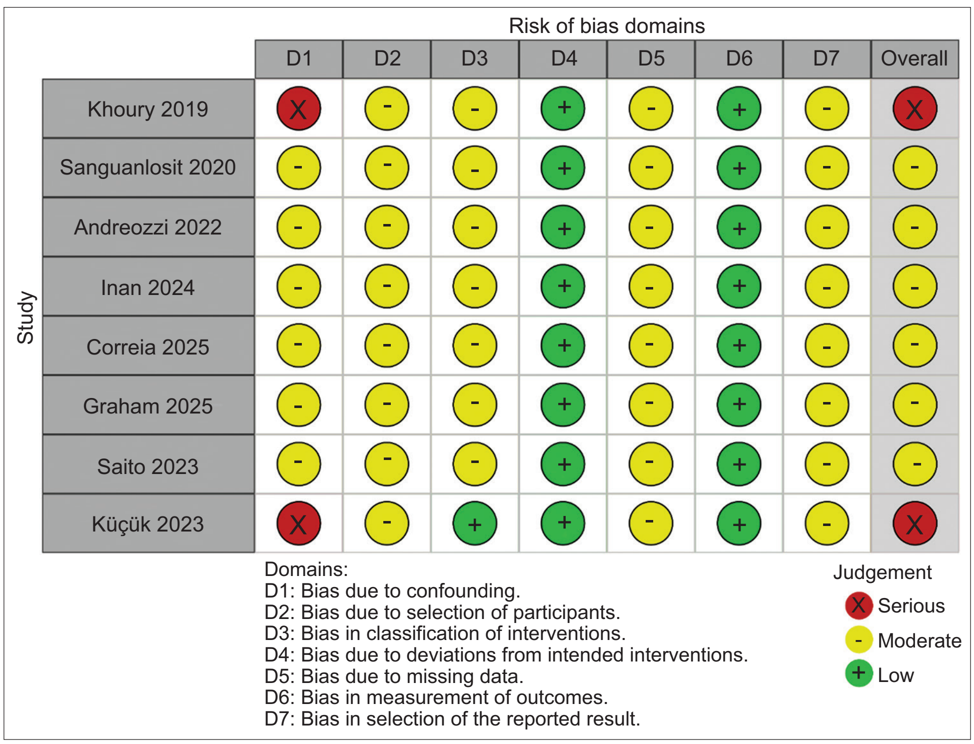


Supplementary Figure 6 Difference in total bilirubin levels between patients with and without spontaneous common bile duct stone passage [21-24]
SD, standard deviation; MD, mean difference; CI, confidence interval



Supplementary Figure 7 Difference in ALP between patients with and without spontaneous common bile duct stone passage [21-25]

SD, standard deviation; MD, mean difference; ALP, alkaline phosphate



Supplementary Figure 8 ROBINS-I (2016) risk of bias traffic-light plot [18-25]