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Original article

# Predictive factors of spontaneous common bile duct clearance and unnecessary ERCP in patients with choledocholithiasis

Fábio Pereira Correia [a,*], Henrique Coelho [a], Mónica Francisco [a], Gonçalo Alexandrino [a], Joana Carvalho Branco [a], Jorge Canena [a,b], David Horta [a,b], Luís Carvalho Lourenço [a,b]

[a] Gastroenterology Department, Hospital Prof. Dr. Fernando Fonseca, Amadora 2720-276, Portugal
[b] Gastroenterology Center, Hospital CUF Tejo/ Nova Medical School – Faculdade de Ciências Médicas, Lisbon 1600, Portugal

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ABSTRACT

*Background:* Endoscopic retrograde cholangiopancreatography (ERCP) is the first-line procedure for choledocholithiasis treatment. However, it is associated with a 10 % rate of adverse events. Spontaneous migration of common bile duct (CBD) stones occurs in 6–33 % of choledocholithiasis cases, making ERCP avoidable. This study aimed to identify predictors of spontaneous CBD stones' migration.

*Methods:* Retrospective study including patients diagnosed with choledocholithiasis and submitted to ERCP. Patients were divided into 2 groups considering spontaneous stone migration (i.e.: the absence of CBD stones on ERCP). Data on patients' characteristics, imaging findings, biochemical analysis, and ERCP procedure were analyzed to identify predictors of spontaneous migration of CBD stones.

*Results:* 334 patients with a mean age of 71.7 years were included in the study: 76.6 % without and 23.4 % with spontaneous migration of CBD stones. Although some patients' features (gender and clinical presentation), imaging findings (diameters of the largest stone and CBD), biochemical analysis (bilirubin levels at diagnosis and pre-ERCP), and ERCP procedure characteristics (time from diagnosis to ERCP) were different between groups, only three variables were defined as predictors: the absence of acute cholangitis, the largest stone diameter $\leq$5 mm, and the bilirubin levels pre-ERCP $\leq$ 2mg/dL. When using those variables together there was a chance of 81–86 % to correctly distinguishing patients with and without spontaneous CBD stone migration.

*Conclusion:* The size of the largest stone at diagnosis was validated as a predictor of CBD stones' spontaneous migration. Furthermore, two new predictors were identified: bilirubin levels pre-ERCP $\leq$ 2 mg/dL, and no acute cholangitis at the clinical presentation of choledocholithiasis. EUS and ERCP in the same session should be considered in patients with factors predictive of stone migration, especially when combined, to minimize unnecessary ERCP and possible complications.

## Introduction

Gallstones (or cholelithiasis) affect up to 20 % of the European population and are a major public health problem [1]. Choledocholithiasis is defined as the presence of stones in the common bile duct (CBD) [2,3] and it is present in 3 - 16 % of the patients with gallstones, being more frequent in elderly populations [1,4].

For most choledocholithiasis cases, the recommended diagnostic work-up consists of liver biochemistry and abdominal ultrasound (US) or other cross-sectional imaging (such as computed tomography or magnetic resonance imaging). In patients with insufficient evidence of stones using those techniques but with a persistent clinical suspicion of CBD stones, further imaging with endoscopic ultrasound (EUS) or magnetic resonance cholangiopancreatography (MRCP) should be used [5,6].

Although most patients with choledocholithiasis present symptoms, around 5 - 12 % of choledocholithiasis cases are incidentally discovered during the evaluation of cholelithiasis [4]. However, between the two groups (symptomatic vs asymptomatic), there are no differences in the occurrence of unfavorable outcomes [5], both presenting equal risk of developing life-threatening complications such as acute pancreatitis, acute cholangitis, or obstructive jaundice [4,5]. Thus, current guidelines advise the removal of CBD stones in all patients who are fit enough to tolerate the intervention [5].

* Corresponding author at: Rua Direita nº17 Casais do Júlio 2525-285 Atouguia da Baleia, Portugal.
*E-mail address:* fabio.correia@ulsasi.min-saude.pt (F.P. Correia).

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Endoscopic retrograde cholangiopancreatography (ERCP) is the first-line procedure for the removal of CBD stones. Although ERCP is very effective, it is also associated with frequent and sometimes life-threatening complications including pancreatitis, hemorrhage, infection, and perforation [7]. Some studies have reported spontaneous migration of CBD stones to occur in 6 – 33 % of choledocholithiasis cases [8–13], making the ERCP procedure unnecessary. Some factors have been indicated as predictors of CBD stones' spontaneous migration such as the largest stone's size [8,10,11,13,14], the number of stones [11,13], and the time between imaging diagnosis and ERCP procedure [10]. However, there is a lack of consistency among studies, with most only reporting the size of the largest stone.

This study aims to retrospectively evaluate the rate of spontaneous CDB stone migration in patients with choledocholithiasis at a Portuguese referral center. It also intends to identify potentially predictive factors of CDB stones' spontaneous migration to prevent unnecessary ERCP procedures.

## Material and methods

### *Population*

Patients with an imaging diagnosis of choledocholithiasis who underwent ERCP (with success) between January 2020 and June 2023 were included. The diagnosis of choledocholithiasis was based on non-invasive imaging studies, including abdominal ultrasound (US), computed tomography (CT), and magnetic resonance cholangiopancreatography (MRCP). Patients without a native papilla (i.e., with previous ERCP) and with altered biliopancreatic anatomy (Billrooth I or II and Roux-Y) were excluded from the study. Institutional review board approval was obtained.

### *Endoscopic retrograde cholangiopancreatography (ERCP)*

All ERCP procedures were performed at the Gastroenterology department of Hospital Professor Doutor Fernando Fonseca, Lisbon, Portugal, a high-volume center (> 500 procedures/year). After biliary cannulation, a cholangiogram was performed to assess the presence of stones in the common bile duct (CBD). In patients without lithiasis on initial cholangiogram, the bile duct was explored with a Dormia basket or Fogarty balloon to exclude the presence of microlithiasis or biliary sludge. Spontaneous migration was considered when there was no lithiasis or biliary sludge.

### *Data collection*

The following data were collected: (1) patient characteristics: age and gender; (2) imaging findings at diagnosis: number of stones, dimension of the largest stone, and CBD diameter; (3) laboratory tests: levels of alanine transaminase (ALT) and total bilirubin at diagnosis and pre-ERCP; (4) time between diagnosis and ERCP; (5) ERCP findings: the presence of choledocholithiasis (number of stones and size of the largest stone); and (6) post-ERCP complications.

### *Statistical analysis*

The Shapiro-Wilk test was used to assess the normal distribution of all continuous variables. In univariate analysis, continuous variables were analyzed using the Welch test, and categorical variables using Pearson's chi-squared test or Fisher's exact test. Multiple logistic regression analyses were performed to determine the predictive variables. The area under the curve (AUC) for the receiver operating characteristic curve (ROC) and the precision-recall (PR) curve was used to compare multiple logistic regression models. A *p-value* $< 0.05$ was considered statistically significant. All analyses were performed using the R studio Version 2024.04.2 + 764 and the following packages: glmnet, pROC, PRROC, ggplot.

## Results

### *Cohort description*

In total, 334 patients with native papilla and imaging diagnosis of choledocholithiasis underwent ERCP between January 2020 and June 2023 at the Gastroenterology Department of Hospital Professor Doutor Fernando Fonseca, Lisbon, Portugal. The demographic and clinicopathological characteristics of the patients are represented in Table 1.

In general, the studied cohort had a patient' mean age of 71.7 ± 17.4 and 60.8 % females. Regarding the clinical presentation of choledocholithiasis, most patients were asymptomatic with altered liver tests/imaging findings (39.5 %) or presented with acute cholangitis (33.5 %). The most common method used to diagnose choledocholithiasis was the CT scan (49.1 %), followed by the abdominal ultrasound (34.1 %), and the MRCP (16.8 %). Using those methods, in most cases (64.4 %) only a single stone was observed. The diameter of the largest stone mainly varied between 6 and 9 mm (43.7 %) and the CBD diameter mean was 11.7 ± 4.0 mm (Table 1).

The ERCP procedure was generally safe with adverse events only occurring in 4.8 % of the cases (Table 2). Although most patients (65.5 %) were submitted to ERCP within 7 days post-diagnosis, a spontaneous stone migration was observed in 23.4 % of the cases (Table 2). Furthermore, both ALT and Bilirubin median serum levels decreased from diagnosis to ERCP (219.0 UI/L to 76.0 UI/L for ALT and 3.4 mg/dL to 1.1 mg/dL for bilirubin). Lithiasis was observed in 76.6 % of the cohort, being mainly characterized by the presence of only one stone per patient (43.7 %) and the largest observed stone's diameter higher or equal to 10 mm (57.0 %, Table 2).

**Table 1**
Demographic and clinicopathological characteristics of patients.

| Patients' characteristics | $n = 334$ |
|---|---|
| **Demographic characteristics** | |
| Age, mean ± SD [range] (years) | 71.7 ± 17.4 [21–101] |
| Female gender, *n* (%) | 203 (60.8) |
| **Clinical presentation of choledocholithiasis, *n* (%)** * | |
| Asymptomatic choledocholithiasis | 132 (39.5) |
| Acute cholangitis | 112 (33.5) |
| Obstructive jaundice | 54 (16.2) |
| Acute pancreatitis | 39 (11.7) |
| Other | 1 (0.3) |
| **Method for choledocholithiasis diagnosis, *n* (%)** | |
| CT scan | 164 (49.1) |
| Abdominal ultrasound | 114 (34.1) |
| MRCP | 56 (16.8) |
| **Number of stones at diagnosis, median [range]** | 1 [1–5] |
| **Number of stones at diagnosis, *n* (%)** | |
| 1 stone | 221 (66.2) |
| 2 stones | 49 (14.7) |
| 3 stones | 22 (6.6) |
| ≥ 4 stones | 38 (11.4) |
| NA** | 4 (1.2) |
| **Diameter of the largest stone at diagnosis, *n* (%)** | |
| ≤ 5 mm | 84 (25.2) |
| 6–9 mm | 146 (43.7) |
| ≥ 10 mm | 96 (28.7) |
| NA** | 8 (2.4) |
| **CBD diameter, mean ± SD [range] (mm)** | 11.7 ± 4.0 [5–25] |

* The same patient can present more than one clinical presentation.
** Data not collected.
ALT: Alanine Aminotransferase; CBD: Common Bile Duct; CT: Computed tomography; ERCP: Endoscopic Retrograde Cholangiopancreatography; MRCP: Magnetic Resonance Cholangiopancreatography; SD: standard deviation.

**Table 2**
ERCP procedures characteristics.

| ERCP procedures | $n = 334$ |
|---|---|
| **Time from diagnosis to ERCP, median [range]** | 5 [0.5–360] |
| **Time from diagnosis to ERCP, *n* (%)** | |
| < 1 day | 5 (1.5) |
| 1 - 7 days | 219 (65.5) |
| 8 - 29 days | 66 (19.8) |
| ≥ 30 days | 44 (13.2) |
| **ALT levels (UI/L)** | |
| At diagnosis, median [range] | 219 [5–2099] |
| Pre-ERCP, median [range] | 76 [5–2416] |
| Bilirubin (mg/dL) | |
| At diagnosis, median [range] | 3.4 [0.2–25.3] |
| Pre-ERCP, median [range] | 1.1 [0.2–20.7] |
| **Post-ERCP complications, *n* (%)** | |
| Pancreatitis | 6 (1.8) |
| Bleeding | 6 (1.8) |
| Perforation | 3 (0.9) |
| Bacteriemia | 1 (0.3) |
| None | 318 (95.2) |
| **Existence of CBD stones, *n* (%)** | |
| Yes | 256 (76.6) |
| No | 78 (23.4) |
| **Number of CBD stones at ERCP, *n* (%)** | |
| Sludge | 24 (9.4) |
| 1 stone | 112 (43.7) |
| 2 stones | 40 (15.6) |
| 3 stones | 25 (9.8) |
| ≥ 4 stones | 55 (21.5) |
| **Diameter of the largest CBD stone at ERCP, n (%)** | |
| ≤ 5 mm | 44 (17.2) |
| 6–9 mm | 66 (25.8) |
| ≥ 10 mm | 146 (57.0) |

ALT: Alanine Aminotransferase; CBD: Common Bile Duct; ERCP: Endoscopic Retrograde Cholangiopancreatography.

*Variables associated with spontaneous CBD stones' migration*

Initially, associations between spontaneous CBD stones' migration and patients' demographic and clinicopathological variables were studied (Table 3). In brief, the analysis showed that patients with spontaneous CBD stones' migration tended to be younger (66.3 vs. 73.3 years; $p = 0.003$) and to more frequently present asymptomatic choledocholithiasis (59.0 % vs 33.6 %, $p < 0.001$) or acute pancreatitis (19.2 % vs 9.4 %, $p = 0.030$). Additionally, those patients also presented lower levels of bilirubin at diagnosis (2.0 mg/dL vs 4.4 mg/dL, *p-value* < 0.001) and pre-ERCP (0.8 mg/dL vs 4.4 mg/dL, *p-value* < 0.001), as well as smaller CBD diameters (9.7 mm vs 12.3 mm, *p-value* < 0.001) and stones' sizes (*p-value* < 0.001). As expected, the existence of acute cholangitis and shorter periods between diagnosis and ERCP seemed to work as contraindicators for spontaneous stones' migration (acute cholangitis: 10.3 % vs 40.6 %, *p-value* < 0.001; time: 29.9 days vs 12.8 days, *p-value* < 0.001).

*Predictors of CBD stones' spontaneous migration*

To verify which of the variables associated with spontaneous stone migration were effective predictors, a multiple logistic regression model was applied. Of the 9 identified variables, only 3 showed to be predictors of CBD stones' spontaneous migration: acute cholangitis, the largest CBD stone's diameter at diagnosis, and bilirubin levels pre-ERCP (*p*-value < 0.05, Table 4). Interestingly time was not correlated with CBD stones' spontaneous migration as previously reported [10,12] or with bilirubin levels pre-ERCP (Fig. 1).

A new multiple logistic regression model was created using the three predictive variables (**Annex 1**). To determine the best cut-offs for each predictive variable, different multiple logistic regression models were created combining the different variables' cut-offs. The areas under the curve (AUC) of receiver operating characteristic (ROC) and precision-recall (PR) curves were used to compare models (Table 5).

Although two models presented an AUC-ROC = 0.81, the associated AUC-PR was low (< 0.60). This suggested that the general good performance of those models (and consequently of the predictive variables) was mainly based on predicting well the absence of spontaneous migration. This was expected since the original dataset was imbalanced, i.e., presented much more patients without spontaneous migration than patients with that condition (80:20 ratio). The final variables' cut-offs were defined through the model that combined the highest metrics. Thus, the final predictor variables of CBD stones' spontaneous migration were the absence of acute cholangitis, CDB stones diameter at diagnosis

**Table 3**
Patients' demographic and clinicopathological characteristics according to the existence of CBD stones' spontaneous migration.

| Variables | With spontaneous migration ($n = 78$) | Without spontaneous migration ($n = 256$) | *p*-value |
|---|---|---|---|
| **Age (years), mean** | **66.3** | **73.3** | **0.003** |
| Female gender, *n* (%) | 48 (61.5) | 155 (60.5) | 0.980 |
| Clinical presentation of choledocholithiasis, *n* (%) * | | | |
| **Asymptomatic choledocholithiasis** | **46 (59.0)** | **86 (33.6)** | **<0.001** |
| **Acute cholangitis** | **8 (10.3)** | **104 (40.6)** | **< 0.001** |
| Obstructive Jaundice | 9 (11.5) | 45 (17.6) | 0.275 |
| **Acute pancreatitis** | **15 (19.2)** | **24 (9.4)** | **0.030** |
| Number of stones at diagnosis, mean | 1.6 | 1.8 | 0.298 |
| **Diameter of the largest stone at diagnosis, *n* (%)** | | | |
| ≤ 5 mm | 42 (53.9) | 42 (16.4) | **< 0.001** |
| 6–9 mm | 29 (37.2) | 117 (45.7) | |
| ≥ 10 mm | 5 (6.4) | 91 (35.5) | |
| NA* | 2 (2.6) | 6 (2.3) | |
| **CBD diameter at diagnosis (mm)** | **9.7** | **12.3** | **< 0.001** |
| **Time from diagnosis to ERCP (days), mean** | **29.8** | **12.8** | **< 0.001** |
| ALT levels (UI/L) | | | |
| At diagnosis, mean | 294.1 | 290.7 | 0.923 |
| Pre-ERCP, mean | 113.8 | 144.3 | 0.184 |
| **Bilirubin (mg/dL)** | | | |
| **At diagnosis, mean** | **2.0** | **4.4** | **< 0.001** |
| **Pre-ERCP, mean** | **0.8** | **2.8** | **< 0.001** |

* The same patient can present more than one clinical presentation.
Variables with statistically significant differences are highlighted in bold.
ALT: Alanine Aminotransferase; CBD: Common Bile Duct; ERCP: Endoscopic Retrograde Cholangiopancreatography.

**Table 4**
Multiple logistic regression analysis of the factors associated with CBD stones' spontaneous migration.

| Variables | Odds Ratio (OR) | IC 95 % | *p*-value |
|---|---|---|---|
| Age (years) | 0.987 | [0.965–1.010] | 0.248 |
| Asymptomatic choledocholithiasis | 0.632 | [0.188–2.087] | 0.451 |
| **Acute cholangitis** | **0.269** | **[0.069–0.972]** | **0.049** |
| Acute pancreatitis | 0.916 | [0.231–3.395] | 0.897 |
| **Diameter of the largest stone at diagnosis** [≤ 5 mm, 6–9 mm, and ≥ 10 mm] | **0.292** | **[0.154–0.525]** | **>0.01** |
| CBD diameter at diagnosis (mm) | 0.976 | [0.851–1.116] | 0.724 |
| Time from diagnosis to ERCP (days) | 1.001 | [0.992–1.009] | 0.830 |
| Bilirubin at diagnosis (mg/dL) | 0.884 | [0.704–1.093] | 0.268 |
| **Bilirubin pre-ERCP (mg/dL)** | **0.546** | **[0.303–0.855]** | **0.021** |

Variables with p-value < 0.05 are highlighted in bold.
CBD: Common Bile Duct; CMDT: Complementary Means of Diagnosis and Therapy. ERCP: Endoscopic Retrograde Cholangiopancreatography.

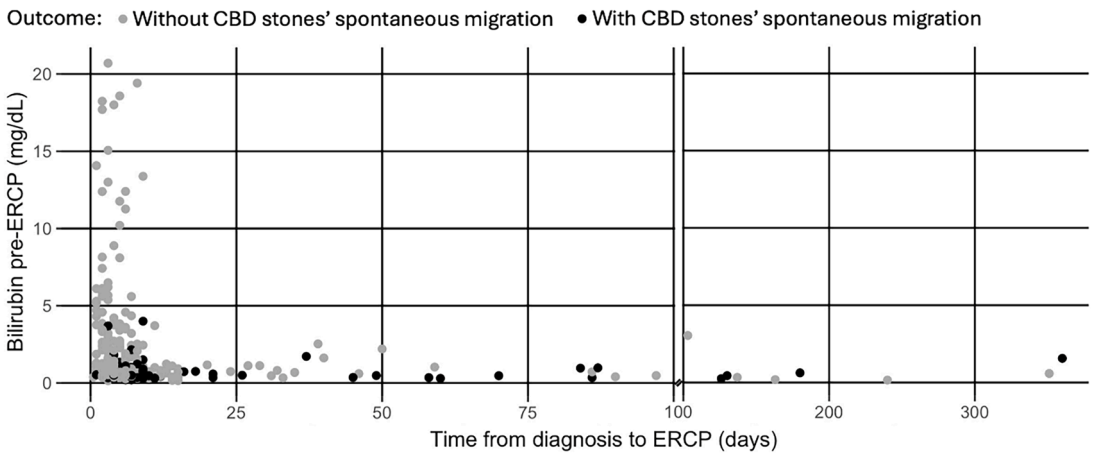


**Fig. 1. Correlation between time from diagnosis to ERCP with bilirubin levels pre-ERCP and spontaneous CBD stones' migration.** Pearson's coefficient for time vs. bilirubin = −0.14, and Spearman's coefficient for time vs. migration = 0.16.

**Table 5**
Best cut-offs for the predictive variables.

| Acute cholangitis | Bilirubin pre-ERCP (mg/dL) | Cut off Stones' dimension (mm) | ROC | PR |
|---|---|---|---|---|
| Yes/No | 0.15 | ≤ 5 | 0.74 | 0.45 |
| | 0.15 | 6–9 | 0.66 | 0.32 |
| | 0.15 | ≥ 10 | 0.74 | 0.38 |
| | 0.50 | ≤ 5 | 0.79 | **0.56** |
| | 0.50 | 6–9 | 0.73 | 0.46 |
| | 0.50 | ≥ 10 | 0.79 | 0.50 |
| | 1.20 | ≤ 5 | 0.79 | **0.50** |
| | 1.20 | 6–9 | 0.73 | 0.39 |
| | 1.20 | ≥ 10 | **0.80** | 0.46 |
| | 2.00 | ≤ 5 | **0.81** | **0.53** |
| | 2.00 | 6–9 | 0.74 | 0.37 |
| | 2.00 | ≥ 10 | **0.81** | **0.47** |
| | 5.00 | ≤ 5 | 0.78 | 0.48 |
| | 5.00 | 6–9 | 0.71 | 0.35 |
| | 5.00 | ≥ 10 | 0.78 | 0.41 |

The 3 higher values for each column are highlighted in bold.
The chosen model is highlighted in grey.
ERCP: Endoscopic Retrograde Cholangiopancreatography; PR: precision-recall; ROC: receiver operating characteristic.

≤ 5 mm, and bilirubin levels pre-ERCP ≤ 2mg/dL (Table 5).

The characteristics of the best predictive cut-offs for each variable are represented in Table 6. In general, a patient presenting acute cholangitis had a two times lower likelihood of CBD stones' spontaneous migration, a patient with stones ≤ 5 mm had approximately four times more chances for spontaneous migration, and a patient with serum levels of bilirubin pre-ERCP ≤ 2 mg/dL was 9 times more probable to have CBD stones' migration (Table 6). When variables were used together, there was a chance of 81–86 % to correctly distinguish patients with and without spontaneous CBD stone migration (Table 5).

**Table 6**
Multiple logistic regression analysis of the CBD stones' spontaneous migration predictors.

| Variables | Odds Ratio (OR) | IC 95 % | *p*-value |
|---|---|---|---|
| Acute cholangitis | 0.237 | [0.091–0.543] | < 0.001 |
| Diameter of the largest stone at diagnosis ≤ 5 mm | 4.234 | [2.161–8.415] | < 0.001 |
| Bilirubin pre-ERCP ≤ 2 mg/dL | 9.224 | [3.139–8.415] | < 0.001 |

## Discussion

This study assessed the predictive factors for CDB stones' spontaneous migration, allowing the identification of patients with no need for ERCP.

Although ERCP is the first-line procedure for the removal of CBD stones, it has a non-negligible rate of life-threatening adverse effects up to 10 % [7,15,16]. In the present study, ERCP adverse effects occurred in nearly 5 % of patients and with a higher in patients submitted to unnecessary ERCP (8 % vs. 4 %). This reinforces the importance of an accurate selection of patients prone to spontaneous biliary clearance.

The rate of spontaneous migration of CBD stones in this study (23.4 %) falls within the range reported in previous studies (6 % – 33 %) [8–13]. However, only one of the three previously identified predictor factors for CBD stones' spontaneous migration—specifically, the size of the largest stone—was validated in this study [8,10,11,13,14]. Although differences in the number of stones and the time from diagnosis to ERCP were observed between patients with and without spontaneous migration of CBD stones, these variables were not predictive factors. Interestingly two new potentially predictive factors of CBD stones' spontaneous migration were identified for the first time in this study: the clinical presentation of choledocholithiasis as acute cholangitis and the serum levels of bilirubin pre-ERCP. Patients presenting acute cholangitis had a two times lower likelihood of CBD stones' spontaneous migration. Acute cholangitis causes significant inflammation and infection, leading to decreased biliary flow. This can impair peristaltic movements and affect spontaneous stone passage [17–18]. In contrast, patients with serum levels of bilirubin pre-ERCP ≤ 2 mg/dL had approximately 9 times more changes of spontaneous CBD stones' migration. Lower bilirubin levels often indicate good overall biliary function. This includes effective biliary motility and the absence of severe obstruction, inflammation, and infection. These factors collectively may affect the likelihood of spontaneous stone migration [14,18,19].

Three different imaging techniques (abdominal US, CT, and MRCP) were used for the diagnosis of choledocholithiasis in the present study. This may represent a bias since different techniques have different sensitivities and specificities in choledocholithiasis diagnosis. Among these techniques, recent literature points to MRCP as the most sensitive test followed by CT and abdominal US [20–23].

Similar to other studies assessing the same problem, an imbalanced dataset (80:20), with fewer cases of spontaneous migration, was analyzed. Although this is a moderate imbalance, it may represent a risk of overfitting for the majority class, which means that the general performance of the model was mainly based on predicting well the absence of spontaneous migration [24]. Thus, it is important to validate the model in different populations to further assess its predictive value.

The results of this study suggest that in patients with a non-invasive imaging diagnosis of CBD stones who present the predictor factors of spontaneous biliary clearance – absence of acute cholangitis, stones' diameter at diagnosis $\leq$ 5 mm, and bilirubin levels at the time of ERCP $\leq$ 2 mg/dL –, the ERCP should be avoided and replaced by a high-sensitivity exam with lower risk of adverse events, such as EUS [24, 25]. By adopting this approach, it would be possible to reduce the risk and cost of patients submitted to unnecessary ERCP. Furthermore, if needed, ERCP can still be performed after the EUS in the same session, reducing repeated sedations, hospital stays, and associated costs [26, 27].

## Conclusion

In conclusion, this study validated the size of the largest stone at diagnosis as a predictor factor of CBD stones' spontaneous migration. Furthermore, two potentially new predictors were identified for the first time: the clinical presentation of choledocholithiasis as acute cholangitis, and the levels of bilirubin pre-ERCP. In patients with these predictive factors for spontaneous clearance of CBD stones, especially if combined, an additional test with high sensitivity (such as endoscopic ultrasound) should be considered to minimize unnecessary ERCPs and possible complications. Further studies including more patients with spontaneous CBD stones' migration should be performed to validate the different predictive variables identified so far: clinical presentation as acute cholangitis, number of stones at diagnosis, diameter of the largest stone at diagnosis, time from diagnosis to ERCP, bilirubin levels pre-ERCP.

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## CRediT authorship contribution statement

**Fábio Pereira Correia:** Writing – original draft, Validation, Project administration, Methodology, Formal analysis, Data curation, Conceptualization. **Henrique Coelho:** Data curation. **Mónica Francisco:** Data curation. **Gonçalo Alexandrino:** Writing – review & editing. **Joana Carvalho Branco:** Writing – review & editing. **Jorge Canena:** Writing – review & editing. **David Horta:** Writing – review & editing. **Luís Carvalho Lourenço:** Writing – review & editing, Conceptualization.

## Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Jorge Canena reports a relationship with Boston Scientific Corporation that includes: consulting or advisory. Jorge Canena reports a relationship with Micro-Tech that includes: consulting or advisory. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.clinre.2024.102515.

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