AUDIT ARTICLE

Short-term outcomes after hepatic resection — perspective from a developing country

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Abstract

Objective: To review the early outcomes of hepatic resection at our hospital.

Methods: This study was conducted at the Aga Khan University Hospital, Karachi, from January 2008 to December 2015, and comprised patients who underwent hepatic resection. We analysed the pathology, magnitude of hepatic resection and short-term outcomes in the patients. Mean and standard deviations were used to describe categorical data whereas frequencies and proportions to describe quantitative data. Univariate analysis was done to look at the factors associated with morbidity, mortality and blood loss during surgery. SPSS 19 was used for data analysis.

Results: Of the 75 participants, 43(57.3%) were males and 32(42.7%) were females. The overall mean age was 52±14 years. Besides, 37(49.3%) patients underwent hepatic resection for underlying hepatocellular carcinoma, with 30(81%) of them being cirrhotic. Major hepatectomy (>3 segments) was performed in 30(40%) patients. Postoperative complications were observed in 30(40%) patients including postoperative liver failure in 3(4%) patients. The presence of one or more co-morbid conditions had a statistically significant association with postoperative morbidity (p=0.018). Mortality rate at 30days and 90days were 3(4%) and 5(6.7%), respectively.

Discussion: Morbidity, mortality and blood loss were comparatively higher in cirrhotic patients.

Keywords: Hepatic resection, Outcome, Morbidity, Mortality, Developing country. (JPMA 67: 1242; 2017)

Introduction

Outcomes after hepatic resection have significantly improved over the last few decades with an improvement in procedure-related mortality from >20% to <5% in most of the experienced centres.[1-4] A number of factors have contributed to this improvement in surgical outcomes, including but not limited to improvised patient selection, innovations in surgical technique, novel devices for bloodless surgery and parenchymal transaction, preoperative portal vein embolisation for contralateral lobe hypertrophy, advanced anaesthetic management, and enhanced postoperative care.[2,5,6] Despite improvements in patient survival, hepatic resection is still associated with significantly high morbidity rates.[7-9] Recent studies from the United States[10] have demonstrated that a high hospital mortality rate of around 10% is still being observed in low-volume hospitals, whereas the hospital mortality rate in high-volume centres is less than 5%.

Despite the establishment of hepatic resection as a therapeutic modality in the Western as well as Far Eastern regions of the world, the development of liver surgery has been suboptimal in most of the developing world including South Asia. Most of the hospitals in the developing countries remain relatively low volume centres for hepatic resection and there are only a limited number of published reports from developing countries on this subject.[11-13] Therefore, we decided to review the early outcomes of hepatic resection at our hospital, which is a low volume centre in a developing country with no transplant facilities. The current study was planned to determine the spectrum of presentation, magnitude of surgical resection and short-term outcomes, including blood loss, morbidity and mortality in patients undergoing hepatic resection.

Patients and Methods

This study was conducted at the Aga Khan University Hospital (AKUH), Karachi, from January 2008 to December 2015, and comprised patients who underwent hepatic resection. The AKUH is a tertiary care hospital with no transplant facilities. Data was retrieved through International Classification of Diseases (ICD)-9 coding system. The patients underwent elective hepatic resection for various benign, malignant and metastatic diseases during the study period. Hepatic resections performed for trauma were excluded. The variables studied included demographics, indication for surgery, type of hepatic resections, duration of surgery, estimated blood loss, transfusion requirements, and any concomitant procedure along with hepatic resection. Postoperative variables included surgical complications, including wound infections, bile leak, intra-abdominal

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collection, and bleeding; systemic complications like liver decompensation, pulmonary infections, and 30-day as well as 90-day mortality. Length of the hospital stay and need for intensive care unit (ICU) stay were also reviewed.

All patients had a triphasic computed tomography (CT) scan or magnetic resonance imaging (MRI) to evaluate the pathology of liver and assess the resectability of tumour. Assessment of functional reserves of liver was based on Child-Pugh class, liver biochemistry and coagulation profile. Preoperative image guided biopsy was done in few patients with diagnostic uncertainty. Patients undergoing hepatectomy received general anaesthesia with invasive monitoring and selective epidural analgesia. All patients underwent an open procedure with selective use of diagnostic laparoscopy in some cases. Intra-operative ultrasound was routinely performed to define the relationship between the tumour and major intrahepatic vessels, any tumour invasion of portal vein or hepatic veins, and to detect any lesions in the contralateral lobe. Parenchymal transection was performed using harmonic scalpel, diathermy or cavitron ultrasonic surgical aspirator (CUSA). Pringle manoeuvre was used only when significant bleeding was encountered. Instead, more attention was paid to lowering of the central venous pressure to below 5 cm of water (H2O) to reduce venous bleeding during transaction. Meticulous attention was paid to the preservation of function in the remnant liver by avoiding prolonged rotation, hypoxic injury, or venous congestion due to overloading of circulation. After transaction, bleeding and any leakage site was carefully repaired with fine sutures. A routine cholangiogram was performed in all patients undergoing left hepatectomy as well as any patient with suspected aberrant anatomy. Fibrin glue was used to seal the raw liver surface at the end of the procedure. Drains were not routinely used.

All patients with major hepatic resection were monitored in the special care unit in the immediate postoperative period. Pain control was provided by continuous epidural analgesia or patient controlled intravenous analgesia. First-line antibiotics were given for about 3 days in the postoperative period. Oral feeding was started as soon as the bowel sounds returned and the early mobilisation was encouraged. Salt free albumin and diuretic agent were selectively used in cirrhotic patients who developed ascites postoperatively. Patients were discharged once clinically stable and regularly followed up in outpatient clinics.

Mean and standard deviations were used to describe categorical data whereas frequencies and proportions to describe quantitative data. Univariate analysis was done to look at the factors associated with morbidity, mortality and blood loss during surgery. Statistical significance was defined as $p<0.05$. SPSS 19 was used for data analysis.

Results

Of the 75 participants, 43(57.3%) were males and 32(42.7%) were females. The overall mean age was 52±14 years. Besides, 47(63%) patients had American Society of Anaesthesiologist (ASA) score of II, but 40(53%) patients had at least one or more associated comorbid conditions. All the patients had a Child-Pugh score of 5 or 6, with 2(2.7%) patients with Hilar Cholangiocarcinoma having

Table-1: Baseline Parameters of Study Population.

Demographics	
Male/Female (n)	43/32
Age (years, mean + SD)	52 ± 14
Co-morbid Conditions	
Hypertension (n, %)	31 (41%)
Diabetes Mellitus (n, %)	23 (31%)
Chronic Obstructive Pulmonary Disease (n, %)	05 (7%)
Basic Laboratory Parameters:	
Haemoglobin (gm/dL, mean + SD)	11.9 ± 1.9
Platelet count (X10E9/L, mean + SD)	257 ± 131
Serum Bilirubin (mg/dL, mean + SD)	0.64 ± 0.6
Serum Albumin (g/dL, mean + SD)	3.5 ± 0.8
Prothrombin time (seconds, mean + SD)	10.67 ± 2.6
ASA Level I/II/III	6/47/22
Cirrhosis	30 (40%)

ASA: American Society of Anaesthesiology.
SD: Standard Deviation.

Table-2: Indications for Surgery and Pathology.

Primary Malignant Pathology (n, %)	46 (61.3%)
Hepatocellular Carcinoma	37 (49.3%)
Carcinoma of Gallbladder	6 (8%)
Hilar Cholangiocarcinoma	2 (2.7%)
Embryonal Sarcoma	1 (1.3%)
Metastatic Malignancy (n, %)	18 (24%)
Metastatic Colorectal Malignancy	10 (13.3%)
Metastatic Neuroendocrine tumour	2 (2.7%)
Metastatic renal cell carcinoma	2 (2.7%)
Adenocarcinoma of stomach (en bloc resection)	1 (1.3%)
Metastatic adrenocortical carcinoma	1 (1.3%)
Metastatic endometrial carcinoma	1 (1.3%)
Metastatic Breast carcinoma	1 (1.3%)
Benign Diseases (n, %)	11 (14.6%)
Focal nodular hyperplasia	2 (2.7%)
Giant Hemangioma	2 (2.7%)
Xanthogranulomatouscholecystitis	2 (2.7%)
Cystadenoma	1 (1.3%)
Liver cell adenoma	1 (1.3%)
Primary Paraganglioma of Liver	1 (1.3%)
Hepatolithiasis	1 (1.3%)
Nonspecific inflammation	1 (1.3%)

Table-3: Extent of Hepatic Resection.

Major Hepatic Resections (> 3 segments)	30 (40%)
Right formal hepatectomy	19 (25.3%)
Right hepatectomy with caudate lobectomy	2 (2.7%)
Right extended hepatectomy	1 (1.3%)
Left formal hepatectomy	4 (5.3%)
Left extended hepatectomy	2 (2.7%)
Central hepatectomy	2 (2.7%)
Minor Hepatic Resections (< 2 segments)	45 (60%)
Radical cholecystectomy and segment IVB and V resection	7 (9.3%)
Left lateral segmentectomy	5 (6.7%)
Segmentectomy / subsegmentectomy	32 (42.6%)
Caudate lobectomy	1 (1.3%)
Additional Procedures	15 (20%)
Left hepaticojejunostomy	2 (2.7%)
RFA / wedge resection of another lesion	4 (5.3%)
Synchronous right hemicolectomy	5 (6.6%)
Sigmoid colectomy	1 (1.3%)
En-bloc total gasterectomy	1 (1.3%)
Right adrenalectomy	1 (1.3%)
Incisional hernia Repair	1 (1.3%)

RFA: Radiofrequency ablation.

high bilirubin level (Table-1).

Moreover, 37(49.3%) underwent hepatic resection for underlying hepatocellular carcinoma (HCC) and 30(81%) of these patients were cirrhotic. All the patients were tested for hepatitis serology and 21(28%) were positive for hepatitis C while 7(9%) had chronic hepatitis B infection. Also, 18(24%) patients underwent hepatic resection for metastatic malignancy and the most common indication was colorectal cancer. A small proportion of patients underwent hepatic resection for symptomatic benign conditions or when the underlying diagnosis was not clear (Table-2). Major hepatectomy (>3 segments) was performed in 30(40%) patients; of them16(53%)had hepatocellular carcinoma with underlying cirrhosis (Table-3).

Furthermore, 63(84%) had a solitary lesion and the mean size of the lesion was 5.8cm. The mean duration of surgery was 300±138 minutes with a mean estimated blood loss (EBL) of 665ml. In a subgroup analysis, estimated blood loss was significantly higher in patients with cirrhosis ($p<0.007$) and patients who underwent hepatic resection for primary hepatic malignancies ($p<0.009$). Estimated mean blood loss was higher in patients who underwent a major hepatectomy but the difference was not statistically significant; on the other hand, the number of pack cells transfused was significantly higher in patients with major hepatectomy ($p=0.003$). Only 3(4%) patients required postoperative mechanical ventilation and were shifted to the intensive care unit, while others were routinely managed in the special care unit with subsequent care in the surgical ward.

Postoperative complications were observed in a total of 30(40%) patients and they were graded according to the Clavien-Dindo classification. Surgical complications were

Table-4: Short term Outcomes of Hepatic Resection.

Perioperative Variables	Overall	Major Resection	Minor Resection	p-value
ASA class ≥ 2 (n, %)	22 (29%)	9 (12%)	13 (17%)	1.000
Cirrhotic Liver (n, %)	30 (40%)	9 (12%)	21 (28%)	0.229
Number of lesions				0.341
◆ Single lesion	63 (84%)	27	36	
◆ More than one lesion	12 (16%)	03	09	
Mean size of lesion (cm ± SD)	5.8±3.9	7.3±5.8	4.8±3.2	0.022
Operating time (minutes, mean ± SD)	300±138	346	269	0.017
Estimated blood loss (ml, mean ± SD)	665±580	680	655	0.856
No of packed red cell transfused (mean+SD)	2 ± 1.67	2	1	0.010
Need for ICU stay (n, %)	3 (4%)	2	1	0.602
Margin of Resection on Pathology				1.00
◆ R_0	72 (96%)	29	43	
◆ R_1	02 (2.6%)	01	01	
◆ R_2	01 (1.3%)	00	01	
Overall Morbidity (n,%)	30 (40%)	14	16	0.349
Clavien-Dindo classification (I/II/III/IV/V)	9/4/9/5/3	3/2/6/1/2	6/2/3/4/1	0.405
30-day Mortality	3 (4%)	2	1	0.560
90-day Mortality	5 (6.7%)	3	2	0.383

ASA: American Society of Anaesthesiology
SD: Standard Deviation
ICU: Intensive care unit.

Table-5: Univariate analysis of factors for morbidity and 90-day mortality.

Variables		Morbidity	p-valve	90-day Mortality	p-value
Age	≤ 60	19	0.922	2	0.278
	>60	11		3	
Gender	Male	17	0.924	2	0.417
	Female	13		3	
Comorbids	21	0.018	2	0.536	
No comorbids	9		3		
ASA level	≤ II	18	0.098	2	0.119
	>II	12		3	
Tumour	Malignant	25	0.901	5	0.289
	Benign	5		0	
Pathology	HCC	17	0.3	3	0.621
	Other tumours	13		2	
Major Hepatic resection	14	0.336	3	0.345	
Minor hepatic resection	16		2		
Duration of surgery	< 300mins	11	0.391	2	0.901
	< 300mins	19		3	
EBL	≤ 500ml	16	0.45	3	0.578
	>500ml	14		2	

ASA: American Society of Anaesthesiology
HCC: Hepatocellular carcinoma
EBL: Estimated blood loss.

noticed in 15(20%) of the patients including surgical site infection in 12(16%), bile leak in 4(5.3%), intra-abdominal collection in 4(5.3%) and postoperative haemorrhage in 1(1.3%) patient. Isolated systemic complications were observed in 5(6.7%) patients, while another 6(8%) patients had combined surgical and systemic complications. Moreover, 3(4%) patients had isolated liver decompensation with progressive worsening of liver function tests and 5(6.7%) had ascites requiring diuretics. Besides, 7(9.3%) patients had pulmonary complications including pneumonia or pleural effusion, while 1(1.3%) had Takotsubo's cardiomyopathy.

Moreover, 72(96%) patients underwent an R0 resection based on pathology report, while 2(2.6%) had an R1 resection and both of them had underlying HCC. Overall, 3(4%) patients expired within 30days of hepatic resection and all of them had underlying cirrhosis and developed progressive liver decompensation in the postoperative period that did not respond to all the supportive treatment. Also, 2(2.6%) more patients died in 3 months making the 90-day mortality at 5(6.7%). One patient with primary hepatic embryonal sarcoma had an R2 resection due to extent of the disease and developed postoperative haemorrhage and liver failure resulting in mortality. The second patient had metastatic adrenocortical tumour and presented later with dehydration and acute renal failure resulting in death (Table-4).

A univariate analysis was done to identify the factors associated with postoperative morbidity and 90-day mortality. The presence of one or more co-morbid condition had a statistically significant association with postoperative morbidity (p=0.018). On the other hand, age more than 50 years, gender, nature of tumour, extent of surgical resection or blood loss had no significant association with short-term postoperative outcomes. Morbidity rate in patients with and without underlying cirrhosis was 50% and 33%, respectively, but the difference was not statistically significant (p=0.149).

Mean length of stay in hospital was 9.5±3 days and the mean follow-up duration was 8±11 months. Recurrence of the disease was observed in 10(13.3%) patients at one year of follow-up including 8(10.7%) patients with HCC and 2 (2.7%) patients who underwent hepatic resection for metastatic disease. For patients with HCC, recurrences were managed by transarterial chemoembolisation in 3(4%) patients, radiofrequency ablation of tumours in 2(2.7%) patients and medical therapy in the remaining patients. Multimodal therapy with chemotherapy and radiotherapy was given to the patients for colonic and adrenocortical carcinoma recurrence (Table-5).

Discussion

Hepatic resection has progressed from a high-risk surgery to an established therapeutic modality with indications ranging from primary hepatobiliary malignancy to metastatic diseases.[8,14] Progressive improvement in

mortality rates over the years has evolved this procedure into a safe therapeutic option for carefully selected patients.[9] However, in the developing world with limited resources and scarcity of technology for proper preoperative workup and energy devices for bloodless surgery, hepatic resection is not still performed routinely in many centres since it is considered a difficult procedure associated with major blood loss and serious postoperative complications.[11]

Formal hepatic resections at our centre started in 2008 by a single hepatobiliary surgeon. A number of limitations in our work environment have resulted in slow development of this specialty at our hospital over the years. Some of the contributing factors include the lack of proper referral system for the patients, the absence of facilities for sophisticated preoperative workup in high-risk patients, lack of modern instruments and infrastructure, and affordability of such procedures since the patients need to pay out of their pockets for medical treatment. Slow growth of such a demanding procedure over the years also results in a long learning curve for the associated support staff. Another important limiting factor is the absence of liver transplant facilities at our centre, which restricts the extent of liver resection in relatively high-risk cirrhotic patients. Despite such overwhelming constraints, we have managed to perform hepatic resections in our low volume centre with early outcomes being comparable to the specialised centres.

We had an overall morbidity rate of 40%; although this figure seems relatively high, it is comparable with that of large series published previously.[9,15] The main causes of morbidity in our study included wound infections (16%), bile leak (5.3%), intra-abdominal collections (5.3%), pulmonary complications (9.3%) and ascites (6.7%).These morbidities prolonged the postoperative recovery period, but were successfully managed conservatively. Our patient population was characterised by high population of patients with HCC (49.3%) and hence with cirrhosis (40%). Hepatic resection in cirrhotic patients is more challenging than resections in normal livers with increased risk of bleeding, septic complications and liver failure.[16,17] Several authors have emphasised the importance of strict selection in terms of liver function reserves in ensuring favourable perioperative outcomes in patients with chronic liver disease.[18] Indocyaninegreen (ICG) clearance[19] and CT volumetry[20] are commonly used in the developed countries to assess functional liver reserves; but our selection was based on Child-Pugh score due to non-availability of such sophisticated facilities.

Our 30-day mortality rate was 4% and mortality at one year was 13.3%, which is comparable to the Western as well as Far Eastern figures of 5.8% and 8.4%, respectively.[6,10] Several studies have compared morbidity and mortality rates among high volume and low volume centres which suggests mortality rates are significantly lower (1.5% - 6.2%) in high volume centres compared with low volume centres (3.7% - 24.4%) due to greater experience and high level of care provided.[21,22] Despite being a low volume centre our 30-day mortality rate is comparable and so low volume centres in developing world should be encouraged to do resections where patients might not be able to reach or afford high volume centres.

We tried to evaluate the factors associated with morbidity and mortality in our study, but the only significant association was the presence of associated comorbids in patients undergoing liver resection. In a similar previous study from South Asia, the presence of comorbid illness was found to be significantly associated with post-hepatectomy morbidity and an independent risk factor for postoperative mortality.[11] Presence of underlying cirrhosis in our patients resulted in significantly higher blood loss and overall higher morbidity rates, but the difference was not statistically significant. Our univariate analysis failed to demonstrate any significant association of short-term outcomes with other preoperative variables and this could be either due to overall small number of patients or diversity of underlying pathology in this cohort of patients.

Conclusion

Despite limited resources and low volume set-up, hepatic resection can be performed in our set-up with reasonable early postoperative outcomes. Morbidity, mortality, estimated blood loss and average transfusion requirement was comparatively higher in cirrhotic patients which can be further minimised with better patient selection, meticulous surgical technique and use of novel energy devices. There is a need to increase awareness among the patients about improving outcomes as well as train and encourage surgeons from developing countries to take up such demanding surgical procedures.

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