

Initial Experience of Surgical Microwave Tissue Precoagulation in Liver Resection for Hepatocellular Carcinoma in Cirrhotic Liver

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Abstract

Background: Surgical Hepatic resection has been considered as the first-line treatment which is most effective and radical treatment for hepatocellular carcinoma in cirrhotic liver. However, hepatic resection, in the presence of cirrhosis is associated with high risk of hemorrhage; thus, good clinical results can only be achieved by minimizing operative blood loss. The tremendous progress in microwave technology has recently attracted considerable attention. Here we describe the treatment outcomes achieved at our institution for intraoperative use of the microwave tissue precoagulation in hepatic resection as part of our strategy for the treatment of HCC.

Methods: Twenty-six selected patients received elective hepatic resections using intraoperative microwave tissue precoagulation as their initial therapy for hepatocellular carcinoma in cirrhotic liver. The patients who were enrolled for our study were chosen according to the Barcelona criteria for HCC management. The safety, therapeutic effect and recurrence were prospectively evaluated and analyzed.

Results: All the procedures were completed as planned. The median duration of the operation was 118 (range, 65-250) minutes with a median resection time of 45 (range 30-80) minutes. The median blood loss for resection was 165 (range, 100-750) mL. One patient required blood transfusion. The average time taken to coagulate the anticipated liver transection plane was less than 15 min. There was no operative mortality. The median postoperative hospital stay was 6 days. The median follow-up of patients was 14 months. At last follow up, recurrent tumors were noted in three (11.5%) of the patients (local in one and remote in two of the patients).

Conclusion: Our initial results show that surgical microwave tissue precoagulation in liver resection for hepatocellular carcinoma in cirrhotic liver is safe and effective treatment. It achieves an acceptable recurrence rate. Longer follow-up is required to determine the long-term outcome of this new treatment modality.

Keywords: Hepatic resection; Microwave ablation; Microwave tissue coagulator; Liver cirrhosis; Hepatocellular carcinoma

Introduction

Hepatocellular Carcinoma (HCC) is the fifth most common cancer and the third most common cause of cancer death in Egypt [1]. Surgical Hepatic resection has been considered as the first-line treatment which is most effective and radical treatment. Because of HCC is usually associated with poor liver function owing to chronic hepatitis or liver cirrhosis, techniques that can eradicate the tumor and also preserve liver function are needed [2,3]. Moreover, hepatic resection, in the presence of cirrhosis, raises special problem of the high risk of hemorrhage. Thus, good clinical results can only be achieved by minimizing operative blood loss. The tremendous progress in microwave technology has recently attracted considerable attention in reducing bleeding from the liver parenchyma by coagulating the tissue before liver transection. Compared with RFA, this technique is much faster and creates a larger ablation zone [4-8]. Liver tissue precoagulation with microwave technology is a novel and efficient technique which allows anatomical resection to be performed safely and easily, and helps prevent intrahepatic metastasis via portal flow during the transaction with minimal morbidity and mortality for liver transection [9-12]. Here we describe the treatment outcomes achieved at our institutions for intraoperative use of the microwave tissue precoagulation in hepatic resection as part of our strategy for the treatment of HCC.

Patients and Methods

Twenty-six consecutive patients with primary diagnosis of Hepatocellular Carcinoma (HCC) on top of liver cirrhosis were recruited for the study in the department of Hepatobiliary surgery

National Hepatology and Tropical Medicine Research Institute "NHTMRI and Theodore Bilharz Research Institute (TBRI). This is a prospective study which was approved by the Ethical Committee of Theodor Bilharz Research Institute (TBRI). Written informed consent was obtained from each patient before treatment. The diagnosis was based on of reliable clinical criteria fulfilling association with viral hepatitis, or liver cirrhosis and typical imaging findings and raised HCC-related tumor markers namely, Alpha-Fetoprotein (AFP) according to the Barcelona criteria of the European Association for the Study of the Liver confirmed by histological confirmation of tumor tissue taken from biopsy samples [3].

All patients were subjected to full clinical examination, laboratory investigations for blood picture, coagulation profile, liver and kidney functions testing. The location of the HCC was evaluated with abdominal Ultrasonography (US) confirmed by Computed Tomography (CT). The requirements for inclusion in our study were presence of resectable disease without vascular invasion or extra hepatic spread, Child-Pugh

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class A and B liver cirrhosis, (INR) <1.6, platelet count >60000/mm³. Patients requiring major hepatic resection (>three segments) were excluded from this study. Any coagulopathy was corrected before the procedure. Patients were treated by applying pre-coagulation of the liver transection lines using microwave cluster antennas positioned in parallel on the line of resection by open approach.

Operative Procedure

The procedures were performed under general anesthesia. Prophylactic antibiotics were routinely administered. An open laparotomy was done via a right subcostal incision with possible upper midline extension if necessary or with a left subcostal extension in a chevron fashion for the resection of the left lobe tumor. The peritoneal cavity was thoroughly explored to exclude extrahepatic disease. Mobilization of the liver was done in all cases. Intraoperative ultrasound (Aloka, Tokyo, Japan) was used to exclude lesions not detected preoperatively, to define the location, number and size of the tumor and to guide insertion of the microwave applicator. To prevent thermal injury, surrounding organs were cooled by continuous irrigation with ice-cold saline. Microwave generator in this study was (Model HS-15M, Heiwa Electronic Ind., Ltd., Osaka, Japan). This device emits microwaves of 2.45 MHz in frequency and 12 cm in wavelength. Its maximum output is 150 watts. Microwave assisted liver resection was performed using a cluster of 13 gauge diameter antennas of 17 and 22cm length. Intraoperative ultrasound was used again, to assess that the line of resection was done. Then, Glisson's capsule was incised with monopolar diathermy and cluster antennas were inserted perpendicularly about 5 cm deeper into the liver parenchyma. Then, the antennas were progressively retracted to the liver surface after 5-10 minutes when usually the color of the liver parenchyma has been changed due to complete coagulation of resection line. The liver parenchyma is dissected by sharp blade between the lesion and the remaining liver leaving 2-3 cm safe oncological margin. For patients who have had two tumors; the largest tumor was resected as described above meanwhile; the smaller tumor was totally ablated by the same microwave technology. Resected specimens were sent for histopathological examination for depth of tissue coagulation along the tumor-negative transection margin.

Primary endpoints documented were total operative time, time for liver parenchyma transection and intraoperative blood loss blood transfusion requirements. Secondary endpoints included postoperative complications, mortality and Intensive Care Unit (ICU) and hospital stay. In all patients, biochemical liver function tests were monitored before and after resection. All values expressed as means ± SD. A paired t test was used to compare liver function tests before and after resection. P<.05 was considered significant.

Postoperative follow-up were carried out after 1 month, and then every 3 months during the first 2 years, and every 6 months thereafter. It involved laboratory investigations for liver function tests, Serum AFP, chest X-ray, U/S and contrast Computed Tomography (CT) of the abdomen. The CT was evaluated by a radiologist experienced in liver tumors. A liver biopsy was performed if recurrence was suspected. Any intra- or extra-hepatic recurrence was documented. Main outcome measures were operative mortality and morbidity and recurrence rate. The date of disease recurrence was dictated by the first imaging study showing recurrence. Local recurrence was defined as disease occurring adjacent to the surgical site, whereas remote recurrence was defined as tumor occurring at a distant site. Multifocal recurrence was defined as multiple intrahepatic tumors at distant sites.

Results

Patients with hepatocellular carcinoma recruited were 19 men and 7 women with a median age of 53 (range, 42-68) years. All patients were hepatitis C positive. Histological findings revealed that all patients had HCC on top of liver cirrhosis. Ten patients belonged to Child's B staging, while the rest were Child's stage A. The median tumor diameter was 3.8 cm (range, 2 -7cm). 24 patients had solitary tumors, and two patients had two tumors (Table 1).

All the procedures were completed as planned. We performed limited resection in five patients, subsegmentectomy in eighteen patients, and segmentectomy in three patients. The median duration of the operation was 118 (range, 65-250) minutes with a median resection time of 45 (range 30-80) minutes. The average time taken to coagulate the anticipated liver transection plane was less than 15 min. The median blood loss for resection was 165 (range, 100-750) mL. Intraoperative blood transfusion was required in only one Child's B patient. There was no postoperative mortality. The median postoperative hospital stay was 6 (range, 2-13) days. All Patients were admitted in ICU for 1-2 days. Five patients stayed in ICU ≥ 2days. All patients had a postoperative increase of liver enzymes and serum bilirubin level which normalized within 7 days (Table 2). Complications occurred in five (19%) of the patients. only one was liver resection-related in the form of bile leak needing endoscopic biliary stent. Histopathology revealed that the depth of tissue coagulation was 3-5 mm. It provided an additional tumor-negative margin at the resection border.

The median follow-up of patients was 14 (range, 4-26) months, and their treatment outcomes are summarized in Table 3. At last follow up, recurrent tumors were noted in three of the patients (11.5%). Two of those patients with recurrence have had multinodular HCC at presentation. Recurrent tumors were local in one patient and were

	Variable
Male: female ratio* n (%).	19(73%):7(27%)
Child-Pugh class*	
A	10(38.4%)
B	16(61.5%)
C	0(0%)
Tumor size*	
2-3 cm	7 (29.3%)
3-5 cm	11(42.3%)
≥5 cm	8(30.6%)
Tumor nodularity*	
Uninodular	24(92.3%)
Multinodular	2(7.6%)
Tumor localization*	
Right lobe	22 (84.6%)
Left lobe	3 (11.5%)
Bilobar	1(3.8%)
Serum AFP** (ng/ml)	461.0 ± 5279.5

*Qualitative variables are expressed as number (percentage)

** Quantitative variables as mean value ± SD for

Table 1: Demographic and Clinical Characteristics of Patients.

	Pre-Resection	1 st Postoperative Day	7 th Postoperative Day
Serum albumin** (g/dl)	3.72 ± 0.03	2.78 ± 0.13	3.02 ± 0.23
Total bilirubin** (mg/dl)	1.03 ± 0.79	2.03 ± 0.04	1.06 ± 0.39
AST(IU/L)	26.5 ± 10.1	115.8 ± 10.10	47.33 ± 1.11
ALT(IU/L)	31.2 ± 4.3	263 ± 0.81	78.34 ± 0.62

Table 2: Liver functions before and after resection.

Median blood loss, ml (range)	165 (100–750)
Median transection time, min (range)	45(30–80)
Median total operation time, min (range)	118 (65-250)
Median hospital stay, days	6 (2-13)
Patients staying in ICU for ≥2 days, n	5
Complications	
Fever	2(3.8%)
Renal dysfunction	2(7.6%)
bile leak	1(7.6%)
Intrahepatic recurrence	
Local	1
Distant	2

Table 3: Operative, postoperative and follow up data.

remote in two of the patients. All patients survived until the time of censorship.

Discussion

The major technical difficulty in liver resection for cirrhotic patients is related to a higher risk of bleeding because of the presence of portal hypertension with Porto systemic collaterals at the back of the liver, and coagulopathy as a result of compromised liver function or thrombocytopenia in patients with hypersplenism. Furthermore, maintaining adequate liver function regardless of whether the resection is anatomic or not may be of greater importance. No superiority was seen in survival and early tumor recurrence when HCC was treated by anatomic resection [13,14]. However, small, non-anatomical resection causes more bleeding. Techniques for liver resection often require hepatic inflow occlusion (Pringle's maneuver) during transection of liver parenchyma. Furthermore, clamping of hepatic pedicles increases the potential risk of liver dysfunction from ischemia-reperfusion injury particularly in patients with underlying chronic liver disease [15,16]. The use of the microwave tissue coagulator has been found to minimize blood loss. Moreover, because of the more or less bloodless intrahepatic surgical field, liver transection could be carried out at a slower and more easily [17-19].

Our study describes our initial experience of that innovative technique involving the use of intraoperative microwave tissue precoagulation in hepatic resection as part of our strategy for the treatment of HCC. It was found to offer bloodless liver resection field without the use of sutures, surgical knots, clips, glue or hepatic pedicle clamp. When this procedure is used carefully, the surgeon can perform a liver resection with minimal blood loss. Intraoperative blood transfusion was required in only one of twenty-six patients operated upon by hepatic resection in our study. Data of patients with HCC subjected to liver resection performed by the Cavitron Ultrasonic Surgical Aspirator (CUSA) technique (n=13) at last three years in our unit revealed that Intraoperative blood transfusion was required in 10(76.9 %) with CUSA technique; which is significantly higher than that in the present study in which Intraoperative blood transfusion was required in only one patient. However, the comparison may be biased by the fact that the number of patients underwent major hepatectomy was higher. There was no significant difference between techniques in mortality, morbidity, liver dysfunction or intensive therapy unit and hospital stay.

There was no postoperative mortality and the morbidity is encountered is acceptable because of the smaller surgical insult to the patient. This coincides with literature review that Child-Pugh grading, operating time, postoperative length of stay, and preoperative serum albumin level were independent predictors of morbidity and Blood loss, Child-Pugh grading, operating time and preoperative serum

albumin level were independent predictors of mortality hepatectomy cases [20]. In this small experience, bile leak was encountered in only one case. This might be because following coagulative necrosis the cut surface of the liver parenchyma is homogeneous and no individual bile duct structure or blood vessel can be identified. The technique is easy to teach, and surgeons with a good knowledge of liver anatomy can apply it to segmental resections although the technique has not yet been used for a major liver resection. It may encourage surgeons to perform more liver resections and popularize liver surgery as a "safe" therapeutic modality in the management of liver tumors. This technique represents a considerable step in making laparoscopic liver resection safer and more feasible for many liver surgeons [21,22].

From the oncological point of view, non-anatomical liver sparing resection has the advantage of saving as much of liver parenchyma as possible in liver cirrhosis patients considering that anatomical resection was not found more advantageous in terms of tumor recurrence or survival in HCC patients. Moreover, microwave tissue precoagulation in hepatic resection lines helps prevent intrahepatic metastasis via portal flow due to tissue shrinkage and dissection with permanent closure of vascular and biliary branches. The depth of tissue coagulation of 3-5 mm provides an additional tumor-negative margin at the resection border. In the current study, two of our patients with recurrence have had multinodular HCC at presentation in agreement with Izumi et al., 2001 who found that patients who had more than two hepatocellular carcinoma nodules accompanied by HCV infection, had a high incidence of recurrence of HCC in the remnant liver after curative treatment [23].

Further experience and establishment of the technique should be done before expanding its indication to major hepatectomy. The application of microwave-assisted liver resection close to hilum and hepatic veins confluence requires more experience. Dissection of those structures before applying this device remains crucial. In fact, during the last two months we performed successful liver resection in further five patients (left hepatectomy in two, bi-segmentectomy of segments V and VIII in two, left lateral segmentectomy in one patient). The follow-up data of those patients and forthcoming experience will be reported in our next report.

Conclusion

Our initial results show that surgical microwave tissue precoagulation in liver resection for hepatocellular carcinoma in cirrhotic liver is safe and effective treatment. It achieves an acceptable recurrence rate. Longer follow-up is required to determine the long-term outcome of this new treatment modality.

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