

# Predictive factors of occult cystobiliary fistula after conservative surgical treatment of the hepatic hydatid cyst

## A retrospective study of 105 patients



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### Predictive factors of occult cystobiliary fistula after conservative surgical treatment of the hepatic hydatid cyst. A retrospective study of 105 patients

**OBJECTIVES:** The objective of our study was to determine the predictive factors of their occurrence during conservative surgical treatment of the hepatic hydatid cyst (HHC).

**PATIENTS AND METHODS:** We carried out a retrospective review of patients who had undergone conservative surgical treatment of the HHC during 6 years. Univariate analyses were used to determine the predictive factors of an occult cystobiliary fistula (CBF).

**RESULTS:** This current study included 105 patients. Concerning the predictive factors of an CBF regardless of its pattern of evolution, we noted that the presence of fistula was statistically correlated with the a cyst size (bigger than 8.65 cm ;  $p = 0.003$ ) and with advanced age ( $p=0.035$ ). Interestingly enough, the correlation to a degenerated cyst ( $p=0.069$ ) were of little significance.

**CONCLUSION:** The size of the cyst greater than 8.65 cm and the advanced age are the risk factors of CBF according to our study.

**KEY WORDS:** Biliary Fistula, Diagnosis, Echinococcosis, Hepatic, Prevention and control

### Introduction

The liver hydatid cyst is a benign disease per se which could lead to serious complications. The most common and the most life-threatening sequel remains the cystobiliary fistula. Cystobiliary fistulas (CBF) are fistulas whose diameter is less than 5 mm. they complication the course of liver hydatid cyst in 12 to 37% of the cases <sup>1,2</sup>.

The objective of our study was to determine the predictors of their occurrence during hydatid cyst conservative surgery.

### Material and Methods

We included in this retrospective study the patients operated on due to liver hydatid cysts over a period of six years. In the general and digestive surgery department of the Habib Bourguiba University Hospital, Sfax, Tunisia. We excluded from of fistulas bigger than 5 mm with or without hydatid fragment migration and cysts which were radically excised. The parameters set to investigate the different correlation were age, sex, cyst number, cyst size, stage and recurrent or ruptured cyst. Univariate analyses were performed to elicit the poten-

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tial predictors of frank cystobiliary fistulas and fistulas revealed thanks to methylene blue and regardless of its preoperative mode be it frank or revealed by methylene blue. The chi-square test was used to compare observed frequencies (qualitative variables). Where not applicable, the chi-square test was replaced with Fisher's test. The observed averages. The threshold of significance was set at 5%.

## Results

The overall number of patients included in the study was 105. The patients mean age was 37 years (range 6-81 years) and the sex ratio was 0.43 (32 men and 73 women). The cysts were single in 70 patients (66.7%) and multiple in 35 patients (33.3%) the mean cyst size was 9.3 cm. the cyst stage, referred to in 68 subjects was unilocular (I, II) in 30 patients and multilocular in 38 ones. Among the 105 patients studied, 7 patients (6.6%) had frank cystobiliary cysts. In those who had the fistulas sutured, the postoperative course was uneventful in 5 (72%) and an external biliary fistula was noted in 2 patients (28%). The fistula did not require any revision surgery. The mean daily flow was 450 cm<sup>3</sup> (10-800 cm<sup>3</sup>). Spontaneous drainage occurred after a mean time of 25 days. In the 98 patients without frank biliary fistulas, 84 patients were not investigated using methylene blue test. In the 84 patients who were initially frank biliary cyst free, and in whom fistulas were not investigated by means of methylene blue, 82 (97%) had an uneventful post-operative course while 2 (2.4%) had an external fistula not requiring revision surgery and

TABLE I - Predictive factors of the methylene-blue test practiced by the surgeon.

		CBF SV(-); FBM(+)		CBF SV(-); FBM(-)		p
		N	%	n	%	
Age		37,5		36,83		0,592
Sex	M	3	3,1	28	28,6	0,520
	F	11	11,2	55	56,1	
Recurrent cyst	yes	3	3,1	3	3,1	0,036
	no	11	11,2	81	82,7	
Complicated cysts	yes			6	6,1	0,589
	no	14	14,3	78	79,6	
Number of cysts	one	11	11,2	55	56,1	0,539
	multiple	3	3,1	29	29,6	
Size of cyst (cm)		11,8		8,54		0,023
Type of cyst	Uniloculated	1	1,6	28	43,8	0,009
	Multiloculated	10	15,6	25	39,1	

CBF SV+: Spontaneously visible cystobiliary fistula; FMB +: fistula searched for using methylene blue; FMB -: fistula not searched for using methylene blue.

TABLE II - Predictive factors of a spontaneously visible occult cystobiliary fistula.

		CBF SV(+)		CBF SV(-)		p
		N	%	n	%	
Age		45,29		36,76		0,257
Sex	M	1	1	31	29,5	0,673
	F	6	5,7	67	63,8	
Recurrent cyst	yes					1
	no	7	6,7	6	5,7	
Complicated cysts	yes					1
	no	7	6,7	67	63,8	
Number of cysts	one	4	3,8	66	62,9	0,684
	multiple	3	2,9	32	30,5	
Size of cyst (cm)		13,75		9,06		0,035
Type of cyst	Uniloculated	3	4,4	35	51,5	0,624
	Multiloculated	1	1,5	29	42,6	

CBF SV+: Spontaneously visible cystobiliary fistula; CBF SV -: Spontaneously Non-visible cystobiliary fistula.

whose mean flow was 45 cm<sup>3</sup> and spontaneous drainage occurred with an average duration of 8 days. As for the patients having had the methylene blue test, 9 of them (64 %) presented no fistulas and 5 others (36%) had a sutured fistula and the course was uneventful for 4 patients and an external fistula was found in one patient only and did not necessitate revision surgery as the mean flow was 35 cm<sup>3</sup> and drainage occurred after a mean duration of 35 days.

To study the correlations, we used univariate analyses and compared both groups under investigation according to age, sex, cyst number, cyst size, cyst ruptured aspect or recurrent cyst, and cyst stage. We first investigated potential predictors preoperatively while the surgeon was performing the methylene blue test and then looked at the risk factors for frank cystobiliary fistulas (Table I)

Performing the methylene blue test by the surgeon looking for a cystobiliary fistula is statistically correlated with recurrent cysts, big-sized cysts and reshaped cysts (III, IV).

### 1. PREDICTORS OF FRANK CYSTOBILIARY FISTULAS

The mean diameter of cysts with frank cystobiliary fistulas was significantly greater (p=0,035) than that of cysts without frank cystobiliary fistulas. There was no frank cystobiliary fistula smaller than 9 cm (Table II).

### 2. PREDICTORS OF OCCULT CYSTOBILIARY FISTULAS REVEALED BY THE METHYLENE BLUE TEST

Concerning the predictors of occult cystobiliary fistulas revealed by methylene blue (VIS group vs VIS - group),

TABLE III - Predictive factors of occult cystobiliary fistulas not spontaneously visible and demonstrated by the methylene-blue test.

		CBF SV(-) FMB(+) BF(+)		CBF SV(-) FMB(+) BF(-)		
		N	%	n	%	p
Age		52,4.		29,22	0,038	
Sex	M			21,4	0,14	
	F	5	35,7	6	42,9	
Recurrent cyst	yes	3	21,4	8	57,1	0,505
	no	2	14,3	1	7,1	
Complicated cysts	yes	4	28,6	7	50	1
	no	1	7,1	2	14,3	
Size of cyst (cm)		15,25		9,5	0,044	
Type of cyst	Uniloculated			1	9,1	1
	Multiloculated	6	54,4	4	36,4	

CBF SV+: Spontaneously visible cystobiliary fistula; FMB +: fistula searched for using methylene blue; FMB -: fistula not searched for using methylene blue; BF +: Presence of biliary fistula; BF -: no biliary fistula.

TABLE IV - Predictive factors of an occult cystobiliary fistula regardless of its mode of development.

		CBF SV(+) ou BF(+) after MBT		CBF SV(-) et BF(+) after MBT		p
		N	%	n	%	
AGE	48,25	35,91	0,035			
Sex	M	1	1	31	29,5	0,101
	F	11	10,5	62	59	
Recurrent cyst	yes	2	1,9	4	3,8	0,082
	no	10	9,5	89	84,8	
Complicated cysts	yes			6	5,7	1
	no	12	11,4		82,9	
Number of cysts	one	8	7,6	62	59	1
	multiple	4	3,8	31	29,5	
Size of cyst (cm)	14,5	8,64	0,003			
Type of cyst	Uniloculated	1	1,5	29	42,6	0,069
	Multiloculated	7	10,3	31	45,6	

CBF SV +: Spontaneously visible cystobiliary fistula; CBF SV -: Spontaneously non visible cystobiliary fistula; BF +: Presence of biliary fistula; BF -: no biliary fistula; MBT: methylene blue test.

presence of occult cystobiliary fistulas revealed thanks to methylene blue was correlated with an important cyst size (15, 25 mean size (p=0,044)). Especially noteworthy was the absence of cystobiliary fistulas in cysts smaller than 10 cm and in older patients (mean age 29 years in the absence of cystobiliary fistulas vs 52 years in the presence of cystobiliary fistulas) as show in Table III.

### 3. PREDICTING FACTORS OF CYSTOBILIARY FISTULA INDEPENDENTLY OF ITS MODE OF REVELATION

As for the possible risk factors of cystobiliary fistulas, we noted that the presence of a cystobiliary fistula, frank or revealed by methylene blue was significantly correlated with a big cyst size (absence of cystobiliary) fistulas in cysts smaller than 8.65 cm) and the patient's advanced age (mean age of 36 years in the absence of a cystobiliary fistulas versus 48,5years in the case of a cystobiliary fistula). Equally interesting were the correlations with recurrent cysts (p= 0,082) reshaped cysts which were of only borderline statistical significance (Table IV).

Overall, the patient's advanced age was tightly correlated with the presence of an occult cystobiliary fistula but revealed by methylene blue and with the presence of a cystobiliary fistula frank o detected thanks to methylene blue. The big size of the cyst was correlated significantly with the presence of a frank cystobiliary fistula and the revelation of a cystobiliary fistula during the methylene blue test. The cyst stage and the recurrent aspect of the cyst were found to be different and had a borderline statistical significance concerning the revelation of frank fistulas or revelation after the methylene blue test. However, the patient's gender, the notion of rupture and the number of cysts were not correlated in anyway with the presence or cystobiliary fistula search.

To sum up, a cyst size (greater than 8 cm) and to a lesser degree, the patient's advanced age were likely to be the most correlated parameters with cystobiliary fistulas be they detected preoperatively or postoperatively.

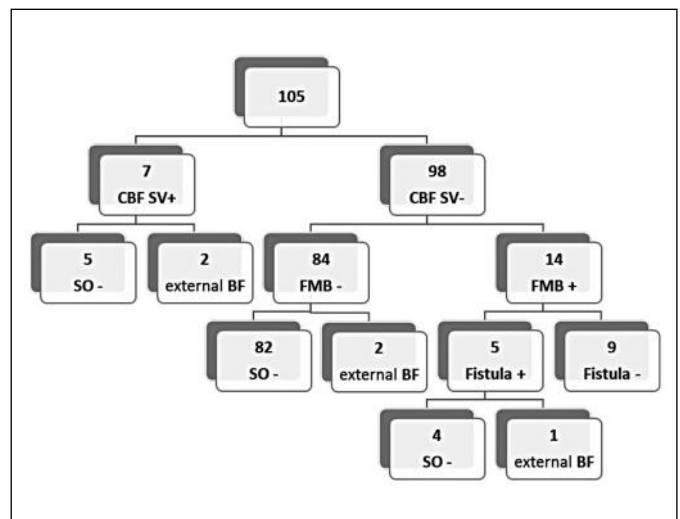


Fig. 1: Representation of our series

CBF SV+: Spontaneously visible cystobiliary fistula; CBF SV -: Spontaneously non visible cystobiliary fistula; FMB +: fistula searched for using methylene blue; FMB -: fistula not searched for using methylene blue; Fistula +: Presence of biliary fistula; Fistula -: no biliary fistula; BF: Biliary fistula; SO: surgical outcomes.

TABLE V - Summary chart of the different selected studies.

	N	Year	Etude	Predictors factors	p
Demircan <sup>4</sup>	222	1992-2002	retrospective	Size of cyst > 8.5 cm ALP > 250 U/L Total bilirubin > 17.1 mol/L GGT > 34.5 U/L Eosinophil > 0.09 Age, sex, pain, nombre, location of the cyst (Left lobe or Right lobe), type of cyst (unilocular, multilocular, degenerated), recurrent, GGT, ASAT, ALAT	0.02 0.001 0.03 0.01 0.02 NS
Altı <sup>6</sup>	116	1992-2000	Prospectivecomparative	Nausea and vomiting ALP > 144 U/L Total bilirubin > 13.5 µmol/l Size of cyst > 14.5 cm Age, sex, pain, nombre, location of the cyst (Left lobe or Right lobe), type of cyst (I, II, III, IV), recurrent, GGT, ASAT, ALAT, Leukocystosis	0.04 0.04 <0.01 <0.01 NS
Kilic M. <sup>9</sup>	102	1998-2006	retrospective	Size of cyst (>10.2 cm) Age, sex, nombre, location of the cyst (Left lobe or Right lobe), type of cyst (I, II, III, IV), GGT, ASAT, ALAT, Total bilirubin	<00.5 NS
Bedioui <sup>10</sup>	391	1996-2006	retrospective	Size of cyst >9 cm	<0.0001
Unalp <sup>8</sup>	183	1998-2008	retrospective	Size of cyst >10 cm Total bilirubin >1.2 mg/dL ALP > 133 U/L Leukocystosis >10,000/mm <sup>3</sup> Age, sex, nombre, location of the cyst (Left lobe or Right lobe), type of cyst (unilocular, multilocular, degenerated), GGT, ASAT, ALAT	0.001 0.007 0.041 0.002 NS
Atahan <sup>2</sup>	15	2003-2007	retrospective	high levels of GGT age, number of cysts, type of cyst, recurrent, ALP, ASAT, ALAT	<00.5 NS
Kayaalp <sup>11</sup>	93	1997-2007	Prospectivecomparative	Nombre of cyst ≥2 Complicated cysts Age, sex, location of the cyst (Left lobe or Right lobe), type of cyst (unilocular, multilocular, degenerated), recurrent, GGT, ALP	0.02 0.01 NS

NS: non-significant; p statistically significant if <0.05

ALP = alkaline phosphatase; ALT = alanine aminotransferase; AST = aspartate aminotransferase; GGT = γ -glutamyl transferase

## Discussion

Although the liver hydatid cyst is a common pathology in many countries, the available publications, most of them retrospective, have shown low levels of evidence. Cystobiliary fistulas occur in 10 to 37 % of the cases <sup>3</sup>. In our series, the cystobiliary fistulas that resulted in biliary leakage preoperatively or postoperatively were observed in 14 patients (13.3%). In Orhan Demircan's series <sup>4</sup>, 41 patients out of the 191 studied cases had cystobiliary fistulas (21%). Rather more significant were the biliary fistulas gone unnoticed preoperatively and emerging postoperatively. The size of these fistulas was not these fore specified (big fistula or small one). Cystobiliary fistulas can be frankly seen at the bottom of the residual cavity after cyst drainage. A part from the cases where cystobil-

iary fistulas are suspected when the cyst's content is tinged with bile or frankly bilious their diagnosis remain difficult <sup>5</sup>. It could be explained by the asymptomatic aspect at the time of operation, and by the fact that the presence of a totally occult fistula peroperatively which does not result in leakage visible in the residual cavity after drainage and which goes unnoticed and postoperatively leads to biliary leakage. The difficulty of its coming into evidence on cholangiography either because of the happened prior to cyst drainage and therefore cystobiliary communication cannot be show due to the elevated pressure inside the cyst and the small size of the cystobiliary fistula or because the opacification occurred after cyst drainage. Thus, cystobiliary communication cannot be demonstrated as a consequence of insufficient filing of intra hepatic biliary ducts by the contrast medium <sup>6</sup>.

In the current study, peroperative cholangiography was not helpful in cystobiliary fistula diagnosis either because it was performed on a closed cyst or the cystobiliary fistula was revealed by methylene blue or again the contrast medium filling pressure was insufficient. In the studies of Demircan and et al.<sup>4</sup>, cholangiography failed to reveal small cystobiliary fistulas owing to the extremely high pressure within the cyst and/or the tiny size of the cystobiliary fistula. Searching for cystobiliary fistulas can be done by injection of methylene blue either by direct puncture of the gallbladder or via a transcyst drainage after cholecystectomy<sup>7</sup>. Besides the cases where cholecystectomy was performed out of necessity, it is quite reasonable puncture procedure or again of its ablation even when it is not pathological.

In our patients, cholecystectomy was performed in most cases on principal and not out of necessity. Of interest, no morbidity specific to cholecystectomy was observed. Several risk factors have been identified in the cystobiliary fistula formation. A comparative prospective study conducted by Ataly<sup>2</sup> and investigating 116 patients found that potential predictors are nausea, vomiting, a cyst size equal to or greater than 14.5 cm, hypereosinophilia and biological cholestasis. In a retrospective study carried out by Demircan and al.<sup>4</sup>, concerning 222 operated on for liver hydatid cysts, looked into the potential risk factors for a cystobiliary fistula gone unnoticed peroperatively and detected only postoperatively because of a postoperative biliary leakage. After the surgery, a cystobiliary fistula was observed in 41 patients (21.5%). There was no correlation between the postoperative biliary leakage and the intervention type (capitonnage, omentoplasty and external drainage), the cyst number, the cyst recurrent aspect and cyst site. Inversely, it was noted that postoperative biliary leakage was correlated with the cyst diameter (>8.5 cm with  $p = 0,001$ ) and a biological cholestasis. In accord with ours, Unalp and al.<sup>8</sup> showed in a study investigating 183 patients that alkaline phosphatase (ALP) higher than 133 U/l, -glutamyl transferase (GGT) higher than 50 U/l and bilirubin rate greater than 1.2 mg/dl, a cyst size bigger than 10 cm are predictors of a cystobiliary fistula. According to kilic<sup>9</sup> and Bedioui<sup>10</sup> only a cyst size (greater than 10 and 9 cm respectively) has been considered as a potential risk factor for a cystobiliary fistula. Yet, all these studies have shown that there was no correlation between occurrence of the postoperative biliary fistula and territory (age, sex), cyst type, cyst site and the conservative surgical technique performed except in Kayaalp's study<sup>11,12</sup> where multiple cysts and complicated cysts were considered as risk factors for cystobiliary cysts (Table V).

*Thus, we can conclude that the main predictors of a cystobiliary fistula in the case of a liver hydatid cyst with a statistically significant  $p$  are a cyst size larger than 9.6 cm and the presence of a cholestasis syndrome. These data are in accord with the results of our study in which a later disturbance of liver biology has to be taken into account.*

## Conclusion

The size of the cyst greater than 8.65 cm and the advanced age are the risk factors of Occult cystobiliary fistulas according to our study.

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