A New Preoperative Categorization and Potential Preoperative Indicator for Cysto-Biliary Fistula in Hydatid Hepatic Disease

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The objective of this study was to determine the risk for cysto-biliary fistula (CBF) and preoperative predictive factors in patients with hepatic hydatid disease (HHD) with high levels of hepatobiliary enzymes (HLE) alone. The risk of CBF and predictive factors in patients with HHD whose only sign of fistula was HLE is unknown. A total of 116 patients without clinical and radiologic signs who were operated for HHD were categorized into 2 groups: patients with and without HLE. The patients with HLE were defined as "usual suspicious." The potential preoperatively predictive factors for CBF were retrospectively analyzed in this group. Our data included 18.1% of patients (n = 21) with CBF and 69.2% of patients (n = 81) with HLE. The usual suspicious group contained 24.7% of patients (n = 20) with CBF. The risk of CBF was 11-fold higher in the usual suspicious group (95% confidence interval, 1.4–86.7). The red cell distribution width (RDW) was higher in patients with CBF than in patients without CBF in the usual suspicious group ($P = 0.006$). The performance of the RDW, with a cutoff value of 13.75%, was found to be suboptimal for predicting CBF for patients in the usual suspicious group (area under the curve, 0.661; 95% confidence interval, 0.525–0.798). We defined a new

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preoperatively high-risk group with HLE alone; this definition can help to identify patients at risk for preoperatively undetectable CBF. The RDW was not found to be sufficient for the discrimination of usual suspicious group with CBF.

Key words: Hepatic hydatidosis – Biliary fistula – Red cell distribution width – Elevated liver enzymes

Cysto-biliary fistula (CBF) is the most common complication of hepatic hydatid disease (HHD),[1] with an incidence of 21%–37%; however, the true incidence of CBF is unclear.[2–4] CBF can be diagnosed preoperatively by obvious clinical symptoms and by the detection of CBF or an intrabiliary cystic finding on radiologic or endoscopic retrograde cholangiopancreatography (ERCP), perioperatively by findings of hydatid fluid stained with bile or a biliary opening in a cyst cavity, and postoperatively by a finding of biliary leakage.[3] CBF was categorized as 2 forms, based on perforation size: frank CBF and occult CBF.[5] Frank CBF occurs in 5%–17% of patients and refers to untroubled diagnostic process of CBF due to complete or partial obstruction of the common bile duct by the contents of a hydatid cyst.[6,7] In clinical practice, preoperative therapeutic ERCP, with a success rate of 80%–100%, is recommended in patients with frank CBF.[8] In this way, planning to remove hydatid contents within the bile ducts and to prevent postoperative biliary fistulae is easy to some degree.[8] However, occult CBF, which occurs in 13%–37% of patients, remains preoperatively undetectable because no clinical and radiologic findings are present due to the small opening between the cyst wall and small biliary channels.[5,6] Occult CBF can be identified and sutured at surgery by observing the opening of the biliary duct in the cystic cavity, but patients with preoperatively or perioperatively undetected CBF are candidates for postoperative biliary complications.[9] Biliary leakage is the most common postoperative complication associated with CBF and causes the length of hospital stay to increase.[6] Additionally, these patients can require early surgery due to increased septic complications and sclerosing cholangitis risk.[5] Therefore, predicting these patients and performing an early preoperative intervention with ERCP is of great importance. For this reason, some studies defined some predictive markers such as cyst diameter, white blood cell count (WBC), and certain hepatobiliary enzyme levels for CBF.[5,6,9] Red cell distribution width (RDW) was also added to the other variables that are possible risk factors for CBF in this study. RDW measures variability in erythrocyte size and shape.[10] RDW is also regarded as an inflammatory marker,[11] and it has not been studied as a variable for patients with HHD.

Preoperatively, high levels of hepatobiliary enzymes (HLE) in patients are not a clear criterion for decision making regarding the prophylactic process to prevent postoperative complications associated with CBF, whereas a consensus has been reached on HLE as a preoperative warning against CBF.[5,6,9] HLE in patients with HHD can be dependent solely on bile duct compression or on the space-occupying mass effect of the cyst. Moreover, only bile duct compression was determined in patients who underwent ERCP for preoperatively probable frank CBC at various rates (0% and 30%).[8] Therefore, it is unknown exactly whether all patients with HHD who had preoperative HLE are suitable candidates for the preoperative invasive process to prevent the postoperative complications associated with CBF. However, patients without any clinical or radiologic signs and with completely normal hepatobiliary enzymes can be considered to have less occult CBF than that defined in the literature no providing a clear description of preoperative occult CBF.

In the present study, we aim to examine the risk of patients with higher levels of all or some hepatobiliary enzymes and without any signs of CBF. The second objective in this study is to identify possible predictive preoperative factors of CBF in this group.

Methods

Study design

We retrospectively collected data on a total of 131 patients who were surgically or only endoscopically treated for HHD at Adana Numune Training and Research Hospital after receiving institutional ethics committee approval (A.N.E.A.H.E.K. 2013/35). The computerized and documentary archives of patients were used in this study. The patients with distant hydatid cysts and preoperatively complicated cysts such as liver abscesses and
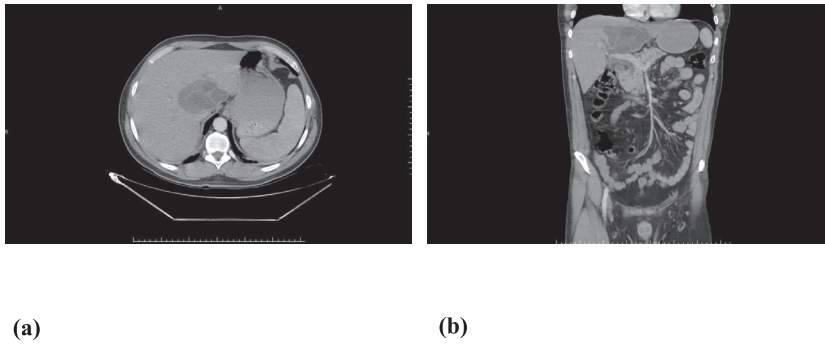
Fig. 1 A 24-year-old man with symptomatic hepatic hydatid disease. (a) Axial and (b) coronary contrast enhanced CT image demonstrating hepatic hydatid cyst obviously dilated main bile duct. Patient was classified as having a frank CBF, due to the detection cholangiohydatidotis on ERCP.

spontaneous cyst rupture, as identified by clinical features, laboratory findings, ultrasonography, or/ and computed tomography (CT), were excluded from the screening. All patients had available complete blood cell count (Cell-Dyn 3700, Abbott Diagnostics Division, Irving, Texas) and liver function test (Cobas Integra 800 Chemistry Analyzer, Roche Diagnostics, Indianapolis, Indiana) results. All patients received albendazole (10 mg/ kg per day) before and after invasive treatment. Patients who underwent only ERCP and preoperative ERCP with cholangiohydatidotis and patients who underwent surgery with findings of bile-stained perioperative cyst content or postoperative biliary leakage received a diagnosis of CBF. Fifteen patients with obvious preoperative clinical symptoms of CBF such as obstructive jaundice (total bilirubin > 2 mg/dL, direct bilirubin > 1.5 mg/dL or other clinical and radiologic signs), acute cholangitis, or radiologic signs such as communication between the cyst wall and bile ducts and dilation of the main bile duct were defined as having symptomatic HHD (Fig. 1). All of the symptomatic patients underwent preoperative treatment or only ERCP. Thirteen of these patients (86.7%) had CBF. They were classified as having frank CBF and received an intervention of endoscopic sphincterotomy. Five of the patients receiv-

ing a CBF diagnosis did not undergo surgery after being treated by therapeutic ERCP because of their poor health status due to other medical conditions. We did not identify CBF in the 2 remaining symptomatic patients, and they underwent surgery. The remaining 116 patients comprised our study population; these patients were without obvious preoperative radiologic signs and clinical features selected from our data for determining patients in whom preoperatively diagnosing CBF is difficult. These 116 patients were categorized into 2 groups: with HLE and without HLE, named usual suspicious HHD and asymptomatic HHD, respectively. Factors associated with CBF were analyzed in 116 patients. Then, the risk for CBF was determined according to whether patients had or did not have HLE. The usual suspicious HHD group was then divided into 2 groups, group 1 and group 2, for patients with and without CBF (Fig. 2), respectively. The distribution of all patients with HHD is shown in Fig. 3. Group 1 was defined as suspected CBF. Groups 1 and 2 were compared according to the variables such as demographic characteristics, cyst features, and hepatobiliary enzyme levels. The optimal cutoff for significant continuous variables was calculated by area under the receiver operating characteristic (ROC) curve (AUC) analysis.
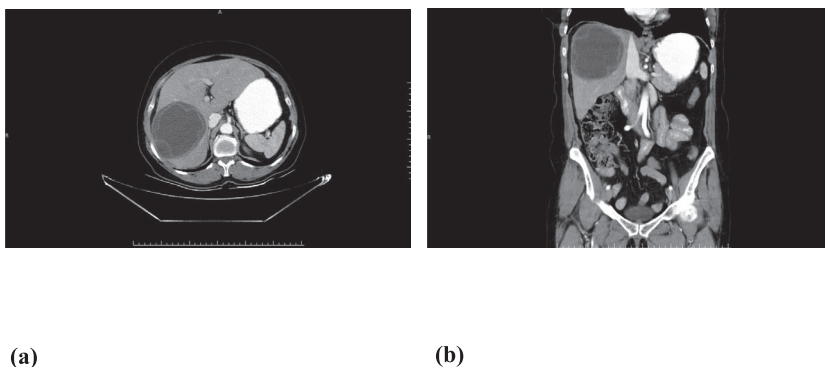
Fig. 2 A 31-year-old woman with hepatic hydatid disease. (a) Axial and (b) coronary contrast enhanced CT image demonstrating hepatic hydatid cyst. Patient with high level of enzymes was classified as without CBF according to preoperative observation and postoperative monitoring.
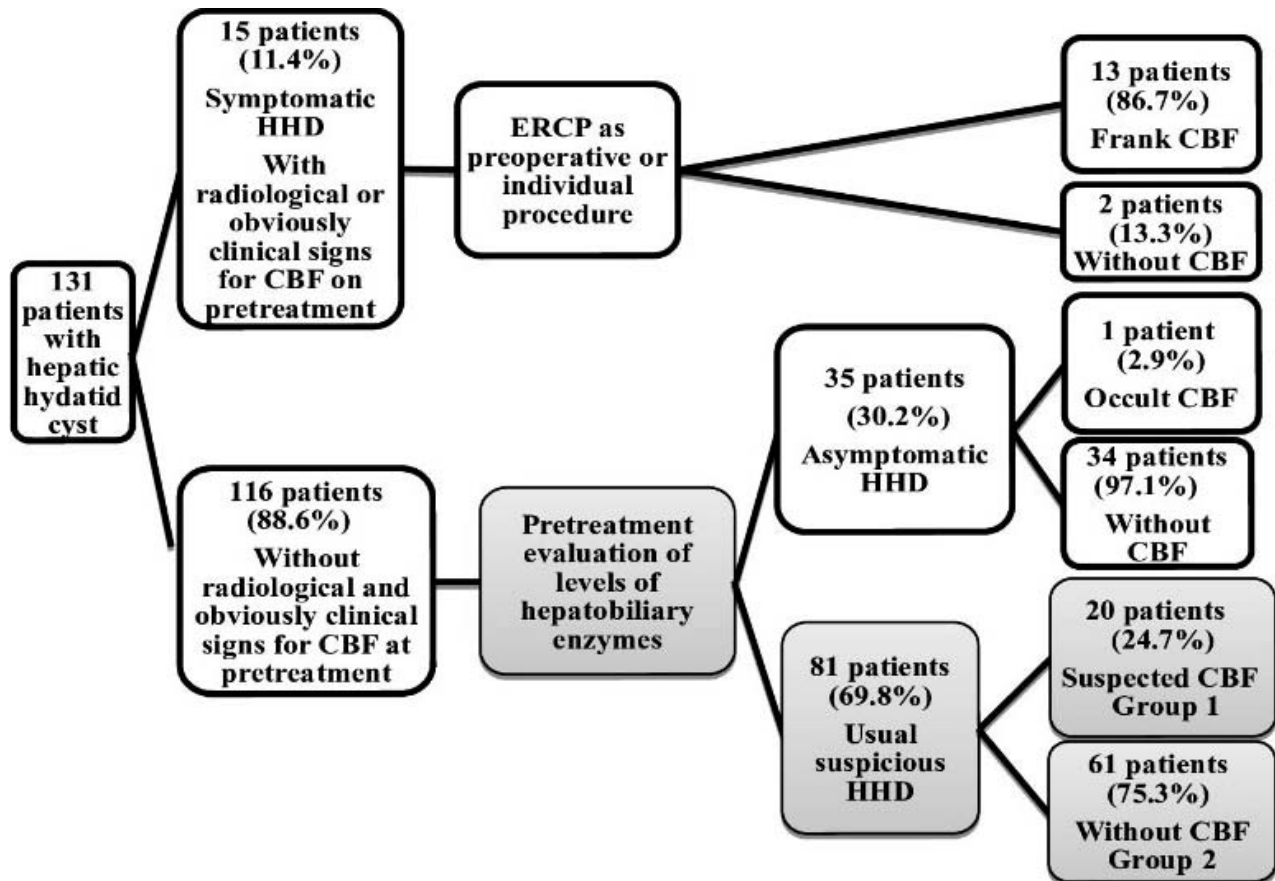
Fig. 3   Patient enrollment and categorization.

Variables

Information regarding the medical history associated with HHD, physical examination, radiologic, findings and laboratory findings of all patients was documented. The following data were collected: age, sex, WBC, RDW, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), γ-glutamyl transpeptidase (GGT), total bilirubin (T.Bil), direct bilirubin (D.Bil), ultrasonography findings such as the cyst type, diameter and Gharbi score, recurrent disease, ERCP term, surgery type, hospital stay duration, postoperative complications (systematic and local), and mortality. A standard fixed set of laboratory values was obtained on admission for all patients with HHD.

Gharbi's classification (type 1, absolute fluid collection; type 2, fluid collection with a split wall; type 3, fluid collection with septa; type 4, heterogeneous echogenic form; type 5, reflecting thick wall)[12]

was conducted according to the definition of a cyst on ultrasonography.

The upper limit of normal for liver function test results in our laboratory were as follows: AST > 32 U/L; ALT > 33 U/L; ALP > 105 U/L; GGT > 40 U/L; T.Bil level ≥ 0.8 mg/dL; and D.Bil level ≥ 0.3 mg/dL. Our data did not contain acute or chronic parenchymal or biliary liver disease and chronic hyperbilirubinemia.

Surgery

All of the surgical procedures were conducted via an open approach. The surgical treatment of cysts was achieved by partial cystectomy. The protocol described below was applied for partial cystectomy in our clinic. A 3% hypertonic saline solution was used as a scolicidal agent. At the beginning of the surgery, the pericystic area was covered with 3% hypertonic saline-adsorbed compresses to protect the area around the cyst from parasitic infection. Then, the cyst was opened by making a small

Table 1   Comparison of all of the patients according to cysto-biliary communication

Variables	No CBF (n = 95)	CBF (n = 21)	P
Age (years) (mean ± SD)	44.8 ± 15.9	37.5 ± 16.0	NS
Sex (n, %)			NS
Male	46 (85.2)	8 (14.8)	
Female	49 (79.0)	13 (21.0)	
WBC (10^3/μL)	8.2 ± 2.5	9.1 ± 3.1	NS
RDW (%)	13.9 ± 1.7	15.3 ± 2.6	0.004
AST (U/L) (mean ± SD)	26.6 ± 17.1	47.4 ± 35.4	NS
ALT (U/L) (mean ± SD)	26.0 ± 18.7	50.1 ± 41.9	0.02
ALP (U/L) (mean ± SD)	103.9 ± 88.9	116.0 ± 97.6	NS
GGT (U/L) (mean ± SD)	52.3 ± 53.2	89.8 ± 66.0	0.01
T.Bil (mg/dL) (mean ± SD)	0.5 ± 0.2	0.8 ± 0.5	0.03
D.Bil (mg/dL) (mean ± SD)	0.1 ± 0.1	0.3 ± 0.3	0.02
Levels of hepatobiliary enzymes			0.004
Higher for some or all enzymes (n, %)	61 (75.3)	20 (24.7)	
Normal for all enzymes (n, %)	34 (97.1)	1 (2.9)	
Cyst diameter (cm) (mean ± SD)	76.0 ± 24.9	81.3 ± 22.4	NS
Cyst type (n, %)			NS
Solitary	67 (82.7)	14 (17.3)	
Multicentric	18 (78.3)	5 (21.7)	
Multifocal	10 (83.3)	2 (16.7)	
Gharbi score (n, %)			NS
2	27 (87.1)	4 (12.9)	
3	42 (75.0)	14 (25.0)	
4	26 (89.7)	3 (10.3)	
Recurrence at diagnosis			NS
No	86 (81.9)	19 (18.1)	
Yes	9 (81.8)	2 (18.2)	
Postoperative hospital stay (mean ± SD)	5.2 ± 2.5	17.0 ± 13.1	<0.001

NS, nonsignificant.

incision, and the cyst cavity was drained. At this time, the cyst fluid was observed to detect whether it contained bile. Hypertonic solution-soaked compresses were placed in the cavity after the germinative membrane was removed. The compresses were collected 10 minutes later to detect biliary leakage. CBF was controlled with primary suture in cases with a viable opening and with T-tube drainage in cases in which the biliary opening was not detected in the cystic cavity. Cavity management could be conducted via omentoplasty or external drainage by the individual surgeons.

Statistical analysis

Kolmogorov-Smirnov and Shapiro-Wilk tests were used to assess normality. Continuous data are presented as the mean ± SD, whereas differences between groups were analyzed by Mann-Whitney U tests. Categorical variables were analyzed with χ^2 or Fischer's exact tests. A *P* value of <0.05 was considered statistically significant. ROC analyses were used to evaluate the predictive performances of significant variables according to an optimal cutoff value for CBF. AUC values between 0.7 and 0.8 represent considerable discrimination. All statistical tests were performed using SPSS software, version 18.0 (SPSS Inc, Chicago, Illinois).

Results

The study population included 116 patients with a mean age of 43.7 ± 16.4 (range, 19–85) years; 62 of the patients (53.4%) were women. Of the total, 21 (18.1%) patients had CBF. The rates of suspected and occult CBF were 17.2% (n = 20) and 0.8% (n = 1), respectively. Usual suspicious HHD was found in 69.8% (n = 81) of patients. Hepatobiliary enzyme levels were completely normal in 30.2% (n = 35) of patients. The type of operative procedure for cyst treatment included partial cystectomy (n = 115). Cavity management was conducted via omentoplasty (n = 110) or external drainage (n = 5). Patients who underwent surgery received a CBF diagnosis perioperatively (n = 9) by perioperative observation or postoperatively (n = 11) by biliary leakage detection. Perioperatively determined CBF was controlled with T-tube drainage (n = 9) because no invisible cysto-biliary opening was found in any of the patients. One suspected CBF patient who did not undergo surgery due to high operative risk underwent only ERCP and endoscopic sphincterotomy, with the aim to diagnose and treat this condition; this patient received a CBF diagnosis via the observation of cholangiohydatidotis. Six operated patients underwent postoperative ERCP for endoscopic sphincterotomy treatment in cases with a longer postoperative duration or with a high-output fistula. The systemic and local morbidity rates in operated patients were 10.9% (n = 13) and 20.2% (n = 24), respectively. Systemic morbidities included cardiopulmonary failure in 7.8% (n = 9) and renal failure in 2.6% (n = 3). Local morbidities included wound infection in 9.5% (n = 11), intra-abdominal abscess in 4.3% (n = 5), and biliary leakage in 9.5% (n = 11). No mortality was found in our patients within 30 days after surgical treatment or ERCP. The demographic and other clinical characteristics of the patients with and without CBF are summarized in Table 1. Age, sex, cyst diameter, cyst type, Gharbi

Table 2 Comparison of HHD patients with high levels of enzymes but no radiologic and obvious clinical signs according to cysto-biliary communication

Variables	No CBF (n = 61)	Suspected CBF (n = 20)	Univariate P
Age (years)			
(mean ± SD)	44.2 ± 16.3	37.9 ± 16.3	NS
Sex (n, %)			NS
Male	35 (83.4)	8 (18.6)	
Female	28(68.4)	12 (31.6)	
WBC ($10^3/\mu$L)	8.6 ± 2.5	9.2 ± 3.2	NS
RDW (%)	14.0 ± 1.8	15.3 ± 2.7	0.006
AST (U/L)			
(mean ± SD)	30.2 ± 20.1	49.0 ± 35.5	NS
ALT (U/L)			
(mean ± SD)	30.5 ± 21.1	56.0 ± 44.1	NS
ALP (U/L)			
(mean ± SD)	126.0 ± 103.5	119.8 ± 98.5	NS
GGT (U/L)			
(mean ± SD)	70.0 ± 59.3	93.7 ± 65..2	NS
T.Bil (mg/dL)			
(mean ± SD)	0.5 ± 0.3	0.8 ± 0.5	NS
D.Bil (mg/dL)			
(mean ± SD)	0.2 ± 0.1	0.3 ± 0.3	NS
Cyst diameter (cm)			
(mean ± SD)	75.8 ± 27.4	82.9 ± 21.8	NS
Cyst type (n, %)			NS
Solitary	46 (78.0)	13 (22.0)	
Multicentric	10 (66.7)	5 (33.3)	
Multifocal	5 (71.4)	2 (28.6)	
Gharbi score (n, %)			NS
2	15 (83.3)	3(16.7)	
3	28 (66.7)	14 (33.3)	
4	18 (85.7)	3 (14.3)	
Recurrence at diagnosis			NS
No	54 (75.0)	18 (25.0)	
Yes	7 (77.8)	2 (22.2)	
Postoperative length of hospital stay			
(mean ± SD)	5.3 ± 2.1	17.5 ± 13.2	<0.001

score, recurrent disease, WBC, AST, and ALP did not significantly differ between the patients with and without CBF ($P > 0.05$). The RDW, ALT, GGT, T.Bil. and D.Bil levels were higher in patients with CBF than in patients without CBF ($P < 0.05$). The mean length of hospital stay was significant longer in patients with CBF (range, 0–50 days) than in patients without CBF (range, 2–20 days; $P < 0.001$). CBF was higher in patients with a higher level of any enzyme than normal for all enzymes ($P = 0.004$; Table 1). The risk of CBF was approximately 11-fold greater higher in patients with HLE than in patients with normal enzyme levels [odds ratio (OR), 11.1; 95% confidence interval (CI), 1.43–86.7]. The usual suspicious HHD group was then divided into 2

groups: group 1 (suspected CBF) and group 2 (no CBF but HLE). Group 1 was compared with group 2 regarding demographic and clinical characteristics, and no significant difference was found for age, sex, cyst diameter, cyst type, Gharbi score, recurrent disease, or WBC, AST, ALT, ALP, GGT, T.Bil, and D.Bil levels. Only the RDW was significantly different for CBF in the suspected CBF group. The mean length of hospital stay was also significantly longer in group 1 (range, 0–50 days) than in group 2 (range, 2–13 days; $P < 0.001$; Table 2). The RDW, with a cutoff value of 13.75%, presented a poor discriminating variable among patients with usual suspicious HHD for CBF (AUC, 0.661; 95% CI, 0.525–0.798). At the accepted cutoff value for RDW of 13.75%, the specificity and sensitivity were 63% and 70%, respectively.

Discussion

HHD is a zoonotic disease caused by the most common form of *Echinococcosis granulosus* and is endemic in Turkey and in other Middle East and Mediterranean countries.[9,13] CBF is the most common complication of HHD; when not recognized or treated preoperatively, CBF can result in a series of complication in the preoperative, postoperative, or late postoperative period.[6,8] In addition, the length of hospital stay is extended by these complications of CBF, as shown in this and other studies.[5,9] Preoperative diagnosis and treatment of CBF are important for preventing these undesirable results. Preoperatively, ERCP and endoscopic sphincterotomy are suggested for diagnosis and treatment, particularly in patients with frank CBF.[8] However, the routine use of preoperative ERCP for suspected CBF remains controversial.[8] The most important reason for this ambiguity is patients without clinical-radiologic finding for preoperative diagnosis of CBF.[8,14] Therefore, current studies have focused on predicting occult CBF to identify patients without obvious clinical and radiologic findings who require intervention with preoperative ERCP, but these studies have resulted in some confusion regarding the preoperative choice of diagnosing frank or occult CBF. Particularly, the selection of occult CBF patients according to HLE has differed among studies, although HLE are well described as having a predictive role for CBF in patients with occult CBF.[4,6,9,14–17] Some studies have used occult CBF as the terminology to describe patients with HLE and without obvious clinical and radiologic findings, whereas other studies describe patients

with HLE as having frank CBF.[4–6,9,14,16] These different descriptions of possible preoperative CBF may cause confusion for the practical use of defined predictive markers in various studies. In our initial data, the rate of frank CBF was 86.7% (n = 13) among 15 symptomatic patients. The literature mentioned that only bile duct compression could be determined in 0%–30% of patients who underwent ERCP for preoperatively probable frank CBF.[8] Preoperative clinical or radiologic signs could be dependent on bile duct compression by cyst in our symptomatic patients without CBF. The remainder of our patients in the main data set belonged to 2 groups: patients with normal hepatobiliary enzyme levels and patients with HLE. We defined the group of patients with HLE but without any clinical and radiologic signs as usual suspicious CBF. We think that these patients may represent the source of confusion for defining occult CBF in prior studies. Moreover, patients who have only HLE as a preoperative sign for CBF have not been evaluated in the previous literature. Generally, hepatobiliary enzymes with varying levels are all affected by hepatic disease. Our data showed that CBF was more often found in patients with HLE (P = 0.004) and that the risk of CBF was higher (approximately 11-fold) in these patients. In other words, the rate of occult CBF in patients who had no preoperative signs of CBF was 0.86%, which was much lower than rates in the literature (13%–37%).[5,6] We think that our result may be connected with the clear definition of occult CBF used; these patients may not require any preoperative examination for CBF. However, CBF was identified in only 24.7% of patients with usual suspicious HHD. If these patients who have solely HLE are considered to have frank CBF, 75.3% of patients will go unnecessarily ERCP. In practice, physicians choose eligible candidates for ERCP from among patients with especially minimally raised hepatobiliary enzymes based on their individual experiences; this procedure is not standardized.

Many studies have shown that hepatobiliary enzymes were increased in patients with CBF, but there are differences in these results according to each enzyme. In their study describing a prognostic scoring system for CBF, Saylam et al found that high levels of direct bilirubin and ALP, along with a higher WBC and an elevated cyst diameter, were higher in patients with CBF; however, they excluded patients with HLE and intervened with ERCP.[6] Demircan et al and Unalp et al found associations between CBF and HLE such as ALT, AST, ALP,

GGT, and bilirubin, as well as between CBF and WBC. They included patients with any hepatobiliary enzyme levels.[5,9] Atli et al found that high levels of ALT, T.Bil, and ALP were associated with occult CBF.[4] Our results were generally consistent with the literature. In our data on 116 patients, ALT, GGT, T.Bil, and D.Bil levels were significantly higher in patients with CBF. ALP was not a significant variable for CBF in our study. Atahan et al founded that ALP was not specific for occult CBF and that elevated GGT was the only significant variable in patients with occult CBF,[14] whereas Demircan et al determined that elevated ALP levels were more specific than high GGT levels.[9] These different results may be dependent on several reasons such as the inclusion of different patient groups in different studies, nonspecific hepatobiliary enzyme studies for HHD and CBF, especially ALP, levels not originating from the liver. Moreover, in our study, no enzyme levels showed significant differences according to whether CBF was identified in patients with usual suspicious HHD, even if the mean enzyme levels were higher in patients with CBF than in patients without CBF. A borderline relationship between CBF and the T.Bil or D.Bil was determined, but it was not significant (P = 0.56, P = 0.59, respectively). This result may be attributed to the small sample size in our study. Some previous studies have discussed that the passage of cystic fluid into minor biliary ducts and the reabsorption of bile from the cystic cavity may be responsible for the high levels of enzymes.[4,6] These comments might be not originating from the liver valid for patients with CBF, but they do not explain the high levels of enzymes in patients without CBF. Moreover, parenchymal damage and small bile duct compression, dependent on the mass effect of the cyst, may result in increased hepatobiliary enzyme levels in both patients with and without CBF.

Recent studies investigating predictive variables for CBF have generally evaluated WBC as an inflammatory marker. WBC has been defined as independent risk factor in some studies,[5,6] whereas other studies have not found any relationship between WBC and CBF, similar to our results.[4,9,14] Additionally, we found that RDW, as the only variable, was significantly higher in patients with CBF than in patients without CBF, but the AUC for RDW > 13.75 revealed unsatisfactory discrimination for CBF in the usual suspicious patients. Chronic inflammation due to occult CBF could be the source of this relationship. A positive correlation has been

found between RDW and inflammatory markers such as C-reactive protein and the erythrocyte sedimentation rate in various studies.[11,18] In addition, the potential prognostic significance of elevated RDW was shown in inflammatory diseases such as acute pancreatitis, inflammatory bowel disease, and sepsis in other studies.[10,18–20] Moreover, Hu *et al* found a positive correlation between RDW and total bilirubin or ALP levels in various liver disease such as primary biliary cirrhosis, alcoholic cirrhosis, primary hepatocellular carcinoma, and liver cirrhosis,[21] but they did not identify any relationship between CBF and AST or ALT levels. Elevated RDW in hepatic disease appears to be associated more with destruction of the bile epithelium than of the liver parenchyma, which may explain the elevated RDW in CBF.

Some of studies mentioned the relationship between increased cyst diameter and CBF.[4–6,9,17] The cause of this relationship can be speculated destructive effect on both the cyst wall and stretching of the bile channels due to increasing intracystic pressure with increasing cyst diameter.[6] However, some of studies did not identify this relationship.[14,15] We also did not any find a significant association between CBF and increasing cyst diameter, although the median cyst diameter was higher in patients with CBF than in patients without CBF. Our results may be dependent on the small sample size in this study. Notwithstanding, a recently increased cyst diameter is still not an indication for preoperative ERCP in cases in which CBF is suspected.[8]

The limitation in our study is its retrospective nature. We could not collect data on other preoperative minor inflammation in patients, even if patients could not have a major preoperatively inflammatory condition such as an upper respiratory tract infection, which can be frequently observed. The specificity of the RDW could perhaps be increased by conducting prospective studies that consider preoperative inflammation. Additionally, our sample size may be criticized, but it is similar to that in other studies investigating CBF in patients with HHD.[2,4,6]

Conclusion

The risk of CBF in patients with HLE was much higher among patients who had no accompanying preoperatively clinical and radiologic signs for CBF. However, this result may not apply to frank CBF because approximately three-fourths of patients with HLE did not have CBF. Preoperatively

higher RDW was defined as an independent risk factor for CBF, but the cutoff value of 13.75% was not useful for discriminating suspected CBF. Further research, with a larger sample size, is required to increase the predictive value of RDW and to identify the exact mechanisms underlying the association between RDW and CBF. We also believe that this study will guide other studies focused on patients newly defined as usual suspicious HHD and on the relationship between RDW and CBF.

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