J Hepatobiliary Pancreat Surg (2005) 12:27–30
DOI 10.1007/s00534-004-0946-z

Journal of HBP Surgery

Assessment of hepatic reserve for the indication of hepatic resection: how I do it

Gian Massimo Gazzaniga, Stefano Cappato, Fiorenza E. Belli, Claudio Bagarolo, and Marco Filauro

Department of Surgery, HPB Unit, Galliera Hospital Genova, Via A. Volta 1, 16100 Genova, Italy

Abstract
Despite the careful selection of cirrhotic patients with hepatic neoplasms, liver resection for these patients remains associated with greater risk than in patients without underlying liver disease. The most rational indications for resective surgery in patients with hepatic neoplasms and cirrhosis are nonprogressive cirrhosis and good functional reserve. Therefore, evaluation of hepatic reserve is mandatory for hepatectomy candidates. Because of the complexity of hepatic function, a single, reliable liver function test is not yet available. However, a good multifactorial system that combines several elements (clinical, laboratory, functional, and volumetric evaluation) does provide sufficient data for determining the safe limitis of hepatectomy.

Key words Liver · Hepatectomy · Hepatic reserve

Introduction

The risk of postoperative liver failure depends upon both the quantity and the quality of the liver parenchyma spared by resection. It is generally agreed that, in normal liver, the paramedian sector, the posterolateral sector, segments I and IV, and the left lateral segment account, respectively, for 30%, 35%, 20% and 15% of the entire organ volume.[1] However, this estimation does not take into account tumor mass, or the frequent dystrophy of cirrhotic liver. An accurate measurement can nowadays be obtained by computed tomography (CT)-assisted image analysis.

Assessment of the functional reserve of cirrhotic liver is more difficult to achieve compared with normal liver. The most common assessment relies on the Child-Pugh classification, which includes clinical (ascites and encephalopathy) and laboratory (serum bilirubin, albumin, and prothrombin time) parameters. It has been demonstrated that the incidence of postoperative mortality and liver failure correlates closely to this classification.[2,3] Resection is therefore contraindicated in patients who are grade C at the time of surgery. Only limited resection should be allowed in patients who are grade B. Quantitative testing of liver function may allow the prognostic assessment of patients undergoing surgery. In grade A cirrhotic patients, several models have, retrospectively, been developed to assess the extent of a safe resection, as a function of bromosulfthalein or indocyanine green clearance, the glucose tolerance test, the redox tolerance index, or a combination of these. Yet these tests are not always easily available. Furthermore, they may be influenced by functional hepatic blood flow (i.e., hepatic blood supply and intrahepatic/extrahepatic shunt) or minor degrees of biliary obstruction. Consequently, their reliability has not generally been confirmed. Superimposed acute alcoholic hepatitis, as well as chronic active viral hepatitis, identified by raised preoperative transaminase levels, are also associated with increased risk and should be considered, at least temporarily, as operative contraindications.

Analytic liver function tests and the Child-Pugh classification

The term "liver function tests" implies standard tests for the measurement of synthetic cell function (serum albumin), excretory function (serum bilirubin), and the inflammatory activity of hepatocytes (serum glutamine-oxalacetic transaminase). The utility of these single tests in monitoring the immediate liver function is rather low and may reflect extrahepatic pathological processes.[4] Moreover, the value is absolutely limited regarding the disease etiology and morphological changes.

Offprint requests to: G.M. Gazzaniga, Via Volta 8, 16100 Genova, Italy
Received: May 19, 2004 / Accepted: September 1, 2004

However, these tests can be used by combining them with scoring systems such as the Child–Pught score. The Child's classification of liver diseases was originally described to assess operative risk in cirrhotic patients undergoing surgery for variceal bleeding. The original classification included five elements (serum bilirubin, serum albumin, ascites, encephalopathy, and nutritional status), which were used to place patients in one of three classes: Child's classes A,B, and C.[5] Pugh later modified the original classification by substituting prothrombin time for nutritional status and introducing 1 to 3 points for each element.[6]

The use of the classification, over the years, has been extended to predict outcome in cirrhotic patients who have undergone abdominal surgery. Furthermore, it has been demonstrated that the incidence of postoperative mortality closely correlates to this classification. Child A patients are suitable candidates for surgical resection, while only limited resection should be allowed in Child B patients. Resection is therefore contraindicated in Child C patients.[7]

Recent studies, nevertheless, show that up to 60% of Child A patients with cirrhosis associated with portal hypertension (as measured by a hepatic venous pressure gradient of > 10 mm Hg) experience liver decompensation (ascites, jaundice, or encephalopathy) after surgery.[8]

Therefore, in Child A patients, several models have been developed to assess the extent of a "safe" resection, with parameters such as preoperative liver biopsy, clearance of xenobiotics, and measurement of hepatic volume. Their role, however, is still controversial.

Liver biopsy

Liver biopsy is the standard criterion in the evaluation of the etiology and severity of liver disease. Grading of necro-inflammatory changes and staging of structural alterations are relevant requirements for the surgeon. Several different scoring systems are now available. The Italian "Gruppo Italiano Patologia Apparato Digerente" (GIPAD) scoring system has been adopted by our group.[9] The activity score is defined as a numerical index, from 0 (no activity) to 3 (severe damage), while structural alterations (fibrosis score) use a scale from 0 (no fibrosis) to 4 (cirrhosis).

Several authors have demonstrated that signs of moderate or severe inflammation on Intraoperative liver biopsy were significantly more frequent in patients who developed postoperative liver failure.

Clearance of xenobiotics

Even though the "clearance" approach has been carefully considered over the past 25 years, it has not yet achieved widespread clinical use, because each test reflects only a single aspect of the various functions of the liver.

Quantitative testing of liver function (QTLF) includes the aminopyrine breath test (microsomal liver function), galactose elimination capacity (cytosolic liver function), sorbitol clearance (liver plasma flow), and indocyanine green clearance (liver perfusion).[10]

Hepatic clearance function is related to liver perfusion, the transfer of solutes from blood to hepatocytes, hepatic volume, and the numbers and enzymatic composition of hepatic cells.[11] Certain liver tests, such as the indocyanine green, sorbitol, and galactose clearance tests, depend mainly upon hepatic perfusion. Others, such as galactose-eliminating capacity, primarily depend on the functional capacity of the liver. The 13C-aminopyrine breath test, to evaluate severity of disease in patients with hepatitis C virus-related chronic liver disease, has been proposed recently.[12] The metabolism of these substances occurs in the microsomal monooxygenase system, with the participation of cytochrome P-450. Problems with the analysis of the tests may be, therefore, related to environmental factors, smoking, and drug administration. Aminopyrine breath test results are particularly appropriate in patients with chronic liver disease, even though the test has shown low sensitivity in the presence of cholestasis (biliary tumors).

The experience of donor evaluation determined the introduction of the lidocaine-monoethylglycinexylidide (MEGX) test to assess liver function in cirrhotic patients. The lidocaine is metabolized to MEGX almost exclusively by cytochrome P-450. MEGX values in a venous blood sample after 15 min reflect liver function. The experience of the transplant surgical team in Bologna has shown that the lidocaine test appears to be more reliable than the Child's classification in quantifying the extent of hepatic insufficiency.[13] The injection of lidocaine, at the dose required for the test, was, nevertheless, not free of side effects, and this test was dismissed by our group early. The aminopyrine breath test is particularly appropriate in evaluating viable liver mass. The methionine breath test could be used to evaluate the oxidative capacity of liver mitochondria. A combination of these breath tests, exploring both mitochondrial and microsomal function, has been proposed in the early phase after liver transplant in order to evaluate the graft outcome.[14]

Measurement of liver volume

The risk of postoperative liver failure also depends upon the parenchyma spared by the resection. Estimations of normal liver resection do not take into account

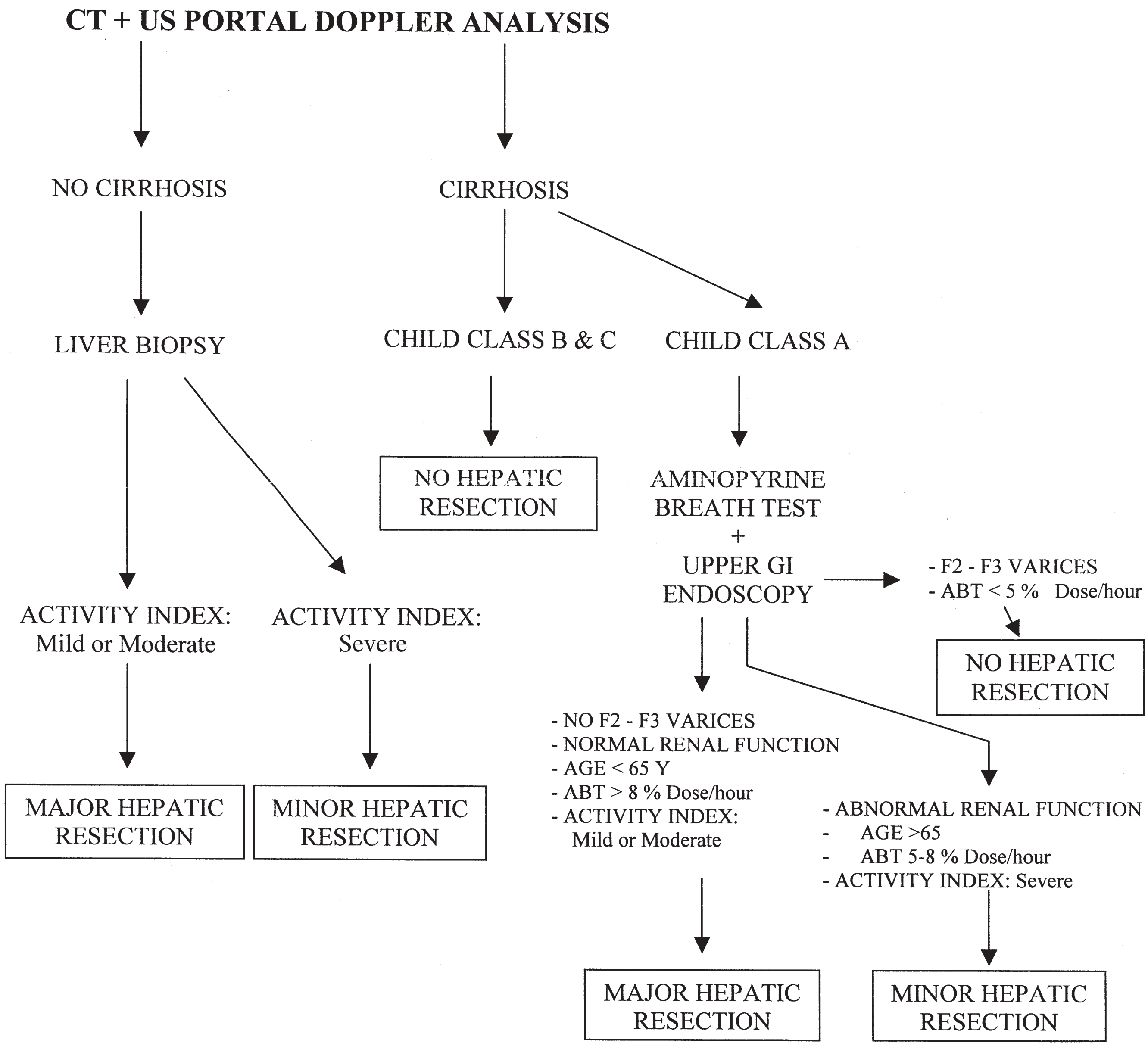

Fig. 1. Diagnostic algorithm, *CT*, computed tomography; US, ultrasonography; GI, gastrointestinal; *ABT*, aminopyrine breath test; *Y*, years

the dystrophy of a cirrhotic liver. Preoperative measurements of liver volume can be obtained using contrast computed tomography (CT). Nowadays, triphasic whole liver spiral CT scan is considered the gold standard. Because anatomical landmarks for hepatectomy simulation are blood vessels, the second (portal venous) phase is always used in our protocol.

The anatomical resection ratio is calculated according to the following formula:

Anatomical resection ratio (%) = resection volume − tumor volume/total liver volume − tumor volume × 100

CT volumetry has, nevertheless, shown different results from the functional resection ratio, as evaluated by radionuclide scanning.[15] This latter evaluation method has shown that CT volumetry may overestimate the resection volume in patients with unilateral portal venous flow decrease or stenosis/occlusion, because it calculates values for lobes which become hypo-functioning. Although, on the one hand, this phenomenon may be appropriate to avoid post-resection failure; on the other, it may reduce the number of potential surgical candidates. Various complex models have been applied to evaluate hepatic function. One recent model, which combines patient- and organ-specific data—the liver resection index (LRI)—was developed to analyze the risk of hepatic resection without discrimination of lesions.[16] In patients with primary liver tumors, the LRI is not a significant predictor of risk. We conclude that the inclusion of the aminopyrine breath test limits the value of the index and should, consequently, be replaced.

Selection of patients

The diagnostic algorithm used to select patients at our institute is shown in Fig. 1.

Conclusions

Improved operative technique and equipment, and improved postoperative intensive care, have resulted in additional indications for hepatic resection of primary liver tumors and liver metastasis. The evaluation of potential postoperative hepatic functional reserve is one of the most important preoperative studies for hepatectomy candidates. Surgical indications should be carefully evaluated. Given the complexity of hepatic function, a single reliable liver function test is not yet available. A good multifunctional system (clinical, laboratory, functional, and volumetric evaluation) that combines several elements can, nevertheless, provide sufficient data to determine the safe limits of hepatectomy.

Among patients with hepatic neoplasms and cirrhosis, those with nonprogressive cirrhosis and good functional reserve present with the most rational indication for resective surgery. The indication for resection must, however, be considered in relation to the therapeutic alternatives.

References

1. Mazziotti A, Cavallari A (1997) Techniques in liver surgery: Medic Med, Greenwich.
2. Nagao T, Inoue S, Goto S, et al. (1987) Hepatic resection for hepatocelular carcinoma: clinical features and long term prognosis. Ann Surg 205:33–40
3. Noun R, Jagot P, Farges O, Sauvanet A, Belghiti J (1997) High pre-operative serum alanine transferase levels: effect on the risk of liver resection in Child grade A cirrhotic patients. Wordl J Surg 21:390–394
4. Morgan DJ, Elliot SL, Ghabrial H (1991) Quantitative liver function test: a realizable goal? Can J Gastroenterol 5:77–85
5. Child CG III, Turcotte JG (1964) Surgery and portal hypertension. In: The liver and portal hypertension. Child CG III (ed). WB Saunders, Philadelphia pp 50–64
6. Pugh RN, Murray-Lyon IM, Dawson JL, et al. (1973) Transection of the oesophagus for bleeding oesophageal varices. Br J Surg 60:646–649
7. Franco D, Capussotti L, Samaja C, et al. (1990) Resection of hepatocellular carcinomas: results of 72 European patients with cirrhosis. Gastroenterology 98:733–738
8. Cohnert TU, Rau HG, Buttler E, et al. (1997) Preoperative risk assessment of hepatic resection for malignant disease. World J Surg 21:396–401
9. Guido M, Faa G (1998) La diagnosi morfologica delle epatiti croniche. Requisiti minimi del referto istopatologico. Pathologica 90:176–182.
10. Herold C, Heinz R, et al. (2001) Quantitative testing of liver function in patients with cirrhosis due to chronic hepatitis C to assess disease severity. Liver 21:26–30
11. Moseley RH (1996) Evaluation of abnormal liver function test. Med Clin N Am 80:887–906
12. Giannini E, Fasoli A, et al. (2002) 13 C-Aminopyrine breath test to evaluate severity of disease in patients with chronic hepatitis C virus infection. Aliment Pharmacol Ther 16:717–725
13. Ercolani G, Mazziotti A, Grazi GL, et al (1996) Evaluation of the liver function with the lidocaine (MEGX) test. Proc 2nd World IHPBA Congress, Bologna, vol 1, pp 143–147
14. Di Campli C, Angelini G, Armuzzi A, et al. (2003) Quantitative evaluation of liver function by the methionine and aminopyrine breath test in the early stages of liver transplantation. Eur J Gastroenterol Hepatol 15:727–732
15. Akaki, S, Okumura Y, Sasai N, et al. (2003) Hepatectomy simulation discrepancy between radionuclide receptor imaging and CT volumetry: influence of decreased unilateral portal venous flow. Ann Nucl Med 17:23–29
16. Cohnert TU, Rau Hg, et al. (1997) Preoperative risk assessment of hepatic resection for malignant disease. World J Surg 21:396–394