

Hepatic resection for T2-3 gallbladder carcinoma: a retrospective analysis of 12 resectable cases

A ressecção hepática para o carcinoma da vesícula biliar estádios T2-3: análise retrospectiva em 12 casos operados

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ABSTRACT

Objective: To report on a group of 12 patients with advanced gallbladder adenocarcinoma at a General Hospital and describe the outcomes (surgical morbidity - mortality and long-term survival) following hepatic resection. **Methods:** The authors present a series of twelve patients with invasive gallbladder adenocarcinoma who underwent hepatic resection at the General Surgery Service of the Hospital de Ensino da Faculdade de Medicina do ABC, in Santo Andre. The study period was from 2001 to 2007. There were twelve hepatic resections, all associated with hilar lymphadenectomy (IVB-V bisegmentectomy = 9 and right trisectionectomy = 3). There were ten women and two men and all patients were Caucasian. The age range was 52 to 72 years. The preoperative symptoms were biliary colic (n = 6), dyspepsia (n = 4), acute cholecystitis (n = 1) and jaundice (n = 1). The diagnosis was made by radiographic images in the preoperative period in seven patients; all of them were confirmed by frozen section during surgery. Five patients submitted to open cholecystectomy (n = 4) and laparoscopic cholecystectomy (n = 1) had their diagnoses confirmed postoperatively by histological analysis. **Results:** The operative time varied between 180 and 340 minutes. Four patients received transfusions. The blood loss varied between 200 and 2500 ml. The hospital stay varied from 7 to 16 days. There were two major complications in two patients and both were treated conservatively, one biliary leakage and one reversible hepatic failure. There was no mortality. The TNM stage distribution was: T2N0M0 (n = 4), T2N1M0 (n = 2), T3N0M0 (n = 4) and T3N1M0 (n = 2). Only one patient presented affected surgical margin (T3N1M0) and died with both peritoneal and liver recurrence after a 9-month follow-up. Other three patients presented recurrence (13 to 28 months of follow-up) and died. The three-year survival rate

was 33.3% (n = 4). **Conclusion:** The radical surgical treatment with hepatectomy plus hilar lymphadenectomy may offer a long term prognosis to localized gallbladder adenocarcinoma with both minimal morbidity and mortality.

Keywords: Hepatectomy; Gallbladder neoplasms/surgery; Adenocarcinoma

RESUMO

Objetivo: Avaliar os resultados (morbidade, mortalidade da cirurgia e sobrevida a longo prazo) do tratamento cirúrgico no adenocarcinoma da vesícula biliar em um grupo de 12 pacientes operados em um hospital geral. **Métodos:** Os autores estudaram 12 pacientes com diagnóstico de adenocarcinoma invasor da vesícula biliar submetidos à hepatectomia no Serviço de Cirurgia Geral do Hospital de Ensino da Faculdade de Medicina do ABC, Santo André, no período entre os anos de 2001 a 2007. Desse grupo, dez eram do sexo feminino e dois, do sexo masculino. Quanto à etnia, todos eram da raça branca, com idade variando de 52 a 72 anos. Em relação aos sintomas pré-operatórios foram observados: cólica biliar (n = 6), síndrome dispéptica (n = 4), colecistite aguda (n = 1) e icterícia obstrutiva (n = 1). Em sete pacientes, o diagnóstico foi sugerido por exame de imagem pré-operatório e confirmado no intra-operatório por exame de congelação. Em cinco, o diagnóstico foi realizado após a colecistectomia aberta (n = 4) ou laparoscópica (n = 1). **Resultados:** No total foram realizadas nove bissegmentectomias centrais inferiores (ressecção dos segmentos IV-B + V) com linfadenectomia hilar e três hepatectomias ampliadas para o segmento IV. O tempo cirúrgico variou de 180 a 340 minutos. Quatro pacientes foram transfundidos.

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O sangramento intra-operatório variou de 200 a 1500 ml e o tempo de internação, de 7 a 16 dias. Houve 2 complicações em dois pacientes, uma fístula biliar e uma insuficiência hepática transitória. Nenhum paciente foi reoperado e não houve óbitos no período pós-operatório. Em relação ao estadiamento TNM foi observado: T2N0M0 (n = 4), T2N1M0 (n = 2), T3N0M0 (n = 4) e T3N1M0 (n = 2). Apenas uma paciente apresentou margem microscópica comprometida (T3N1M0) e faleceu por recorrência peritoneal e hepática aos nove meses de seguimento. Outros três pacientes apresentaram recorrência e faleceram da doença (entre 13 e 28 meses de seguimento). A sobrevida global em 3 anos foi 33,3% (n = 4). **Conclusão:** O tratamento cirúrgico radical do carcinoma de vesícula biliar com ressecção hepática e linfadenectomia hilar pode levar a uma sobrevida prolongada com baixa morbimortalidade.

Descritores: Hepatectomia; Neoplasias da vesícula biliar/cirurgia; Adenocarcinoma

INTRODUCTION

Gallbladder carcinoma was described for the first time by Maximilian Destoll, in 1777⁽¹⁾. However, it was Keen⁽²⁾ who first performed hepatic resection with a curative purpose to treat this neoplasm. Although it is rare, the malignant gallbladder neoplasm ranks sixth among the most frequent cause of cancer in the gastrointestinal tract and is the first cause of cancer in the biliary tract⁽³⁾.

Despite improvements in the postoperative support and more aggressive surgical treatment, the overall survival of patients with gallbladder carcinoma is still low. Failures in early treatment are due to the insidious course which can invariably be confused with benign diseases that are clinically less important⁽⁴⁾. As a disastrous effect, the diagnosis is often made at an advanced stage of the disease. Exuberant symptoms such as jaundice, palpable mass, changes in the bowel habit and ascites invariably represent the disease in the end-stage or advanced with low curability⁽⁵⁾.

More recently, based on better outcomes particularly from Japanese specialists (hepatic resections combined with regional or extended lymphadenectomy) there has been a resurgence of the curative surgical treatment of this neoplasm. For more advanced stages, such as T2 or

T3, most recent studies suggest performing some type of hepatectomy⁽⁴⁻¹¹⁾. The curative options suggested for treatment vary from a resection of IV-B and V segments, also called inferior central bisegmentectomy (S4B + S5) to right hepatectomy extended to segment IV^(3-4,7,12-20).

OBJECTIVE

The objective of this study was to describe the early postoperative results and the long-term survival of patients with stages T2-3 gallbladder carcinoma that underwent hepatic resection.

METHODS

A total of 22 patients with gallbladder adenocarcinoma were diagnosed by the General Surgery Service Hospital de Ensino da Faculdade de Medicina do ABC, in the city of Santo André, São Paulo, between July 2001 and July 2007. Twelve patients underwent some type of hepatectomy as surgical treatment. Resections were distributed as follows: right hepatectomy extended to segment IV (n = 3) and inferior central bisegmentectomy (S4B + S5, n = 9). The epidemiological features are shown in Chart 1.

In seven patients, the preoperative examinations showed radiological images suspect of gallbladder neoplasm whereas in the other five patients the diagnosis was made by histological findings after cholecystectomy for a presumably benign disease. Among these five patients, one presented occlusive jaundice and choledocholithiasis at the imaging examinations. This patient underwent endoscopic papillotomy and was cholecystomized (open approach) after normalization of the bilirubin levels. Another patient underwent emergency open cholecystectomy due to acute cholecystitis while the other three patients underwent elective cholecystectomy due to symptomatic cholelithiasis with biliary colic (open approach = 2 and laparoscopic approach = 1). The period between cholecystectomy and definitive surgery varied between one and three months.

Chart 1. Epidemiological characteristics

Characteristics	Cases											
	1	2	3	4	5	6	7	8	9	10	11	12
Sex	F	F	F	F	F	F	F	M	F	M	F	F
Age	52	72	68	70	66	72	70	68	65	61	71	59
ASA	II	II	II	III	I	II	I	I	I	I	I	I
Associated diseases	Alcohol abuse	SAH	SAH	SAH+DMII	-	SAH	-	-	-	-	-	-
Symptoms	Biliary colic + weight loss	Dyspeptic syndrome	Obstructive jaundice	Acute cholecystitis	Biliary colic	Biliary colic	Dyspeptic syndrome	Dyspeptic syndrome	Dyspeptic syndrome			

ASA = American Society of Anesthesiologists (scores); SAH = systemic arterial hypertension; SAH + DMII = systemic arterial hypertension + diabetes mellitus type II

All patients underwent complete abdominal ultrasound and all presented biliary lithiasis. The number of gallstones varied from two to ten, and the diameter ranged between 3 and 40 mm. Eleven patients, except one who underwent emergency surgery due to acute cholecystitis, were submitted to abdominal computed tomography (CT) in the preoperative period, and four patients to abdominal nuclear magnetic resonance (NMR). Some radiological preoperative abnormality suspect of neoplasm was seen in nine patients. The abnormalities seen included: vegetating fungoid heterogeneous lesion; focal and calcified thickening; diffuse thickening; dilation of the extrahepatic biliary tract and heterogeneous mass occupying the entire gallbladder fossa. The most frequent anatomical site of neoplasms was the fundus (n = 6) and the mean size was 3.6 cm. Distribution of the preoperative radiological findings (type of abnormality found, size of lesion, location and estimated TNM staging) and type of surgery are shown in Chart 2.

The preoperative levels of the tumor markers carcinoembryonic antigen (CEA) and CA 19.9 of all patients were measured. The level of CEA varied between 2.5 and 500 ng/ml while the level of CA 19-9 varied between 28 and 800 ng/ml. When the normal levels were taken into account, eight out of twelve patients (66.66%) presented increased levels of both CEA and CA 19-9 (Chart 3).

A total of nine IV-B + V bisegmentectomies and three hepatectomies extended to segment IV were performed. After surgical treatment, all patients were followed up at three-month intervals (up to two years) and at six-month intervals (between two and five years). At each return visit, in addition to the physical examination, the patients underwent examinations to measure the levels of CEA and CA 19-9, complete abdominal ultrasound, abdominal/pelvic computed tomography and plain chest X-ray. Recurrence was considered only in cases of unequivocal radiological documentation and, whenever possible, with histological confirmation.

Chart 2. Distribution of radiological findings and type of surgery

Findings	Cases												
	1	2	3	4	5	6	7	8	9	10	11	12	
US/CT or NMR	Mass in gallbladder fossa	Mass in gallbladder fossa	Mass in gallbladder fossa	Vegetating lesion – in the main biliary system	Focal thickening + calcification	Choledocholithiasis Biliary tree dilation	Diffuse thickening	-	-	Mass in gallbladder fossa	Vegetating lesion –main biliary system	-	
Type of surgery	S4B + S5	S4B + S5 + VB + caudate	S4B + S5	S4B + S5 + VB + caudate	S4B + S5	S4B + S5	S4B + S5	S4B + S5	S4B + S5	S4B + S5	RH + IV	RH + IV	RH + IV + VB + caudate
Site (lesion)	Fundus	Body	Fundus	Body	Fundus	Fundus	Fundus	Fundus	Fundus	Fundus	Diffuse	Infundibulum	Cystic
Size (cm)	3	6	2	4	3	2.1	2.5	2.7	3.3	6	3	3.7	
Estimated preoperative tumor staging	T3	T3	T2	T2	T3	Postop. diagnosis	Postop. diagnosis	Postop. diagnosis	Postop. diagnosis	T3	T2	Postop. diagnosis	

S4B + S5 = inferior central bisegmentectomy; RH + IV = right hepatectomy + segment IV; VB = main biliary system; Postop. = postoperative

Chart 3. Distribution of markers and biochemical tests

Markers and tests	Cases											
	1	2	3	4	5	6	7	8	9	10	11	12
CEA Mean = 82.0 ng/ml)	100	500	35	2.5	85	3.5	3.3	3.8	2.7	91.3	31.5	126
CA 19-9 Mean = 111.6 ng/ml)	190	325	98	28	183	25	2.7	20.2	16.3	127	253	71.7
Alkaline phosphatase	500	750	33	10	25	38	10	34.2	12.4	16	732	267
Total bilirubin	1.6	2	1	0.6	0.8	1	0.7	1.7	1.5	1.2	0.4	1.1

CEA up to 4.0 ng/ml and CA 19-9 up to 39 ng/ml; CEA = carcinoembryonic antigen; CA 19-9 = tumor marker

RESULTS

Early surgical results are shown in Chart 4 and the postoperative histological findings are shown in Chart 5. There were no deaths in the postoperative period. Three patients presented a major complication each and there were no minor complications. No patient was reoperated. The overall morbidity in the current series was 25%. One patient, who underwent extended bisegmentectomy with resection of the caudate lobe and of the main biliary tree, presented a high output biliary fistula that resolved with conservative treatment. A patient who also underwent IV-B + V bisegmentectomy and presented compensated micronodular cirrhosis of alcoholic etiology (Child A) showed postoperative hepatic insufficiency that was clinically reverted. Another patient, who underwent extended right hepatectomy, presented bronchopneumonia that was resolved with wide spectrum antibiotic therapy.

A total of eleven surgeries presented free margins (R0), while one presented a microscopically compromised margin (R1). This R1 resection was performed in a tumor measuring about six centimeters (in the longest axis) located in the body with invasion of the infundibulum (inferior hepatic margin microscopically

compromised). No patients underwent multidisciplinary treatment with radiotherapy or chemotherapy.

The follow-up varied between 11 and 48 months. Four patients presented relapses and died from the disease. Coincidentally, one of the patients presented a microscopically positive margin of hepatic section and also three lymph nodes affected. This patient showed disease relapse both in the peritoneum and in the liver, within eight months after surgery. The patient evolved with antral/pyloric occlusion syndrome and underwent new surgery, further evolving to death in the postoperative period (at nine-month follow-up). Three other patients presented relapses in a period varying between six and 19 months after the surgical treatment with a 11-to-28-month survival. The eight remaining patients were alive until the end of this study without relapse, in a follow-up period of 11 to 48 months. Four patients were alive and with no disease for at least 36 months until the end of the study, with a total disease-free survival of 33.3% in three years. The late surgical results are shown in Chart 6. The Figure 1 shows the magnetic resonance of a vegetating lesion inside the gallbladder. Figures 2, 3 and 4 show the macroscopic findings of surgery and Figure 5 presents a schematic diagram of the surgical technique.

Chart 4. Distribution of early surgical results

Early surgical results	Cases											
	1	2	3	4	5	6	7	8	9	10	11	12
Operative time (minutes)	260	280	240	340	180	185	260	190	225	350	380	410
Median = 276,6												
Estimated bleeding (ml)	200	1,500	800	600	700	500	1,000	600	500	2,000	1,500	1,200
Median = 950 ml												
Length of stay (d)	9	18	8	7	9	10	8	7	7	16	10	11
Median = 9d												
Complications	Hep. Ins.	BF	-	-	-	-	-	-	-	BCP	-	-
Transfusion	-	+	-	-	-	-	+	-	-	+	+	+
Type of surgery	S IV-B + V	S IV-B + V	S IV-B + V	S IV-B+V	S IV-B + V	RH +IV	RH+ IV	RH + IV				

ml = milliliters; d = days; Hep. Ins. = hepatic insufficiency; BF = biliary fistula; BCP = bronchopneumonia; SIV-B + V = inferior central bisegmentectomy; RH+IV = right hepatectomy extended to segment IV

Chart 5. Distribution of histological findings

Histological findings	Cases											
	1	2	3	4	5	6	7	8	9	10	11	12
Macroscopy	nodular	nodular	papilliferous	papilliferous	nodular	tubular	tubular	papilliferous	papilliferous	papilliferous	papilliferous	nodular
Mode of spread	Liver-bed type	Hilum type	Liver-bed type	Hilum type	Liver-bed type	Hilum type						
TNM	T2N0M0	T3N1M0	T2N0M0	T3N0M0	T2N1M0	T3N0M0	T3N0M0	T2N0M0	T2N0M0	T3N0M0	T3N0M0	T3N1M0
Differentiation	I	III	II	I	II	III	II	I	I	I	I	III
Dissected versus affected lymph nodes	7(0)	15(3+)	8(0)	10(0)	14(1+)	10(0)	10(0)	12(0)	13(0)	9(0)	14(0)	14(2+)

Chart 6. Distribution of late results

Late results	Cases											
	1	2	3	4	5	6	7	8	9	10	11	12
Survival (months)	29	11	18	28	39	12	37	11	25	38	48	13
Status	Alive with no disease	Deceased due to disease	Alive with no disease	Deceased due to disease	Alive with no disease	Deceased due to disease	Alive with no disease	Deceased due to disease				
Relapse	-	+	-	+	-	+	-	-	-	-	-	+
Site		Peritoneum + liver		Peritoneum		Liver + lungs						Peritoneum + liver
Operative time versus relapse (months)		9		19		7						6

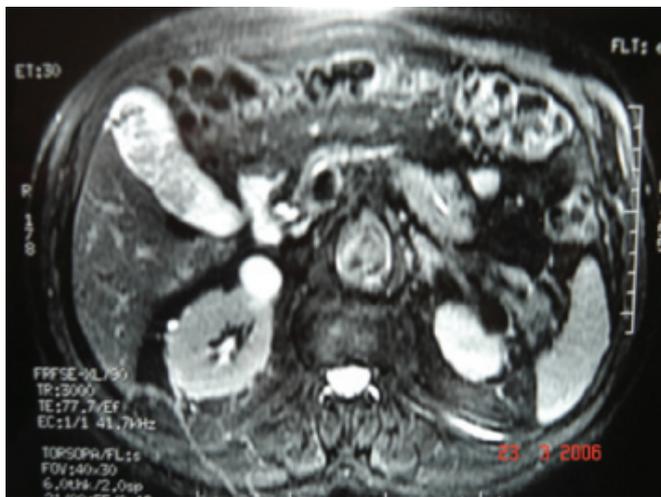


Figure 1. Nuclear magnetic resonance – heterogenous vegetating lesion inside the gallbladder

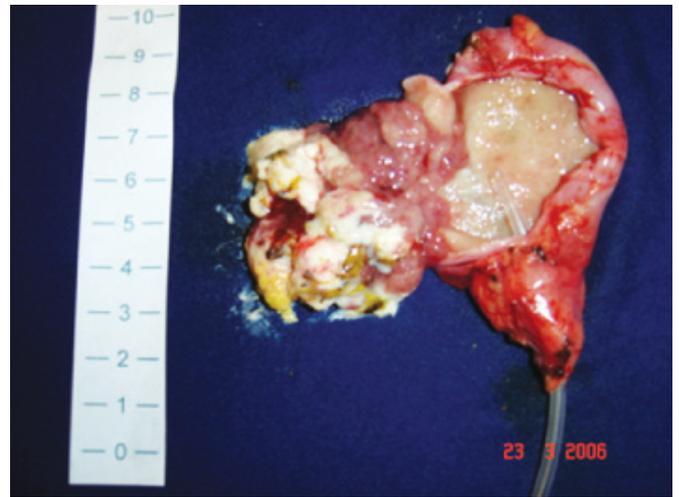


Figure 2. Macroscopic finding – vegetating lesion inside the gallbladder



Figure 3. Specimen of inferior central bisegmentectomy (segments IV-B and V)

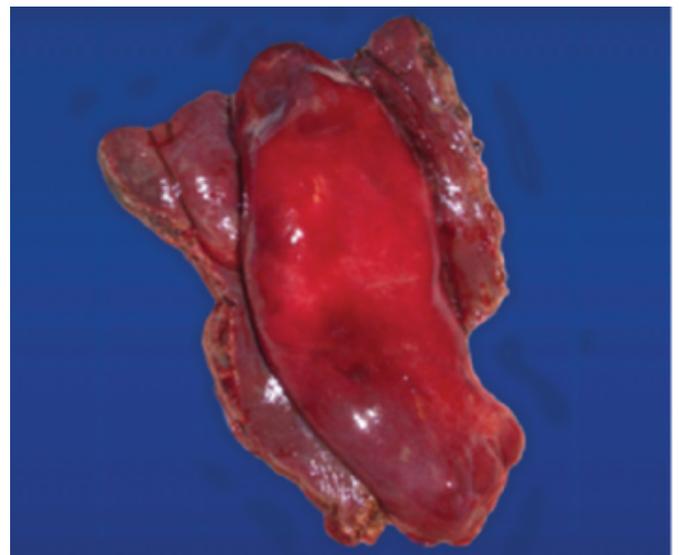


Figure 4. Specimen of inferior central bisegmentectomy (segments IV-B and V) with gallbladder resection in monoblock

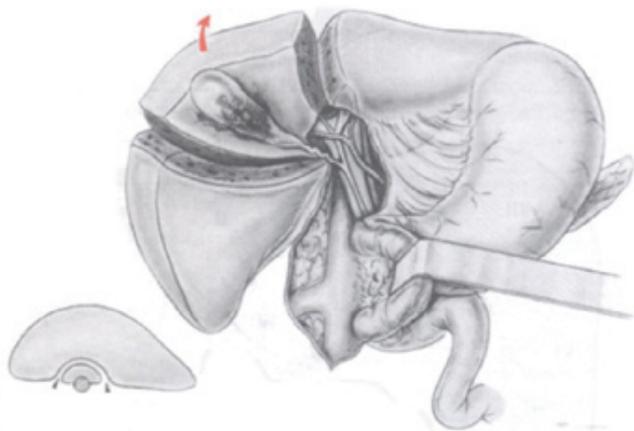


Figure 5. Surgical technique for bisegmentectomy IV-B+V, based on Cubertafond et al⁽³⁰⁾, 1990 (authorized reproduction)

DISCUSSION

Although the etiology of the gallbladder carcinoma is unknown, some authors have considered the presence of gallstones as a risk factor for this neoplasm⁽¹¹⁾. Evidence favoring this association is in the fact that 65 to 90% of patients with gallbladder neoplasm present gallstones by the time of diagnosis⁽⁵⁾. Additionally, it was observed that the risk of developing gallbladder carcinoma is greater and directly proportional to the size of gallstones. According to Diehl⁽²¹⁾, the relative risk of developing gallbladder carcinoma in individuals with gallstones between 2.0 and 2.9 cm of diameter is 2.4 when compared with the overall population with no gallstones, and it goes up to 10.1 if the gallstones are larger than 3 cm in diameter. In this current series, all patients presented gallstones with diameters varying between 0.3 and 4 cm, and eight patients presented gallstones larger than 2 cm. Although the sample was small, this finding coincides with the abovementioned theory that the large gallstones may favor the development of gallbladder carcinoma.

Gallbladder carcinoma was more commonly described in the fundus and it may appear as a focal wall thickening, a polypoid – vegetating lesion or even as a plaque in the mucosa⁽²²⁾. Macroscopically, it can be divided into three types: papilliferous, tubular or nodular. Papilliferous tumors invade the hepatic surface less frequently and present lower frequency of lymph node involvement⁽¹⁹⁾. On the other hand, the tubular or nodular tumors have more hepatic and hilar infiltration as well as greater lymph node involvement. However, in the present series, most patients coincidentally presented tumors in the fundus of papilliferous pattern (n = 6). In this group, no patients presented lymph node involvement. Nevertheless, three patients with nodular pattern also presented lymph node

involvement. The only histological finding in this series was adenocarcinoma which was in agreement with the literature data, in which this type of carcinoma was found in 80 to 95% of cases⁽²³⁻²⁴⁾.

Localized gallbladder carcinoma has no specific symptoms. Pain in the right hypochondrium, weight loss, anorexia, nausea and vomiting, jaundice and abdominal distension are the symptoms most commonly described⁽⁵⁾. The presence of jaundice was associated with an extremely poor prognosis. Surgical unresectability in icteric patients represents 44%. Patients with advanced disease may also present a palpable mass, irregular liver and ascites⁽⁵⁾.

In 1% of the patients, gallbladder carcinoma is incidentally discovered during routine cholecystectomy or even at a later stage with histological evaluation of the surgical specimen. However, in only 20% of cases the neoplasm is restricted to the gallbladder – unfortunately, the great majority of patients present upon diagnosis invasion of adjacent organs or distant metastases. However, the gallbladder neoplasm should be suspected in patients with a long history of oligosymptomatic chronic calculous cholecystitis who recently started presenting changes in their symptoms. This neoplasm has a higher incidence in elderly individuals. About 90% of patients are aged over 50 years and the incidence peak is between 70 and 75 years. It is usually more frequently found in females in a 3:1 ratio. In this present series there was also a predominance of females, although it was even higher than described, with a 6:1 ratio. On the other hand, the mean age of patients was under 66 years, which is younger than data reported in the literature⁽⁵⁾.

Knowledge about the natural history of gallbladder carcinoma, especially its dissemination pattern, has been fundamental for the progression of its management. Fahim et al.⁽²⁵⁾ described the modes of spread (contiguity, lymphatic, hematogenic, neural, peritoneal and intraductal). The gallbladder lymphatic drainage is primarily directed to the lymph nodes along the main biliary system which correspond to the first drainage station (N1). Subsequently, to the pancreatic-duodenal lymph nodes (superior, anterior and posterior), portal lymph nodes (posterior) and in the course of the common hepatic artery which are considered as the second drainage station (N2). Finally, the drainage heads to the lymph nodes of the celiac trunk, superior mesenteric and para-aortic vessels which correspond to the third drainage station (N3). Hilar lymph nodes are only affected by retrograde drainage. The lymph node involvement rate depends on the macroscopic type of the tumor, depth of invasion and grade of differentiation, and it varied between 54% and 64%⁽⁵⁾. For T1b tumors, it is about 15.5% for primary chains (N1) and it reaches

40% to 60% for primary chains or even about 20% for secondary chains in T2 tumors⁽²⁴⁾. In T3 or T4 tumors, however, the more distant involvement such as para-aortic lymph nodes (N3) can reach rates of 19% to 25%^(18,26). The majority of patients presents advanced stages with intense symptoms and low respectability rate⁽⁴⁾.

Although the diagnosis of gallbladder carcinoma is histological (surgical specimen), it must always be suggested in cases of a suspect radiological image. This way, patients with a clinical picture compatible with cholelithiasis (biliary colic or dyspeptic syndrome) may coincidentally present in imaging studies a suspect lesion that should be better radiologically evaluated. The radiological images (ultrasound or computed tomography) more frequently associated with the gallbladder carcinoma are:

- tumor mass that replaces the gallbladder (36-45%);
- gallbladder wall thickening (19-47%);
- vegetating mass in the gallbladder lumen (14%)⁽²⁷⁾.

It has been reported that tumor size is strictly related to tumor extension by the time of diagnosis; therefore, tumors measuring over one centimeter are probably malignant, whereas those smaller than one centimeter are supposedly benign and related to cholesterol polyps. Gallbladder wall thickening, both focal and diffuse, has been the most difficult manner to establish the preoperative diagnosis of gallbladder cancer since it can be undistinguishable from acute cholecystitis. In the current series, most patients presented polypoid lesions or a mass in the gallbladder fossa which were in conformity with the findings in the medical literature. Only one lesion presented as focal thickening and calcification. Nuclear magnetic resonance (NMR) has been the most sensitive examination to detect the tumor extension. With NMR it is possible to accurately assess the invasion of the hepatic parenchyma or even the surrounding structures, in addition to allowing better assessment of the vascular structures and the main and secondary biliary trees. Therefore, it is paramount to establish the preoperative resectability⁽²⁷⁾.

Both CA 19.9 and CEA markers may be increased in the gallbladder carcinoma and have occasionally contributed to the diagnosis, especially in anicteric patients⁽¹⁴⁾. These markers showed similar sensitivity (approximately 70%); however, the specificity of CA19.9 was higher than that of CEA (90% versus 71%)⁽²⁸⁾. In our cases, both markers were elevated in the majority of patients evaluated in the preoperative period and with no difference among them. It should be emphasized that all patients were anicteric. Despite the small sample reported, this finding signals that the association of the suspect image with increased markers

in anicteric patients may contribute to the preoperative diagnosis of gallbladder carcinoma.

Treatment of the gallbladder carcinoma is still a challenge and a controversy to surgeons. If, on the one hand, the extended surgery with hepatectomy and regional lymphadenectomy may prolong the patient's survival, on the other hand it is still associated with considerable morbidity and mortality^(4-10,13,16-17,20). The surgery must be customized for each case, both right hepatectomy extended to the IV segment or inferior central bisegmentectomy (resection of segments IV-B and V) or even central hepatectomy (resection of segments IV, V and VIII) have been accepted by most specialized services as long as the margins are respected, which must be free of neoplasm involvement^(4-6,11-12,14,29). Therefore, for T2-3 tumors restricted to the gallbladder fundus or body, without hilar invasion ("liver-bed type") and especially without infiltrative growth (with little invasion to the liver), inferior central bisegmentectomy (S4B + S5) can be performed without any change in the final oncological outcome. The main advantage of this surgery is greater preservation of the hepatic parenchyma compared with right hepatectomy, without compromising the oncological radicality^(8,11,13,16). This surgery seems to present less morbidity than the extended right hepatectomy, especially in relation to the postoperative hepatic insufficiency and transoperative hemorrhage. On the other hand, for more advanced tumors (T3 or T4) and with predominantly distal presentation (infundibulum and cystic ductus region) or with hilar invasion ("hilum type") and infiltrative character in depth towards the hepatic bed, the surgery with best oncological results has been the right hepatectomy extended to segment IV^(4-6,9,12,14,29). It should be emphasized that the remaining hepatic volume is the limiting factor to this type of resection and it must be greater than 25% or up to 30% to assure a lower index of postoperative hepatic insufficiency^(12,29). In our service, the management has been similar. In all lesions suspect of gallbladder neoplasm in the preoperative imaging examination, the patient is explored with an extended right subcostal incision and a detailed inventory is carried out with rigorous assessment of the peritoneal, hepatic and lymph node dissemination routes (N2-N3). In case of any evidence of spread, the tissue is promptly submitted to biopsy and the specimen is sent to histological analysis by means of frozen examination. If positive, the resection is interrupted. If no dissemination is present, cholecystectomy is primarily performed (in the anterior lesions or even in the posterior lesions with no clear hepatic involvement). After that, the gallbladder is longitudinally opened and the cystic duct is marked; the sample is sent to frozen biopsy examination. If it is positive for neoplasm, lymphadenectomy along the

path of hepatoduodenal ligament (N1) is performed jointly with dissection of N2 lymph nodes, such as the pancreatic-duodenal (superior, anterior, posterior), retroportal lymph nodes and the nodes located along the common hepatic artery. Although there are studies showing increased survival in patients with affected lymph nodes who undergo extended lymphadenectomy, we believe that in this disease such procedure has a decisive role in the staging and prognostic evaluation, thus properly superseding its therapeutic character.

At the same time, an hepatic resection is performed, either an inferior central bisegmentectomy (S4B + S5) or right hepatectomy extended to the IV segment depending on factors such as the patient's morbidity status, place and type of tumor spread and remaining hepatic volume. Specifically, for cases in which the tumor presents obvious invasion of the hepatic parenchyma, the surgery is performed as a single block with resection of the gallbladder jointly with segments IV-B and V or with the right lobe (segments IV, V, VI, VII and VIII). Therefore, S4B + S5 has been reserved for cases of tumors limited to the gallbladder fundus or body and without hilar invasion (liver-bed type). For tumors located in the infundibulum, cystic ductus or large tumors next to or with invasion of the hilar region (hilum type), the surgery performed is the right hepatectomy extended to the segment IV if the volume of the remaining left lobe is greater than 25%⁽⁴⁾, as observed in three cases of the current series.

The inferior central bisegmentectomy (S4B + S5) we perform in our department follows the technical standardization described by Cubertafond et al.⁽³⁰⁾. There is some controversy in the resection (as a block) of the biliary tree and of the caudate lobe in a systematic manner. If, for some authors, it is always performed to facilitate hilar lymphadenectomy and to increase surgical radicality, for others it must be reserved only for cases of invasion of these structures or even insufficient margins. The systematic resection has not increased survival and it still leads to high morbidity, especially in cases of biliary fistulas^(4-5,12,14). We have not performed the resection of the main biliary tree in a routine and systematic fashion. This management has been reserved only for cases in which the neoplasm affects the ductus hepatocholedochus or in cases where the margin of the cystic duct tends to be suspicious or even affected. Therefore, in only three patients we performed the joint resection of the main biliary tree (up to, inclusive, the confluence of the hepatic ductus) and the caudate lobe. The reconstruction used in all these cases has been the end-to-side intrahepatic hepaticojejunostomy of 70 cm in an excluded loop, retrocolic as per advocated by Blumgart et al.⁽²⁹⁾. In patients with an indication

of hepatectomy (stage T2 or higher) who underwent previous laparoscopic cholecystectomy, similar to other authors we have routinely performed the resection of the scar at the portal sites, from the skin up to the parietal peritoneum^(4,11).

The morbidity observed in this current series is close to that reported in the literature, which varied between 13% and 30%^(16,31). The main complications were infections, such as intracavitary abscesses or pneumonia; but pleural effusion and biliary fistulas were also described. We should emphasize that the two cases with complications were treated conservatively with no need of surgical intervention. One of them evolved with a biliary fistula, a common complication mainly in resections involving the caudate lobe and performance of intrahepatic biliodigestive anastomosis. This fistula was medically treated and closed spontaneously on the 30th postoperative day. The other complication in the series, a transient hepatic insufficiency, was also resolved with conservative medical treatment. This patient presented compensated hepatopathy that was not suspected in the preoperative period. It was recognized that even the minor hepatic resections were associated with postoperative hepatic insufficiency in this type of patient.

The survival observed in patients with gallbladder carcinoma was directly proportional to tumor thickness, lymph nodes involvement (TNM staging) and resection (R0). After curative resection (R0), survival varied from 60% to 80% within five years for T2 tumors, and between 15% and 50% within five years for T3 tumors⁽⁴⁾. Although the sample was small, the survival of four patients was over 36 months. Eight patients were alive and without disease in a follow-up period that varied between 11 and 48 months until the conclusion of the present study. Despite the fact it was a short follow-up period, only four patients presented relapses and one of them had an affected margin (R1). On the other hand, almost all resections were R0. Additionally, these results may have been obtained through an appropriate preoperative diagnosis and extended surgery with hepatectomy and lymphadenectomy associated to a still higher number of well differentiated tumors and with low lymph node involvement.

CONCLUSION

Although the invasive gallbladder carcinoma (stages T2-T3) is usually a neoplasm with an extremely poor prognosis, an adequate preoperative diagnosis associated to correct surgical treatment (hepatic resection with free margins and hilar lymphadenectomy) may lead to prolonged survival in selected cases with minimal morbidity and zero mortality.

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