

Postoperative Morbidity and Mortality after Liver Resection. Retrospective Study on 133 Patients

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Rezumat

Morbiditatea și mortalitatea postoperatorie după rezecția hepatică. Studiu retrospectiv pe 133 de pacienți

Introducere: Rezecția hepatică a cunoscut de-a lungul timpului o dezvoltare impresionantă, atât prin lărgirea plajei de indicații ale acestei proceduri, cât și prin apariția unor modificări și artificii tehnice menite să reducă rata morbidității și a mortalității postoperatorii.

Material și metodă: Studiul de față este un studiu retrospectiv și prezintă o analiză a unui lot de 133 pacienți internați în cadrul Compartimentului de Chirurgie Hepatică a Spitalului Clinic Municipal de Urgență Timișoara, în perioada ianuarie 2000 - noiembrie 2011 și la care s-a intervenit chirurgical fie pentru o tumoră hepatică primară (benignă sau malignă), fie pentru o tumoră hepatică secundară. Toate cazurile au fost analizate din punct de vedere al etiopatogeniei, investigațiilor preoperatorii și intraoperatorii, al indicației și tipului de hepatectomie realizat, al tehnicii operatorii folosite și a evoluției postoperatorii.

Rezultate: Lotul de studiu cuprinde un număr de 133 de pacienți. Din totalul pacienților, 100 (75,19%) au fost diagnosticați cu tumori hepatice primitive, la 70 de pacienți (70% din tumorile primare) acestea survenind pe un fond cirotic. La 33 de pacienți (24,81%), afectarea hepatică a fost secundară, cel mai frecvent fiind implicate tumorile colo-

rectale (19 pacienți). Din totalul rezecțiilor hepatice, 21 (15,79%) au fost hepatectomii majore. Restul au fost hepatectomii minore, incluzând o trisegmentectomie (V, VI, VII), 51 de bisegmentectomii și 60 de rezecții hepatice limitate la un singur segment. În 89 de cazuri (66,92%) s-a folosit clampajul, la 65 de pacienți (73,03%) fiind vorba despre clampaj pedicular iar 24 dintre pacienți (26,97%) au beneficiat de clampaj selectiv extraglissonian. Din cei 33 de pacienți cu determinări secundare hepatice, 12 (36,36%) au beneficiat de rezecții sincrone. Cea mai frecventă complicație în lotul studiat a fost reprezentată de insuficiența hepatică postoperatorie, întâlnită la 45 de pacienți (33,83%), într-un caz aceasta (2,22%) fiind ireversibilă, cu decesul pacientei. La 34 de pacienți (75,55%) din cazuri, insuficiența hepatică a fost întâlnită la pacienți cirofici, în restul cazurilor fiind vorba de pacienți cu hepatectomii majore. Insuficiența hepatică a apărut la 35 (77,78%) dintre cazurile la care s-a folosit clampaj, 4 dintre acestea fiind după clampajul selectiv extraglissonian. Dintre cei 45 de pacienți cu insuficiență hepatică postoperatorie, 31 (68,89%) au fost transfuzați, 25 de pacienți (55,55%) primind mai mult de 2 unități de sânge. Din totalul pacienților, 3 (2,25%) au decedat postoperator.

Concluzii: Rezecția hepatică poate fi efectuată și la pacienții cirofici cu o morbiditate acceptabilă și cu mortalitate minimă. Cea mai frecventă complicație după rezecția hepatică întâlnită în lotul studiat a fost reprezentată de insuficiența hepatică postoperatorie, aceasta fiind în majoritatea cazurilor reversibilă.

Cuvinte cheie: tumoră hepatică, hepatectomie, complicații, insuficiență hepatică

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Abstract

Introduction: Hepatic resection had an impressive growth over time, both by broadening the range of its indications and the occurrence of changes and technical tricks in order to reduce postoperative mortality and morbidity.

Material and methods: This study is a retrospective study presenting an analysis of 133 patients hospitalized in the Department of Hepatic Surgery in City Hospital Timisoara, between January 2000 and November 2011, in which a surgical intervention was performed, either for a primary hepatic tumor (benign or malignant) or a secondary liver tumor. All cases were analyzed in terms of etiopathogenesis, preoperative and intraoperative investigations, indication and type of hepatectomy performed, the surgical technique used and postoperative evolution.

Results: The study group comprises 133 patients. From the whole group, 100 patients (75.19%) were diagnosed with primitive liver tumors, in 70 patients (70% of primary tumors) HCC occurring on a cirrhotic liver. Liver disease was secondary in 33 patients (24.81%), colorectal tumors being most commonly involved (19 patients). Of all liver resections, 21 (15.79%) were major hepatectomies. The remaining were minor hepatectomies, including a trisegmentectomy (V, VI, VII), 51 bisegmentectomies and 60 liver resections limited to one segment. Vascular clamping was used in 89 cases (66.92%), pedicular clamping in 65 patients (73.03%) and selective extraglissonian clamping in 24 patients (26.97%) respectively. Of the 33 patients with liver metastases, 12 (36.36%) received synchronous resections. The most common complication in our study group was postoperative liver failure, found in 45 patients (33.83%), being irreversible in one case (2.22%), followed by the death of the patient. In 34 patients (75.55%), hepatic failure was seen in cirrhotic patients and the other cases were patients with major hepatectomies. Hepatic failure occurred in 35 patients (77.78%) with vascular clamping, four of them after selective clamping. 31 of the patients (68.89%) with postoperative liver failure were transfused, 25 patients (55.55%) receiving more than 2 units of blood. Of all patients, 3 (2.25%) died postoperatively.

Conclusions: Respecting the principles of liver surgery, hepatic resection can be performed, even in cirrhotic patients, with acceptable morbidity and minimal mortality. The most common complication after hepatic resection, in our study group, was postoperative liver failure, which was mostly reversible.

Key words: liver tumor, hepatectomy, complications, liver failure

Introduction

First described many centuries ago (1), hepatic resection has begun to develop in the mid-twentieth century, along with the first anatomical liver resection reported in 1949 in Kyoto

University by Honjo and later in Europe (1952) by Lortat-Jacob (2). Subsequently, hepatic resection had an impressive growth, both by broadening the range of its indications and the occurrence of changes and technical tricks in order to reduce postoperative mortality and morbidity.

Hepatic resection is the treatment of choice for a wide variety of liver tumors, benign or malignant, the latter, whether primary or secondary (3). In the malignant tumors of the liver, hepatic resection is indicated whenever it is possible, being the only potentially curative treatment option in these conditions and which provides the best long term survival (4).

Material and Methods

This study is a retrospective study presenting an analysis of 133 patients hospitalized in the Department of Hepatic Surgery in City Hospital Timisoara, between January 2000 and November 2011, in which a surgical intervention was performed, either for a primary hepatic tumor or a secondary liver tumor.

All cases were analyzed in terms of etiopathogenesis, preoperative and intraoperative investigations, indication and type of hepatectomy performed, the surgical technique used and postoperative evolution. All patients were preoperatively diagnosed with tumors in the liver by using imaging techniques: ultrasound, computed tomography, magnetic resonance or PET-CT, which allowed assessing the extension and resectability of liver tumors.

Treatment has been dictated by tumor location, stage of disease, liver parenchyma status, histological type and presence or absence of complications. Liver parenchyma status was assessed by routine biochemical tests (bilirubin, transaminases, alkaline phosphatase, gamma GT, albumin, prothrombin time), and also viral screening, especially in patients with hepatocellular carcinoma. We didn't use indocyanine green clearance for any patient. The incision used in most cases was bilateral subcostal incision, shorter to the left and with a midline extension (Mercedes). The type of performed hepatic resection, type of vascular clamping used and the quantity of blood administered were evaluated.

The method used for hepatic resection was the combined approach for most cases, meaning vascular access in order to control the bleeding and parenchymal transection with identification and ligation of the bilio-vascular elements at the hepatic resection line. We performed Bismuth technique in 24 cases. This method combines the advantages of both techniques Lortat-Jacob and Ton That Tung, limiting blood loss during transection and avoiding devascularization of the remaining parenchyma (5). Vascular approach was performed either at the hepatic pedicle (pedicular clamping), or to the right or left pedicle in an extraglissonian manner (selective clamping). We abandoned dissection and isolation of the elements of the right or left glissonian pedicle, making their pinching together, avoiding a laborious dissection that increases the risk of complications, especially in cirrhotic patients. Intermittent clamping was used to reduce the impact

of hepatectomy on hepatic function, 15 minutes in patients with macroscopically normal liver and 10 minutes in cirrhotic patients with 5 minutes break, repeated up to 3 times. In cirrhotic patients with small, marginal tumors, we did not use clamping in order to avoid the impact of hepatic resection on liver function, using a primary parenchymal approach (Ton That Tung).

At least 25-30% of total liver volume was preserved in a macroscopically normal liver. In patients with Child A cirrhotic liver, remaining hepatic volume was at least 50%, while in Child B patients, interventions were limited to segmentectomies. Liver parenchymal transection was performed using Kelly clamps (most common) or ultrasound dissector (CUSA) and biliary or vascular elements were tied off (if thicker than 2 mm) or coagulated at the hepatic resection line. In performing this surgical step, we tried to follow some goals:

- Maximum shortening of this surgical step, without compromising hemo- and bilistasis at the resection line (general anesthesia should not exceed 3 hours);
- Continuing parenchymal transection between clamping periods, using bimanual compression of the resection line;
- We introduced as a mandatory step a thorough verification of the resection line after declamping, in order to identify potential small biliary fistulas

Knowing that both, extended clamping and blood loss, reflected in need of transfusion, are factors with a negative impact on liver function in cirrhotic patients (6,7), we tried to create a balance, adapted for each case, between blood loss and clamping periods. Drainage of Morrison's pouch was used in all cases.

In the postoperative complications, postoperative liver failure was defined as the postoperative appearance of one or more of the following: total bilirubin over 2.5 mg% per day, ascites produced in excess (more than 0.5 l / day) externalized on drain/appreciated using ultrasound or development of various degrees of hepatic encephalopathy. Postoperative mortality was defined as death within 30 days postoperatively.

Results

The study group comprises 133 patients, 77 (57.89%) males and 56 (42.11%) females. From the whole group, 100 patients (75.19%) were diagnosed with primitive liver tumors, 11 (11%) cases of benign tumors (2 hemangiomas and 9 nodular focal hyperplasia) and 89 cases (89%) of hepatocellular carcinoma which occurred on a cirrhotic background in 70 patients (70% of primary tumors) – 55 patients with liver cirrhosis Child A and 15 patients with liver cirrhosis Child B. Liver disease was secondary to extrahepatic malignancies in 33 patients (24,81%), colorectal tumors being most commonly involved (19 patients). In other cases, we found gastric tumors in 3 patients, lung tumors in 2 patients, pancreatic tumors in 2 patients, ovarian tumor in 2 patients and one case for each of breast tumor, prostate adenocarcinoma, lymphoma, melanoma and renal cell carcinoma respectively.

Of all liver resections, 21 (15.79%) were major hepatectomies, including a left hepatectomy extended to segments V, VIII and I and a right hepatectomy extended to segment IV. The remaining 112 resections (84.21%) were minor hepatectomies, including a trisegmentectomy (V, VI, VII), 51 bisegmentectomies (segments 2 and 3 – 22 cases; segments 6 and 7 – 16 cases; segments 4 and 5 – 4 cases; segments 5 and 8 – 3 cases; segments 7 and 8 – 3 cases; segments 5 and 6 – 2 cases; segments 3 and 4 – 1 case) and 60 liver resections limited to one segment (segment 6 – 16 cases; segment 5 – 12 cases; segment 4 – 8 cases; segment 8 – 7 cases; segment 3 – 6 cases; segment 7 – 5 cases; segment 2 – 5 cases; segment 1 – 1 case).

Vascular clamping was used in 89 cases (66.92%), 65 patients (73.03%) with pedicular clamping and 24 patients (26.97%) extraglissonian selective clamping. We used clamping in all 21 major hepatectomies (pedicular clamping in 16 patients and selective clamping in 5 patients). In patients with minor hepatectomies, we used clamping in 68 cases (pedicular clamping in 49 patients and selective clamping in 19 patients). Of the 33 patients with liver metastases, 12 (36.36%) received synchronous resections, 11 cases of colorectal cancer and 1 case of gastric cancer.

Of the 133 patients, 59 (44.36%) developed one or more complications. In our study, the most common complication was the postoperative liver failure, found in 45 patients (33.83%), being reversible in 44 cases (97.78%) and irreversible in one case (2.22%), followed by the death of the patient. Among the patients with hepatic failure, 41 (91.11%) were diagnosed with hepatocellular carcinoma, the other 4 cases (8.89%) being colorectal tumors (3 cases) and one case of metastatic renal cell carcinoma in a patient with post viral chronic HBV. We found a residual hepatic impairment at discharge in only 3 cases, meaning that the stabilizing of the liver function parameters was over the values found at the hospital admission. In 36 cases (80%), hepatic failure was seen in cirrhotic patients; the other 9 cases (20%) were all patients with major hepatectomies. Hepatic failure occurred in 35 patients (77.78%) with vascular clamping, 4 of them after selective extraglissonian clamping. 31 of the patients (68.88%) with postoperative liver failure were transfused, 25 patients (55.55%) receiving more than 2 units of blood. All cirrhotic patients where we performed major hepatectomy developed a degree of hepatic insufficiency. Transient elevations of serum transaminases have been reported in all patients, without relation to postoperative liver failure.

Postoperative bleeding of more than 500 ml / 24 h and upper gastrointestinal bleeding were the most common complications after liver failure, being found in 11 (8.27%) and 13 cases (9.77%) respectively, all with favorable outcome that did not require reinterventions.

Biliary fistulas were found in 4 patients (3%), one of them developing an abdominal abscess secondary to bile leak, with subsequent appearance of septic shock and death. The other patients had a spontaneously favorable outcome.

In synchronous resection, we found a case of intestinal fistula (at the site of ileotransverse anastomosis) with

subsequent generalized peritonitis which required reintervention, multiple organ failure and death. Other complications encountered after liver resection were the intra-abdominal abscess in 2 cases (1.5%) and a right basal pneumonia in one case (0.75%), all with favorable outcome under conservative treatment.

Of the 133 patients who received liver resection, we had 3 deaths (2.25%) - an irreversible liver failure occurred in a patient with hepatocellular carcinoma associated with Child B cirrhosis and two postoperative complications occurred in patients with colorectal liver metastases (biliary leak in one case and intestinal fistula in a patient with synchronous resection).

Discussion

Although hepatic resection has experienced impressive growth in recent decades, it is still burdened by a relatively high rate of postoperative morbidity, especially postoperative liver failure in cirrhotic patients, secondary to associated comorbidities, underlying liver disease and particularly an insufficient volume of the remaining liver (8). Along with liver failure, bleeding, biliary fistulas and septic complications are the main problems after liver resection (9). Perioperative mortality, which declined in recent years, remains far below 5% (9,10) and tends to 0 in experienced centers.

The study group includes 133 patients who received liver resection for benign or malignant liver tumors, primitive or secondary, in the Department of Hepatic Surgery of City Emergency Hospital Timișoara.

The fact that hepatocellular carcinoma (HCC) develops in up to 90% of cases on cirrhotic liver (11), explains the large number of cirrhotic patients in the examined casuistry, HCC representing the prevailing pathology in our study (66.92%). This feature is due both to geographical distribution and some aspects of addressability, existing large differences in the distribution of pathology in the examined groups, even in our country, in different geographical regions. In a study conducted in our country on 445 patients, Popescu et al (12) show that of the 460 liver resections, 79 were performed for hepatocellular carcinoma, 28 of them on a cirrhotic liver. In a study on 1803 consecutive patients, Jarnagin et al (13) talk about 1021 cases of colorectal liver metastases and only 375 hepatic resections performed for primary hepatic or biliary cancers.

Despite the high percentage of cirrhotic patients in the examined group, the rate of complications (44.36%) in our group is consistent with the data found in the literature. Presenting their experience with 1059 noncirrhotic patients undergoing major hepatectomy, Mullen et al (14) reported complications occurring in 43% of the patients. Andres et al (15), in a study on 726 patients with elective liver resection reported that 36% of the patients had at least one complication, while Jarnagin et al (13) had a 45% postoperative morbidity. We believe that this aspect is due to both, adapting clamping period for each case and paying attention to liver transection, lowering the rate of complications at the

resection line. We can also find in the medical literature lower percentage of postoperative morbidity. Schroeder et al had a postoperative complications rate of 32% (16), while Popescu et al (12) and Belghiti et al (17) report morbidity rate of 21% and 22% respectively.

Knowing the negative impact of prolonged clamping and blood loss on cirrhotic liver (6,7), we avoided extension of the clamping beyond the limits we have imposed, even if this would reduce blood loss. We also tried to reduce blood loss by any means (decreasing transection time, using bimanual compression, etc.) except clamping extension.

Higher rate of postoperative liver failure (33.83%) is due on the one hand to the large number of cirrhotic patients (70 patients, representing 52.63% of all hepatic resections), and on the other hand to the definition taken as reference for the assertion of liver failure. It is difficult to compare and extrapolate results from clinical trials because of the large number of definitions of postoperative liver failure (PLF) found in the literature (8), leading to large discrepancies regarding the rate of PLF. Schroeder et al (16) found a 32.1% rate of PLF defined as a >100% increase in serum bilirubin. When PLF is defined by 50-50 criteria (prothrombin index <50% and serum bilirubin > 2.9 mg/dL on post-operative day 5) Balzan et al (18) reported their experience with 775 patients and found a rate of 3.5%. Jarnagin et al (13) defined PLF as prolonged hyperbilirubinaemia, clinically apparent ascites, prolonged coagulopathy and/or hepatic encephalopathy and had a PLF rate of 5.5%.

Hepatic insufficiency was not a major life-threatening complication (one death among patients with hepatic impairment), as defined and accepted by us, most of them being reversible under liver support therapy.

Carefully checking the resection line and completing hemo- and bilistasis, even in a modified cirrhotic liver parenchyma, we obtained literature accepted percentages in resection line related complications (biliary fistulas, postoperative bleeding). Capussotti et al. (19) published a study on 610 patients with liver resection, where biliary fistulas occurred in 3.6% of cases, our rate of 3% being consistent with these data. Regarding postoperative bleeding, Popescu et al (12) found a rate of 4.1% in 445 patients with hepatic resection, while Andres et al (15) had a postoperative bleeding rate of 6% after 726 elective liver resections.

Mortality of 2.25% seen in our group is consistent with the data published in the literature. This aspect is extremely important, considering that the percentage of cirrhotic patients is well above the average described in the literature. Furthermore, only one death out of three was linked directly to hepatic failure. Asiyanbola et al (20) in a systematic MEDLINE review which included 7073 patients who underwent hepatic resection, out of which 23.2% had cirrhosis found a mortality rate of 3.6%. There are several centers that report zero mortality after hepatic resections, but this depends, beside experience of the center, on how the study group was made, the type of pathology encountered, the type of surgery performed, whether interventions were elective or not. Itoh et al (21), in a recently published study, reported zero mortality

after 304 hepatic resections performed for liver tumors or to procure grafts for living donor liver transplantation.

Conclusions

The aspect that remains to be solved for liver resection refers to its performance in cirrhotic patients, because in patients with macroscopically normal liver this intervention came to be performed with minimal morbidity and mortality. Thus, the key is not necessary to minimize blood loss by extended clamping or to reduce the clamping time increasing blood loss, but to find a balance between clamping time and blood loss.

Respecting the principles of liver surgery, hepatic resection can be performed even in cirrhotic patients with acceptable morbidity and minimal mortality. Postoperative hepatic insufficiency is a relatively common complication in cirrhotic patients, but it is reversible in most cases.

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