LIVER RESECTION: 10-year experience from a single institution

Julio Cezar Uili **COELHO**[1, 2], Christiano Marlo Paggi **CLAUS**[2], Tiago Noguchi **MACHUCA**[1], Wagner Herbert **SOBOTTKA**[1] and Carolina Gomes **GONÇALVES**[2]

ABSTRACT - ***Background*** – Liver resection constitutes the main treatment of most liver primary neoplasms and selected cases of metastatic tumors. However, this procedure is associated with significant morbidity and mortality rates. ***Aim*** – To analyze our experience with liver resections over a period of 10 years to determine the morbidity, mortality and risk factors of hepatectomy. ***Patients and methods*** – Retrospective review of medical records of patients who underwent liver resection from January 1994 to March 2003. ***Results*** – Eighty-three (41 women and 42 men) patients underwent liver resection during the study period, with a mean age of 52.7 years (range 13-82 years). Metastatic colorectal carcinoma and hepatocellular carcinoma were the main indications for hepatic resection, with 36 and 19 patients, respectively. Extended and major resections were performed in 20.4% and 40.9% of the patients, respectively. Blood transfusion was needed in 38.5% of the operations. Overall morbidity was 44.5%. Life-threatening complications occurred in 22.8% of cases and the most common were pneumonia, hepatic failure, intraabdominal collection and intraabdominal bleeding. Among minor complications (30%), the most common were biliary leakage and pleural effusion. Size of the tumor and blood transfusion were associated with major complications ($P = 0.0185$ and $P = 0.0141$, respectively). Operative mortality was 8.4% and risk factors related to mortality were increased age and use of vascular exclusion ($P = 0.0395$ and $P = 0.0404$, respectively). Median hospital stay was 6.7 days. ***Conclusion*** – Liver resections can be performed with low mortality and acceptable morbidity rates. Blood transfusion may be reduced by employing meticulous technique and, whenever indicated, vascular exclusion.

HEADINGS – Liver, neoplasms, surgery. Neoplasm metastasis. Carcinoma, hepatocellular. Hepatectomy. Risk factors.

INTRODUCTION

The first liver resection was performed in 1716 by Berta who removed partially the liver of a trauma patient[9]. After that, it took more than a hundred years to von Bruns, in 1870, to perform the procedure again in a soldier of the Franco-Prussian war[1]. However, the first successful elective liver resection, a left lobectomy in a patient presenting with a hepatic mass, was performed only in 1888 by Langenbuch[9]. In 1908, a great technical advance was implemented by Pringle, who established the vascular control of the liver by compressing the portal triad, a maneuver subsequently named after him[27]. However, the real breakthrough in liver surgery was set by COUINAUD in 1957, when he extensively described the portal segmental hepatic anatomy which nowadays provides the rationale for segment-oriented resections[5].

The aim of the present study is to evaluate our 10-year experience with liver resections, mainly the indications, perioperative features and pathological findings in order to determine risk factors, morbidity and mortality of hepatectomy.

PATIENTS AND METHODS

Medical records of patients who underwent liver resection at the Digestive Surgery Division, "Hospital de Clínicas", Federal University of Parana, Curitiba, PR, Brazil, between January 1994 and March 2003 were reviewed. A protocol was created in order to obtain the following data: age, sex, relevant past medical history, including cirrhosis, chronic hepatitis and previous neoplasm, indication of hepatectomy, intraoperative data such as tumor location, extension of resection, employment of vascular exclusion, blood transfusion requirements and procedure duration, information related to the pathologist report (tumor size and histological type), and data regarding postoperative outcome, mainly postoperative complications, mortality index and hospital stay.

Operative Procedure

A bilateral subcostal incision was employed in all procedures, with an upward midline extension whenever necessary. Cholecystectomy, when the gallbladder was present, was performed for right hepatectomy. Whenever vascular exclusion was necessary, it was performed as a continuous occlusion of the portal triad with a vascular clamp for up to 60 minutes in non-cirrhotic patients and up to 30 minutes in cirrhotic patients. No pre-conditioning occlusion was employed. Parechymal transection was performed by blunt dissection with a Kelly clamp and ligation of vessels and bile duct branches. Eletrocoagulation was also widely employed. Operative blood transfusion was defined as the number of packed red cells infused during the operation and in the immediate postoperative period.

Nomenclature and Surgery Extension

The type of resection was classified according to the anatomical nomenclature of COUINAUD[5]. Resections were considered extended when involving five or more segments

[1] Digestive Surgery Division, "Hospital de Clínicas", Federal University of Parana and [2] Hospital Nossa Senhora das Graças, Curitiba, PR, Brazil.
Address for correspondence: Dr. Julio Coelho - Rua Bento Viana, 1140 – apt. 2202 - 80240-110 – Curitiba, PR. – Brazil.

(extended right lobectomy and extended left hepatectomy), major when three or four segments were involved (right and left hepatectomies), and minor when one or two segments were resected or whenever a non-anatomical resection was performed.

Postoperative Complications and Mortality

Complications leading to life-threatening conditions were classified as major. These included major postoperative bleeding, any organic failure, intra-abdominal abscess, sepsis and portal vein thrombosis. Complications with no fatal potential were considered minor and included pleural effusion, wound infection, urinary tract infection and atelectasis. Biliary leakage was also considered a minor complication since it was self-limited in the majority of cases.

Operative mortality was defined as any death occurring during the surgical procedure or within the 30th postoperative day. When death occurred in the same admission of the surgical procedure, it was defined as hospital mortality.

Statistical Analysis

Values were expressed as mean ± standard deviation. In univariate analysis, quantitative variables were compared using the Mann-Whitney test and qualitative variables using Fisher's exact test. Variables found to be statistically significant at a level of $P<0.05$ were evaluated for a multivariate analysis using the stepwise logistic regression model. Significance was also defined as $P<0.05$ for this statistical model.

RESULTS

A total of 83 liver resections were performed during the study period. Forty-one patients were women and 42 men. The mean age was 52.7 years, ranging from 13 to 82. In 37 patients (44.6%) an underlying chronic disease was detected in the preoperative evaluation, usually systemic hypertension or diabetes mellitus. Chronic liver disease was diagnosed in 13 patients (15.7%). The operations performed are summarized in Table 1.

TABLE 1 - Operative procedures

Procedure	n
Extended Resections	17
Right lobectomy	14
Left extended hepatectomy	3
Major resections	34
Right hepatectomy	22
Left hepatectomy	12
Minor resections	32
Bisegmentectomy	7
Segmentectomy	14
Non-anatomical resection	11

The indications for liver resection are listed in Table 2. The most common indication was secondary hepatic malignancy, which occurred in 41 patients (49.3%). Colorectal carcinoma was the primary tumor in 36 of these cases. Stomach, gallbladder, kidney, breast and ampulla of Vater were the primary site of the tumor in one case each. Primary hepatic malignancy was the indication for resection in 24 patients (28.9%): hepatocellular carcinoma in 19 (22.9%), cholangiocarcinoma in 4 (4.8%), and angiosarcoma in 1 (1.2%). Of the patients with hepatocellular carcinoma, seven had liver cirrhosis and one chronic hepatic disease. Hepatic resection was performed for benign conditions in 18 patients, 3 with focal nodular hyperplasia, 3 with hematoma, 3 with fibrotic nodule, 2 with adenoma, 2 with hemangioma, 2 with cyst, 1 with biliary fistula, 1 with left hepatic duct stenosis associated with cholangitis, and 1 with cirrhotic nodule.

TABLE 2 - Indications for liver resection

Diagnosis	n
Malignant tumors	65
Metastasis	41
Hepatocellular carcinoma	19
Cholangiocarcinoma	4
Angiosarcoma	1
Benign lesions	18
Focal nodular hyperplasia	3
Hematoma	3
Fibrotic nodule	3
Adenoma	2
Hemangioma	2
Cyst	2
Biliary fistula	1
Duct stenosis	1
Cirrhotic nodule	1

The mean operative time was 290 minutes, ranging from 120 to 630 minutes. The longest mean operative time (340 minutes) was observed in patients who underwent extended resections. Pringle's maneuver was employed in 28 patients (33.7%). Thirty-two patients (38.5%) required blood transfusion, with a mean of three units of packed red cells.

Complications were observed in 37 patients (44.5%) and they are shown in Table 3. Major complications occurred in 19 patients (22.8%). Pneumonia was the commonest major complication, occurring in seven patients (8.4%). Hepatic insufficiency developed in six cases (7.2%) and it was associated with the highest mortality rate of the study (50%). In this group, four patients underwent an extended resection and two a major resection. Intrabdominal fluid collection was observed in six patients. In four of them, abscess formation was diagnosed and successfully treated with either open or percutaneous drainage. In the remaining two, the collection resolved spontaneously with conservative approach. Intrabdominal bleeding occurred in five cases (6%). It was successfully managed with fluid infusion and blood transfusion in three cases. In the other two cases, the patients died of failure of multiple organs and systems.

Major complication rate varied with indication and extension of liver resection. These complications occurred in 2 of 4 patients (50%) who underwent hepatectomy for cholangiocarcinoma, 8 of 19 patients (42.1%) for hepatocellular carcinoma, 7 of 41 patients (17%) for metastatic disease, and 2 of 18 patients (11.1%) for benign conditions. Major complications were observed in 6 of 17 patients (35.2%) who were subjected to extended resections, 9 of 34 (26.4%) to major resections, and 4 of 32 (12.5%) to minor resections.

The size of the tumor correlated with morbidity. The mean size of the tumor was 9.42 cm in patients with major complications and 6.22 cm in patients with minor complications.

TABLE 3 - Postoperative complications*

Complications	n (%)
Major complications	19 (22.8%)
Pneumonia	7 (8.4%)
Hepatic insufficiency	6 (7.2%)
Intraabdominal fluid collection	6 (7.2%)
Intraabdominal bleeding	5 (6.0%)
Myocardial infarction	1 (1.2%)
Portal vein thrombosis	1 (1.2%)
Minor complications	25 (30%)
Biliary leakage	11 (13.2%)
Pleural effusion	11 (13.2%)
Atelectasis	2 (2.4%)
Urinary tract infection	2 (2.4%)
Wound infection	2 (2.4%)

*Some patients had more than one complication

Blood transfusion was needed in 13 of 19 patients (68%) with major complications and only in 21 of 83 patients (32.8%) without major complications. Tumor size correlated with the requirement of blood transfusion. In the group of patients who received blood transfusion, the mean tumor size was 9.14 cm, whereas in the group of patients without transfusion, the mean size was only 5.39 cm.

Major complications occurred in 2 of 13 patients (15.3%) with chronic hepatic illness, and in 16 of 70 patients (22.8%) with normal liver function.

In the univariate analysis, only the size of the tumor and the requirement of blood transfusion were associated with major complications ($P = 0.0185$ and $P = 0.0141$, respectively). In multivariate analysis, no statistical significance was observed for any variable (Table 4).

TABLE 4 - Statistical analysis of variables for postoperative major complications

Variable	*P* value univariate	*P* value multivariate
Age	0.1898	NE
Underlying chronic disease	1	NE
Chronic hepatic disease	0.7229	NE
Previous surgery	0.5982	NE
Indication	0.7495	NE
Extent of resection	0.0582	NE
Pringle's maneuver	0.0952	NE
Operative time	0.0843	NE
Blood transfusion	0.0141	0.4343
Tumor size	0.0185	0.1860

NE – variables not eligible for multivariate analysis

Minor complications were observed in 25 patients (30%). Biliary leakage and pleural effusion were the most common, occurring in 11 patients each (13.2%). Biliary leakage was minimal and resolved spontaneously in nine patients (10.8%). In the remaining two (2.4%), surgical reintervention was necessary. Operative time and the extension of resection correlated with biliary leakage ($P = 0.0343$ and $P = 0.193$, respectively). Pleural effusion occurred in 17% of the right hepatectomies and in 9% of left hepatectomies.

The operative mortality occurred in seven patients (8.4%). Hypovolemic shock was the main cause of death, which occurred in one patient during the surgical procedure and in two, during the postoperative period. Two patients died due to hepatic insufficiency, one due to acute myocardial infarction and one due to intra-abdominal sepsis. Statistical analysis revealed that increased age (64.71 ± 9.66) and use of Pringle's maneuver correlated with operative mortality ($P = 0.0395$ and $P = 0.0404$, respectively). One patient died of hepatic insufficiency in the 34th postoperative day, accounting for a hospital mortality of 9.6%. The median hospital stay was 6.7 days.

DISCUSSION

Despite improvements in chemoembolization, cryosurgery and other modalities of treatment, liver resection remains the procedure of choice in the management of most primary liver tumors[25]. Liver transplantation is the best approach in selected cases, mainly in patients with liver cirrhosis and small tumors[12]. Hepatectomy is the mainstay treatment of selected patients with metastatic liver tumors, especially those in which the primary site is the large bowel[3]. However, this procedure has been associated with significant morbidity and mortality.

The most common indication of liver resection in our series was metastatic liver tumors, accounting for 49.3% of cases, followed by primary hepatic malignancy, with 24%. These results are similar to those of a recently published multicentric study reporting the outcomes of 2,097 patients subjected to hepatectomy. In this series, 52% of the patients underwent resection for metastatic disease and 16% for primary liver malignancy[6].

Liver resection has been associated with high morbidity and mortality. The reported morbidity has ranged from 16.2% to 81%[4, 23, 30]. This enormous range is partially due to the heterogeneity of the published series, with major differences in indication, extension of hepatic resection, percentage of patients with cirrhosis and definition of postoperative complication. Our rate of 44.5% is considered high when compared to others. However, we stress that a meticulous data review was employed so that complications such as pleural effusion were considered even when thoracocentesis and chest tube drainage were not required. Fatal complications occurred in 22.8% of patients and, analyzing specific complications, our rates are similar to those of major international centers. For instance, intra-abdominal sepsis occurred in 4.8% of our resections, as compared to 6.9% and 3% in the reports of MIYAGAWA et al.[21] and LAI et al.[17], respectively.

Risk factors for complications following hepatic resection have been addressed by others. NOGUCHI et al.[24] detected albumin, glutamic oxaloacetate transaminase, serum total bilirubin, plasma disappearance rate of indocyanin green and 75 g oral glucose tolerance test as factors associated with increased morbidity. YAMANAKA et al.[32] reported age as a risk factor. MIYAGAWA et al.[21] demonstrated, in a multivariate analysis, that operation duration, extension of resection and preoperative cardiovascular disease correlated with postoperative complication period. Surprisingly, this author observed, in a univariate model, that a histologically normal liver (except for the tumor) was associated with higher morbidity rates. This finding was possibly due to the more extensive liver resections performed in patients without underlying

liver disease. In addition to this finding, we also observed that the size of tumor and blood transfusion were predictors of major postoperative complications. Blood transfusion has long been associated with tumor recurrence[20,23] and also with morbidity and mortality[7,11,14,28]. KOOBY et al.[15] revealed that perioperative blood transfusion is a risk factor for poor outcome after liver resection. The greatest effect was in the perioperative course, where the transfusion was an independent predictor of operative mortality, minor and major complications and duration of hospital stay. This effect was dose-related. The preoperative detection of patients at risk for bleeding is important in order to schedule an autologous transfusion to improve outcome[20]. Although extension of liver resection was not a predictor factor of complication in our study, MIYAGAWA et al.[21] found that extension of resection correlated with postoperative complication in a multivariate model. This difference may be due to a smaller number of patients in our study.

Liver resection in patients with cirrhosis presented a mortality rate of 58% by 1970.[10] In the eighties, Asian and Western countries reported rates of 20%[13, 16]. Due to advances in perioperative management, refinement of surgical technique, reduced hospital stay and reduced requirement for intensive care unit monitoring, the mortality rates in the nineties reached a plateau near 10%.[22]. Our 8.4%-rate is similar to those of other centers, although zero-mortality rate has been reported by a few highly specialized centers[8, 31].

In our study, Pringle's maneuver and increased age were associated with mortality. In an evaluation of extended liver resections, WEI et al.[34] demonstrated that the presence of associated diseases and perioperative blood transfusion were risk factors for mortality. In that study, Pringle's maneuver was also a predictor of morbidity. However, in a prospective randomized trial, Pringle's maneuver was associated with less blood loss and better postoperative liver function without increasing neither complication nor morbidity rates[19,30]. These different findings may be due to limited cohort. Age was also described as a risk factor by DIMICK et al.[6], who found, in a recent multicentric study, that low-volume hospitals for hepatectomies, patients older than 65 years of age, major liver resection, primary hepatic malignancy as indication for resection and severity of hepatic dysfunction were all independent predictors of mortality.

Biliary complications represent another major topic in liver surgery. In a recent report, TANAKA et al.[29] published a leakage rate of 7.2%, with a significant number of the patients with this complication requiring reintervention. In a series of 5.5% of biliary leakage, LAM et al.[18], in agreement with BISMUTH et al.[2], concluded that intraoperative dye tests significantly reduced fistula rates. In our series the leakage rate was 13.2%. However, leakage was minimal in most cases, resolving spontaneously in a few days. Thus, we agree with others[22], that the routine use of dye tests is not justified, since only a small percentage of patients need reintervention. In addition, even with routine assessment of leakage with this test, cases of biliary fistula are still observed[18].

In conclusion, our findings demonstrate that liver resection can be performed with low mortality and acceptable morbidity rates. The impact of blood transfusion on perioperative outcome highlights the need for advances in control of operative blood loss. Blood transfusion may be reduced by employing meticulous surgical technique and, whenever indicated, vascular exclusion.

Coelho JCU, Claus CMP, Machuca TN, Sobottka WH, Gonçalves CG. Ressecção hepática: experiência de 10 anos de uma única instituição. Arq Gastroenterol 2204;41(4):229-33.

RESUMO - ***Racional*** – A ressecção hepática constitui o principal tratamento da maioria das neoplasias primárias do fígado e de casos selecionados de tumores metastáticos. Entretanto, este procedimento está associado a taxas expressivas de morbidade e mortalidade. ***Objetivo*** – Analisar a experiência com hepatectomia em um período de 10 anos para determinar os fatores de risco, a morbidade e a mortalidade das ressecções hepáticas. ***Pacientes e Métodos*** – Revisão retrospectiva dos prontuários médicos dos pacientes que foram submetidos a hepatectomia no período de janeiro de 1994 a março de 2003. ***Resultados*** – Foi realizada hepatectomia em 83 pacientes (41 mulheres e 42 homens) durante o período do estudo. A idade média dos pacientes foi de 52,7 anos, com variação de 13 a 82 anos. As principais indicações de ressecção hepática foram carcinoma do intestino grosso metastático (36 pacientes) e carcinoma hepatocelular (19 pacientes). Hepatectomias ampliadas e maiores foram realizadas em 20,4% e 40,9% dos pacientes, respectivamente. Transfusão sangüínea foi necessária em 38,5% das operações. A morbidade total foi 44,5%. Complicações com risco de vida ocorreram em 22,8% dos casos e as mais comuns foram pneumonia, insuficiência hepática, coleção intra-abdominal e sangramento intra-abdominal. Entre as complicações menores (30%), as mais comuns foram extravasamento biliar e derrame pleural. O tamanho do tumor e transfusão sangüínea foram associadas com complicações maiores ($P = 0,0185$ e $P = 0,0141$, respectivamente). A mortalidade operatória foi de 8,4% e os fatores de risco relacionados com a mortalidade foram idade avançada e realização de exclusão vascular ($P = 0,0395$ e $P = 0,0404$, respectivamente). O período de internação médio foi de 6,7 dias. ***Conclusão*** – As hepatectomias podem ser realizadas com baixa mortalidade e aceitável morbidade. Transfusão sangüínea pode ser reduzida com o emprego de técnica meticulosa e quando indicada, a exclusão vascular.

DESCRITORES – Neoplasias hepáticas, cirurgia. Metástase neoplásica. Carcinoma hepatocelular. Hepatectomia. Fatores de risco.

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