

Gallbladder carcinoma. Surgical management of gallblad-der carcinoma.

An analysis of 37 cases



Ann. Ital. Chir., 2018 89, 6: 501-506
pii: S0003469X18029202

Florin Graur*/**, Emil Mois*/**, Simona Margarit*/**, Claudia Hagiu*/**, Nadim al Hajjar*/**

*University of Medicine and Pharmacy "Iuliu Hatieganu", Cluj-Napoca, Romania

**Regional Institute of Gastroenterology and Hepatology "Prof. O. Fodor", Cluj-Napoca, Romania

Gallbladder carcinoma. Surgical management of gallblad-der carcinoma. An analysis of 37 cases

BACKGROUND & AIMS: Gallbladder carcinoma is a rare yet very aggressive cancer. In this study we evaluate the presentation, staging, procedures, complications and survival of patients with gallbladder carcinoma.

MATERIAL AND METHODS: Data at presentation, operative findings, postoperative evolution, complications and survival data were analyzed for 37 patients with gallbladder carcinoma (as cohort study) confirmed at histopathology between January 2005 and December 2011 in Surgical Department of Regional Institute of Gastroenterology And Hepatology "Octavian Fodor" Cluj-Napoca, Romania.

RESULTS: In 12 cases we had the suspicion of GBC (gallbladder carcinoma) before surgery, in 6 cases GBC was suspected intraoperatively and in 19 cases only after the histopathology exam. Radical cholecystectomy was considered in 9 cases (24.32%); 4 cases with cholecystectomy alone (patients with Tis-T1) and in 5 cases liver resection was associated. **CONCLUSION:** The GBC has a low incidence (0.35% out of all cholecystectomies), the females being more affected (F:B=4.3:1). GBC was associated with low resectability rate (24.32%) and having a bad prognosis (survival under a year in stages T3 and T4). In most cases the diagnosis was hidden by an acute inflammatory process (acute cholecystitis) and the diagnosis was made after surgical intervention, therefore, the histopathology is crucial in these situations.

KEY WORDS: Gallbladder carcinoma, Jaundice, Palliative treatment, Resection, Survival

Introduction

Gallbladder carcinoma (GBC) is a silent and the same time a very aggressive disease with early metastasis. A new study reports that the incidence is 2.5 of 100.000 people ¹. Despite all the effort of the medical world, it is discovered incidentally in most of the cases, after a cholecystectomy (as a T1-T3 stage) or intraoperatively

(when is T3-T4). Because the diagnosis is made in advance stage, the prognosis is poor. Females are more predicted (2.6 times than man) for gallbladder carcinoma (is the first cause of cancer death for women in Chile), 3/4 of patients having over 75 years ¹.

Surgery remains the only curative treatment for gallbladder carcinoma (this cancer is resistant to radiotherapy) but not all the time is possible a radical resection. Chemotherapy is only used after surgery, such as gemcitabine and oxaliplatin, but has no preventive effect. The gallbladder carcinoma is radioresistant.

A complete resection is the only change for cure, but most of the patients present at the hospital in advanced stages. The Glenn procedure indicated in GBC consists of resection of the gall bladder with non anatomical wedge resection of 2 cm of liver surrounding the gall bladder with lymph node resection in the hepatoduodenal ligament. Some studies promote more extensive resec-

Pervenuto in Redazione Luglio 2018. Accettato per la pubblicazione 2 Settembre 2018

Correspondence to: Emil Mois, Regional Institute of Gastroenterology and Hepatology "Prof. O. Fodor", Str. Croitorilor 19-21, Cluj-Napoca, Romania; (e-mail: dr_emil_mois@yahoo.com)

tions like anatomical IVb+V segments resection or right/left extended hepatectomies associated with common bile duct resection and pancreatoduodenectomy or lymph dissection in the interaorto-caval space²⁻⁶. In stages T_{is} or T_{1a} the simple cholecystectomy is enough as radical treatment, but in stages T_{1b}, T₂ and T₃ the open surgery with radical cholecystectomy is mandatory. The T_{1b} stage is debatable, some surgeons consider the simple cholecystectomy as sufficient. The T₄ stage is generally unresectable⁷.

Aggressive surgical therapy of gallbladder cancer demonstrates a longer survival, instead of a limited resection. This study aims to evaluate the survival of the patients with gallbladder carcinoma according to stages and other clinical data.

Material and Method

Between January 2005 and December 2011 in our clinic were performed 10586 cholecystectomies. On a retrospective study, we discovered a number of 37 cases of GBC based on anatomopathological results. The analyzed parameters were: admission data, lab tests, histopathological results, treatment and survival. The statistical analysis was performed with IBM® SPSS® Statistics ver. 20.0.0 using Kaplan-Meier survival method.

Results

Among 10586 cholecystectomies only 37 were GBC which represents a small incidence in our area (0.35%). The number of cholecystectomies performed during 2005-2011 (> 95% laparoscopic cholecystectomies) is represented in Fig. 1, while Fig. 2 represents the number of gallbladder carcinoma between 2005 and 2011. Median age of the series was 69.02 (38-92); 30 (81%) were women and 7 (19%) were men (F:B=4.3:1). The

average of hospitalization was 12,16 days (3-57). Table I shows the data of all 37 patients.

In 30 cases the major symptom was pain in the right hypochondrium (14 having also jaundice, average for the total bilirubin was 7.75), 2 patients accusing weight loss too.

At the abdominal ultrasound the gallbladder lithiasis was discovered in 33 cases, 20 with acute cholecystitis and 4 with a subhepatic tumor.

Other preoperative investigations discover liver metastasis (3 cases - 2 at CT and 1 at abdominal ultrasound), adenopathy of the hepatic artery, retroperitoneal and interaortocaval (3 cases discovered at CT scan).

When stratifying the cases following AJCC 7th ed 2010, stage II and IIIA are more prominent with 12 cases each, followed by stage IVB with 5 cases (Fig. 3)

Taking into account only the T category, stages T2 and T3 are represented with 14 cases each (Fig. 4).

Patients with jaundice are in advanced stages (stages 3-4) with a very low rate of resection or survival.

In 8 cases we had the suspicion of GBC before surgery, in 8 cases GBC was suspected intraoperatively and in 21 cases only after the histopathology exam (57.75% were diagnosed after pathology examination).

In most of the cases there was no preoperative or intraoperative suspicion of GBC, but of acute cholecystitis with edema or sclerous cholecystitis. In the cases with preoperative or intraoperative suspicion of GBC, the lymph node dissection and liver resection were performed if there was a radical intent of resection.

Cholecystectomy was performed in 34 cases (91.89%) associated with: coledoco-duodeno-anastomosis in 2 (5.40%) cases, biliary-enteric Roux-in-Y drainage in 3 (8.10%) cases, T-tube drainage in 2 (5.40%) cases, in 5 (13.51%) cases was performed a radical resection with a partial liver resection (1 case with transverse colon resection) and in 1 case an open stent insertion. Radical cholecystectomy was considered in 4 cases with cholecystectomy alone and in 5 cases with partial liver resec-

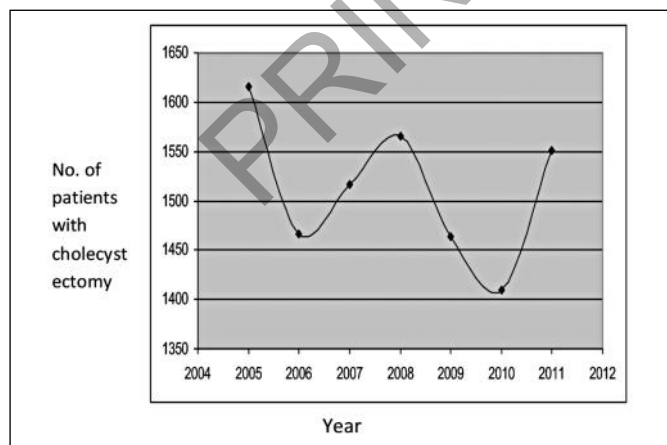


Fig. 1: Number of cholecystectomies during 2005-2011.

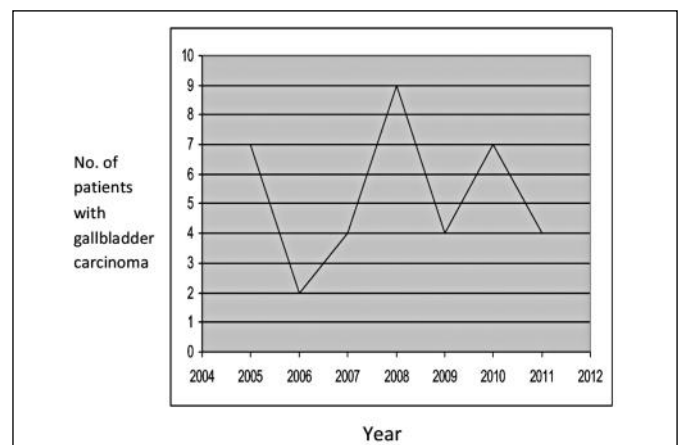


Fig. 2: Number of GBC during 2005-2011.

TABLE I - Patients data

Factors	No	Observations
Sex		
Male	7	
Female	30	
Age		
< 65 yrs	9	
> 65 yrs	28	
Main presenting symptom		
Pain	30	
Jaundice	14	
Other	2	
Suspicion of GB carcinoma		
Preoperative	8	
Intraoperative	8	
Postoperative (histopathology)	21	
Ultrasound findings		
Gallbladder lithiasis	33	
Acute cholecystitis signs	20	
Subhepatic tumor	4	
AJCC stage		
0	3	
I	1	
II	12	
III a	12	
III b	3	
IV a	1	
IV b	5	
Treatment		
Laparoscopic cholecystectomy	14	3 ERCP + stent insertion; 1 ERCP + sphincterotomy; 1 reintervention for fluid subhepatic collection
Open cholecystectomy	7	
Cholecystectomy + Choledoco-duodenoanastomosis	1	
Cholecystectomy + choledoco-duodenoanastomosis + wirsungo-jejunoanastomosis	1	1 reintervention for wirsungo-jejunoanastomosis fistula
Cholecystectomy + hepatico-jejunoanastomosis	3	
Cholecystectomy + partial liver resection	5	
Cholecystectomy + open stent insertion	1	
Cholecystectomy + T-tube drainage	2	1 reintervention for false fluid collection
Open stent insertion	1	1 ERCP+ sphincterotomy
Exploratory laparotomy + biopsy	2	

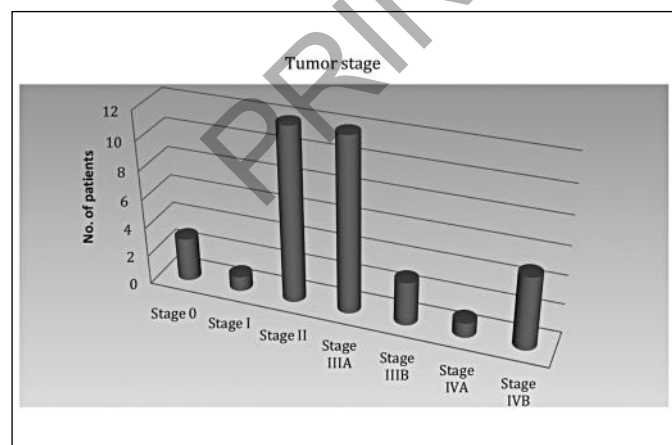


Fig. 3: Staging of GBC (AJCC 7th ed., 2010).

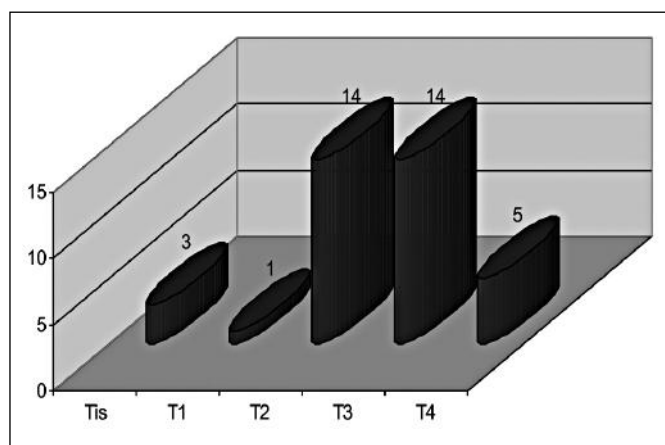


Fig. 4: Tumor (T) Classification (AJCC 7th ed., 2010).

TABLE II – Means and Medians for Survival Time

T stage	Mean ^a				Median			
	Estimate	Std. Error	95% Confidence Interval		Estimate	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound			Lower Bound	Upper Bound
Tis	1770.000	61.518	1649.424	1890.576	1683.000	–	–	–
T1	490.000	.000	490.000	490.000	490.000	–	–	–
T2	450.480	154.185	148.277	752.683	261.000	137.829	.000	531.145
T3	252.000	133.976	.000	514.594	61.000	12.124	37.236	84.764
T4	254.750	91.998	74.435	435.065	199.000	178.000	.000	547.880
Overall	452.713	108.503	240.047	665.379	199.000	90.380	21.856	376.144

^a Estimation is limited to the largest survival time if it is censored

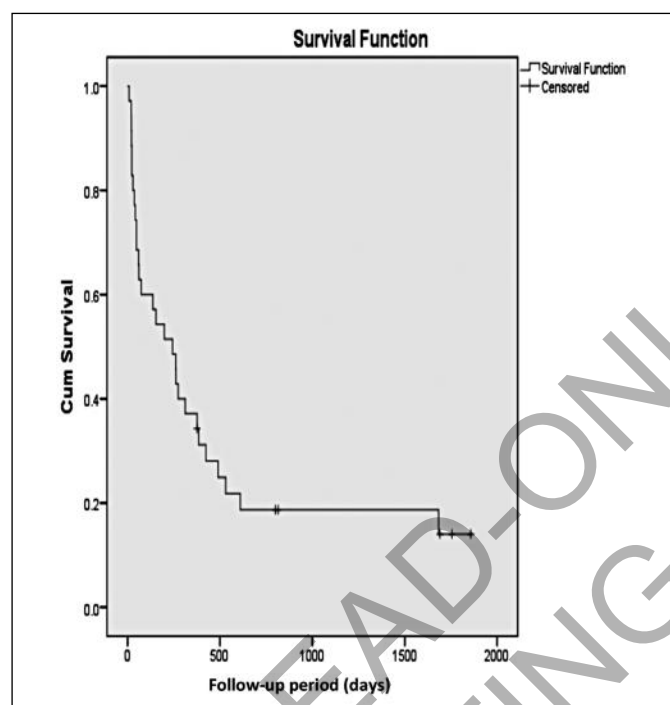


Fig. 5: Five years estimated survival.

tion (total of 9 cases – 24.32%). In 2 cases were performed exploratory laparotomies with biopsies and in 1 case an open stent insertion was possible. In 4 cases was necessary a second intervention: 3 cases of fluid collection and 1 for haemostasis of the wound.

In 7 cases was performed an ERCP, 4 for stent insertion and sphincterotomy, and 2 cases for main bile duct lithiasis (in one case the ERCP was aborted because of a duodenal ulcer bleeding).

The resectability rate with a radical intent was low – 24.32%, the reintervention rate 10.81% and one perioperative death.

Mean estimated overall survival time is 452.71±108.50 days (range 240.04-665.37) and median estimated overall survival time is 199.00±90.38 days (range 21.85-376.14) (Table II).

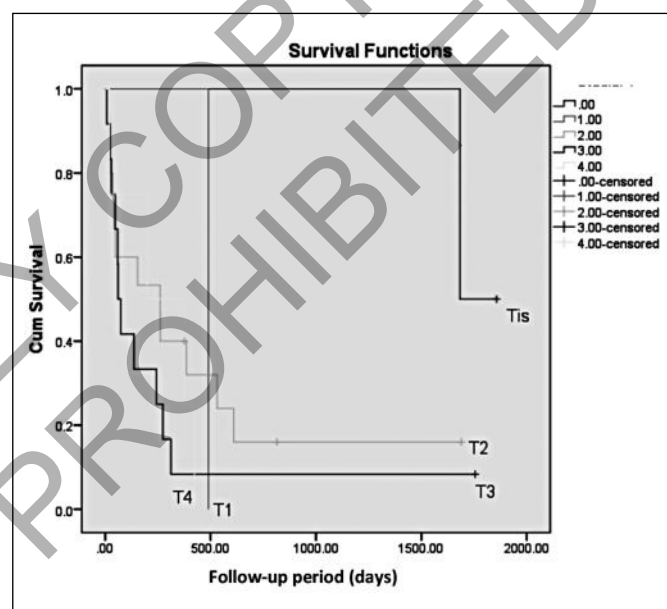


Fig. 6: Survival stratified on T stage.

Discusions

The incidence of gallbladder carcinoma varies between 1% to 3% of cholecystectomies⁸⁻¹¹, while in our series was a low incidence – 0.35% of cholecystectomies. Females are more prone to develop gallbladder carcinoma, one factor could be the lithiasis itself as carcinogenic stimulus – in our series 89.18% of patients had gallbladder lithiasis (literature data ranges between 70% and 90%)¹². The literature shows a 70% prevalence of females, while in our study was 81.08%⁹. Mean age varies between 59.7 and 67 years^{6,9}, while in our study it was 69 years. The mean hospitalisation period is 15 days⁶ – in our series it was 12.16 days.

Preoperative diagnosis of GBC is very difficult, only the suspicion of the examiner could improve the early diagnosis. One important etiologic relation is with gallbladder lithiasis, the longer stay of the stones in the gallbladder the higher the risk for GBC.

Riassunto

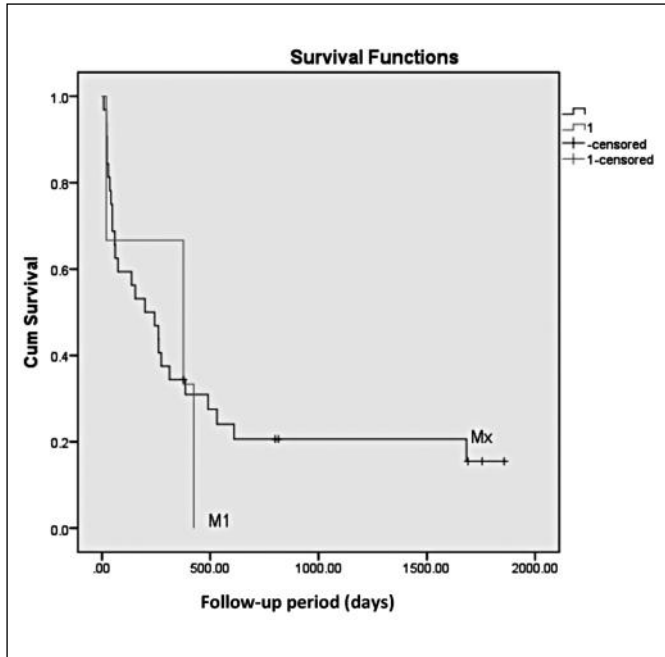


Fig. 7: Survival stratified on M stage

Only 10-20% are diagnosticated in the early stages (stages 0-1) ^{7,9} – 10.81% in our series, while almost half of the cases had jaundice at admission, with a very low rate of resectability – 24.32%. Data in the literature reports a resectability between 17% and 47% ¹⁰. The reported morbidity is about 27.5% ⁹ and in our series the reintervention rate is about 10.81%. Survival data in the literature shows a 5-year survival rate varying between 18% and 58% after radical resection ^{13,14}.

Conclusion

The incidence of GBC is below data in the literature, but other data are in the limit of the ranges. Also the suspicion of GBC is very low before and during surgery and this is one cause for paliative resection in some cases, because some patients will not come back for a reintervention. In most of the cases the carcinoma is hidden by a benign pathology like acute cholecystitis. The survival is better in early stages with a chance for radical resection, while in the advanced stages presenting with jaundice the prognosis is more reserved. The histopathological exam of any specimen removed during cholecystectomy is essential in many cases to diagnose a hidden gallbladder carcinoma. This could be life saving in many cases when the patients are recalled and operated radically. Such an approach could improve the survival of a very aggressive cancer.

Il carcinoma della cistifellea è raro ma molto aggressivo. In questo studio valutiamo la presentazione, la stadiazione, le procedure, le complicanze e la sopravvivenza dei pazienti con carcinoma della colecisti.

Si è proceduto all'analisi dei dati circa la presentazione, la condotta operatoria, l'evoluzione postoperatoria, le complicanze e i dati di sopravvivenza di 37 pazienti con carcinoma della colecisti (come studio di coorte) confermati a livello istopatologico tra il gennaio 2005 e il dicembre 2011 nel dipartimento di chirurgia dell'istituto regionale di gastroenterologia ed epatologia "Ottaviano Fodor" Cluj-Napoca, Romania.

I risultati sono che in 12 casi il sospetto di GBC (carcinoma della colecisti) era insorto prima dell'intervento chirurgico, in 6 casi il GBC è stato sospettato intraoperatoriamente e in 19 casi la diagnosi è avvenuta solo all'esame istopatologico. La colecistectomia radicale è stata considerata in 9 casi (24,32%): in 4 casi con colecistectomia semplice (pazienti con Tis-T1) e in 5 casi con associata una resezione epatica.

Per la conclusione si considera che il GBC ha una bassa incidenza (0,35% su tutte le colecistectomie), e le donne sono le più colpite (F: B = 4,3: 1). Il GBC è risultato con ridotta possibilità di resezione nel 24,32% dei casi, e con prognosi sfavorevole (sopravvivenza inferiore a un anno nelle fasi T3 e T4). Nella maggior parte dei casi la diagnosi è risultata occultata da un processo infiammatorio acuto (colecistite acuta) con chiarimento diagnostico soltanto ad intervento chirurgico completato, pertanto l'istopatologia è fondamentale per il chiarimento definitivo in queste situazioni.

References

1. Feng, F.L., et al., *Role of radical resection in patients with gallbladder carcinoma and jaundice*. Chin Med J (Engl), 2012; 125(5): 752-6.
2. Gagner M, Rossi RL: *Radical operations for carcinoma of the gallbladder: Present status in North America*. World J Surg, 1991; 15(3): 344-47.
3. Gall FP, et al.: *Radical operations for carcinoma of the gallbladder: Present status in Germany*. World J Surg, 1991; 15(3):328-36.
4. Ogura Y, et al.: *Radical operations for carcinoma of the gallbladder: Present status in Japan*. World J Surg, 1991; 15(3): 337-43.
5. Bartlett DL., et al.: *Long-term results after resection for gallbladder cancer. Implications for staging and management*. Ann Surg, 1996; 224(5):639-46.
6. Scheingraber S, et al.: *The standardized surgical approach improves outcome of gallbladder cancer*. World J Surg Oncol, 2007; 5:55.
7. Zhu AX, et al: *Current management of gallbladder carcinoma*. Oncologist, 2010; 15(2):168-81.

8. Morera Ocon, F.J., et al.: *Gallbladder cancer in a regional hospital*. Cir Esp, 2009; 86(4):219-23.
9. Manterola C, Vial, M, Roa JC: *Survival of a cohort of patients with intermediate and advanced gallbladder cancer treated with a prospective therapeutic protocol*. Acta Cir Bras, 2010; 25(3):225-30.
10. Panagiotis Paliogiannis et al.: *Preneoplastic and neoplastic gallbladder lesions occasionally discovered after elective videocholecystectomy for benign disease A single centre experience and literature review*. Ann Ital Chir, 2013; 84: 281-85. Published online 8 October 2012 pii: S0003469X12019781
11. Faik Tatli et al.: *Incidental gallbladder cancer at cholecystectomy*. Ann Ital Chir, 2017; 88, 5:399-402; pii: S0003469X17026665
12. Wang RT, et al.: *Gallbladder carcinoma: Analysis of prognostic factors in 132 cases*. Asian Pac J Cancer Prev, 2012; 13(6): 2511-514.
13. Puhalla H, et al.: *Long-term follow-up of surgically treated gallbladder cancer patients*. Eur J Surg Oncol, 2002; 28(8):857-63.
14. Ito H, et al.: *Treatment outcomes associated with surgery for gallbladder cancer: A 20-year experience*. J Gastrointest Surg, 2004; 8(2): p183-90.

READ-ONLY COPY
PRINTING PROHIBITED