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Impact of DAAS on Resection of HCC on Cirrhotic Liver, Outcome and Prognosis

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Abstract

Hepatocellular Carcinoma (HCC) is one of the leading causes of death from cancer in the world. Direct-acting Antiviral (DAA) therapy has revolutionized the treatment of Hepatitis C Virus (HCV) infection, with very high rates of Sustained Virology Response (SVR) and an excellent safety profile. The procedures performed were: 22 cases done major RT hepatectomies (32.4%). 12 cases underwent Lt Lateral hepatectomy (17.6%) 34 cases underwent non anatomical resection (50%). Time of hepatic transection was performed is 192 min average range (135 to 250 min). The average blood loss was 825 ml (range 50-1600 ml).

The treatment approach for Hepatocellular Carcinoma (HCC) depends on the stage and extent of disease, the severity of the underlying liver disease, and the overall performance status of the patient.

Keywords: Hepatocellular Carcinoma (HCC) • Direct-acting Antiviral (DAA) • Hepatitis C Virus (HCV) • Sustained Virology Response (SVR) • Hepatic fibrosis

Introduction

Hepatocellular Carcinoma (HCC) is one of the most common malignancies worldwide [1]. It is frequently found in association with liver cirrhosis. Viral hepatitis B and C are particularly major risk factors for HCC with incidence varies according to geographic area [2].

Hepatocellular Carcinoma (HCC) is one of the leading causes of death from cancer in the world. Direct-Acting Antiviral (DAA) therapy has revolutionized the treatment of Hepatitis C Virus (HCV) infection, with very high rates of Sustained Virology Response (SVR) and an excellent safety profile [3]. The presence of advanced hepatic fibrosis prior to treatment is recognized as a significant risk factor for HCC development after achieving SVR; however, not all patients with advanced hepatic fibrosis develop HCC [4]. Recently, new antiviral therapies with interferon-free medications have been introduced, such as the Direct Acting Antivirals (DAA) treatments which have shown a high effectiveness with SVR rates above 90%. Direct Acting Antivirals (DAAs) are molecules that target specific nonstructural proteins of the virus, resulting in disruption of viral replication and thereby infection [5].

Aim of the work: is to analyze hepatic resection in cirrhotic patients previously taking DAAS either surgically or laparoscopically treated with CUSA (Cavetron Ultrasonic Surgical Aspirator) and Habib™ 4 × bipolar, handheld, disposable RF device, Harmonic scalpel device.

Literature Review

Patients and methods: 68 consecutive patients with previously taken DAAS against hepatitis C with discovered small focal lesion during routine HCC meeting twice weekly national liver institute, 23 cases in left lobe 45 cases in right lobe, 16 cases females and 52 cases males, were randomized to one of different dissection strategies. From August 2016 and September 2018. All patients were put in preoperative data as: 1) Demographic and clinical data, 2) Age and sex [6].

Co-morbidity: (DM, hypertension and other co-morbid risk factors).

Clinical presentation: 1) Asymptomatic (discovered during routine follow up). 2) Symptomatic (ex. abdominal pain, weight loss).

Pre-operative assessment: Abdominal US and α-FP and PCR for HCV.

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Inclusion criteria: Patients with liver cirrhosis of child grade A. Resectable hepatocellular carcinoma. Patients with good performance status.

Exclusion criteria: Child B or C. Portal hypertension. History of HCC (after surgical resection or loco regional ablation). Patients with co-infection with HBV and HIV. Bad performance status. Large focal lesion with portal vein thrombosis [7,8].

Preoperative outcome: Hepatic resection for HCC in the presence of cirrhosis is a major operation associated with a significant risk of morbidity and mortality. Wedge hepatic resection is the first-line treatment for cirrhotic patients with small HCC and preserved liver function.

Intraoperative procedures: The following data were collected type and extension of resection. Amount of blood loss and blood transfusion. Operative time associated procedures. Operative morbidity and mortality. Use of intraoperative ultrasonography. Non anatomical resection and anatomical resection.

Postoperatively: All patients were admitted to ICU for 24-72 h according to homodynamic stability including; vital signs, urine output, drain's output and blood or fresh frozen plasma transfusion.

Postoperative laboratory data: LFTs, PT and PC% and CBC on postoperative day 1, 3, 5 and at time of discharge.

Abdominal ultrasound with Doppler study for intraperitoneal collection and portal vein thrombosis on postoperative day 1, 3, and at time of discharge. Hospital stay was recorded from the day of operation till the day of discharge. Outcome after short term follow up (6 months). Mortality recurrence liver decompensating [10-12].

Results

68 consecutive patients were analyzed prospectively 56 cases male (82.3% women), 12 female cases (17.7% men). Ages ranged from 32 to 84 years. 23 cases (36.5%) underwent laparoscopic technique by Harmonic scalpel, 12 cases (17.8%) converted to open surgical resection.

The procedures performed were: 22 cases done major Rt hepatectomies (32.4%). 12 cases underwent Lt lateral hepatectomy (17.6%) 34 cases underwent non anatomical resection (50%). Time of hepatic transection was performed is 192 min average range (135 to 250 min). The average blood loss was 825 ml (range 50–1600 ml). The mean postoperative stays were nine days range (7-11 days) for all the patients. Forty two cases had no ascites (61.8%), 16 cases (23.5%) had minimal ascites, 8 cases (11.7%) had moderate ascites while marked ascites was occurred in two cases (3.5%). Hepatic encephalopathy was detected in one case (1.8%) while no cases had hematemesis. Histopathology (post operatively specimens) was grade II (83,9%) (moderately differentiated) and 11 specimens (16.1%) was grade III (Poorly differentiated) [13].

Lymph vascular Invasion present at 10 cases (15%) while only one case (1.5%) with perineural invasion.

Resected surgical margin is more than 1 cm in 48 specimens (70.1%) while less than 1 cm in 8 specimens (11.8%) twelve of them (17.6%) surgical margin is involved by tumor.

AS regarding pathological staging: 34 patients (50%) was at T_1 and 22 patients (32.9%) was at T_2 while only 12 cases (17.5%) at T_3.

Recurrence: The overall recurrence number was 12 cases (17.5%). The recurrent group had shown 4 cases (6%) unifocal lesion and one case (1.5%) multifocal lesions and 3 case (4.5%) had shown tumor size (≤ 5 cm), 2 cases (7%) had shown tumor size (>5 cm). There was no significant between size, number of the tumor and recurrence [14].

Site of recurrence was identified as follows: Fore cases (6%) had developed marginal recurrence, 1 cases (1.5%) had developed adjacent lobe recurrence and 7 cases (10.5%) had developed extrahepatic recurrence (1 cases bone metastasis and the other case was lung metastasis).

Mortality and morbidity: Only 3 cases died. The cause of death in first patient was due to due to intra-operative bleeding and multi organ failure. The cause of death in the other two patients (3%) was liver cell failure [15].

Discussion

The treatment approach for Hepatocellular Carcinoma (HCC) depends on the stage and extent of disease, the severity of the underlying liver disease, and the overall performance status of the patient.

Treatment consists of 4 main strategies: Surgery (e.g. resection and liver transplant), locoregional procedures (e.g. ablation and transarterial embolization), systemic therapies, and best supportive care [16]. The key question is to discover the mechanism responsible for the higher rate of HCC recurrence in patients treated with DAAs. The rapid onset of HCC recurrence upon DAA treatment suggests a sudden increase in cell proliferation without the counterbalance of the immune system. However, it is unlikely that DAAs have a direct effect on tumor cell growth, based on the evidence that protease inhibitors reduce the incidence of cancer in HIV patients [17]. The presence of advanced hepatic fibrosis prior to treatment is recognized as a significant risk factor for HCC development after achieving SVR, however not all patients with advanced hepatic fibrosis develop HCC. Natural killer group 2 (Member D) associated with cancer immunity changes during DAA therapy [18,19]. It is possible that small HCCs that are not visible by imaging techniques, after treatment with DAAs will have aggressive tumor growth [20].

Conclusion

The Egyptian ministry of health and the national committee for the control of viral hepatitis have treated approximately one million Egyptian patients since 2014, with cure rates over 90% using various DAA combinations. One of the major challenges following the introduction of DAAs was the failure of a significant number of patients (approximately 40%) to return for evaluation of SVR. It was observed that, the critical interval between the end of HCV treatment with DAA regimen and appearance of HCC lesions was (5.60 ± 2.54) month with range from (0.5-12) months, Two lesions of them appeared during treatment. The tumor was more than 5 cm which may support that DAA boosting the growth of invisible HCC.

Hepatocellular Carcinoma (HCC) is a major cause of cancer related death worldwide. In selected patients, surgical treatment in the form of either resection or transplantation offers a curative option.

There was an improvement in postoperative complications in patients treated by Habib trademark 4 sealers (bipolar device) for reducing ischemia–reperfusion damage due to absence the Pringle maneuver and for reducing the risk of morbidity. However ultrasonic dissector (CUSA) easy, versatile take long respectable time, excess blood loss and blood transfusion. Other as harmonic scalpel, good haemostatic device, take short operative time not need Pringle maneuver less blood loss and transfusion.

Recommendation

Caution should be used when considering the HCC with IFN-free therapy because many additional factors are associated with tumour occurrence or recurrence. This issue should be confirmed to avoid panic because millions of hepatitis C patient's were/are/will is using DAAs in the past, present, and future.

HCV-infected patients with underlying cirrhosis who treated with DAAs should still be closely monitored and followed during antiviral therapy and screened for HCC even after treatment and SVR.

Finally, because all enrolled patients showed chronic liver disease status, a well-designed, well-controlled, randomized study of a large population is required.

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