

## **Preoperative Volumetric and Functional Evaluation for Hepatic Resection in a Cirrhotic Liver**

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### **ABSTRACT**

Twenty three cirrhotic patients who underwent hepatic resection for hepatocellular carcinoma (HCC) between January 1996 and August 1999 at the National Cancer Institute of Cairo University (NCI) were submitted to preoperative volumetric evaluation of their tumor, resected liver and preserved liver. They were also assessed by the modified child (Pugh and Paul Brousse) scoring systems. Sixteen patients with child class A underwent less than 50% resection of their liver and 7 patients with child class B underwent less than 25% resection of their liver. Only one early postoperative mortality was recorded (4.4%) and the rate of postoperative complications was 60.9%. The intraoperative blood loss, intensive care and overall hospital stay were also evaluated. The estimation of parenchymal hepatic resection rate (PHRR) by volumetric and functional assessment proved to be an efficient tool for achieving safe hepatic resection in cirrhotic patients.

**Key Words:** *Volumetry - Hepatic resection - Cirrhosis.*

### **INTRODUCTION**

Hepatocellular carcinoma (HCC) is frequently associated, worldwide, with liver cirrhosis. This association ranges from 50% in France [3] to almost 85% in Asia [12,26]. In the United Kingdom, the figures reported lie between 68% and 74% [10,15]. Although hepatic resection in non-cirrhotic patients has become an established and safe procedure, mortality in cirrhotic patients is unfortunately elevated, ranging between 12% and 37% [3,9,11,16].

Since hepatic resection is the only curative treatment for HCC [18], a lot of research work was directed towards improving the results of surgery in cirrhotics. The old belief that major liver resections were not feasible in cirrhotic livers [21] had to be reconsidered after the publication of many series reporting less than 4% operative mortality rates [6,16].

The most frequent postoperative complications reported in cirrhotics are in order, liver insufficiency, variceal bleeding, ascitis, infection and intraabdominal bleeding [14,17,23,29]. Accordingly an accurate evaluation of the functional reserve of the liver and its capacity to regenerate is essential before embarking onto hepatic resection in a cirrhotic patient. The functional reserve of the liver depends on two factors: (a) volume of the non-tumorous liver and (b) functional efficiency of the remaining hepatocytes. Hence, it is important not to consider the amount of liver resected, but the quantity and quality of the remaining hepatic parenchyma [2].

As early as 1969, Stone and his colleagues [22] roughly estimated the volumes of the various liver sectors and segments and expressed them as percentages of the whole organ (Fig. 1). However, this rule of thumb is not always accurate since it does not take into account neither the tumor volume, nor the possible atrophy or hypertrophy of any liver segment [2,18] (Fig. 2a,b). So, in a trial to overcome the inaccuracy of Stone's rule, Okamoto and his colleagues in 1984 [18] suggested a more accurate "volumetric study" of liver tumors on computerized tomography (CT) scans. They reproduced the CT slices on transparent paper and by weighing the cut images of each of the tumor, resected liver and preserved liver, they could calculate the approximate volume of each of these [2]. By this method, they estimated the "Parenchymal hepatic resection rate" (PHRR) which they defined as the proportion of resected liver to the entire liver volume after excluding the volume of HCC in both. Their formula was designed as follows:

$$\text{PHRR} = \frac{\text{Volume of liver resected} - \text{Volume of HCC}}{\text{Volume of entire liver} - \text{Volume of HCC}} \%$$

The functional efficiency of the cirrhotic liver can be estimated by several methods like the Child-Turcotte [4], Pugh [19], Child-Paul-Brousse classifications [3] and others [20,24] (Table 1-a,b). Bismuth and his colleagues used this Child Paul-Brousse (Child PB) classification to recommend a rough guide for the estimation of the percentage of functional parenchyma which could be safely removed (PHRR) from a cirrhotic liver, for Child-PB class A it was 50%, for class B 25% and for class C it was 17% [3].

**Segmental anatomy of the liver on CT scans: (Fig. 3-a, b,c)**

Contrast enhanced CT cuts taken near the diaphragm show the inferior vena cava (INC) and emerging from it in a fan like appearance, the 3 main hepatic veins. At this level, it is easy to identify the 4 major hepatic sectors. The middle hepatic vein (M) corresponds to Cantlie's line which, in more caudal cuts, is represented by an imaginary line drawn between the gall bladder (GB) fossa and the IVC. This line divides the liver into right and left hemilivers (Fig. 3-a,b).

On the other hand the umbilical fissure, or fissure for ligamentum teres divides the left hemiliver into a lateral sector (segment II, III) and a medial sector (segment IV). It is indicated by a notch on the anterior surface of the liver just to the left of Cantlie's line and in higher cuts, it corresponds to the left hepatic vein (Fig. 3-b,c). Continuous with the umbilical fissure, is the fissure for ligamentum venosum which runs in a transverse direction and it demarcates segment I also called caudate lobe (c), which is posterior to it (Fig. 3-b,c). The boundary between the anteromedial sector of the right hemiliver (Segments V, VIII) and the posterolateral sector (segment VI, VII) is identified by extrapolating the line of the right hepatic vein (R) onto lower CT sections (Fig. 3-a). Each of these two sectors is subdivided into superior (segments VII, VIII) and inferior (segments V, VI) by the right portal vein (pvr) which runs horizontally from left to right and that can be seen in central cuts [1] (Fig. 3-c).

## PATIENTS AND METHODS

The present study was held between January 1996 and August 1999 and included 23 patients

all of whom had HCC associated with liver cirrhosis. Their age ranged between 41 and 68 years. They were 14 males and 9 females. Cirrhosis was histologically demonstrated in preoperative needle biopsy in 5 cases and suggested by preoperative imaging in 18 cases.

Preoperative evaluation of all patients included Alphafetoprotein (AFP) serum level, routine blood tests such as blood picture, blood sugar, kidney and liver function tests such as serum albumin, bilirubin, AST, ALT and prothrombin time and concentration. Abdominal ultrasound and CT scans were performed for all patients using a cycle time of 5 seconds at intervals of 1 cm. To demarcate the tumor margin intravenous contrast was used in 16 patients.

The patients were assigned to one of the groups of modified Child classification according to their liver functions and to whether there was any evidence of ascitis or encephalopathy (Table 2).

For practical purposes, factor II was ignored and only prothrombin concentration was taken into account with the other factors of child PB classification. All patients underwent upper gastrointestinal endoscopy to elucidate the presence of oesophageal or gastric varices and 9 out of 23 patients showed signs of impending bleeding and underwent prophylactic sclerotherapy.

Volumetric evaluation of CT tracings of all the patients was undertaken. Each individual CT slice was reproduced onto transparent paper. The liver borders were first traced and then, the different lines marking the various segments of the liver were drawn and projected onto all tracings. Finally, the circumference of the tumor was outlined (Fig. 4). The tracings were all cut out with scissors and accurately weighed by means of a precision scale. A simple calculation of the whole liver volume, the tumor volume and the volume of liver to be resected could be made using the equation of Heymsfield et al. [7] designed as follows:

$$\text{Liver volume} = \sum x \frac{\text{Tracing weight} \times 28.4 \times \text{thickness of CT slice (cm)}}{\text{Weight of } 1 \text{ cm}^2 \text{ of tracing paper}}$$

Where  $\sum$  = the sum of individual slices.

And 28.4= the magnification index.

In this formula the tracing weight differed for each evaluated area. Finally, the PHRR was calculated for each patient using the formula suggested by Okamoto et al. [10].

Hepatic resection was undertaken for each patient according to his or her Child PB class, taking into consideration that the maximum PHRR allowed for group A would not exceed 50% and for group B: 25% [3]. Evaluation of the intraoperative and early postoperative complications was then undertaken to appraise the combined volumetric and functional evaluation of these patients and to study the reflection of the PHRR on the results of hepatic resection in cirrhotic patients.

## RESULTS

Twenty three patients were included in this study and they all had HCC associated with cirrhosis. Their ages ranged between 41 and 68 years with a mean age of 56.8 years. They were 14 males and 9 females. HCC was diagnosed by preoperative needle biopsy in 8 out of the 23 cases while in the remaining patients, it was diagnosed by high AFP level and radiological characteristics of the tumor. Cirrhosis was histologically demonstrated in preoperative needle biopsy in 5 out of the 23 patients and suggested radiologically by preoperative ultrasound or CT scan in the rest of the patients.

The tumors were located in the right hemiliver in 12 out of the 23 patients and in the left hemiliver in 11 out of the 23 patients (Table 2).

Upon functional evaluation (as shown in table 2), 16 patients were assigned to Child PB class A and 7 to class B. None of the patients included in this study who class C. In group A, 7 out of 16 patients underwent right hemihepatectomy (Fig. 5-a,b and Fig. 6-a,b) 6 out of 16 were submitted to left hemihepatectomy (Fig. 7) and 3 out of 16 to different types of segmentectomy. These included segmentectomy (VI) in one patient (Fig. 8), segmentectomy (VI) and (VII) in another patient and segmentectomy (II) and (III) in the last patient. In group B, no patient underwent right hemihepatectomy, while 2 out of 7 patients were submitted to left hemihepatectomy and 5 out of 7 underwent different types of segmentectomy. These were segmentectomy (VI) in 2 patients, segmentectomy (VI) and (VII) in another patient and segmentectomy (II) and (III) in 2 patients (Fig. 9).

Upon volumetric evaluation of the CT scans the average number of CT slices covering the whole liver was 17.8 slices (range: 16 to 23). The PHRR was calculated for each case and it is shown in table (3). For patients with Child PB class A, it ranged from 17.3% to 50% with a mean of 36.8% and for those with Child PB class B, it ranged from 14.2% to 24.8% with a mean of 20.4%. It should be noted here that the PHRR did not exceed 50% for the patients in class A or 25% for those in class B.

The duration of surgery ranged from 2.2 to 4.7 hours for all patients with a mean of 3.6 hours. Blood transfusion was needed intraoperatively for 12 out of 16 patients in class A with a mean amount of 2.2 units of blood (range 0-5 units) and 3 out of 7 patients among those in class B with a mean amount of 1.8 units (range 0-4 units).

Thirteen of the 16 patients in class A (81.3%) needed postoperative intensive care for a mean duration of 8.7 days (range 2-21 days) and three of the 7 patients in class B (42.9%) were kept in the intensive care for a mean duration of 5.2 days (range 1-12 days). The hospital stay for the patients with class A ranged from 13 to 26 days (mean hospitalization: 20.2 days) while for those with class B, it ranged from 14 to 22 days (mean: 17.4 days). No intraoperative mortality was encountered while 1 patient (4.4%) died on the 11th postoperative day. Postoperative complications were noticed in 14 out of the 23 patients (60.9%), which are shown in table (4).

The single postoperative mortality was due to severe hemorrhage from oesophageal varices in a patient with class A who underwent right hemihepatectomy. This patient developed multiple organ failure within 2 days.

The most common complication encountered was liver insufficiency (LI). This was defined as a rise of serum bilirubin > 5 mg% for more than 2 weeks or > 15 mg% at any time. It could be associated with coagulopathy or hypoalbuminaemia (requiring albumin supplementation) or amoniacal encephalopathy. It occurred in 3 patients (13%). It was temporary in all three, where two of them regained a normal bilirubin level after 6 and 11 days respectively and only one was discharged with a bilirubin level of 2.3 gm%. Ascitis developed in 2 patients (8.7%). It was minimal in one and re-

quired no paracentesis, while in the other patient it needed repeated tapings. Hematemesis was encountered in 2 patients (8.7%). In one of them it originated from missed varices which was fatal (on postoperative day 11), while in the other, it responded to conservative treatment since immediate endoscopy had revealed only minimal gastric erosions that were treated conservatively and the patient was discharged on the 22nd day.

Septic complications occurred in 2 patients (8.7%). One of them developed a right subphrenic abscess following right hemihepatectomy. It was drained percutaneously through an ultrasonographically guided catheter on day 12 and the patient was discharged 6 days later. The other patient developed mild wound sepsis that subsided on repeated dressings and the patient was discharged on day 16. Biliary leakage was noticed in 2 patients. It was temporary and required no intervention since it was freely drained by the hemovacs. Both patients were discharged after it stopped on days 18 and 26 respectively. Renal insufficiency occurred in only 1 patient (4.4%) whose urinary output gradually dropped to less than 350 ml per day, his blood urea rose to 120 and his serum creatinine rose to 3.5 mg/dl. The condition started on the 7th postoperative day and responded favorably to liver support, accurate fluid and electrolyte regulation and dopaminergic renal stimulation. It resolved on postoperative day 12 and the patient was discharged 5 days later. Other miscellaneous complications like chest infection and deep venous thrombosis were seen in 2 patients but these were not serious and respond-

ed promptly to medical treatment and the patients were discharged on days 15 and 22 respectively. The overall complication rate was close among patients with class A (62.5%) and those with class B (57%).

Table (1-a): Child-Pugh score to assess severity of cirrhosis [19].

Parameter	Points		
	1	2	3
Albumin (g/dl)	> 3.5	2.8-3.5	< 3.5
Bilirubin ( $\mu$ mol/l)	< 25	25-40	> 40
Prothrombin time (sec. above normal)	< 4	4-6	> 6
Ascitis	None	Mild	Moderate
Encephalopathy (grade)	0	I-II	III-IV

Class A= 5-6 points, Class B= 7-9 points, Class C= 9-15 points.

Table (1-b): Child-Pugh brousse score for functional evaluation of the cirrhotic liver [3].

Criteria	Points
Clinical ascitis	1
Clinical encephalopathy	1
Serum bilirubin > 30 mmol/L	1
Serum albumin < 30 g/L	1
Prothr. T % + factor II %	1
$\frac{2}{2}$	
Prothr. T. % + factor II %	2
$\frac{2}{2}$	

Class A= 0 Class B= 1-2 points Class C= > 2 points

Table (2): Location of tumor, extent of resection and child PB classification in 23 cirrhotic patients with HCC.

Location of tumor	Child PB-A		Child PB-B		Total
	Extent	No.	Extent	No.	
* Right 1/2 liver (12)	• Right 1/2 Hepatectomy	(7)	• Right 1/2 Hepatectomy	(0)	7
	• Segmentectomy VI	(1)	• Segmentectomy VI	(2)	3
	• Segmentectomy VI-VII	(1)	• Segmentectomy VI-VII	(1)	2
* Left 1/2 liver (11)	• Left 1/2 Hepatectomy	(6)	• Left 1/2 Hepatectomy	(2)	8
	• Segmentectomy II-III	(1)	• Segmentectomy II-III	(2)	3
Total		16		7	23

Table (3): PHRR as calculated by preoperative volumetry in 23 cirrhotic patients.

PHRR (%)	Mean PHRR
Child PBA 17.3 18.2 20.4 28.2 33.2 35.6 37.5 38.1 38.8 43.9 44.1 44.5 45.8 46.2 47.6 50	36.8%
(16 patients)	
Child PBB 14.2 14.8 17.7 22.6 23 24.7 24.8	20.4%
(7 patients)	

Table (4): Postoperative complications after liver resection in 23 cirrhotic patients with HCC.

Complication	n° of patients	%
Liver insufficiency	3/23	13
Ascitis	2/23	8.7
Hematemesis	2/23	8.7
Sepsis	2/23	8.7
Biliary leakage	2/23	8.7
Renal insufficiency	1/23	4.4
Miscellaneous	2/23	8.7
Total	14/23	60.9

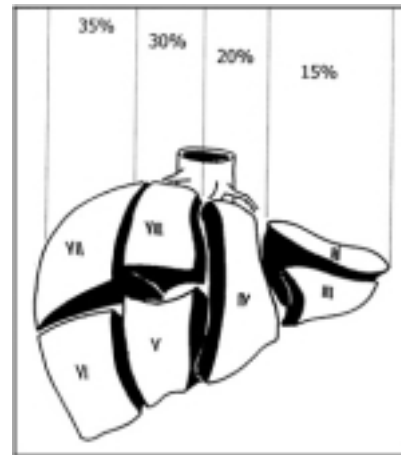
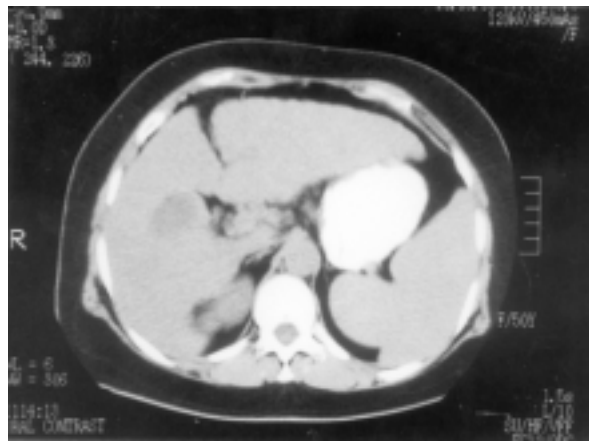


Fig. (1): Average volume % of different sectors in a normal non-cirrhotic liver (Stone et al., 1969).



(A)



(B)

Fig. (2): A- Preoperative CT showing HCC in a female occupying seg. (V) - (VIII) in an atrophied right 1/2 liver with compensatory hypertrophy of the left hemiliver.  
 B- Postoperative CT after right hemi hepatectomy (PHRR= 43.9%).

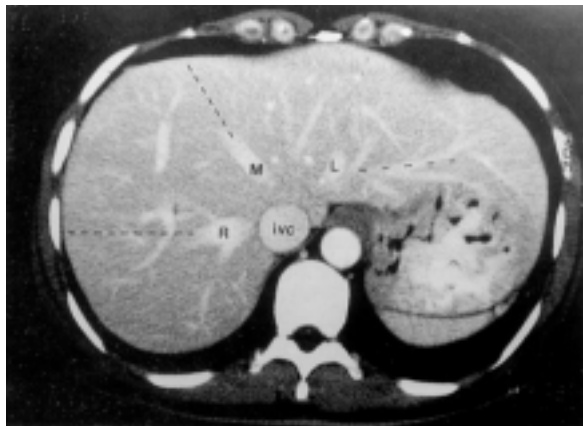


Fig. (3,a): Contrast enhanced abdominal CT cut near the diaphragm, showing IVC and emerging from it the 3 main hepatic veins: right (R), middle (M) and left (L).

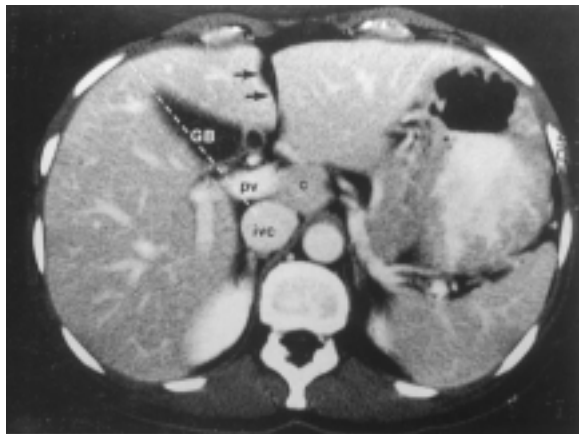


Fig. (3,b): Lower cut showing the umbilical fissure (of ligamentum teres) shown by thick arrows, gall bladder fossa (GB), inferior vena cava (IVC), Cantlie's line joining the last two structures, the main portal vein (PV) and the caudate lobe (c).



Fig. (3,c): Further lower cut showing right division of portal vein (pvr) and caudate lobe (c) posterior to the fissure for ligamentum venosum, shown by thin arrows.

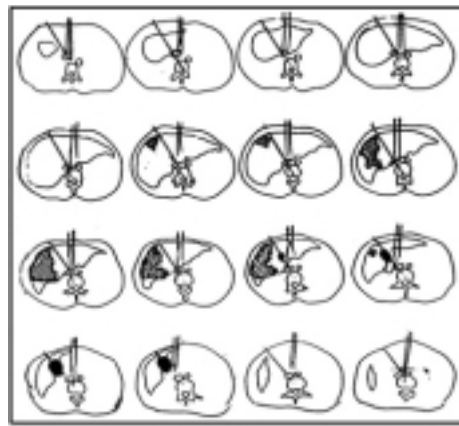
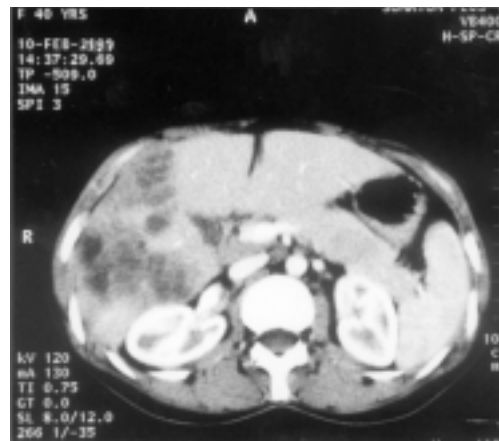
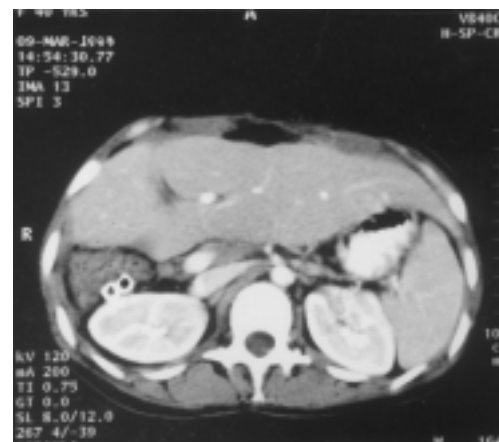


Fig. (4): Schematic representation of the CT tracings of a patient with HCC of seg. VI, VII, VIII used for volumetric study:

- = Gall
- ⊘ = Tumor.
- = Cantlie's line.
- == = Left sagittal fissure (for lig. teres).



(A)



(B)

Fig. (5): A- Preoperative CT showing HCC of seg. (V, VI, VII, VIII) in a female aged 40 years. B- Postoperative CT of the same patient after right hemihepatectomy. (PHRR= 28.2%).



(A)



(B)

Fig. (6): A- Preoperative CT showing HCC of seg. (V, VI, VII, VIII).

B- Postoperative CT of the same patient after 3 months showing left lobe hypertrophy after right hemihepatectomy (PHRR= 47.6%).



Fig. (7): Early postoperative CT after left hemihepatectomy (Seg. II, III, IV) (PHRR= 33.2%).



Fig. (8): Postoperative CT after segmentectomy (VI) (PHRR= 14.8%).

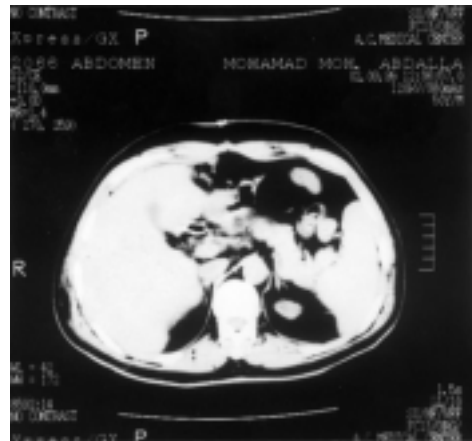


Fig. (9): Postoperative CT after segmentectomy (II,III) (PHRR= 14.2%).

## DISCUSSION

In the past, liver cirrhosis has been traditionally considered as a contraindication to hepatic resection because of its association with high mortality rates ranging from 13 to 37% [3,9,11,16]. Accordingly only patients with adequate hepatocellular reserve should be considered candidates for resection, while those patients who cannot tolerate resection due to advanced cirrhosis should be identified and offered other alternatives to hepatectomy in the form of local ablative therapies including intralésional injectional therapies, cryoablative therapy and thermal ablative therapies (e.g. radiofrequency ablation); or regional therapies including hepatic artery infusion chemotherapy and hepatic artery chemoembolization [28].

The combination of preoperative volumetric assessment and functional evaluation of the liv-

er was proved by many studies to be an efficient tool aiming at improving the results of hepatic resection in cirrhotic patients [3,11,16,18].

Volumetric assessment for PHRR evaluation by the transparent paper technique advocated by Okamoto et al. [18] was used in this study. It proved to be simple and inexpensive. Nonetheless it was time consuming and not error free. The above mentioned authors themselves reported an average difference of 10% and 7% between the CT calculations and the actual volumes of resected liver and tumor respectively [18]. They explained this discrepancy by some organ movement during respiration and incomplete resolution of the tumor from the rest of the liver on one hand and of the liver from the surrounding structures on the other hand. Currently, many CT scanners include software capable of direct volumetric measurements through the CT computer itself, which makes the procedure of PHRR calculation easier, faster and more accurate [27].

According to Stone's rough rule (Fig. 1) [22], the right hemiliver represents 65% and the left hemiliver represents 35% of the liver. Nevertheless, 6 patients with class A underwent right hemihepatectomy and 2 patients with class B underwent left hemihepatectomy (table 2). These major hepatectomies could be successfully undertaken without exceeding the maximal PHRR allowed by Bismuth and his colleagues for class A patients (50%) and class B patients (25%) [3]. This discrepancy is due to two facts. On one hand, Stone's rule is applicable only to non-cirrhotic livers, while in cirrhotic livers, atrophy of some segments and compensatory hypertrophy of some others change the relative volumes of different hepatic sectors and segments. On the other hand, the subtraction of the tumor's volume from both the resected and the total liver volume in Okamoto's equation [18] for PHRR calculation also adds to the inability of blind application of Stone's rough rule.

To further illustrate this latter point, a look at the CT tracings shown in Figs. (5 & 6) shows that right hemihepatectomy could be represented by a PHRR of 28.2% in one patient and 47.6% in the other patient. This discrepancy could be explained by the fact that in the first patient the right hemiliver was largely replaced by the voluminous tumor while in the second patient the tumor was central and small. When

the tumor's volume was subtracted from that of the right hemiliver, in Okamoto's equation, the PHRR representing the amount of functioning parenchyma resected varied largely, as illustrated by these two figures.

Functional evaluation according to the modified Child (PB) classification was found to be easy and of reasonable cost. Nevertheless, newer methods have been advocated by many authors, with possible better accuracy namely, Indocyanine Green (ICG) clearance test, where hepatic resection is not recommended in patients with ICG clearance of less than 5 ml/min/kg [6,18].

Intraoperative blood loss was minimal considering the number of major resections performed in this study (7 out of 23 right hemihepatectomies and 8 out of 23 left hemihepatectomies). This is due to adequate patient selection that was made possible by accurate preoperative functional assessment of the cirrhotic liver. Child PB class A patients required more blood units than those of class B probably because of the higher proportion of hemihepatectomies performed in this group (13/16 versus 2/7).

The mean duration of intensive care (8.7 and 5.2 days) and overall hospital stay (20.2 and 17.4 days) were slightly longer in patients with class A compared to those with class B. Again this is probably due to the higher proportion of major resections performed on the patients with class A.

The morbidity and mortality figures of this study were favorably comparable to other series dealing with hepatic resection in cirrhotic patients. No intraoperative mortality was encountered in the present series while the reported rate in many other studies ranged between 2.3 and 30.7% [3,5,8,13,17,23,25]. The 30 day mortality rate was 4.3% which is lower than many other series reporting early postoperative mortality rates of 18% to 35.8% [6,18]. The postoperative complications encountered were similar to other studies dealing with hepatic resection in cirrhotics. These were mostly temporary and responded to conservative measures. In accordance with most other series, liver cell failure was the most common postoperative complication and it was seen in 13% of cases. It was reported by other authors to range between 0% and 28.5% [3,8].

This fact alone emphasizes on the prime importance of calculating the functional capacity of the preserved liver after resection of the tumorous liver, by both volumetric and functional preoperative evaluation.

Ascitis, hematemesis, sepsis and biliary leakage, each occurred respectively in one patient (8.7% each). These were similarly found by other large series as fairly common postoperative complications after resection in cirrhotic livers. Ascitis was reported to occur in 0-16% [8,14], hematemesis in 1-10% [8,28], sepsis in 0-8.3% [8,13] and biliary leakage occurred in 0-8.3% [3,13].

The low postoperative mortality and complication rates obtained in this study in addition to the absence of intraoperative mortality were all in favor of the importance of volumetric and functional assessment for accurate calculation of the PHRR aiming at successful resection in a cirrhotic liver.

### **Conclusion:**

At present, liver cirrhosis is no longer being considered as an absolute contraindication to hepatic resection. An easy way to identify patients who will survive resection with acceptable morbidity is by calculating the PHRR by accurate volumetric and functional assessment of the cirrhotic liver. The preoperative calculation of PHRR will allow the surgeon to identify patients who are candidates for resection from others who should be given other therapeutic alternatives. It will also define the type of resection and its extent. Rough estimation of the amount of liver resected, based on Stone's rule, can give false results while volumetric evaluation by Okamoto's equation is certainly more accurate since it takes into consideration both the tumor's volume and the possible atrophy and hypertrophy of different liver segments caused by cirrhosis.

Volumetry methods by the transparent paper technique of Okamoto et al. [18] and functional assessment by the modified Child classification are simple and inexpensive for reaching this goal. Nevertheless, more expensive and complicated techniques can be used instead, namely new CT machines supplied with special software capable of volumetric calculation, ICG clearance test and intraoperative ultrasonography which will allow more accurate localization

of the tumor and avoid inadvertent injury to important structures. With further perfection and refinement, these techniques will probably acquire, in the near future, a more important role in achieving safe resection of tumors in cirrhotic livers.

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