



ARAŞTIRMA MAKALESİ
RESEARCH ARTICLE
CBU-SBED, 2023, 10 (2): 98-103.

Karaciğer Hidatik Kist Ameliyatı Sonrası Biliyer Fistül Gelişiminde Risk Faktörlerinin Retrospektif Analizi

Retrospective Analysis of Risk Factors in the Development of Biliary Fistula After Liver Hydatid Cyst Surgery

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Gönderim Tarihi / Received:27.10.2022

Kabul Tarihi / Accepted: 14.04.2023

DOI: 10.34087/cbusbed.1210769

Öz

Giriş ve Amaç: Kistik ekinokokkozis (KE), Echinococcus granulosus larvalarının neden olduğu paraziter bir hastalıktır. KE benign karakterde bir hastalık olmasına rağmen komplike kistler varlığında morbiditesi yüksektir. En önemli komplikasyonlar safra yollarının fistülizasyonu ve intraperitoneal kist rüptürleridir. Bu çalışmada kistik ekinokokkozis cerrahisi sonrası gelişen biliyer fistülün üzerine etki eden faktörleri incelemeyi amaçladık.

Gereç ve Yöntemler: 2011-2021 yılları arasında KE nedeniyle ameliyat edilen hastalar geriye dönük olarak incelendi. Ameliyat edilen tüm hastaların demografik bilgileri, KE lokalizasyonu, kist boyutu, KE sınıflandırması, cerrahi teknikler ve hastanede kalış süreleri kaydedildi. Tüm veri türlerinin kategorik değişken üzerindeki etkisi ikili lojistik regresyon kullanılarak analiz edildi.

Bulgular: Hastaların 299'u (%60,2) kadın, 198'i (%39,8) erkekti. Safra fistülü olan ve olmayan grupta yaş ortalamaları sırasıyla 40.78 ± 15.48 ve 41.27 ± 15.36 idi. Safra fistülü olan ve olmayan grup arasında ortalama kist boyutları sırasıyla 101.75 ± 35.38 ve 94.01 ± 35.43 idi ve aralarında istatistiksel olarak anlamlı bir farklılık bulduk ($p=0.01$). WHO sınıflamasına göre kist yerleşimi ve kist tipi, kistobiliyer fistül üzerinde istatistiksel olarak anlamlı bir etkiye sahipti (sırasıyla $p=0.00$, $p=0.00$). Kist tiplerine göre analiz, CE1, CE2, CE3A ve CE3B kistlerinin biliyer üzerinde istatistiksel olarak anlamlı derecede etkili olduğunu gösterdi. Fistül oluşumu CE1 tipi kistler diğer kist tiplerine göre daha etkiliydi. CE2, CE3A ve CE3B kistleri CE1'e göre daha az etkiliydi.

Sonuç: Sol lob yerleşimli karaciğer kist hidatiklerinde ve CE1 kistlerinde safra kaçağı riski daha fazladır. Büyük kistlerde safra kaçağı görülme sıklığı artar.

Anahtar Kelimeler: Kistik ekinokokkozis, Paraziter Karaciğer Hastalığı, Safra fistülü.

Abstract

Objective: Cystic echinococcosis (CE) of the liver is a parasitic disease caused by the larvae of Echinococcus granulosus. Although CE is a disease with benign characteristics, its morbidity is high in the presence of complicated cysts. The most important complications are fistulisation of the biliary tract and intraperitoneal cyst ruptures. In this study, we aimed to examine the factors affecting the biliary fistula that developed after cystic echinococcosis surgery.

Materials and Methods: Patients who underwent surgery for CE between 2011 and 2021 were analyzed retrospectively. Demographic information, CE localization, cyst size, CE classification, surgical techniques and

hospitalisation time of all operated patients were recorded. The effect of all data types on the categorical variable was analyzed using binary logistic regression.

Results: Of the patients, 299 (60.2%) were female, and 198 (39.8%) were male. The mean age was 40.78 ± 15.48 and 41.27 ± 15.36 years in the group with and without bile fistula, respectively. The mean cyst sizes were 101.75 ± 35.38 and 94.01 ± 35.43 between the groups with and without biliary fistula, respectively, and we found a statistically significant difference between them ($p= 0.01$). Cyst location and cyst type according to WHO classification had a statistically significant effect on the cystobiliary fistula ($p= 0.00$, $p= 0.00$, respectively). Analysis by cyst types showed that CE1, CE2, CE3A, and CE3B cysts were statistically significantly effective on biliary fistula formation. CE1 type cysts were more effective than other cyst types. CE2, CE3A, and CE 3B cysts were less effective than CE1.

Conclusion: The risk of bile leakage is higher in hepatic hydatid cysts located in the left lobe and in CE1 cysts. The incidence of bile leakage increases in large cysts.

Keywords: Biliary Fistula, Cystic echinococcosis, Liver Diseases, Parasitic

1. Introduction

Cystic echinococcosis (CE) of the liver is a parasitic disease caused by the larvae of *Echinococcus granulosus* [1]. It is more prevalent in regions associated with livestock, such as Asia, Africa, South America and Central Europe. In Turkey, the Eastern Anatolia Region is endemic to this disease. CE can be detected in varying sizes. It can be detected incidentally asymptotically or manifest with abdominal pain and a palpable mass. Although CE is a disease with benign characteristics, its morbidity is high in the presence of complicated cysts. The most important complications are fistulization of the biliary tract and intraperitoneal cyst ruptures [2]. Cystobiliary fistula (CBF) can be detected in two types, frank and occult. Frank type can be detected in the preoperative period, while occult type fistulas occur after the operation or interventional procedures [3].

Patients with a cystic echinococcosis with cystobiliary communication may experience a prolonged postoperative recovery period and require additional radiological imaging and interventional treatment methods such as endoscopic retrograd cholangio pancreatography (ERCP) [4]. In cases without proper drainage in the postoperative period, bile may accumulate in the cavity due to bile leakage, an infection may develop, and as a result, the patient may present again with an abscess. To avoid such complications, many surgical techniques such as omentoplasty, cholecystectomy, and T-tube drainage are routinely used in cavity management [5, 6, 7, 8]. Despite this, biliary fistula formation after CE surgery is still a cause of morbidity.

This study aimed to analyze the factors affecting the development of biliary fistula after cystic echinococcosis surgery and to determine the risk factors. Accordingly, the secondary aim was to contribute to studies that will minimize complications through the management of modifiable risk factors.

2. Materials and Methods

This study was approved by Erzurum Atatürk University Faculty of Medicine Ethics Committee (No: 4/11/2021–Approval number 7-51). All

procedures in this study involving human participants were performed in accordance with the 1964 Declaration of Helsinki and its later amendments.

All patients who were operated on with the diagnosis of CE in the Hepatobiliary Surgery service of Erzurum Atatürk University University Research Hospital between 2011 and 2021 were retrospectively analyzed (n: 497). The data of the patients were retrieved electronically from the hospital information system and manually from the patients' archive files and evaluated. CE patients treated percutaneously with interventional radiology were not included in the study. Demographic information (age, gender), CE localization, cyst size, CE classification according to WHO [9], surgical techniques (cystotomy and omentoplasty, cholecystectomy, partial cystectomy), and hospitalization time of all operated patients were recorded. The effects of these characteristics, which are considered possible risk factors, on the development of biliary fistula were investigated.

2.1 Statistical Analysis

Quantitative parameters were given as arithmetic mean±standard deviation, while categorical variables as numbers and percentages. Distribution of numerical data was evaluated with Shapiro–Wilk test, Kolmogorov–Smirnov test, and histogram graphics. Numerical data that did not show normal distribution within the two groups were compared with the Mann Whitney U test. Categorical data were also compared with the Pearson chi-square test. The effect of all data types on the categorical variable was analyzed using binary logistic regression. Data were analyzed at a 95% confidence interval and significance value was accepted as $p<0.05$. SPSS version 26 software was used for statistical analysis.

3. Results and Discussion

3.1. Results

The general characteristics of the patients are shown in Table 1. Of a total of 497 patients, 352 (70.8%) did not develop biliary fistula, while 145 (29.1%) did. Of the patients, 299 (60.2%) were female, and 198 (39.8%) were male. The lowest age was 19, and

the highest was 83 among the treated patients. The mean age was 41.27 ± 15.48 and 40.78 ± 15.36 years in the group with and without bile fistula, respectively. The mean hospital stay was 13.97 ± 7.34 and 13.61 ± 7.34 days in the group with and without biliary fistula, respectively. Of all cases, 325 (65.4%) of the cysts were in the right lobe, 107 (21.5%) were in the left lobe, 25 (5%) were bilobar,

and 40 (8%) were centrally located. In patients who developed biliary fistula, 230 (65.3%) of the cysts were in the right lobe, 90 (25.6%) in the left lobe, 15 (4.3%) were bilobar, and 17 (4.8%) were centrally located. In the other group, 95 (65.5%) of the cysts were in the right lobe, 17 (11.7%) in the left lobe, 10 (6.9%) were bilobar, and 23 (15.9%) were centrally located.

Table 1. Patients' characteristics

| Parameters | | Non Bile Fistula (n: 352) | Bile Fistula (n:145) | p |
|--------------------|-----------------------------|---------------------------|---------------------------|------------|
| Age | | 40.78 ± 15.36 (83-19) | 41.27 ± 15.48 (20-83) | *0.69 |
| Gender | Female | 217 (61.6%) | 82 (56.6%) | **0.29 |
| | Male | 135 (38.4%) | 63 (43.4%) | |
| Cyst type | CE1 | 140 (39.8%) | 27 (18.6%) | **0.000022 |
| | CE2 | 82 (23.3%) | 56 (38.6%) | |
| | CE3A | 58 (16.5%) | 30 (20.7%) | |
| | CE3B | 36 (10.2%) | 22 (15.2%) | |
| | CE4 | 36 (10.2%) | 10 (6.9%) | |
| Cyst Location | Right Lobe | 230 (65.3 %) | 95 (65.5%) | **0.000009 |
| | Left Lobe | 90 (25.6 %) | 17 (11.7%) | |
| | Bilobar | 15 (4.3%) | 10 (6.9%) | |
| | Centre Lobe | 17 (4.8%) | 23 (15.9%) | |
| Cyst size | | 94.01 ± 35.43 (41 – 221) | 101.75 ± 35.38 (40 - 198) | *0.01 |
| Surgical Technique | Cystotomy | 270 (76.7 %) | 68 (46.9 %) | **0.000011 |
| | Cystotomy + Omentoplasty | 0 | 30 (20.7%) | |
| | Cystotomy + Cholecystectomy | 81 (23%) | 22 (15.2%) | |
| | Partial Cystectomy | 1 (0.3%) | 25 (17.2%) | |
| | | | | |
| Hospital Duration | | 13.61 ± 7.83 | 13.97 ± 7.34 | *0.46 |

* p value calculated using Mann-Whitney U test

** p value calculated using Pearson Chi-Square test

Among those who developed cystobiliary fistula, 27 (18.6%) had CE1, 56 (38.6%) had CE2, 30 (20.7%) had CE3A, 22 (15.2%) had CE3B, and 10 (6.9%) had CE4 hydatid cysts. Of the patients who did not develop cystobiliary fistula, 140 (39.8%) had CE1, 82 (23.3%) had CE2, 58 (16.5%) had CE3A, 36 (10.2%) had CE3B, and 36 (10.2%) had CE4 hydatid cysts. Being performed on 338 (68%) of all cases, cystotomy was the most frequently performed surgical method. Cholecystectomy was performed along with cystotomy in 113 (22.7%) patients.

Binary logistic regression analysis was used to analyze the factors affecting the development of biliary fistula in patients with CE (Table 2). According to this analysis, although the decrease in cyst size showed that the risk of development of biliary fistula increases, this factor may not be taken into account due to the small confidence interval and the p value close to the threshold (p: 0.038, OR:

0.994, %95 CI: 0.988 – 1.000). On the contrary, we found a significant difference in mean cyst sizes between the two groups (Table 1, p= 0.01). Mean cyst size was 94.01 ± 35.43 (41 – 221) cm in patients without biliary fistula (n: 352), and mean cyst size was 101.75 ± 35.38 (40 – 198) cm in patients with biliary fistula. Accordingly, the mean cyst sizes are higher in patients who develop biliary fistula.

Cyst location and cyst type according to WHO classification had a statistically significant effect on the CBF (p= 0.00, p= 0.00, respectively). While cysts located in the right lobe are effective on the development of biliary fistula, cysts located in the left lobe increase the risk of CBF more than cysts located in the right lobe (p= 0.01, OR: 2.130, %95 CI: 1.177 – 3.854). Cysts located in the right lobe also increase the risk of CBF more than centrally located cysts. Cysts located in the right lobe increase the risk of CBF more than cysts located centrally (p= 0.00, OR:0.279, 95% CI:0.137- 0.568). Bilobar localization of the cyst, on the other hand, had no effect on the development of biliary fistula.

In conclusion, the risk of biliary fistula formation is higher in left lobe cysts, while bilobar cysts have no effect on biliary fistula formation.

Analysis by cyst types showed that CE1, CE2, CE3A, and CE3B cysts were statistically significantly effective on biliary fistula formation. Whereas, CE4 cysts had no effect on the development of biliary fistula (p: 0.183). CE1 type cysts were more effective than other cyst types. CE2, CE3A, and CE3B cysts were less effective than CE1 (Table 2).

Table 2. Binary logistic regression analyze

| | OR | 95%CI | P |
|--------------------|-----------|------------------|-----------------|
| Age | 1.005 | 0.991-1.019 | 0.479 |
| Gender | 0.785 | 0.515-1.196 | 0.259 |
| Cyst size | 0.994 | 0.988-1.000 | 0.038 |
| Right lobe | | | 0.00003 |
| Left lobe | 2.130 | 1.177-3.854 | 0.012 |
| Bilobar | 0.658 | 0.276 – 1.569 | 0.345 |
| Centre lobe | 0.279 | 0.137 – 0.568 | 0.00004 |
| CE 1 cyst | | | 0.00005 |
| CE 2 cyst | 0.265 | 0.152 – 0.463 | 0.000004 |
| CE 3A cyst | 0.322 | 0.172 – 0.601 | 0.0001 |
| CE 3B cyst | 0.292 | 0.145 – 0.591 | 0.001 |
| CE 4 cyst | 0.562 | 0.240 – 1.314 | 0.183 |

3.2. Discussion

CBF is common in patients with cystic echinococcosis and is the most significant cause of morbidity. Two theories have been proposed about its pathogenesis. The first is that the hydatid cyst compresses the bile duct walls and causes necrosis and fistula over time. The second is the leaks that occur when the pressure on the small bile ducts opening into the hydatid cyst is removed [10]. These leaks can be of occult or frank type [11]. Their incidence varies in various series and is between 3% and 37%[5,6]. In our series, the incidence of cystobiliary fistula in patients who underwent liver hydatid cyst surgery was 29.2%, occult type cysto biliary communication was 26.4%, and frank type was 2.8% [12].

In patients with CE presenting with cholangitis or jaundice, it can be understood that bile ducts are opened into the cyst and a CBF has developed. It has been shown that endoscopic interventions to be performed in the preoperative period in these patient groups reduce bile leakage in the postoperative period, thus reducing morbidity [13] In addition, more care is taken in the intraoperative period in conservative surgeries and primary suturing is attempted while minding bile leakage. Patients who

have undergone radical surgery such as cystectomy, resection, and peri-cystectomy have lower risk of bile leakage. However, the application of a major surgical technique due to a benign disease is controversial as it will prolong the operation time and cause morbidity [7, 14, 15]

Medical, surgical, and PAIR (Puncture-aspiration-injection-reaspiration) methods are used for the treatment of CE, depending on the size and type of the cyst. While medical treatment with albendazole is preferred for hydatid cysts smaller than 5 cm, invasive procedures can be applied for larger cysts PAIR treatment should be considered primarily for CE1, CE3, and CE2 type hydatid cysts whose medical condition is not suitable for surgery according to the WHO classification [9]. In CE 4 hydatid cysts, if infected fluid contents are present, percutaneous intervention or, if appropriate, surgical treatment may be considered. There is no need for any treatment for a CE5 cyst since it is an inactive hydatid cyst Percutaneous treatments are minimally invasive surgical methods and should be considered in suitable cases because they are less risky and costly [16]. Percutaneous catheter or surgical treatment is more appropriate in the case of minor bile duct opened into the cyst.

Cyst type and size are taken into account in the management of liver hydatid cysts. We revealed that cyst types have an effect on bile leakage. We found that CE1 type cysts were the type that increased the risk of biliary fistula formation the most while CE4 type cystshad no effect. For this reason, we think that minor bile leaks should be paid attention to when performing surgical treatment in CE1, CE2 ve CE3 cysts.

There are studies in the literature reporting the size of the cyst as an important determinant of the presence of CBF. Atlı et al. concluded that a cyst diameter of >10.5 cm was a significant predictor of cyst rupture, whereas a cyst diameter of >14.5 cm was significant for occult CBF. Demircan et al. reported that a cyst diameter of >8.5 cm was a predictor of biliary fistula [17, 18, 19] In addition, there are also studies reporting that there is no relationship between cyst sizes and CBF development [20]. In present study, we could not reveal that cyst size affects the formation of CBF as a risk factor by regression analysis. However, due to the significant difference in cyst sizes between the two groups, we think that larger cysts develop more CBF. Also, we suggest considering the use of a catheter if percutaneous treatment is to be applied in large-sized CE1 cysts. Because, if there is cystobiliary fistula, the large size of the pouch in large cysts may cause the development of an abscess in this pouch. Our study suggests that because of the most increased risk in CE1 cysts, these patient groups should be followed more closely to prevent morbidity after the procedure or surgery.

There are not many studies about the anatomical location of the cyst for CBF. However, it has been reported that there is no difference with its location [20]. Bilobar cysts had no effect in this study. We found that cysts located in the left lobe also increased the risk of developing biliary fistula 2 times more than cysts located in the right lobe. Therefore, a closer follow-up is required after the procedure in cysts in the left lobe.

In our series, we mostly performed conservative surgery. Fistula developed less frequently in patients who underwent cholecystectomy and repaired bile leakage. In addition, we found that postoperative bile leakage was higher in patients who underwent partial cystectomy. Therefore, we think that cholecystectomy and leakage control from the cystic duct are a reliable method, especially in patients with biliary contamination into the cyst. In addition, we recommend performing radical resection, such as pericystectomy, instead of partial cystectomy, when necessary.

The limitations of our study are its retrospective design and the inclusion of only patients who underwent surgery, not those who were followed up with percutaneous or medical treatment. However, considering the number of patients examined, it is indeed one of the longest series in the literature. It is a unique study in terms of investigating the risk of bile leakage. It will contribute to studies on cysto biliary communications, which is the most significant factor determining morbidity and mortality in liver hydatid cysts.

4. Conclusion

The risk of bile leakage is higher in hepatic hydatid cysts located in the left lobe and in CE1 cysts. The incidence of bile leakage increases in large cysts.

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