Annals of Gastroenterology (2026) **39,** 543-551

Cystic duct anatomical variations and the risk of choledocholithiasis: a systematic review and meta-analysis

Dimosthenis Chrysikos*, Nikolaos Taprantzis*, Amir Shihada, Theodore Troupis

Athens Medical School, National and Kapodistrian University of Athens, Greece

Abstract

Background Cystic duct anatomy is clinically significant for surgery and stone formation, yet the literature lacks a systematic analysis linking variations to common bile duct stones. This study investigated their prevalence and risk for choledocholithiasis.

Methods We systematically searched PubMed, Embase, Web of Science and Scopus for studies on cystic duct morphology and choledocholithiasis. Pooled prevalence, risk ratios (RRs), and odds ratios were calculated using R; heterogeneity and bias were assessed via AQUA and Peter's tests.

Results High (17.2%) and posterior (13.8%) insertions were most prevalent. Factors significantly associated with choledocholithiasis included a long cystic duct (RR 1.50, 95% confidence interval [CI] 1.18-1.90), low insertion (RR 1.46, 95%CI 1.06-1.76), spiral course (RR 1.41, 95%CI 1.06-1.86), and posterior insertion (RR 1.32, 95%CI 1.07-1.60). Lithiasis patients exhibited wider cysto-choledochal angles (47.1° vs. 40.8°). Geographic analysis revealed a high prevalence of low insertion in African populations (21.8%) and spiral ducts in East Asians.

Conclusions Cystic duct variations significantly increase susceptibility to choledocholithiasis and pose surgical challenges. As these complex anatomical courses and configurations are often missed, preoperative imaging is essential. Early identification enables safer surgical planning, reduces biliary injury risk, and can guide tailored strategies to prevent lithiasis in high-risk groups.

Keywords Choledocholithiasis, cystic duct, anatomy, risk factors

Ann Gastroenterol 2026; 39 (5): 543-551

Introduction

The anatomical configuration of the cystic duct plays a critical role in patients' clinical assessment and management. Its significance is evident, both during surgical procedures involving the extrahepatic biliary tree, and in the pathophysiological development of bile duct stones. The normal, or most commonly reported, anatomical configuration of that structure is a right mid-lateral insertion to the common bile duct, with an approximate length of 2-4 cm [1,2]. Although the existing literature reports the presence of a normal anatomy in 51-72% of all cases, the position of the insertion, the course and the length of the cystic duct show a great degree of variability [3].

An association between the existence of certain cystic duct variations and the development of choledocholithiasis has been proposed by some studies [3,4]. However, no previous meta-analysis or systematic review has aimed to explore that relationship in detail. Accordingly, this study aimed to report the prevalence of the clinically important cystic duct variations, along with their variability across different investigative methods, areas and sexes. Notably, this analysis also calculated the risk ratio (RR) for every available cystic duct variation, quantifying the risk association between anatomy and choledocholithiasis. The clinical interpretation of the results, as well as the surgical challenges of such variations, are discussed below.

Anatomy Department and Surgical Anatomy Unit, Athens Medical School, National and Kapodistrian University of Athens, Greece (Dimosthenis Chrysikos, Nikolaos Taprantzis, Amir Shihada, Theodore Troupis)

Conflict of Interest: None

*Equal contributions, joint first author

Correspondence to: Nikolaos Taprantzis, Department of Anatomy, Athens Medical School, National and Kapodistrian University of Athens, Mikras Asias 75, Athens, Greece, e-mail: nichostap@gmail.com

Received 31 January 2026; accepted 5 April 2026; published online 9 July 2026

DOI: https://doi.org/10.20524/aog.2026.1095

Materials and methods

We systematically searched through the PubMed, Embase, Web of Science and Scopus databases—using key words such as "cystic duct variations", "cystic duct anatomy", "cystic duct" AND "choledocholithiasis", "extrahepatic biliary anatomy", "extrahepatic biliary variations" AND "choledocholithiasis", "cysto-choledochal angle" AND "choledocholithiasis", "anatomical study"—in order to collect data that would fit the criteria of our review. The search and study selection process followed the PRISMA guidelines [5] (Supplementary Table 1). Since this paper used only published data, no institutional review board approval or any other consent were needed.

Our search was limited to studies reported in the English language, while additional data were found by screening the references of the articles retrieved. The final set of studies and articles was decided based on the predefined selection criteria, which included studies that reported the presence of different cystic duct variations and/or their association with choledocholithiasis only through the usage of magnetic resonance cholangiopancreatography (MRCP). Additionally, distinct clinically relevant anatomical variations (e.g., posterior and anterior insertion, high or low insertion, medial insertion, parallel or spiral anatomy), as well as their presence in males and females, were recorded so as to calculate and investigate the frequency of these characteristics. Finally, this review did not include animal studies, abstracts from conferences, or any study that did not report the data sufficiently.

Subgroup analyses stratified by geographic area were conducted to explore the variability between different regions. The geographic moderator was categorized as Europe, America, East Asia (Japan, Korea, China), South Asia (India, Pakistan, Sri Lanka), Middle East (Iran, Saudi Arabia, Iraq), West Asia (Turkey, Anatolian populations). Since the 3D rendering ability of MRCP makes it substantially superior to other methods of visualization (e.g., direct surgical view), only studies that utilized MRCP were included in this analysis, in order to avoid any potential bias and provide more clinically relevant data.

Definitions

Low insertion and high insertion referred to joining of the cystic duct into the common bile duct in the lower third and upper third, respectively. Anterior and posterior insertion referred to the front and back end of the common bile duct, respectively. Medial insertion was defined as joining to the left side of the common bile duct. A long cystic duct was defined as one with a length greater than 2 cm, while a short duct was less than 5 mm long. A parallel cystic duct referred to a parallel course along the common hepatic duct. A spiral path referred to a cystic duct that twined around the common hepatic duct before inserting either anteriorly or posteriorly. Finally, the cysto-choledochal angle (CCA) was defined as the angle between the cystic duct and the common bile duct at the site of insertion.

Statistical analysis

We performed a meta-analysis using R (version 4.3.2) and RStudio, employing the "meta" and "metafor" packages for statistical analysis. To assess the association between cystic duct anatomical configurations and the risk of choledocholithiasis, RRs were calculated from study-level 2×2 contingency tables for dichotomous variables, while odds ratios (ORs) were used for identifying any differences in prevalence between male and female patients. For these comparative analyses, the Restricted Maximum Likelihood (REML) estimator was utilized to calculate the between-study variance (t2). As far as the pooled prevalences are concerned, we employed the Freeman–Tukey double arcsine (PFT) transformation. The rationale for this transformation was to stabilize the variances of proportions, particularly for rare surgical complications with rates approaching 0 or 1, ensuring appropriate study weighting. For these prevalence estimates, the DerSimonian-Laird (DL) estimator was applied. Given the inherent clinical and methodological heterogeneity expected across observational surgical studies comparing varied patient populations, a random-effects model was chosen *a priori* and applied to all analyses. Heterogeneity was assessed using Cochran's Q test and Higgins' I^2 statistic, interpreted as low (0-30%), moderate (30-50%), substantial (50-75%), or considerable (75-100%) heterogeneity. Statistical significance was defined as $P<0.05$. Publication bias was evaluated with Peters' test, and sensitivity analyses were performed using leave-one-out methods to assess the robustness of pooled estimates [6].

Data extraction

Two independent reviewers (DC and NT) conducted their literature search across online databases and collected their results into Microsoft Excel files. The extracted data included raw count data artery prevalence. After completing data extraction independently, the reviewers compared their datasets and resolved discrepancies through consensus. No automated tools were used in the data extraction process. The majority of the studies reported just anatomical data, without a comparison between choledocholithiasis-related groups. The RR was calculated only from studies that provided a direct comparison and association between the 2 groups, ensuring a fair evaluation.

Risk of bias assessment

Risk of bias for each included study was assessed using the Anatomical Quality Assurance (AQUA) tool of Henry *et al* for prevalence studies [7]. Two reviewers (DC and NT) conducted the assessments independently. Each domain of the tool was rated separately, and an overall judgment of risk (low, moderate, or high) was assigned per study. In cases of disagreement, a consensus was reached through discussion. Additionally, to assess the presence of publication

bias, Peters' tests, along with the corresponding plots, were performed for each prevalence analysis [6].

Results

After the completion of our systematic search, 3205 studies were identified from databases and citation searching. Following the removal of duplicates and articles that did not meet the predefined criteria, 1233 studies were assessed for eligibility. Finally, it was decided that 29 studies would be included in the systematic review (Fig. 1). The mean number of patients among the included studies was 321.4 (Table 1).

Low insertion

The overall pooled prevalence of low cystic duct insertion into the common bile duct was 5.6% (95%CI 0.03-0.08). The patient's sex had no significant effect on choledocholithiasis (OR 1.40, 95%CI 0.70-2.82; P=0.331), whereas low insertion was significantly associated with risk (RR 1.46, 95%CI 1.06-1.76; P<0.001)

High insertion

The pooled prevalence for this variation was 17.2% (95%CI 0.10-0.25). The effect of patients' sex was not significant (OR 1.02, 95%CI 0.90-1.15; P=0.862). Finally, the association between high insertion and choledocholithiasis was not significant (RR 1.02, 95%CI 0.32-3.29; P=0.729).

Anterior insertion

Pooled prevalence for this variation was calculated to be at 3.6% with (95%CI 0.02-0.05). The effect of patients' sex was not significant (OR 0.99, 95%CI 0.53-1.82; P=0.879). The association between anterior insertion and the risk of choledocholithiasis was also not significant (RR 1.32, 95%CI 0.82-1.72; P=0.129).

Posterior insertion

Posterior insertion was present in 13.8% of total individuals (95%CI 0.09-0.19). Patients' sex had a significant effect (OR 1.61, 95%CI 1.13-2.32; P=0.008). However, there was a significant association between this variation and choledocholithiasis (RR 1.32, 95%CI 1.07-1.60; P=0.019).

Medial insertion

A cystic duct with a medial insertion to the common bile duct was present in 10.3% of patients (95%CI 0.05-0.16). Patients' sex was not significant (OR 0.99, 95%CI 0.23-4.11;

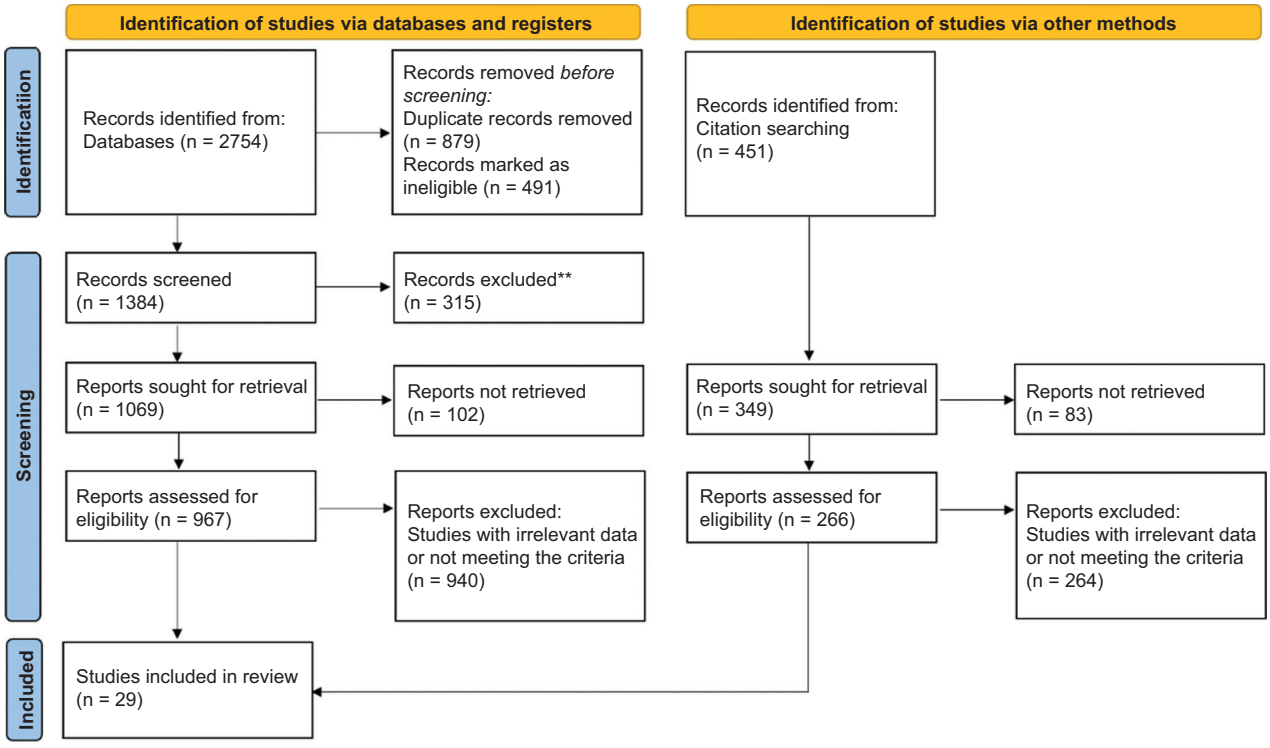

Figure 1 PRISMA flow chart

Table 1 Study characteristics

Author [ref.]	Year	Total individuals	Risk of bias
Sarawagi [8]	2016	198	Low risk
Fujimoto [9]	2020	480	Moderate risk
Gunduz [4]	2021	307	Low risk
Alijiffry [10]	2020	325	Moderate risk
Garg [11]	2022	100	Moderate risk
Tastemur [12]	2020	930	Low risk
Adetepe [13]	2016	1041	Low risk
Krisem [14]	2025	184	Low risk
Taghavi [15]	2017	290	Low risk
Zhu [16]	2024	300	Moderate risk
Gupta [17]	2016	338	Low risk
Agarwal [18]	2023	265	Moderate risk
Sudeep [19]	2024	252	Low risk
Mohammed [20]	2024	307	Moderate risk
Rathnayaka [21]	2023	180	Low risk
Cao [22]	2024	232	Low risk
Karakas [23]	2023	172	Moderate risk
Tsitouridis [24]	2006	622	Low risk
Vijay [25]	2023	226	Moderate risk
Taourel [26]	1996	126	Moderate risk
Dikici [27]	2025	303	Moderate risk
Seretis [28]	2022	284	High risk
Filippo [29]	2008	350	Moderate risk
Haroon [30]	2024	152	Moderate risk
Alparslan [31]	2025	232	Moderate risk
Abdelkareem [32]	2019	302	Low risk
Bozdag [33]	2023	424	Moderate risk
Sipahi [34]	2015	126	High risk
Sherifi [35]	2018	63	Moderate risk

P=0.866). Finally, this variation was not significantly associated with choledocholithiasis (RR 0.98, 95%CI 0.82-1.17; P=0.897).

Low medial insertion

Low medial cystic duct insertion is a specific type of anomaly that was reported in most of the included studies. Its prevalence was found to be 4.8% (95%CI 0.03-0.06). Patients' sex had no significant effect (OR 1.12, 95%CI 0.73-1.72; P=0.580). Nor was there any significant association between this variation and choledocholithiasis (RR 0.70, 95%CI 0.07-6.71; P=0.787).

Parallel

A parallel cystic duct was present in 8.6% of individuals (95%CI 0.04-0.14). The effect of patient's sex was not significant (OR 1.31, 95%CI 0.78-2.19; P=0.300). This variation had one of the weakest connections with the development of choledocholithiasis (RR 0.90, 95%CI 0.38-2.10; P=0.658).

Spiral

A spiral cystic duct was identified in 11.8% of patients (95%CI 0.06-0.18). A male vs. female sex analysis was not feasible, but this anomaly had a significant association with choledocholithiasis (RR 1.41, 95%CI 1.06-1.86; P=0.015).

Short cystic duct

A short cystic duct was a relatively rare anatomical variation, present in only 2.1% of the total individuals (95%CI 0.01-0.03). The effect of patients' sex was not significant (OR 1.56, 95%CI 0.72-3.37; P=0.252). The association of this anomaly with choledocholithiasis was very weak (RR 0.46, 95%CI 0.07-2.91; P=0.521).

Long cystic duct

A long cystic duct was identified in 9.1% of the total individuals (95%CI 0.02-0.20) (Table 2). However, there was a highly significant positive association between this variation and choledocholithiasis development (RR 1.50, 95%CI 1.18-1.90; P<0.001).

CCA

The CCA, or the angle between the cystic duct and the common bile duct at the site of insertion, was calculated for patients with and without choledocholithiasis. The CCA was 47.1° in the former group (95%CI 30.52-63.68°) and 40.8° (95%CI 31.87-49.83°) in the latter. Thus, patients with lithiasis in their bile duct tended to have a wider angle of insertion between the cystic duct and the common bile duct.

Other variations

Two other extremely rare variation were also reported in the literature. Specifically, a double cystic duct was found in 0.38% of the population (95%CI 0.00-0.01), while an insertion of the cystic duct to the right hepatic duct was present in 0.5% of the assessed individuals (95%CI 0.00-0.01).

Table 2 Area subgroup analysis results

Parameters	Posterior insertion (%)	Low insertion (%)	Spiral course (%)	Long cystic duct (%)
South Asia	14.6	5.8	8.6	6.5
West Asia	22.3	4.8	-	8.9
East Asia	11.6	5.2	35.4	13.5
Middle East	3.5	3.6	9.5	5.2
America	-	8.7	-	-
Africa	17.5	21.8	16.9	-
Europe	11.3	6.2	7.1	-
P-value	<0.001	<0.001	0.001	0.009

Area subgroups

For the anatomical variations of the cystic duct that presented with a higher RR for choledocholithiasis, additional subgroup analyses were performed in order to determine how their prevalence varied across different geographical areas and ethnic groups.

For low insertion, the African population presented with a significantly higher prevalence (21.8%) compared to the other areas, while Middle Eastern patients were found to have the smallest prevalence (Fig. 2).

Regarding the posterior insertion of the cystic duct, studies that were conducted in the western part of Asia were associated with greater numbers for this type of variation (22.3%), while the Middle Eastern population again had the lowest prevalence (3.5%) (Fig. 3).

Regarding a spiral course of the cystic duct, the Eastern Asian populations presented with the highest prevalence of this type of variation (35.4%), while the European and south Asian individuals had the lowest prevalence (7.1% and 8.6%, respectively).

Finally, a long cystic duct was more common in Eastern Asian and Western Asian populations, with prevalences of 13.5% and 8.9%, respectively. The Middle East area had the lowest prevalence (5.2%) (Table 2).

Risk of bias assessment

Each study that was included in this analysis was assessed using to the AQUA Tool (Supplementary Table 2). Additionally, Peters' test for funnel plot asymmetry showed no evidence of bias in the prevalence of any of the cystic duct variations assessed (Supplementary Fig. 1-10). In the sensitivity analysis, none of the findings showed any significant change in results or heterogeneity after the omission of each study (Supplementary Table 3).

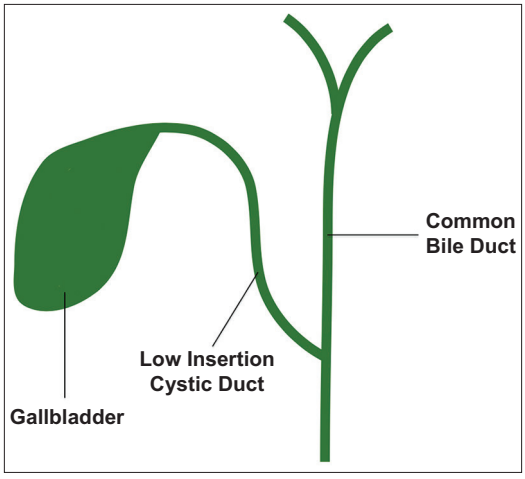

Figure 2 Low insertion of the cystic duct

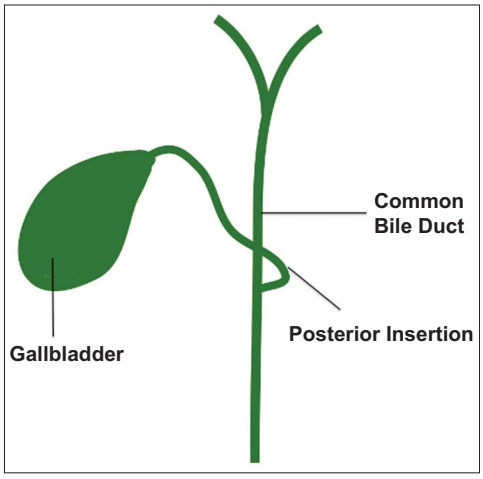

Figure 3 Posterior insertion of the cystic duct

Discussion

This systematic review with meta-analysis investigated, assessed and presented the prevalence of the most clinically significant anatomical variations of the cystic duct, along with their variation across patient's sex and geographic regions. Furthermore, this is the first meta-analysis to investigate the risk and association between each anatomical variation and the development of choledocholithiasis. One other systematic review presented the prevalences of each cystic variation, without analyzing its variability through different moderators and factors [36] (Table 3).

Several variations showed meaningful associations with choledocholithiasis. Low insertion (RR 1.46, 95%CI 1.06-1.76), posterior insertion (RR 1.32, 95%CI 1.07-1.60), a spiral course (RR 1.41, 95%CI 1.06-1.86), and a long cystic duct (RR 1.50, 95%CI 1.18-1.90) were all positively associated with lithiasis. In contrast, anterior, medial, parallel and low medial insertions

Table 3 Comparison of study findings with existing literature

Parameters	Ekwesianya *et al* (%)	Current study (%)
High insertion	14.0	17.2
Anterior insertion	7.6	3.6
Posterior insertion	29.6	13.8
Long cystic duct	2.6	9.1
Double cystic duct	0.5	0.4
Low insertion	11.2	5.6
Medial insertion	9.8	10.3
Parallel course	7.4	8.6
Insertion into right hepatic duct	1.1	0.5
Short cystic duct	3.2	2.1

showed no significant association, while a short cystic duct demonstrated the weakest relationship (RR 0.46, 95%CI 0.07-2.91). Sex-based analysis did not demonstrate a higher prevalence for either gender, with the exception of posterior insertion, which was more prominent in females. Collectively, these findings indicate that cystic duct anatomical variations can be identified equally in both female and male patients.

As far as the geographical analysis is concerned, the results demonstrated that Middle Eastern populations consistently exhibited the lowest prevalence of cystic duct variations associated with the highest risk of choledocholithiasis. In contrast, both Eastern and Western Asian populations showed a higher overall frequency of these high-risk anatomical variants, suggesting a greater susceptibility to anatomy-related choledocholithiasis in these groups. Finally, special mention needs to be made for the African population, whose low insertion prevalence (21.8%), was more than double the frequency for the American population, which was in second place. Hence, it should also be noted that African patients have a stronger association with this highly significant risk factor for development of bile duct stones.

Thus, based on the findings of the present study, patients exhibiting the aforementioned cystic duct variations, which are associated with an increased risk of choledocholithiasis, may warrant assessment and treatment using more radical means. Patients that belong in the aforesaid high-risk groups have a greater need to undergo imaging evaluation in order to determine the presence of this risk factor, which will help in preoperative and management planning.

The exact pathophysiological mechanisms underlying the association between cystic duct anatomical variations and choledocholithiasis remain a subject of ongoing debate. Much of the current literature focuses on altered biliary hemodynamics and primary stone formation. Anomalous configurations inherently increase resistance to bile flow, promoting biliary stasis. Zhu *et al* and Pitt *et al*. [16,37] postulated that this increased resistance significantly reduces bile flux. According to Poiseuille's law, this reduction in flow velocity is associated with greater bile viscosity, which creates a highly lithogenic environment and facilitates the precipitation of primary stones [16,38]. Furthermore, a tortuous or abnormal anatomy may subject the cystic duct mucosa to altered shear stress and constant physical collision from bile flow. The resulting cycle of chronic mucosal injury, localized inflammation and subsequent repair can either act directly as a focal point for stone crystallization, or progressively narrow the ductal lumen, thereby exacerbating stasis [37,38].

However, the specific pathophysiology regarding low-inserting cystic ducts presents a more complex paradigm. While a recent study has established a clear clinical correlation between intrapancreatic low insertion and common bile duct stones [39], the exact mechanical etiology remains elusive. Attributing this association solely to stagnation is controversial, as some authors argue that variations in the duct's course or length are far more likely to cause significant stasis than the insertion site itself [11]. Interestingly, Garg *et al* [4] highlight that structural variations do not universally guarantee downstream stone progression. They propose that severe flow restriction in an abnormal cystic duct might actually trap forming stones within the cystic duct, preventing their transit into the common bile duct and theoretically decreasing the clinical incidence of choledocholithiasis.

Alternatively, the anatomical association may be driven by a migratory mechanism, where existing secondary stones travel from the gallbladder into the common bile duct. Although direct evidence for this specific pathway is currently limited, Tastemur *et al* [12] demonstrated that anterior, posterior, and low medial insertions are associated with a significantly higher coexistence of gallbladder and choledochal stones. This finding supports a mechanical theory wherein certain anatomical insertion angles may facilitate the passage and migration of preexisting gallstones into the main biliary tree.

Building upon this theory, another clinically relevant anatomical variation, albeit reported by a limited number of studies, is a large cystic duct diameter. Krisem *et al* [14] demonstrated a statistically significant relationship (OR 2.22, 95%CI 1.32-3.73) between a dilated cystic duct and choledocholithiasis, suggesting its potential utility as a strong anatomical predictor for stone occurrence. Mechanistically, this aligns with the migratory theory; a case report by Tong *et al* [40] hypothesizes that an abnormally wide cystic duct offers less physical resistance, thereby facilitating the unobstructed transit of preexisting gallbladder stones directly into the common bile duct.

Given the inherent predisposition to primary choledocholithiasis in patients with specific high-risk cystic duct variations, clinical management should focus on mitigating synergistic risk factors. While anatomical morphology is unalterable, studies consistently demonstrate that primary stone formation is multifactorial [11]. Recent multivariate analyses indicate that, alongside ductal anatomy, advanced age, female sex, and specifically modifiable factors such as an elevated body mass index (≥24 kg/m^2), hyperlipidemia and dietary habits are independent risk factors for lithiasis [11,41]. Therefore, when a high-risk anatomical variation (such as a long or low-inserting duct) is identified, clinicians should proactively address these concurrent risks. Advising lifestyle modifications is a critical preventative measure to minimize the cumulative risk of primary bile duct stone development in these susceptible individuals.

All of these variations hold additional significance during surgical operation concerning the gallbladder and the biliary tree. One of the most serious complications during biliary surgery is the failure to accurately identify cystic duct anatomy, resulting in confusion with the common bile duct. In such cases, misidentification may lead to inadvertent transection of the common bile duct [42]. Other variants, such as cystic duct drainage into the right hepatic duct, can distort the hepatocytic triangle, thereby heightening the likelihood of inadvertent biliary injury during dissection. Similarly, the presence of a double cystic duct can lead to significant intraoperative confusion and, if unrecognized, may result in inadequate clipping and postoperative bile leakage [11]. Furthermore, given that low insertion has a relatively high association with stone formation, not identifying such a variation could lead to complications and challenges during endoscopic retrograde cholangiopancreatography.

Moreover, the presence of a long cystic duct can create further challenges for the responsible surgeons. Apart from the great danger of confusing the long cystic duct with the common bile duct and causing a serious iatrogenic injury, an additional risk of transecting or ligating in close proximity to the common bile duct could result in the latter undergoing strictures or narrowing in that area [42]. Patients with a short or absent cystic duct should be carefully assessed during surgery. This group of patients are associated with an unintentional clamping of the common bile and hepatic duct, as the abnormal anatomy of the cystic duct increases the risk of tenting of the 2 aforementioned structures [8].

One procedure that is significantly impacted by the abnormal anatomy of the cystic duct is the endoscopic naso-gallbladder drainage procedure [11]. Such operations rely heavily on the anatomy of the cystic duct, as well as its insertion into the common bile duct. The high failure percentages that several studies have reported seem to be a result of the notably high difficulty of cystic duct cannulation, which is based on the accurate identification of the cystic duct orifice [16,43,44]. However, the high variability of cystic duct insertion into the common bile duct can play a major role in the greater difficulty involved in this procedure. Furthermore, the direction and spatial relativity of the cystic duct compared to the bile duct also play an important role. More precisely, in cases where the cystic duct is located on the left or lower side of the common bile duct, successful wire or catheter cannulation becomes extremely difficult [43].

This analysis is strengthened by a clearly defined and independently executed study selection and data extraction process, which was able to reduce the risk of bias. Another strength was the use of rigorous statistical methodology, including extensive pooled prevalences, subgroup analyses, comprehensive risk of bias and publication bias assessments (AQUA tool, Peters' test), and sensitivity analyses confirming the robustness of pooled estimates. The transparent use of validated tools and open-source statistical packages further enhances the reproducibility and reliability of the findings.

This systematic review and meta-analysis nevertheless had a few limitations. Specifically, several studies were characterized as Moderate or High Risk according to the AQUA tool. Furthermore, high between-study heterogeneity persisted across most analyses, probably reflecting differences in patient groups, clinical factors, and population characteristics. There were some imbalances in the data distribution regarding the sex, and geographic area analyses, which may affect the generalizability of results. There were some limitations to clinical data reporting, as not all studies reported the association between the presence of any variation and choledocholithiasis. It should be noted that, even though high heterogeneity is expected in anatomy-related analyses, it can limit the precision of a single "global mean". Thus, readers should interpret the pooled estimates with caution and contextualize these findings within the field of anatomical meta-analysis.

In conclusion, cystic duct anatomy plays a major role during the clinical and surgical assessment of patients. Variations such as low insertion, posterior insertion, spiral course and long cystic ducts demonstrate the strongest associations with stone formation, particularly in certain geographic populations, including Eastern and Western Asians. Awareness of these variations is essential for guiding surgical planning and minimizing the existing risk factors. Future research should focus more on the impact of these variations on the development of choledocholithiasis, by directly comparing the biliary anatomy between the 2 stone-related groups. Additionally, research from diverse geographical areas could also prove to be useful in obtaining a clearer image of the variation trends of cystic duct anatomy.

Summary Box

What is already known:

- The anatomical configuration of the cystic duct is highly variable, with the standard right mid-lateral insertion present in only 51-72% of individuals
- While individual studies have hypothesized an association between specific cystic duct variations and choledocholithiasis, there was no previous comprehensive meta-analysis quantifying this exact risk

What the new findings are:

- Low insertion, posterior insertion, a spiral course and a long cystic duct are statistically associated with a significantly greater risk of developing choledocholithiasis
- The prevalence of high-risk anatomical variants demonstrates significant geographic variability, highlighted by a notably high frequency of low insertions among African populations and spiral courses in Eastern Asian cohorts
- Sex-based analysis revealed no significant difference in the overall prevalence of cystic duct variations between male and female patients, with the sole exception of posterior insertion being more prominent in females

References

1. Zhou Y, Zha WZ, Zhang YP, Xuan FM, Wang HW, Wu XD. Treatment for recurrent choledocholithiasis: endoscopic? or laparoscopic? A prospective cohort study. *Surg Endosc* 2025;**39**:868-874.
2. Turner MA, Fulcher AS. The cystic duct: normal anatomy and disease processes. *Radiographics* 2001;**21**:3-22.
3. Doherty GM, Way LW. Current Surgical Diagnosis & Treatment. 12th ed./McGraw-Hill Medical; 2005.
4. Gündüz N, Doğan MB, Alacagöz M, Yağbasan M, Söylemez UPO, Atalay B. Anatomical variations of cystic duct insertion and their relationship with choledocholithiasis: an MRCP study. *Egypt J Radiol Nucl Med* 2021;**52**:202.
5. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;**372**:n71.
6. Peters JL, Sutton AJ, Jones DR, Abrams KR, Rushton L. Comparison of two methods to detect publication bias in meta-analysis. *JAMA* 2006;**295**:676-680.
7. Henry BM, Tomaszewski KA, Ramakrishnan PK, et al. Development of the anatomical quality assessment (AQUA) tool for the quality assessment of anatomical studies included in meta-analyses and systematic reviews. *Clin Anat* 2017;**30**:6-13.
8. Sarawagi R, Sundar S, Gupta SK, Raghuwanshi S. Anatomical variations of cystic ducts in magnetic resonance cholangiopancreatography and clinical implications. *Radiol Res Pract* 2016;**2016**:3021484.
9. Fujimoto N, Tomimaru Y, Yamamoto T, et al. Clinical investigation of the cystic duct variation based on the anatomy of the hepatic vasculature. *Surg Today* 2020;**50**:396-401.
10. Aljiffry M, Abbas M, Wazzan MAM, Abduljabbar AH, Aloufi S, Aljahdli E. Biliary anatomy and pancreatic duct variations: a cross-sectional study. *Saudi J Gastroenterol* 2020;**26**:188-193.
11. Garg S, Dutta U, Chaluvashetty SB, et al. The anatomy of the cystic duct and its association with cholelithiasis: MR cholangiopancreatographic study. *Clin Anat* 2022;**35**:847-854.
12. Taştemur Y. Anatomical variations of the cystic duct in Turkish population and their association with biliary track stone. *J Coll Physicians Surg Pak* 2020;**30**:1005-1008.
13. Adatepe M, Adibelli ZH, Esen OS, Imamoglou C, Yildirim M, Erkan N. Anatomic variations of biliary ducts: magnetic resonance cholangiopancreatography findings of 1041 consecutive patients. *Eur Surg* 2016;**48**:296-303.
14. Krisem M, Aleenajitpong N, Tungtrongchitr N. Cystic duct diameter as an independent predictor of choledocholithiasis in patients undergoing magnetic resonance cholangiopancreatography. *Egypt J Radiol Nucl Med* 2025;**56**:77.
15. Taghavi A, Azizi M, Rasekhi A, Gholami Z. Anatomic variations of the cystic duct in magnetic resonance cholangiopancreatography in Shiraz: a cross-sectional study. *Iran J Med Sci* 2022;**47**:48-52.
16. Zhu JH, Zhao SL, Kang Q, Zhu Y, Liu LX, Zou H. Classification of anatomical morphology of cystic duct and its association with gallstone. *World J Gastrointest Surg* 2024;**16**:307-317.
17. Gupta A, Rai P, Singh V, Gupta RK, Saraswat VA. Intrahepatic biliary duct branching patterns, cystic duct anomalies, and pancreas divisum in a tertiary referral center: a magnetic resonance cholangiopancreaticographic study. *Indian J Gastroenterol* 2016;**35**:379-384.
18. Agarwal S, Choudhury PR, Biswas KK, Baruah P, Baro A. Anatomical variations of cystic ducts in magnetic resonance cholangiopancreatography: a retrospective study with 265 patients. *Int J Anat Res* 2022;**10**:8391-8397.
19. Sudeep KC, Banjade UR, Ghimire P. Anatomical variations of the cystic duct assessed by magnetic resonance cholangiopancreatography (MRCP): a cross-sectional study at tertiary center of Nepal. *Journal of Patan Academy of Health Sciences* 2024;**11**:15-20.
20. Mohammed TAA, Abdelmotalab MAA, Abdelaziz OAE. Variations in cystic duct anatomy using magnetic resonance cholangiopancreatography and their clinical significant in the Sudanese. *Sri Lanka Anatomy Journal* 2024;**8**:18-26.
21. Rathnayaka P, Dassanayake Y, Pallewatte A. Analysis of anatomical variations of the cystic duct in magnetic resonance cholangiopancreatography. *Sri Lanka Journal of Radiology* 2023;**9**:1-6.
22. Cao Z, Zhou J, Wei L, He HY, Li J. Effect of the extrahepatic bile duct anatomy on choledocholithiasis and its clinical significance. *World J Gastrointest Surg* 2024;**27**:1363-1370.
23. Karakas HM, Celik T, Alicioglu B. Bile duct anatomy of the Anatolian Caucasian population: Huang classification revisited. *Surg Radiol Anat* 2008;**30**:539-545.
24. Tsitouridis I, Lazaraki G, Papastergiou C, Pagalos E, Germanidis G. Low conjunction of the cystic duct with the common bile duct: does it correlate with the formation of common bile duct stones? *Surg Endosc* 2007;**21**:48-52.
25. Vijay S, Ragupathi S. Magnetic resonance cholangiopancreatographic evaluation of cystic duct anatomical variants in Pondicherry population. *IAIM* 2019;**6**:81-86.
26. Taourel P, Bret PM, Reinhold C, Barkun AN, Atri M. Anatomic variants of the biliary tree: diagnosis with MR cholangiopancreatography. *Radiology* 1996;**199**:521-527.
27. Dikici TF, Fazlıoğulları Z, Özcan AG, Koplay M, Karabulut AK, Uysal İİ. Anatomical study of bile ducts by magnetic resonance cholangiopancreatography. *Med J Bakirkoy* 2025;**21**:83-89.
28. Seretis C, Zohdy M, Padgett B, Janardhanan P. Routine extensive dissection of the cystic duct during laparoscopic cholecystectomy to reduce the risk of residual choledocholithiasis: an unnecessary step and a potentially hazardous concept. *Prz Gastroenterol* 2022;**17**:67-72.
29. De Filippo M, Calabrese M, Quinto S, et al. Congenital anomalies and variations of the bile and pancreatic ducts: magnetic resonance cholangiopancreatography findings, epidemiology and clinical significance. *Radiol Med* 2008;**113**:841-859.
30. Haroon Q, Shamim B, Ajmal R, Irfan N, Nasir S. Cystic duct variations in adult population; a magnetic resonance based cholangiopancreaticography at a tertiary care referral hospital. *J Adv Med Med Res* 2024;**36**:298-304.
31. Alparslan AS, Ocal S, Buldukoglu OC, et al. Effect of biliopancreatic tree anatomy on development of acute gallstone pancreatitis. *BMC Gastroenterol* 2025;**25**:269.
32. Abdelkareem H, Ali R, Jibrini M, et al. A study of the anatomic variations of the pancreatico-biliary system in Palestine: a national study. *Int Surg J* 2019;**6**:1020-1028.
33. Bozdag E, Sonmez S, Somuncu E, Yilmaz S, Basaran C, Bozkurt MA. Extrahepatic biliary tract variations is an effect for acute calculous cholecystitis. *J Coll Physicians Surg Pak* 2022;**32**:991-995.
34. Sipahi M, Erkoç MF, Serin HI, Börekçi H, Banlı O. A novel approach for differentiating etiology of gallstone formation: sistocholedochal angle. *Eur Rev Med Pharmacol Sci* 2015;**19**:1063-1067.
35. Sherifi F, Bajraktari I, Bexheti S, Lahu A, Gashi Z, Shatri J. Anatomic variations of the cystic duct assessed by magnetic resonance cholangiopancreatography. *Ital J Anat Embryol* 2018;**123**:158-164.
36. Ekwesianya AC, Ayantunde BO, Ayantunde AA. A cautionary tale of anatomical variations of the extrahepatic biliary system and their implications for surgical procedures: a systematic literature review. *Surg Radiol Anat* 2025;**47**:145.
37. Pitt HA, Roslyn JJ, Kuchenbecker SL, Doty JE, Denbesten L. The role of cystic duct resistance in the pathogenesis of cholesterol gallstones. *J Surg Res* 1981;**30**:508-514.
38. Luo X, Li W, Bird N, Chin SB, Hill NA, Johnson AG. On the

mechanical behavior of the human biliary system. *World J Gastroenterol* 2007;**13**:1384-1392.
39. Renzulli M, Brocchi S, Marasco G, et al. A new quantitative classification of the extrahepatic biliary tract related to cystic duct implantation. *J Gastrointest Surg* 2021;**25**:2268-2279.
40. Tong M, Li Y, Sun X, et al. Choledocholithiasis caused by anatomical variation of cystic duct: a case report and review of the literature. *Laparosc Endosc Robot Surg* 2022;**5**:40-44.
41. Lam R, Zakko A, Petrov JC, Kumar P, Duffy AJ, Muniraj T. Gallbladder disorders: a comprehensive review. *Dis Mon* 2021;**67**:101130.
42. Mansour S, Kluger Y, Khuri S. Primary recurrent common bile duct stones: timing of surgical intervention. *J Clin Med Res* 2022;**14**:441-447.
43. Woo YS, Lee JK. Endoscopic nasogallbladder drainage in patients with acute cholecystitis: what's predictive factor for technical success? *Gut Liver* 2015;**9**:141-142.
44. Kim JY, Kim KW, Ahn CS, et al. Spectrum of biliary and nonbiliary complications after laparoscopic cholecystectomy: radiologic findings. *AJR Am J Roentgenol* 2008;**191**:783-789.

Supplementary material

Supplementary Table 1 PRISMA checklist

Section and Topic	Item #	Checklist item	Location where item is reported
		TITLE	
Title	1	Identify the report as a systematic review.	Page 1
		ABSTRACT	
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	
		INTRODUCTION	
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 4
		METHODS	
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 5
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 5
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Page 5
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 5-6
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 5-7
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g., for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 5-7
	10b	List and define all other variables for which data were sought (e.g., participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Page 5-7
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool (s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 6-7
Effect measures	12	Specify for each outcome the effect measure (s) (e.g., risk ratio, mean difference) used in the synthesis or presentation of results.	Page 5-6
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g., tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page 5-6
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 5-6
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 5-7
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 5-7
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g., subgroup analysis, meta-regression).	Page 6-7
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Page 5-7
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Page 5-7
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Page 5-7

(*Contd...*)

Supplementary Table 1 (*Continued*)

Section and Topic	Item #	Checklist item	Location where item is reported
		RESULTS	
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 7-8
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Page 7-8
Study characteristics	17	Cite each included study and present its characteristics.	Page 7-8
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Supplementary File
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g., confidence/credible interval), ideally using structured tables or plots.	Page 7-12
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Page 12
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g., confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Page 7-12
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Page 7-13
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Page 10-13
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Page 7-12
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Page 7-12
		DISCUSSION	
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 13-16
	23b	Discuss any limitations of the evidence included in the review.	Page 18
	23c	Discuss any limitations of the review processes used.	Page 18
	23d	Discuss implications of the results for practice, policy, and future research.	Page 13-18
		OTHER INFORMATION	
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 19-20
Competing interests	26	Declare any competing interests of review authors.	Page 19-20
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	

Supplementary Table 2 Risk of bias assessment based on the AQUA tool

Parameters [ref.]	Objectives and subject characteristics	Study design	Methodology characterization	Descriptive anatomy	Reporting of results
Sarawagi [8]	Low risk	Moderate risk	Low risk	Low risk	Low risk
Fujimoto [9]	Moderate risk	Moderate risk	Moderate risk	Low risk	Moderate risk
Gunduz [4]	Moderate risk	Moderate risk	Low risk	Low risk	Low risk
Alijiffry [10]	Moderate risk	Moderate risk	Moderate risk	Moderate risk	Low risk
Garg [11]	Moderate risk	Moderate risk	Moderate risk	Low risk	Moderate risk
Tastemur [12]	Low risk	Low risk	Moderate risk	Low risk	Low risk
Adetepe [13]	Low risk	Moderate risk	Low risk	Low risk	Low risk
Krisem [14]	Low risk	Moderate risk	Low risk	Low risk	Low risk
Taghavi [15]	Low risk	Low risk	Moderate risk	Moderate risk	Low risk
Zhu [16]	Low risk	Moderate risk	Moderate risk	Moderate risk	Low risk
Gupta [17]	Low risk	Moderate risk	Low risk	Low risk	Low risk
Agarwal [18]	Low risk	Low risk	Moderate risk	Moderate risk	Low risk
Sudeep [19]	Low risk	Moderate risk	Moderate risk	Low risk	Low risk
Mohammed [20]	Low risk	Moderate risk	Moderate risk	Moderate risk	Low risk
Rathnayaka [21]	Low risk	Moderate risk	Low risk	Low risk	Low risk
Cao [22]	Moderate risk	Low risk	Low risk	Moderate risk	Low risk
Karakas [23]	Moderate risk	Moderate risk	Moderate risk	Moderate risk	Low risk
Tsitouridis [24]	Low risk	Low risk	Moderate risk	Moderate risk	Low risk
Vijay [25]	Moderate risk	Moderate risk	Moderate risk	Moderate risk	Low risk
Taourel [26]	Moderate risk	Low risk	Moderate risk	Low risk	Moderate risk
Dikici [27]	Moderate risk	Moderate risk	Low risk	Moderate risk	Moderate risk
Seretis [28]	High risk	Moderate risk	Moderate risk	Moderate risk	Low risk
Filippo [29]	Low risk	Moderate risk	Low risk	Moderate risk	Moderate risk
Haroon [30]	Moderate risk	Moderate risk	Moderate risk	Low risk	Low risk
Alparslan [31]	Moderate risk	Moderate risk	Moderate risk	Low risk	Low risk
Abdelkareem [32]	Low risk	Low risk	Moderate risk	Moderate risk	Low risk
Bozdag [33]	Moderate risk	Moderate risk	Low risk	Moderate risk	Moderate risk
Sipahi [34]	Moderate risk	High risk	Moderate risk	High risk	Moderate risk
Sherifi [35]	Low risk	Moderate risk	Low risk	Moderate risk	Moderate risk

Supplementary Table 3 Leave-one-out analysis results. A leave-one-out sensitivity analysis was conducted to assess the influence of each individual study on the overall estimates

Variable	Range of prevalence	I^2 heterogeneity	P-value
Spiral course	8.9-13.7%	≈92%	0.846
Medial insertion	9.4-12.0%	≈96%	0.486
Low insertion	4.3-6.1%	≈91%	0.766
Low medial insertion	3.9-5.3%	≈80%	0.392
High insertion	15.2-18.4%	≈97%	0.303
Anterior insertion	2.9-4.2%	≈85%	0.683
Posterior insertion	12.7-14.2%	≈91%	0.202
Parallel course	7.3-9.1%	≈85%	0.103
Long cystic duct	7.4-10.1%	≈84%	0.292
Short cystic duct	1.8-2.9%	≈92%	0.484

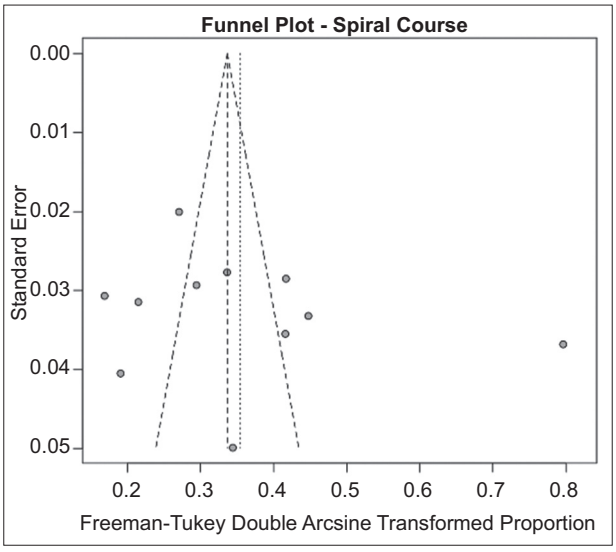

Figure 1 Spiral course
Linear regression test of funnel plot asymmetry
Test result: t = 1.35, df = 9, P-value = 0.215
Bias estimate 228.1644 (SE = 169.0058)

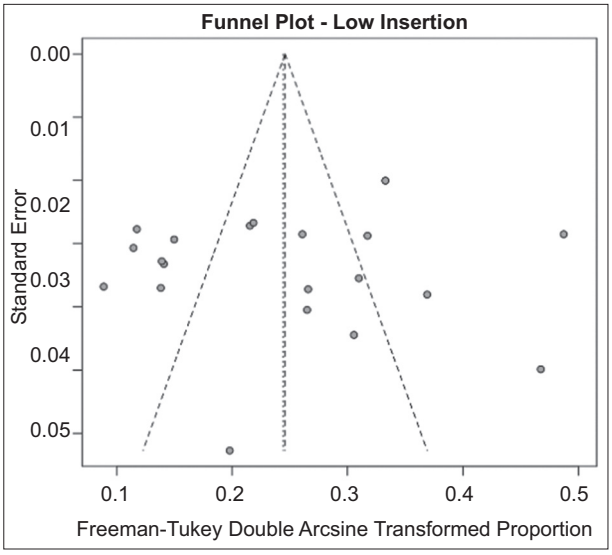

Figure 2 Low insertion
Linear regression test of funnel plot asymmetry
Test result: t = 0.33, df = 18, P-value = 0.742
Bias estimate: 3.4819 (SE = 10.4335)

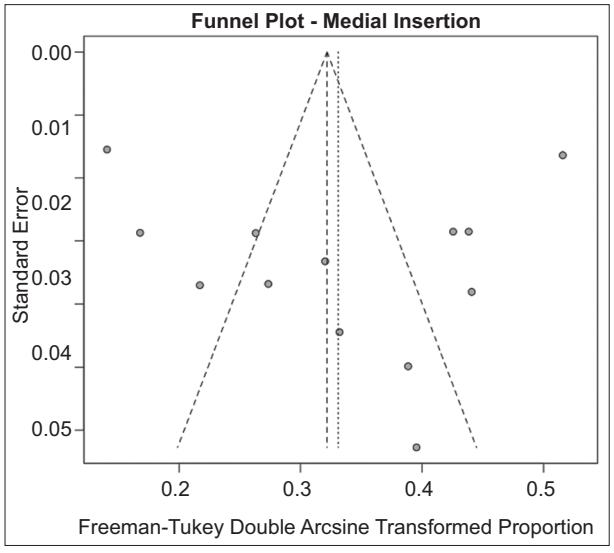

Figure 3 Medial insertion
Linear regression test of funnel plot asymmetry
Test result: t = -1.15, df = 11, P-value = 0.276
Bias estimate: -12.8039 (SE = 11.1657)

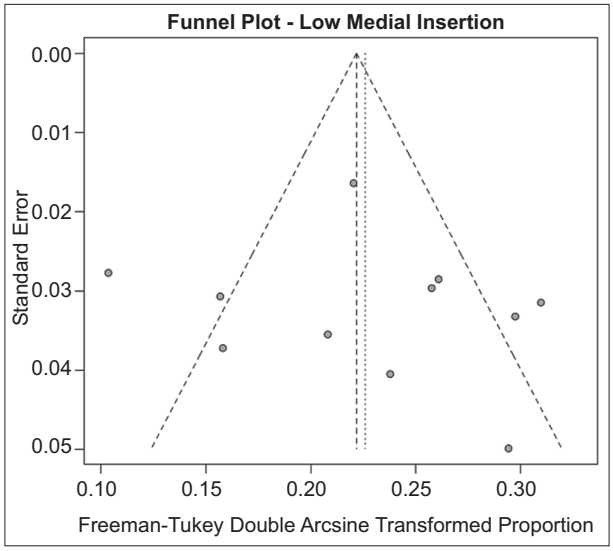

Figure 4 Low medial insertion
Linear regression test of funnel plot asymmetry
Test result: t = 1.05, df = 9, P-value = 0.322
Bias estimate: 7.238 (SE = 6.9044)

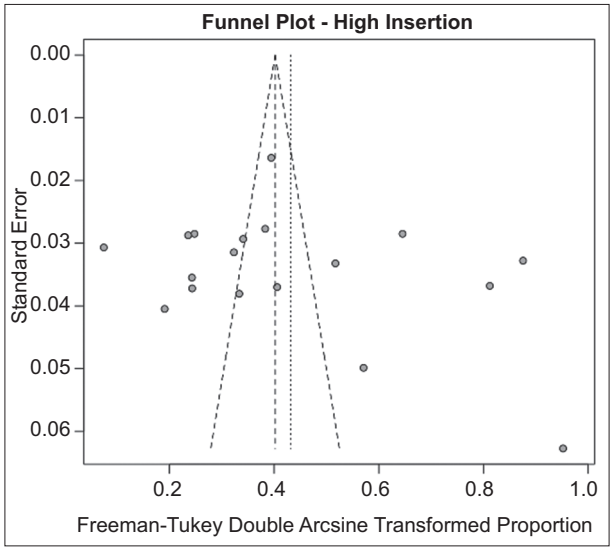

Figure 5 High insertion
Linear regression test of funnel plot asymmetry
Test result: t = 1.85, df = 16, P-value = 0.083
Bias estimate: 32.6701 (SE = 17.6594)

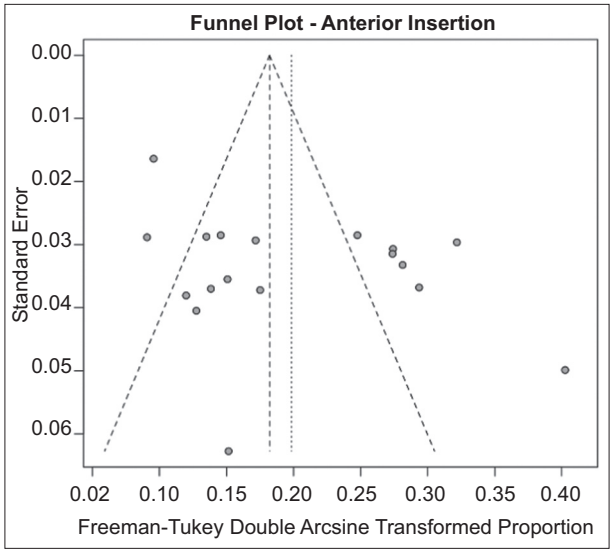

Figure 6 Anterior insertion
Linear regression test of funnel plot asymmetry
Test result: t = 2.05, df = 16, P-value = 0.065
Bias estimate: 17.4783 (SE = 8.5433)

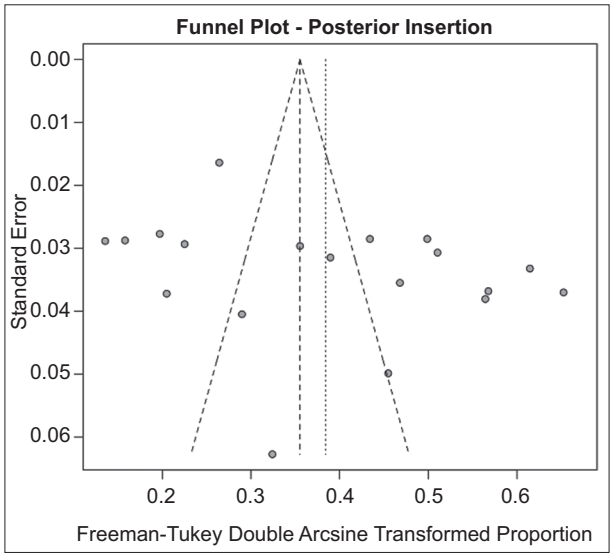

Figure 7 Posterior insertion
Linear regression test of funnel plot asymmetry
Test result: t = 1.55, df = 17, P-value = 0.140
Bias estimate: 23.2822 (SE = 15.0466)

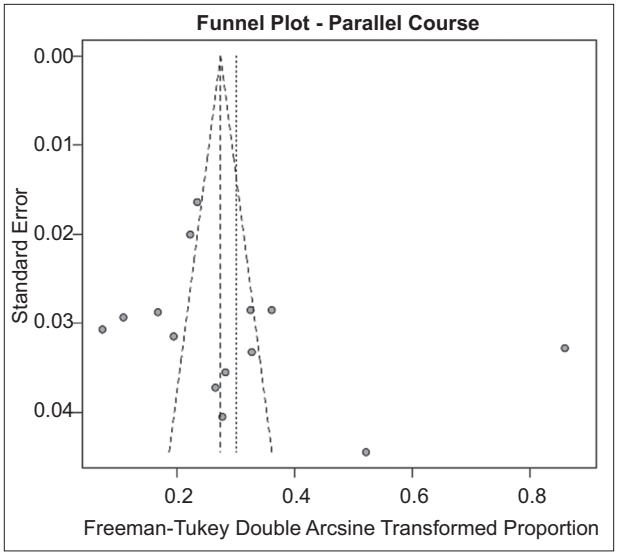

Figure 8 Parallel course
Linear regression test of funnel plot asymmetry
Test result: t = 1.45, df = 12, P-value = 0.172
Bias estimate: 48.0492 (SE = 33.0865)

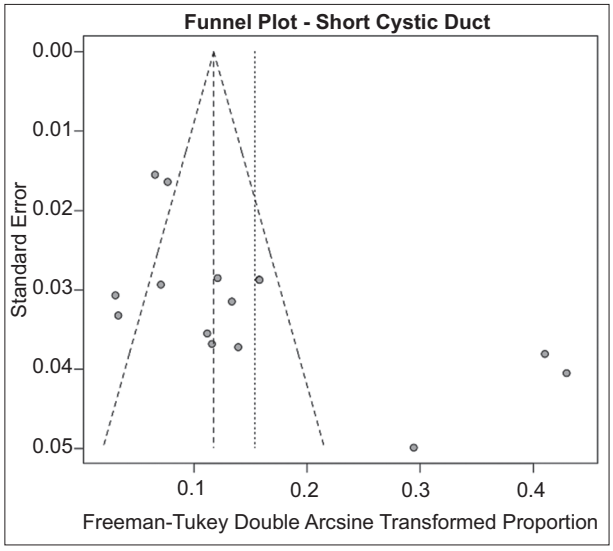

Figure 9 Short cystic duct
Linear regression test of funnel plot asymmetry
Test result: t = 3.14, df = 11, P-value = 0.110
Bias estimate: 44.1657 (SE 14.0793)

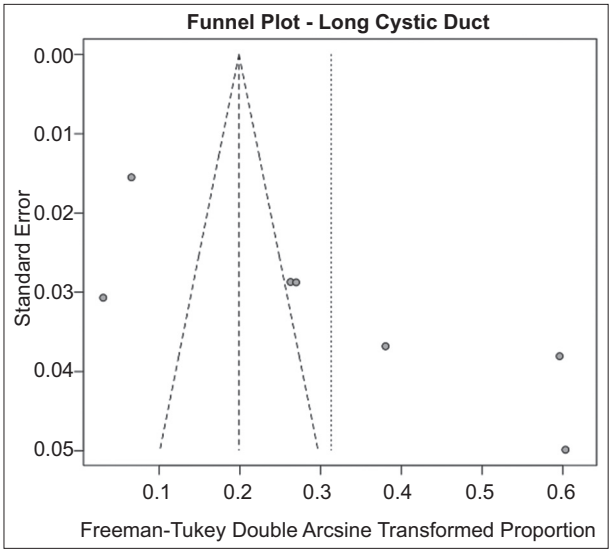

Figure 10 Long cystic duct
Linear regression test of funnel plot asymmetry
Test result: t = 2.12, df = 13, P-value = 0.064
Bias estimate: 23.9927 (SE = 11.3066)