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CLINICAL CHARACTERISTICS OF PRIMARY CARCINOMA OF THE GALL BLADDER

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Summary. *Carcinoma of the gall bladder ranks as the most common malignancy of the biliary tract with a threefold higher incidence in females than males and a tendency to increase in the old age. The aim of this study was: to specify clinical characteristics of primary carcinoma of the gall bladder; to establish a correlation between the clinical and histological stage of the disease; to assess survival time with respect to the histological stage of the disease; and to determine the most optimal surgical treatment with respect to the tumor stage and the patient's general condition. Within 1991-2001, 2,835 cholecystectomies were performed at the Surgical Clinic in Niš. Of a total number of extirpated gall bladders, a malignancy on histopathological examination was found in 16 patients who were further divided into three groups: Group I - patients with the carcinoma that infiltrated all layers of the gall bladder wall and perforated the serosa; Group II - patients with the carcinoma that did not perforate the lamina propria of the musculature; and Group III - patients with inoperable carcinomas. Postoperative survival was highest in patients with early gall bladder carcinoma (22.75 months) and lowest in inoperable carcinomas (3.25 months). Regardless of the modern diagnostic procedures, early diagnosis of gall bladder carcinoma is a rare event. Diagnosis may be left out at operation as well, so it is necessary that all suspicious agents be sent to pathohistological analysis. Simple cholecystectomy is the method of choice in managing early gall bladder carcinoma.*

Key words: *Gall bladder carcinoma, mortality, surgical treatment*

Introduction

Carcinoma of the gall bladder is the most frequent malignancy of the biliary tract, found on 0.1-1% autopsies, that is, 0.2-2% of all surgeries for the gall bladder. In over 70-80% cases, it is associated with cholelithasis, although a correlation between these two entities cannot be determined with certainty (3). Gall bladder carcinoma is more common in females than males (the female-male ratio being 3:1), and its incidence grows with age (3). Gall bladder carcinoma is a localization of carcinoma of extra-hepatic bile ducts with an unfavourable prognosis. According to clinical data, the average survival since diagnosis ranges from 5 to 8 months (6), whilst a 5-year survival is encountered in only 1-6% of all operated patients (11).

The Aim

The aim of this study was: to specify clinical characteristics of primary carcinoma of the gall bladder; to establish a correlation between the clinical and histological stage of the disease; to assess survival time with respect to the histological stage of the disease; and to determine the most optimal surgical treatment with respect to the tumour stage and the patient's general condition.

Material and Method

Within 1991-2000, 2,835 cholecystectomies were performed at the Surgical Clinic in Niš. Routine histopathological examination of extirpated gall bladders was done at the Institute of Pathology of the Clinical Center in Niš. A particular attention was paid to clinically altered gall bladders (swollen or uncritical bladders, acute inflammation of the wall). Inoperable carcinomas of the gall bladder were confirmed intraoperatively in 6 patients on biopsy performed with the use of palliative surgical procedures.

Postoperatively, upon histopathological examination, patients with positive findings were divided into three groups: Group I - patients with the tumour that infiltrated all layers of the gall bladder wall and perforated the serosa; Group II - patients with the carcinoma that did not perforate the lamina propria of the musculature; and Group III - patients with inoperable carcinomas. Survival was monitored postoperatively, with respect to the histological type of the tumour and the stage of the disease.

Results

In the period 1991-2000, 2,835 cholecystectomies were performed at the Surgical Clinic in Niš. Of a total number of extirpated gall bladders, a malignancy on

histopathological examination was found in 16 patients, which is 0.56% of all operated patients.

The study involved a total of 16 patients (13 females and 3 males), between 55-78 years of age, with an average age of 71.3 years.

In 10 patients, a malignancy was not suspected preoperatively, whilst in 6 patients a malignancy in the gall bladder was diagnosed preoperatively. The patients were divided into three groups on the basis of the clinical and histopathological stage of the malignancy.

Group I comprised patients with the tumour that infiltrated the entire wall of the gall bladder. Cholelithasis was found in all patients, and after histopathological examination adenocarcinoma of the gall bladder was established. Survival was also monitored that ranged from 1 to 12 months. The average survival in this patient group was 4.33 months. All patients underwent simple cholecystectomy.

Table 1. Group I (the tumour infiltrates the entire wall of the gall bladder)

AGE / SEX	Cholelithasis	Type of cholecyst.	HP finding	Survival time (months)
55 F	+	A	AC	5
72 M	+	A	AC	1
66 M	+	C	AC	12
65 M	+	C	AC	8
57 F	+	C	AC	4
68 F	+	A	AC	6

Legend: A = acute, C= chronic, AC= adenocarcinoma

Group II comprised patients with the tumour that did not perforate the lamina propria of the musculature. Cholelithasis was found in all patients, and adenocarcinoma of the gall bladder was established after histopathological examination. Survival ranged from 5 to 48 months. The average survival in this group was 22.75 months. All patients underwent simple cholecystectomy.

Table 2. Group II (the tumour infiltrates the wall all the way to the lamina propria of the musculature)

AGE / SEX	Cholelithasis	Type of cholecyst.	HP finding	Survival time (months)
78 F	+	A	AC	5
72 F	+	A	AC	8
71 F	+	C	AC	48
70 F	+	A	AC	30

Legend: A = acute, C= chronic, AC= adenocarcinoma

Group III comprised patients with inoperable carcinoma. Cholelithasis was registered in all patients, and adenocarcinoma of the gall bladder was diagnosed on histopathological examination. Survival was between 1 and 6 months, with an average survival time of 3.25 months. Three female patients underwent palliative surgery as the tumour infiltrated the main bile duct: percutaneous transhepatic choledochal drainage (PTCD) was performed in two patients, and choledochal T-drainage in one. The remaining three patients underwent biopsy for a malignancy.

Table 3. Group III (inoperable tumours)

AGE / SEX	Cholelithasis	Type of cholecyst.	HP finding	Survival time (months)	Surgery
74 F	+	C	AC	1	T-drainage
71 F	+	C	AC	1.5	PTCD
77 F	+	C	AC	4	Biopsy
78 F	+	C	AC	5	PTCD
82 F	+	A	AC	6	Biopsy
85 F	+	C	AC	2	Biopsy

Legend: A = acute, C= chronic, AC= adenocarcinoma

Discussion

The main hypothesis of the study was that there exists a possible correlation between the clinical and histopathological stage of gall bladder carcinoma, as well as that cholecystectomy is the treatment of choice for pre-invasive carcinoma. Carcinoma of the gall bladder ranks as the most frequent malignancy of the biliary tract. Patients commonly do not have any symptoms or have uncharacteristic symptoms even at a later stage of the disease, suggesting a disease of the gall bladder, but not a carcinoma. It is for this reason that proper diagnosis is established comparatively late, often intraoperatively or on histopathological examination.

Gall bladder carcinoma is more common in females than males (the female-male ration being 3:1) and its incidence shows the tendency to increase with age (3). These facts have been found to correlate with our study (13 females: 3 males, with an average age of 71.31 years).

Gall bladder carcinoma treatment is dependant on the disease stage. The stage of gall bladder carcinoma, which is an accidental finding at surgery for clinical benign diseases, is primarily determined on the basis of the invasion depth (T) as the information about the lymph nodes involvement (N) may be inadequate (in a number of cases metastases do not develop in local lymph nodes but regional lymph nodes may be involved; or the lymph nodes of the cystic duct may not have been sent for analysis along with the agents). Wide cholecystectomy is the method of therapeutic choice in treating the tumour that penetrates the lamina propria of the musculature (T2 and T3), since metastases develop in the lymph nodes in 60-80% cases (5). Shirai et al. (9) reported 23 patients out of 41 with a local residue after simple cholecystectomy. The 5-year survival in T2 stage was 90% after wide cholecystectomy compared to 40% after simple cholecystectomy (9). Another study demonstrated that 13 out of 25 patients having the entire gall bladder wall infiltrated appear with a local residue after simple cholecystectomy. This study revealed that the three-year survival after wide cholecystectomy is 91% compared to 28% after simple cholecystectomy (4).

There is much controversy over surgical treatment of T1 stage of the disease. Many authors recommend simple cholecystectomy for this disease stage, as it does not present with lymphatic, vascular, and perineural dissemination of metastases (8). Yamaguci K. and Tsuneyoshi K. (13) treated 31 patients with subclinical carcinoma of the gall bladder, six of whom had T1 stage, no postoperative complications within 10-84 months of simple cholecystectomy, and a 5-year survival rate of 100%. Another group of authors received the same 5-year survival rate of 100% in 39 patients with T1 stage of the disease after simple cholecystectomy (6). A recent study shows that none of 19 patients with T1 stage of the disease after laparoscopic cholecystectomy had lymphatic, vascular and perineural invasion of the malignancy (2). All these studies on surgical treatment of early carcinoma of the gall bladder correlate with the findings of our study: of a total number of patients, 6 were found with an early form of the disease and a survival time of 22.75 months after simple cholecystectomy. The majority of these patients were elderly (over 65 years of age). Due to the early stage of the disease and concomitant chronic diseases, their treatment was limited to simple cholecystectomy, but the obtained results revealed a satisfactory rate of survival.

In the advanced disease stage, no surgical procedure was applied, due not only to an inappropriate preoperative diagnosis but also to the patient's serious general condition and inappropriate ex tempore histopathological examination. These patients had a postoperative survival rate of 4.33 months. However, some studies (2) demonstrated that even after a seemingly radical local excision, residues occur comparatively soon. At surgery on the liver, not a segment of the gall bladder wall should be preserved. The liver resection has not led to better treatment results (5).

In general, resection methods are also the best mode of surgery for inoperable carcinoma of the gall bladder. They give better results with respect to survival and postoperative quality of life (14). Non-resection operative palliative procedures are associated with a high in-hospital lethality of up to 20% (14). The aim of all palliative procedures is to prevent development of obstructive jaundice. The procedures that are applied include: biliodigestive anastomosis, operative bile duct drainage (T-drainage or transhepatic ring drain); endoscopic procedures; and percutaneous transhepatic choledochal drainage. All these procedures, in particular the endoscopic ones, are advantageous in risk patients (elderly, cardio-respiratory unstable). It is for this reason that we applied in two female patients two endoscopic procedures, whilst the third patient underwent intraoperative choledochal decompression. Survival in this group was 3.25 months, which is in correlation with literature data (13).

Conclusion

On the basis of the available literature and the results obtained by this study, the following conclusions are obvious:

1. Carcinoma of the gall bladder ranks as the most frequent malignancy of the biliary tract with a threefold higher incidence in females and an increased incidence in the old age.
2. In spite of the modern diagnostic procedures, early diagnosis is a rare event.
3. Diagnosis of gall bladder carcinoma may be omitted at operation, so it is necessary that all suspicious agents be sent to pathohistological analysis.
4. The surgeon alone should open each extricated gall bladder and examine the wall and its interior.
5. Postoperative survival was highest in patients with early carcinoma of the gall bladder (22.75 months), whist the lowest was registered in inoperable carcinoma (3.25 months).
6. Simple cholecystectomy is the method of surgical choice in treating early carcinoma of the gall bladder.

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KLINIČKE KARAKTERISTIKE PRIMARNIH KARCINOMA ŽUČNE KESE

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Kratak sadržaj. *Karcinom žučne kese predstavlja najčeši malignom bilijarnog trakta koji se tri puta češće javlja kod žena, sa povećanom incidencom u starijem životnom dobu. Cilj ovog rada bio je: utvrdjivanje kliničkih karakteristika primarnih karcinoma žučne kese; uspostavljanje korelacije izmedju kliničkog i histološkog stadijuma bolesti; utvrdjivanje dužine preživljavanja bolesnika vezano za histološki stadijum bolesti i odredjivanje najoptimalnijeg vida hirurškog lečenja vezano sa stadijum tumora i opšte stanje bolesnika. U periodu od 1991. do 2001. godine na Hirurškoj klinici Niš uradjeno je 2835 holecistektomija. Od ukupnog broja odstranjenih žučnih kesa nakon histopatološkog ispitivanja nadjeno je kod 16 bolesnika prisustvo malignog procesa, pacijenti sa pozitivnim nalazom podeljeni su u tri grupe: I grupa pacijenata- karcinom je infiltrisao sve slojeve zida žučne kese i probio serozu; II grupa pacijenata gde karcinom nije probio muscularis propriju i III grupa pacijenata sa inoperabilnim karcinomom. Postoperativno preživljavanje bilo je najduže kod pacienata sa ranim karcinomom žučne kese (22,75 meseci), dok je najkraće bilo kod inoperabilnog karcinoma (3,25 meseca). Uprkos savremenim dijagnostičkim procedurama rana dijagnoza karcinoma žučne kese se postavlja dosta retko. Dijagnoza može se propustiti i tokom operacije te je potrebno sve sumnjive preparate slati na patohistološki pregled. Obična holecistektomija predstavlja metodu hirurškog izbora kod lečenja ranog karcinoma žučne kese.*

Ključne reči: *Karcinom žučne kese, mortalitet, hirurško lečenje*