

*Case reports*

**Treatment of Concomitant Gastric Varices in Patients with Hepatocellular  
Carcinoma at a Single Japanese Institute**

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*Running title:* Treatment for hepatoma with gastric varices

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**ABSTRACT**

**Background/Aims:** Hepatocellular carcinoma (HCC) patients often have esophago-gastric varices due to portal hypertension by chronic hepatitis or cirrhosis. Surgical treatment for gastric varices is necessary when the patient undergoes hepatic resection for HCC, simultaneously. **Methodology:** We examined the clinical demographics, surgical records and outcome in 7 patients undergoing both hepatectomy and Hassab's operation (=decongestion of upper gastric veins and splenectomy) between 1994 and 2007. **Results:** All patients had HCC, including chronic injured liver diseases. Preoperative liver functions were well preserved in all patients. Right hepatectomy was performed in two patients and limited resections in 5. Three patients had postoperative complications and the in-hospital death by hepatic failure was observed in one. Four patients had tumor recurrence within one year and 3 were dead, while, two patients had long-term survival with or without recurrence of HCC. Following Hassab's operation, gastric varices dramatically disappeared. Portal hypertension and hypersplenism were significantly improved. **Conclusions:** Simultaneous operation with Hassab's procedure and hepatectomy is useful and can be safely performed in HCC patients with gastric varices.

**KEYWORDS:** hepatocellular carcinoma, hepatectomy, gastric varix, Hassab's operation

**ABBREVIATIONS:** hepatocellular carcinoma (HCC), indocyanine green retention rate at 15 minutes (ICGR15)

## INTRODUCTION

Hepatocellular carcinoma (HCC) patients often have esophago-gastric varices due to portal hypertension caused by injured liver such as chronic viral hepatitis and cirrhosis (1, 2). Esophageal varices are usually treated using endoscopic procedures such as sclerotherapy or ligation technique (3). When surgical treatment is scheduled, large varices or veins with red color should be treated with endoscopy prior to operation to the reduce risk of postoperative hemorrhage (4). However, in case of gastric varices, endoscopic treatment may be difficult and surgical removal of varicose veins in the upper stomach is more effective than other modalities (5). Therefore, simultaneous treatments such as a Hassab's operation (=decongestion of upper gastric marginal veins and splenectomy) with treatments for HCC should be necessary (6, 7). In the present report, we examined the clinical demographics, surgical records and outcome in 7 HCC patients with gastric varices who underwent simultaneous hepatectomy concomitant with Hassab's operation in the Division of Surgical Oncology, Department of Translational Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences (NUGSBS) between 1994 and 2007.

## CASES

Between 1994 and 2007, Hassab's operation was performed in 10 patients with gastric varices, and 7 of 10 patients had HCC simultaneously. Patients included 3 men and 4 women with ages ranging from 54-77 years (**Table 1**). All patients had HCC with

background liver disease; one patient had chronic viral hepatitis, one had primary biliary cirrhosis and 5 had cirrhosis by viral hepatitis. Child-Pugh classification A was present in 5 patients and B in two. Only one patient had a history of hematemesis and a routine gastroscopy found gastric varices in other patients. Tumor-node-metastasis stage I was found in one patient, II in one, III in 4, and IVA in one (8). **Table 2** shows the operative procedures and patient outcomes. All patients underwent decongestion of the upper gastric marginal veins and splenectomy for gastric varices prior to hepatic resections. Right hepatectomy was undertaken in two patients and limited resections were performed in 5 patients for HCC. Blood loss ranged between 516 and 2960 mL (mean;  $1290 \pm 947$  mL) and 3 patients needed red cell transfusion. Three patients had postoperative complications and in-hospital death from hepatic failure occurred in one patient who underwent limited resection. Four patients had a recurrence of HCC and 3 patients died from tumors. Two patients had a long-term survival and one patient had no tumor recurrence. Findings of gastric varices are shown in **Table 3**. Six patients showed white varix and two patients showed red color sign. Six patients had esophago-gastric varix and all patients had large varices. Follow-up gastroscopy at one month after operation could be performed in 6 patients and varices completely disappeared in 5 patients and one showed a mild esophageal varix. **Figure 1** shows the changes of laboratory data before and after operation. Portal pressure was significantly decreased and indocyanine green retention rate at 15 minutes (ICGR15) was significantly increased. White blood cell

tended to be increased but the change was not significant. Platelet count was significantly increased after operation.

## **DISCUSSION**

In the long history of treatment for gastric varices due to portal hypertension in cirrhotic patients, the usefulness of Hassab's operation has been well recognized, as reported previously (5-7). The operative procedure is safe and gastric varices outcome is positive. Cirrhotic patients often have simultaneous HCC, which must be treated. Hepatic resection is still the most useful option for radical treatment of HCC compared to ablation therapy or chemoembolization (9). Therefore, when it is necessary to treat gastric varices under laparotomy, simultaneous hepatic resection for HCC would be reasonable. Although there is the risk of liver failure in cases of simultaneous operation in cirrhotic patients, previous reports showed the safety and usefulness for this procedure (6, 7).

In the present report, liver function in all patients was well preserved, even in cirrhotic livers. Hepatectomy indication was based on Makuuchi's criteria (10) and, therefore, preoperative conditions of total bilirubin level less than 2.0 mg/dl, ICGR15 less than 40% and no intra-abdominal ascites were basically necessary in the present procedure. If liver function worsens, other modalities for HCC treatment can be selected. In the present series, the preoperative platelet count was lower than 100,000/mm<sup>3</sup> as shown in the figure due to hypersplenism caused by portal hypertension. This parameter is important before hepatectomy to care for intra- or post-operative bleeding tendency

and hepatic failure (11). We preferably apply splenectomy prior to hepatectomy in patients with a low level of platelet count by hypersplenism. Splenectomy in Hassab's operation is also variable to prevent the above complications. Hematemesis as an onset of finding gastric varices rarely occurred and routine gastroscopy for liver diseases was useful as in previous reports (12).

Major hepatectomy could be performed in 2 patients because of strong liver function. We propose that the indication of hepatectomy is not limited by the presence of gastric varix. Hassab's operation was completed in all patients without massive bleeding and, therefore, this procedure can be safely performed regardless of treatment for veins with portal hypertension. Four patients who underwent partial hepatectomy did not need intraoperative blood transfusion. On the other hand, two of three patients requiring red cell transfusion underwent major hepatectomy; however, these transfusion were limited to within 800 mL. In summary, simultaneous Hassab's operation and hepatectomy was safely performed in all patients in the present study. Postoperative outcomes were satisfactory, except for one patient who died due to uncontrolled ascites and subsequent liver failure. This patient had liver function of Child-Pugh B, ICGR15 38%. The uncontrolled ascites can be predicted by the serum hyaluronic acid (HA) level by our study at this stage (13); however, this parameter was not examined at the time of treatment for this patient. If the serum HA level was at a high level, ablation or chemoembolization might have been selected. Long-term prognosis was not well satisfied because of early recurrence in HCC patients with TNM stage III and IVA in our

series. We are not sure whether splenectomy influenced the immune-response to tumor recurrence in our series; however, it is speculated that splenectomy was associated with immune-deficiency for cancer progression (14).

Our recent result showed that massive gastric varices were successfully treated except in one case. Hassab's operation was dramatically effective. Only one patient had a mild esophageal varix, which was easily controlled followed with endoscopic ligation. This effect has been maintained for a long period in all patients, as in previous reports (5, 6). Following splenectomy, hypersplenism, portal flow or pressure may improve as reported previously (15). In the present study, portal pressure dramatically decreased immediately after splenectomy during operation. Lower white cell count or platelet count were significantly improved after splenectomy as well. Increase of platelet count is an advantage for following hepatectomy to reduce risk of hepatic failure. However, the result of ICGR15 became worse; this change might be influenced by hepatectomy.

In conclusion, we examined 7 patients with HCC patients with gastric varices who were treated with simultaneous Hassab's operation and hepatic resection. Six patients safely underwent these operations but one patient died of massive ascites and postoperative hepatic failure. Gastric varices, portal hypertension and hypersplenism were well controlled by Hassab's operation; however, tumor recurrence was still aggressive after operation. Two patients had long-term survival. Simultaneous operation of Hassab's procedure and hepatectomy can be usefully and safely performed in patients with HCC patients with gastric varices.

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**FIGURE LEGEND**

**FIGURE 1** Changes of laboratory data before and after operation. Preop.; preoperation.

Postop.; postoperation.

**TABLE 1** Clinical Demographics of Patients

<b>Case</b>	<b>Age</b>	<b>Gender</b>	<b>Background liver</b>	<b>Viral status</b>	<b>Child-Pugh classification</b>	<b>History of hematemesis</b>	<b>Japanese TNM stage of HCC*</b>
1	63	Female	Cirrhosis	hepatitis C	A	No	I
2	77	Female	Cirrhosis	hepatitis C	B	No	III
3	67	Male	Chronic hepatitis	hepatitis B	A	No	III
4	66	Female	Cirrhosis	hepatitis C	A	No	III
5	73	Female	PBC	none	A	Yes	II
6	54	Male	Cirrhosis	hepatitis B	A	No	IVA
7	57	Male	Cirrhosis	hepatitis C	B	No	III

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**TABLE 2** Operative Procedures and Outcomes

	<b>Hepatectomy</b>	<b>Blood loss (ml)</b>	<b>Postoperative complications</b>	<b>Outcomes</b>
1	Limited resection (S6)*	600	Mild ascites	Survival with tumor recurrence (146) <sup>#</sup>
2	Limited resection (S23 and S48)	516	Uncontrolled ascites Hepatic failure	Dead by liver failure (2)
3	Right hepatectomy	2686	None	Dead by tumor (13)
4	Limited resection (S8)	885	None	Dead by tumor (5)
5	Limited resection (S5)	1337	None	Survival without tumor recurrence (98)
6	Right hepatectomy	2960	Mild ascites	Dead by tumor (15)
7	Limited resection (S8)	1550	None	Survival with tumor recurrence (9)

\*: parenthesis shows segment of the liver.

#: months after operation

**TABLE 3** Findings of Gastric Varices (16)

	<b>Color</b>	<b>Red color sign</b>	<b>Location of esophageal varices</b>	<b>Form</b>	<b>Changes after Hassab's operation at 1 month after operation</b>
1	Blue	negative	Lm*	3	Disappeared
2	Blue	negative	Lm	2	Disappeared
3	Blue	negative	Lm	2	Disappeared
4	White	negative	Li <sup>#</sup>	2	Disappeared
5	Blue	negative	Lm	2	Disappeared
6	Blue	positive	-	3	Disappeared
7	Blue	positive	Li	2	Mild esophageal varix

\*: Middle esophagus

#: Inferior esophagus

FIGURE 1

