

# Regeneration of the liver after hepatectomy in Egyptian patients with schistosomal periportal fibrosis

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## **Abstract**

*Aim: The aim of this work was to assess the safety of liver resection in bilharzial patients with special attention to the ability of the bilharzial liver to regenerate.*

*Methods: The study included patients with liver mass indicated for resection. Patients with pathologically proved pure bilharzeal hepatic fibrosis and who fit in Child-Pugh class A or B were selected. Patients underwent liver resection. They were followed up for one year. They were examined serially for their liver functions and liver volumetry.*

*Results: Forty eight patients had liver resection. Of them, 16 had pure bilharzeal fibrosis. The mean age was  $59 \pm 14$  years. There were eight right hepatectomies, three left lateral segmentectomies, two left hepatectomies, two non-anatomical resections (for cancer gall bladder) and one IVth segmentectomy. Mean operating time was  $155 \pm 73$  minutes. Mean blood loss was  $430 \pm 720.72$  mls. There were neither operative complications nor mortalities. Mean hepatic volumetry was  $854.66 \pm 92.32$ ,  $1003.68 \pm 123.68$ ,  $1166.54 \pm 65.32$  and  $1246.12 \pm 30.87$  mls at one, 12, 24 and 52 weeks postoperative respectively.*

*Conclusions: Resection in bilharzeal liver does not carry added operative risk. Bilharzeal liver has a considerably better regenerating power as compared to cirrhotic liver. It might therefore tolerate resection safely.*

*Key words: Liver resection, volume regeneration, bilharziasis.*

## **Introduction:**

Bilharzial hepatic fibrosis is the commonest cause of portal hypertension in Egypt.<sup>1</sup> Portal hypertension is generally defined as a portal vein pressure above 10 mmHg.<sup>2</sup> Cirrhosis is the main pathology that causes portal hypertension. Cirrhosis is defined as diffuse nodulation resulting from fibrous bands subdividing the liver into regeneration nodules.<sup>3</sup> Non cirrhotic portal hypertension is caused by schistosomiasis (bilharziasis) as well as a variety of conditions including: idiopathic portal hypertension (IPH), non-cirrhotic portal fibrosis and extrahepatic portal venous

thrombosis, hepatic venous outflow tract obstruction, veno-occlusive disease and congenital hepatic fibrosis. The diagnosis of non-cirrhotic portal hypertension is usually made by abdominal ultrasound, upper gastrointestinal endoscopy, normal liver function tests and normal liver histology.<sup>4</sup>

Liver resection is required for the management of a number of pathologies that affect the liver.<sup>5</sup> The amount of liver tissue that can be safely resected depends on the total hepatic volume and the ability of the remaining liver to regenerate.<sup>6</sup> Both features are severely impaired in cirrhotic liver.<sup>7,8</sup>

Bilharzial hepatic fibrosis has some resemblance to cirrhosis, yet it represents a different pathological process.<sup>9</sup> A number of patients who are candidates for resection in Egypt will have bilharzial hepatic fibrosis, being a common endemic disease. To date, there has been very limited research that specifically addressed the effects of resection on bilharzial patients and the ability of bilharzial liver to regenerate.<sup>10</sup>

#### **Aim:**

The aim of this work is to assess the safety of liver resection in bilharzial patients with special attention to the ability of the bilharzial liver to regenerate.

#### **Materials and methods:**

The study included 48 patients admitted for liver resection.

Patients were enrolled according to the following inclusion criteria:

- Past history of bilharzial infestation, positive shistosomal serology or positive urine or stool analysis for shistosomal ova.
- Negative serological markers for hepatitis B and C.
- Child-Pugh class A or B.
- Ultrasonographic confirmation of periportal fibrosis with absence of cirrhotic changes.
- Histopathologic proof of pure shistosomal hepatic fibrosis. Selected patients had been proved to have pure bilharzial hepatic fibrosis by histopathological examination of either preoperative liver biopsy or by examining the post operative specimen.

Patient personal approval to be enrolled in the study had been taken from all patients.

This study has been approved by the Ethical Committee of the Faculty of Medicine University of Alexandria.

All patients were subjected to thorough clinical assessment and comprehensive laboratory workup including liver function tests, hepatitis B surface antigen (HBs Ag), anti-HBc and antibodies against hepatitis C virus (Anti HCV), serum alpha- fetoprotein (AFP) and carcino- embryonic antigen (CEA). Imaging of the liver included B-mode ultrasonography for determination of the degree of liver parenchymal insult (cirrhosis versus

fibrosis). Tri-phasic C.T of the liver. Liver volumetry was calculated using CT data - through image reformatting and manual and automated tracing- and liver biopsy. The appropriate pattern of resection was then performed. Data recorded included the type of hepatic resection performed, the technique used in resection, operative time, operative blood loss and complications.

Patients were reviewed at 1, 12, 24 and 52 weeks postoperatively. They underwent clinical check, liver function assessment, multi-slice CT of the liver and abdomen and liver volumetry. The percentage of liver regeneration was calculated.

#### **Results:**

During a period of two years, 48 patients had liver resections. Of those 16 patients fulfilled the inclusion criteria of the study. They had schistosomal hepatic fibrosis with varying degree of periportal fibrosis as diagnosed by histopathology. They were 14 males and two females. The age ranged between 45 and 72 with a mean of  $59 \pm 14$  years. The indication for resection was hepatocellular carcinoma (HCC) in 7 patients, hemangioma in 4, metastasis from colon cancer in 3 and carcinoma of gall bladder invading the liver parenchyma in two. Ten patients were Child's class A and six patients were Child's class B. None of the patients received oncologic treatment in the form chemo-embolisation, alcohol injection or radiofrequency prior to resection.

Patients had eight right hepatectomies **Figures(1,2)**, three left lateral segmentectomies, two left hepatectomies, two non-anatomical resections (for cancer gall bladder) and one IVth segmentectomy. Selective extrahepatic control of the inflow vessels was achieved in all cases. Control of hepatic veins was done intrahepatic starting by securing the small hepatic veins. Parenchymal dissection was done used Kelly clamp technique. Concomitant colectomy was performed in two cases.

Operative blood loss was  $430 \pm 720.72$ mls. Operating time ranged from 104min to 225min with a mean of  $155 \pm 73$  minutes. There were neither operative complications nor mortalities.

Postoperatively, six patients developed ascitis that was mild in four and moderate in two. All patients responded favorably to medical treatment. No patients developed hematemesis.

All patients attended the 12 weeks and 24 weeks follow-up visits. Eleven patients (11/15, 73.3%) attended the 52 weeks visit **Figure(3)**.

During follow-up visits, patients were clinically examined: There was no ascitis, no jaundice. Liver functions were within normal range **Table(1)**. Patients were able to perform full duty work. Mean hepatic volumetry and the percentage increase in liver volume are shown in **Table(2)**.



*Figure (1): Preoperative CT of a large mass of the right lobe.*



*Figure (2): CT for the same patient in "figure1" one week after undergoing right hepatectomy.*



*Figure (3): CT for the same patient in "figure1" 52 weeks after his right hepatectomy.*

Table (1): Mean values of liver functions postoperatively as compared to preoperative values.

| Liver function test | Bilirubin   | AST         | ALT         | Prothrombin % | Albumin     |
|---------------------|-------------|-------------|-------------|---------------|-------------|
| Pre-operative       | 0.82 ± 0.32 | 84 ± 43.5   | 74.8 ± 43.8 | 84 ± 32       | 3.43 ± 0.9  |
| 12 weeks            | 0.93 ± 0.43 | 63.7 ± 63.3 | 75 ± 33.6   | 86 ± 22       | 3.11 ± 1.8  |
| 24 weeks            | 0.92 ± 0.24 | 59.9 ± 53.4 | 63.5 ± 27.2 | 78 ± 67       | 3.43 ± 2.32 |
| 52 weeks            | 0.84 ± 0.72 | 57.8 ± 62.3 | 62.7 ± 33.4 | 81 ± 83       | 3.56 ± 1.54 |

Table (2): Mean values of liver volumetry and the corresponding calculated percentage of increase liver volume.

| Duration after resection | Liver volumetry  | % increase in liver volume |
|--------------------------|------------------|----------------------------|
| One week                 | 854.66 ± 92.32   | --                         |
| 12 weeks                 | 1003.68 ± 123.68 | 17.43 ± 10.53%             |
| 24 weeks                 | 1166.54 ± 65.32  | 36.49 ± 6.45%              |
| 52 weeks                 | 1246.12 ± 30.87  | 45.80 ± 6.85%              |

### Discussion:

Periportal hepatic fibrosis caused by schistosomal infestation is a pathology that is different from cirrhosis. Bilharzial patients tend to have good hepatic reserve as compared to cirrhotics.<sup>11</sup> This might reflect the good hepatocyte perfusion inspite of the periportal fibrosis caused by the immune reaction against the schistosoma eggs.

In the era of liver transplantation, extensive research has been conducted recently to determine the factors responsible for liver regeneration after hepatectomy.<sup>12,13</sup> The percentage increase of the portal flow to the remaining liver segment seems to be a determining factor that govern the rate of regeneration of the remaining liver.<sup>14</sup>

Coming to the results of the current study, the mean operative blood loss was 430±720.72mls. This compares favorably with that reported for surgery of normal livers: Clavien et al, who reported 100 resections in normal livers, had a median blood loss of 250 mL (range 50-5000 mL).<sup>15</sup> The operative time of 155±73 minutes was also comparable to that of normal liver resection.<sup>16,17</sup>

The percentage increase in liver volume of the studied patients was 17.43%±10.53%,

36.49%±6.45% at 12 and 24 weeks postoperatively. When comparing these values to those reported by Chen et al who found that normal liver increases in volume by 21.2±6.7% and 30.6±12.7% at 3 and 6 months post-resection respectively while cirrhotic livers increase by only 8.5±3.6% and 12.9±4.5% in the same periods. It is noticeable that the rate of regeneration of bilharzial liver is much closer to that of the normal liver compared to cirrhotic liver.<sup>18-20</sup>

Surgery on cirrhotic liver invites high incidence of complications. Operative complications were found to be significantly higher when comparing cirrhotic with non-cirrhotic liver resection.<sup>21,22</sup> There were no major complications among the studied patients.

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