Hepatectomy preoperative planning

Planejamento pré-operatório em hepatectomias

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ABSTRACT

A Hepatectomy can comprise excision of peripheral tumors as well as major surgeries like trisegmentectomies or central resections. Patients can be healthy, have localized liver disease or possess a cirrhotic liver with high operative risk. The preoperative evaluation of the risk of postoperative liver failure is critical in determining the appropriate surgical procedure. The nature of liver disease, its severity and the operation to be performed should be considered for correct preparation. Liver resection should be evaluated in relation to residual parenchyma, especially in cirrhotic patients, subjects with portal hypertension and when large resections are needed. The surgeon should assess the rationale for the use of hepatic volumetry. Child-Pugh, MELD and retention of indocyanine green are measures for assessing liver function that can be used piror to hepatectomy. Extreme care should be taken regarding the possibility of infectious complications with high morbidity and mortality in the postoperative period. Several centers are developing liver surgery in the world, reducing the number of complications. The development of surgical technique, anesthesia, infectious diseases, oncology, intensive care, possible resection in patients deemed inoperable in the past, will deliver improved results in the future.

Key words: Hepatectomy. Hepatic Insufficiency. Liver Cirrhosis. Risk Assessment.

INTRODUCTION

The operations on the liver have been developing since the second half of the 20th century[1]. The description of right hepatectomy in 1952 by Lortat-Jacob gave birth to modern liver surgery[2]. With improvement in surgical technique, anesthetic drugs and intensive care it became possible to perform complex liver resections with very low morbidity and mortality. Liver resections may comprise small peripheral tumor enucleations or large operations, such as trisegmentectomies or central resections. Patients vary between healthy, with localized disease and severely cirrhotic with great operative risk[1].

Operations performed in patients with impaired hepatic functional reserve may present with high rates of morbidity and mortality. Garrison et al. showed in 1984 that 10% of patients with advanced liver disease would be subjected to some kind of surgery other than transplantation in the final two years of their lives[1]. Postoperative infection and subsequent sepsis remains a common complication after hepatectomy (4% to 20%), with significant impact on postoperative mortality, reaching 40% of the death causes[3,4].

Assessing the preoperative risk of liver failure in the postoperative period is critical for determining the appropriate surgical procedure[5]. Inadequate hepatic functional reserve in the remaining parenchyma leads to failure of regeneration and progression to liver failure. No single method is able to provide safe limits for the resection[6].

Good selection of patients is the largest contributor to improved survival after hepatectomies. Careful identification of each patient's overall risk factors, hepatic functional reserve and the volume of the remaining parenchyma is essential for prevention of post-hepatectomy liver failure and improvement in morbidity and mortality[7].

Evaluation of liver function

The classification of Chil-Turcotte-Pugh (CTP) is the simplest form. Even small liver resections are not possible in most patients CTP B and C. However, some studies suggest that traditional methods for estimating the hepatic functional reserve, such as the CTP score, are limited in clinical practice[8, 9].

As for patients with colorectal carcinoma, 50% develop liver metastasis. Hepatic failure can occur when the extent of tumor requires a large resection or when the patient has undergone previous chemotherapy[10,11]. Portal vein occlusion may be the best way to increase the hepatic functional reserve by hypertrophy of the counter-lateral lobe. Scintigraphy with 99 technetium labeled with a sialoglycoprotein analogue (99m-Tc-GSA) is currently the best way to document this compensatory hypertrophy[12].

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However, surgeons need simple tests to evaluate liver function.

Recently, imaging has been used to estimate the volume of the liver remnant , such as computed tomography (CT), ultrasonography (USG) and magnetic resonance imaging (MRI). Data shown by these techniques demonstrate that the hepatic functional reserve is related to hepatic volume[5]. Through information from CT liver cirrhosis can also be analyzed and classified into grades. These grades are significantly correlated with prognosis. Rong et al. (2007) combined this graduation with the liver volume analysis to preoperatively predict the hepatic functional reserve after hepatectomy[5].

Vauthey *et al*. (2000)[13] measured the volume of the liver using helical CT and demonstrated serious postoperative complications when the remnant liver has less than 25% of the initial volume. Normally, the liver can tolerate a trisegmentectomy with resection of the caudate lobe, which results in a reduction of up to 80% of its volume. Conversely, cirrhotic livers cannot tolerate even small hepatic resections[14].

The rational way to utilize hepatic volume is to have the liver volume measured by the same surgeon. Some authors perform this measurement with the use of Adobe Photoshop® software on personal computers. Unfortunately, image analyses softwares permeate more the radiologists' field, with little access to surgeons. Surgical planning should be known by those who analyze the images to predict the liver remaining volume. Volumetric CT softwares are expensive and rarely available[15]. A free program for image analysis called "ImageJ" is available for surgeons. Studies to demonstrate the accuracy of the "ImageJ" for analysis of liver volume by CT in personal computers for patients undergoing major hepatectomy for colorectal metastases were successfully performed[16].

Preoperative Preparation

To correct preoperative preparation, one should take into consideration the nature of liver disease, as well as its severity and type of operation to be carried out[17].

The liver resection should be evaluated for residual parenchyma, especially in cirrhotic patients with portal hypertension. The absence of portal hypertension (hepatic vein gradient less than 10 mmHg) and normal serum bilirubin proved to be the best predictors of good postoperative prognosis, with a 70% five-year survival in these patients. On the other hand, changes in the hepatic vein pressure gradient and elevation of bilirubin were associated with a 30% five-year survival after hepatectomy regardless of CTP classification[18].

After careful preoperative evaluation, CTP A cirrhotics can be submitted to elective surgeries. However, CTP B cirrhotics should not have liver resection or cardiac surgery, but can undergo other procedures after optimization of their clinical condition. As for CTP C cirrhotics it is not recommended for them to be submitted to any type of surgical procedure.

The MELD (Model for End Stage Liver Disease) scale uses the values of bilirubin, creatinine and INR. It can be used as a preoperative parameter. One advantage of it is the fact that it is a continuous scale, which can be performed repeatedly. When low, it indicates patients' stability; one could then recommend surgical procedures when the MELD score is below 10. When the MELD scale is between 10 and 15, one should be cautious to perform operations, which should be carried out in strictly necessary cases. However, in patients with MELD scores above 15, surgical procedures are contraindicated. The presence of portal hypertension (esophageal varices, ascites, splenomegaly with thrombocytopenia) should be investigated as it is a predictor of worse prognosis than the CTP criteria in patients undergoing hepatic resection[19].

In a prospective work 55 patients with hepatocellular carcinoma (HCC) were studied. Forty-six were CPT A and nine B. Liver volumes were measured by CT with contrast in two phases with 10 mm cuts. The percentage of remnant liver was calculated. Liver cirrhosis in the area without tumor was divided into four grades according to CT: grade 0 - homogeneous density, without distortion in shape, spleen moderate in size (index up to 300) and no signs of portal hypertension; grade 1 - heterogeneous density, changes in liver shape with atrophy (hepatic fissure up to 1.5 cm), especially segment 4, 300-600 splenic index and two or three signs of portal hypertension; grade 2 - regenerative nodules, liver atrophy (liver fissure > 1.5 cm) and splenic index above 600 and two to four signs of portal hypertension with moderate ascites (less than 2 cm); grade 3 - greater number of regenerative nodules, quite atrophic liver (fissure > 2 cm) over four signs of portal hypertension, ascites (> 2 cm). The greater the degree of cirrhosis evaluated by CT and the smaller the percentage of remaining liver (PRL), the greater the probability of death after hepatectomy. The error was 2.6% in the preoperatively calculation of PRL by CT and the one postoperatively found[5]. Tu et al. (2007) designed a method to analyze the distribution of survival in relation to PRL and degree of cirrhosis by CT together and found an oblique line that can be used as a predictor of survival based on these two parameters. This line suggests that 40% of PRL is safe in a grade 0 patient but not less than 90% of PRL can be left in grade 3 cirrhotics. It is a noninvasive, inexpensive and easily applicable method[5].

Liver volumetry

The hepatic functional reserve is highly related to the quantity and quality of liver cells. Both liver volume and form reflect this condition[20,21]. Many researchers argue that the larger the liver resection, the greater the chance of liver failure in the postoperative period. On the other hand, the more limited the resection, the greater the chance of tumor recurrence. It is very difficult to predict the volume of the remaining liver, and it is very difficult to estimate the volume to be resected during the operation[22]. There is currently no consensus on the remaining liver volume necessary to avoid liver failure. Many studies[20,23,24] are focused on volume resected, but should take into consideration not only the amount of remnant liver but its quality. The 2007 study by Tu et al. found no difference between the volumes of resected liver, but did find between PRLs[5].

Resection of 50% has been considered safe; however, it was observed that even the removal of small tumors can lead to liver failure, while resection of large tumors may result in long survical[25,26]. This suggests that PRL is probably not the same at different degrees of cirrhosis. One should combine these two parameters to determine the safe size of the hepatectomy.

The hepatic volumetry is deemed faithful and reliable when large resections are mandatory. The rational way to utilize the hepatic volumetry is to have the liver volume measured by the same surgeon.

Lu *et al*. (2004) perform this measurement with the use of Adobe Photoshop® on personal computers. We used Adobe Photoshop® 5.0, Windows 98, 1.31-megapixel digital camera or an Acer 620UT scanner to scan the images. CT with and without contrast in 10 mm sections was scanned by the scanner or digital camera in JPEG format. The areas containing the liver and tumor were outlined. The image histogram was opened and the pixels in the area were measured. After creating an area of 1 cm^2 the number of pixels in this area was copied and input in a Microsoft Excel® spreadsheet. When comparing the 10 liver volumes achieved by this method with the ones achieved by volumetric CT, there was agreement between the groups. Three right lobes calculated by this method were concordant with the surgical specimens after right hepatectomy, with variation of 5%[15].

Another study uses a computer program (ImageJ) to carry out volumetry by the same surgeon. Seventy patients who underwent major hepatectomy (three or more segments) for colorectal metastases were selected. CT was performed in four phases. After resection, the specimen was measured and weighed for comparison. The portal phase of the CT study was used to measure the plane of resection. Three areas of interest were selected: total liver area, area of metastasis, resection area. The areas of metastasis and the area to be resected were manually outlined and calculated by the program. The whole analysis took 25 to 28 minutes. The results showed that ImageJ was able to reproduce the liver volume. For referred patients, who already have the TC exam on CD, the ImageJ eliminates the need to calculate the new CT volumetry. It can be performed by the surgeon without the need of radiologists. The ImageJ can be used for calculation of the hepatic volume, is free and brings volumetry to the surgeon personal computer, regardless of radiologist support[16].

According to studies, the minimum adequate remnant liver function for hepatic resection for colorectal metastases is 25% to 30%[10,11,27]. It is known that cirrhotic, steatotic and post-chemotherapy livers support only minor resections[27,28]. Recent studies apply the combination of hepatic volumetry by CT with functional tests such as indocyanine green and scintigraphy[29,30]. The predictive value of indocyanine green retention is increased if the remnant liver volume is measured by CT prior to hepatectomy[31].

Postoperative liver failure

In a study of 158 surgical patients, 111 undergoing liver resection, liver function tests such as CTP, 15 minutes indocyanine green retention, total liver receptors and volume of liver parenchyma were performed and were compared between patients with and without signs of postoperatively hepatic failure. Multivariable logistic regression showed only the number of liver remaining receptors as a significant parameter for postoperative liver failure[32].

To Fan (2000) the clearance of indocyanine green is the highest accuracy test for hepatic functional reserve. Retention of the green of 14% in 15 minutes is the limit for safe major hepatectomy in cirrhotic patients. Up to 60% of the liver can be resected safely. Steatosis and patients' age also affect the hepatic functional reserve and are risk factors for hepatectomies[7].

Kanzler et al. (2007) claim that, in cirrhotic patients, only Child As with normal bilirubin and no portal hypertension should be candidates for hepatic resection[6]. To Yamagiwa *et al*. (1997) elective operations are possible in Child A patients, procedures with little blood loss are possible in Child B patients, but in Child C only emergency cases should be operated. The limits for surgery in cirrhotic patients are e" 0.04/min indocyanine green, bilirubin d" 3 mg/dl, PT> 50% and R15 e" 40%[33]. According to Pisani et al., the Acute Physiology and Chronic Health Evaluation (APACHE III) was superior to Chid-Pugh for survival prognosis in cirrhotic patients undergoing hepatectomies[34].

A study of 466 cirrhotic patients hepatectomized for HCC was conducted with the goal of creating an algorithm for safe liver resection based on factors of postoperative irreversible liver failure (ILF). The general index of ILF was 4.9%. MELD (<9, 9-10 and >10) and the extent of liver resection were significant factors. Meld <9 showed ILF of 0.4%, Meld 9-10 1.2% for less of one resected segment, 5.1% for one or two segments and 11.1% for three or more segments resected. In this level of MELD, Na^+ >140 rendered lower risk. For Na^+ <140 with resection of one segment, ILF was 2.5% and two or more segments, 5%. In patients with MELD > 10 there was a 15% index of ILF in all resections. They concluded that a simple algorithm, based on MELD and Na^+ may indicate the maximum permissible extent of hepatectomy for HCC in cirrhotics[35].

MELD was created to reflect hepatocellular reserve in cirrhosis. One study divided patients operated for HCC into two groups: group A with 21 patients without cirrhosis and group B comprising 25 patients with cirrhosis. Eighty-six percent of Group A patients underwent major hepatectomy and 40% in group B. Morbidity and mortality were 24% and 4.8% in group A and 64% and 20% in B. MELD values of preoperative, postoperative and delta MELD in group A were respectively 7, 13, and 5, and in group B they were 9.6, 16.8 and 7.2. In group A, the MELD was not predictive of complications, despite the large number of major hepatectomies. In group B, MELD score greater than or equal to nine was associated with higher mortality (84% vs. 41%). Mortality was significantly higher in MELD scores greater than or equal to 15. They concluded that preoperative MELD failed to predict postoperative complications after hepatectomy for HCC in non-cirrhotic, but was indeed a predictive factor in cirrhotics[36].

Extent of resection

The number of resected segments has a profound impact on morbidity and mortality. The complication rate ranges 32% and mortality of less than 1% with zero or one resected segment, progressing to 75% complication rate and 7.8% mortality in patients with resection of six segments. In patients with three or more segments resected the mortality doubled from 3% to 6% when other complex surgical procedure was associated. The estimated blood loss during operation and the number of resected segments were the only predictors of higher morbidity and mortality. Patients who underwent resection of less than three segments had no increase in the number of transfusions or death if another complex procedure was performed. On the other hand, when another procedure was performed with resection of three or more segments there was increase in blood loss, transfusions, morbidity and mortality. The presence of jaundice and thrombocytopenia during the operation represented an increasing risk of death[2].

Belghiti et al. (2002) analyzed 747 hepatic resections and concluded that the only independent predictor of operative mortality in patients with cirrhosis was the performance of concomitant extra-hepatic procedures[3].

Infectious complications

Jarnagin *et al.* (2002) showed a 45% complications rate after hepatectomy, half of them infectious. The most common infections were related to the liver and bile ducts, closely followed by the lung. The most common complication was the presence of a peri-hepatic collection. The mortality rate was 3.1%. Infections accounted for 42% of the death causes[2].

Such high association between infection and mortality after hepatectomies raises questions about the involvement of the liver in the homeostasis of the patient and the functioning of the immune response against micro-organisms of the gastrointestinal tract, especially in the elderly[37].

In 207 hepatectomies performed, Garwood *et al.*[41] (2004) had an infection rate of 3.3% with a mortality of 33% among infected individuals. Infectious complications were responsible for 25% of deaths in hepatectomy. In contrast, they accounted for 9% of death causes in general operations. The largest number of infections was found in resections by cholangiocarcinoma and trauma. Infections increased length of stay in six on average days and antibiotic use in 11 days, with an increase in costs of US$ 55,000 per infected patient. Individuals with infection after hepatectomy were on average five years older and the ones who died as a result of infection were about 15 years older. The number of comorbidities was also higher in infected patients. The only laboratory test associated with postoperative infection was albumin. Regarding surgical procedure, the only factors that increased the risk of infection were the extent and duration of the procedure. Two thirds of infected patients underwent resection of at least three segments. The increase in the residual cavity may serve as a site for infection in addition to more devitalized tissue and greater chance of biliary fistula[38,39]. Surgical time over six hours was also associated with greater chance of infection[40]. The most frequent site was intra-abdominal, followed by pneumonia. The most prevalent bacteria in post-hepatectomy infections were gram-negative enteric bacilli and gram-positive cocci, the *Enterobacter sp*. and *Enterococcus sp*. being the biggest promoters of bacteremia after hepatectomy. In patients who died, the most frequently germ found was the methicillin-resistant *Staphylococcus sp*. Fungal infections by *Candida albicans* were frequently found in cultures. All classes of antibiotics were used with no difference between them[41].

According to Kobayashi and Tanimura (2001) third and fourth generation cephalosporins and carbapenems should be the antibiotics of choice because of the severity of infection and the risk of postoperative infections. The most commonly identified bacteria are *Pseudomonas*, *Enterococcus* and MRSA. Empiric treatment should be performed with carbapenems associated with vancomycin or teicoplanin on suspicion about these two agents[42]. Infected patients who died after hepatectomy had an average 5.3 days delay in the beginning of antibiotics administration than those who survived[41].

Advances in the second half of the twentieth century propelled modern liver surgery. More and more centers are developed in liver surgery in the world, with a decreasing number of complications. Studies are still being done in relation to surgical technique, anesthesia, infectious diseases, oncology and intensive care, enabling resection in patients thought to be inoperable in the past and will provide better results.

R E S U M O

Hepatectomia pode combinar desde a captação pequeno tumor periférico para operações de grande porte como trissegmentectomia ou ressecções central. Os pacientes podem ser saudáveis, com doença hepática localizada ou cirróticos com alto risco operatório. A avaliação pré-operatória do risco de insuficiência hepática pós-operatório é fundamental para determinar o procedimento cirúrgico adequado. A natureza da doença hepática, a sua gravidade e a operação realizada devem ser considerados para correta preparação pré-operatória. A ressecção hepática deve ser avaliada em relação ao parênquima residual, especialmente em cirróticos, pacientes com hipertensão portal e grandes ressecções. O racional para a utilização de volumetria hepática é medida pelo cirurgião. Child-Pugh, MELD e retenção de verde de indocianina são medidas de avaliação da função do fígado que pode ser usado em hepatectomia pré-operatório. Extremo cuidado deve ser tomado em relação à possibilidade de complicações infecciosas com alta morbidade e mortalidade no período pós-operatório. Vários centros estão desenvolvendo a cirurgia de fígado no mundo, com diminuição do número de complicações. O desenvolvimento da técnica cirúrgica, anestesia, doenças infecciosas, oncologia, terapia intensiva, possível ressecção em pacientes considerados inoperáveis no passado, irão proporcionar melhores resultados no futuro.

Descritores: *Hepatectomia. Insuficiência hepatica. Cirrose hepática. Medição de Risco.*

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