

Major Hepatectomies: Outcome and Perspectives from Eastern Nepal

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ABSTRACT

Introduction: Liver resection is a widely used surgical procedure for different benign and malignant pathology, which carries a significant morbidity and mortality (5-10%). Post-hepatectomy liver failure and bile leak are the major complications of major (>3 segments) hepatectomy, and is also the determinant factor for mortality. However, recently due to multimodality development like better surgeons experience, advanced imaging modality and better surgical planning, the outcome has significantly improved. Moreover, with relocation of experienced surgeons, selection of patients and sharing of operative techniques and perioperative care pathways had made possibility of performing major hepatectomy at even low volume academic centre, with almost comparable outcome to high volume centre.

Aim: To study the outcome of major hepatectomy at an academic institute of Nepal, which has a specialised hepatopancreatobiliary unit with its trained surgeon from a high volume centre.

Materials and Methods: Retrospective analysis of all patients undergoing major hepatectomy between December 2015 to July 2017 was done. Patient demographics, clinical characteristics, operative details, morbidity and mortality were recorded.

Results: There were 6 (24%) major hepatectomy, out of 25 liver resection. Five (83.3%) were for malignant pathology: Right hepatectomy-1; Extended right hepatectomy-1; Central hepatectomy-1; Left hepatectomy-3. The mean age of the patient was 50.8 years, with M:F ratio of 1:2. Jaundice was seen in 50% of patients and none required preoperative biliary drainage or portal vein embolisation. The mean operating time, blood loss and transfusion requirement were 216 minutes, 408 mL and one pint respectively. Three (50%) patients developed major bile leak, which was managed conservatively. There was no postoperative, 30-day or 90-day mortality.

Conclusion: Major hepatectomy is a safe and feasible option at our centre despite limited resources and low-volume set-up.

Keywords: Liver resection, Low volume, Morbidity, Mortality

INTRODUCTION

Liver resection is a widely used surgical procedure for different benign and malignant pathology of liver [1]. According to Höhn's classification [2], liver resection is classified as major abdominal surgery, which carries a significant morbidity and mortality. However, this procedure has markedly improved over the past three decades, with mortality rate more than 20% in 1970s to 10% in 1980s to recent reported rates below 5% [3,4].

Post-hepatectomy liver failure and bile leak is the major and dreaded complications of major liver resection and is also the determinant factor for the mortality [5-7]. However, present advancements permit such major procedure to be performed in low volume centres with outcomes comparable to high volume centres in affluent countries [8-10]. The academic institute (BP Koirala Institute of Health Sciences) has a specialised Hepatopancreatobiliary (HPB) unit established in 2015 with its trained surgeon from a high volume centre. This study documents the first successful series of major liver resections from a tertiary care academic centre in Eastern Nepal.

MATERIALS AND METHODS

The present study was a retrospective analysis of all patients undergoing major hepatectomy (resection of three or more Couinaud segments) [11] for different benign and malignant liver disease at BP Koirala Institute of Health Sciences, Nepal. The institute is a 700 bedded hospital with its separate HPB and Gastrointestinal (GI) surgery division. From December 2015 until July 2017, all patients undergoing major hepatectomy in HPB unit were included. A written informed consent was obtained from all patients before surgery. All patients underwent the following to confirm the diagnosis and resectability of liver or biliary tract disease:

1. Complete detailed history and examination, including Body Mass Index (BMI) calculation, ASA score, comorbidities.
2. Laboratory tests: complete blood count, platelet count,

creatinine, electrolytes, liver function test, albumin, total bilirubin, prothrombin time. All laboratory reports were calculated in relation to Child-Pugh's score.

3. Imaging modalities: Chest X-ray, abdominal ultrasound, abdominal Contrast-Enhanced Computed Tomography (CECT), Magnetic Resonance Imaging/Cholangiopancreatography (MRI/MRCP).
4. Patients with technically resectable tumours of any origin with an estimated sufficient Future Liver Remnant (FLR) based on Child-Pugh's score, platelet count, BMI and volume and quality on CECT/MRI were selected for major hepatectomy.

The variables studied included demographics, indication for surgery, need for preoperative biliary drainage, type of hepatic resections, duration of surgery, estimated blood loss, transfusion requirements, and any concomitant procedure along with hepatic resection. The type of liver resections performed was defined using the Brisbane 2000 nomenclature. Postoperative complications consistent with a Clavien-Dindo classification of surgical complication grade \geq IIIa were defined as morbidity. The "50-50" criteria was used to define Post-hepatectomy Liver Failure (PHLF), and the bile leak was graded as per International Study Group for Liver Surgery (ISGLS) [6]. Length of hospital stay, 30-day and 90-day mortality was also reviewed. Follow-up of patients was done by clinical examination, ultrasound/CECT abdomen every three to six months.

STATISTICAL ANALYSIS

Statistical analysis was performed in Microsoft Excel 2007 and results were presented as mean \pm SDs for normally distributed data and median and range for the rest of the variables.

RESULTS

The study identified 6 (24%) adult patients out of 25 liver resections (major and minor) at BP Koirala Institute of Health Sciences, Sunsari, Nepal.

Case	Age (years)	Sex	BMI (kg/m ²)	ASA	CPS	Comorbidity	Total bilirubin (mg/dL)	Platelet count (×10 ³ /μL)	Obstructive Jaundice
1	48	M	19.2	II	A	no	1.0	175	no
2	55	F	17.3	II	A	no	2.5	160	yes
3	50	F	18.2	II	B	no	17	140	yes
4	28	M	20	III	A	no	1.7	210	no
5	70	F	16.5	II	B	DM	20	155	yes
6	54	F	15.2	II	A	no	1.0	190	no

[Table/Fig-1]: Patients demographics and clinical profile.

CPS: Child-pugh score; DM: Diabetes mellitus; BMI: Body mass index; ASA: American society of anaesthesiologists

Case	Diagnosis	Treatment	OT (min)	EBL (mL)	PRBT	Major morbidity	LOS (days)	Pathology	Follow-up* (months)
1	RPC	LH	175	200	no	no	7	RPC	Well (20)
2	GB cancer, Right portal pedicle involvement	ERH, BDE	225	350	no	Ascites	14	pT3N1M0R0	Well (18)
3	HC (Bismuth-corlette Type IIIa)	RH, BDE	230	410	Yes (1 pint)	Bile leak (Grade B)	22	pT2N0M0R0	Well (12)
4	UESL (intratumour bleeding)	CH	240	620	Yes (2 pint)	Ascites	15	pT3N0M0R1	Recurrence (6)
5	HC (Bismuth corlette Type IIIb)	LH, BDE	250	520	Yes (1 pint)	Bile leak (Grade B)	20	pT2N1M0R0	Well (8)
6	Intrahepatic cholangiocarcinoma	LH	180	350	Yes (1 pint)	Bile leak (Grade B)	9	pT1b N0M0R0	Well (6)

[Table/Fig-2]: Diagnosis, intraoperative details and outcome.

RPC: Recurrent pyogenic cholangitis; GB: Gall bladder; HC: Hilar cholangiocarcinoma; LH: Left hepatectomy; ERH: Extended right hepatectomy; BDE: Bile duct excision; RH: Right hepatectomy; CH: Central hepatectomy; OT: Operative time; EBL: Estimated blood loss; PRBT: Packed red blood cell transfusion; LOS: Postoperative length of stay

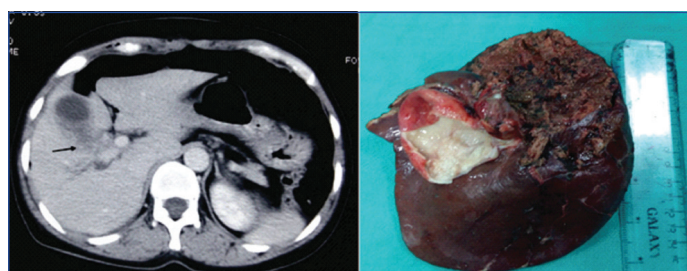
*There were no post-hepatectomy liver failure, reoperation, readmission and 30 and 90-day mortality.

The number of female patients was higher than that of male patients. The demographic profile, operative details and outcome of all the patients are summarised in [Table/Fig-1,2].

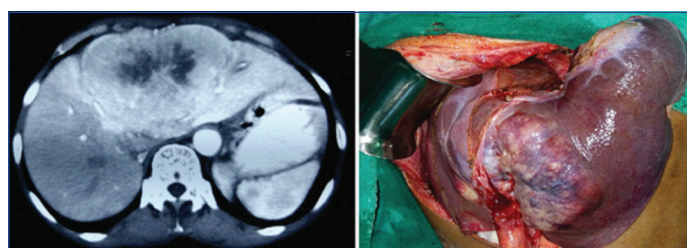
The mean age of the patients was 50.8 years. Three (50%) patients were having below normal BMI as per WHO classification with mean value of 17.7 kg/m² [Table/Fig-3]. Five patients (83.3%) were in ASA 2 category and one patient was in ASA 3 category. The associated comorbidity (Type 2 diabetes mellitus) was present in one (16.6%) patient. Obstructive jaundice was seen in three patients (50%). Five patients (83.3%) required major hepatectomy for malignant cause [Table/Fig-4,5]. Concomitant bile duct excision with reconstruction was required in three patients (50%). None of the patients in present study was in acute cholangitis or severe malnutrition requiring preoperative biliary drainage/portal vein embolisation. Two patients requiring concomitant bile duct resection and one patient with left hepatectomy for intrahepatic cholangiocarcinoma developed bile leak (Grade B) in postoperative period, which was managed with radiological percutaneous drainage (Clavin-Dindo Grade III) [Table/Fig-2,3]. None of the patient developed post-hepatectomy liver failure despite few patients with high serum bilirubin (>10 mg%) undergoing upfront surgery. There was no reoperation, readmission or mortality for

Extended right hepatectomy (S4b/5/6/7/8)	1 (16.6)
Central hepatectomy (S4/5/8)	1 (16.6)
Combined resection of adjacent organs, bile duct excision, n (%)	3 (50)
Operating time (minutes, mean±SD)	216.6±31.5
Estimated blood loss (mL, mean±SD)	408.3±146.6
Units of Packed red blood cell transfused (median)	1
Postoperative length of hospital stay (days, mean±SD)	14.5±5.8
Overall Major Morbidity, n (%)	5 (83.3)
Bile leak (Grade B)-	3 (50)
Ascites	2 (33.3)
In hospital, 30 and 90-day mortality	nil

[Table/Fig-3]: Baseline parameters and outcomes of major hepatectomy.



[Table/Fig-4]: Computed Tomography (CT) scan (left) and intraoperative image (right) of patients with gallbladder cancer with right portal pedicle involvement (arrow) requiring extended right hepatectomy.



[Table/Fig-5]: Computed Tomography (CT) scan (left) and intraoperative image (right) of patients with left liver intrahepatic cholangiocarcinoma requiring left hepatectomy.

Age (years, mean±SD)	50.8±13.6
Male:Female (M:F)	1:2
ASA-II	5 (83.3)
ASA-III	1 (16.6)
BMI (kg/m ²) (mean±SD)	17.7±1.7
Comorbidity	
Diabetes mellitus, n (%)	1 (16.6)
Obstructive jaundice, n (%)	3 (50)
Total serum bilirubin (mg/dL) (median; range)	2.1 (1 to 20)
Platelet count (×10 ³ /μL, mean±SD)	171±25.4
Pathology	
Benign, n (%)	1 (16.6)
Malignant, n (%)	5 (83.3)
Major Hepatectomy, n (%)	
Left hepatectomy (S2/3/4)	3 (50)
Right hepatectomy (S5/6/7/8)	1 (16.6)

any complication. Two out of the five patients with malignant aetiology underwent postoperative adjuvant chemotherapy. After mean duration of 12.8 months follow-up of all patients are performing well with one patient having disease recurrence.

DISCUSSION

The present study is the first review of major hepatic resections in an Eastern Nepal and we have shown that this surgery is safe in terms of mortality/morbidity and is comparable to high-volume tertiary centres carrying out similar procedures [12,13].

Postoperative mortality has been well reported in large series from both low and high volume centres with available results consistently reporting inpatient and 90-day mortality rates of less than 5 to 8% [3]. Although the morbidity was high (83%), there were no mortality in present series, and the study clearly illustrates the safety of the procedure in our centre (BP Koirala Institute of Health Sciences, Sunsari, Nepal).

Bile leak is the most common complication and technical challenge to manage for surgeon after major hepatectomy. The reported incidence widely varies depending on the extent of hepatectomy and associated adjacent organ resection [14]. In one of the multi-institutional study, the proportion of patients developing bile leak was 8% after minor hepatectomy, more than 12% after major hepatectomy and the figure exceeded 30% after hepatectomy with bile duct reconstruction [15]. Bile leak after liver resection can lead to sepsis, organ space infection, prolonged hospital stay and cost, reoperation, readmission and a liver failure [16]. In the present case, we had 50% of patients with Grade B bile leak (Clavin-Dindo Class IIIa surgical complications) which was managed successfully by prolonged management of intraoperatively placed drain coupled with percutaneous radiological drainage of abdominal collection. This complication, although led to prolonged hospital stay, was devoid of any re-exploration and re-admission. The high incidence in present study could be presumed due to the small sample size and malignant pathology (hilar cholangiocarcinoma) requiring extrahepatic bile duct excision and reconstruction, a high risk group for bile leak.

Post-hepatectomy liver failure is the most dreaded complication after hepatectomy and is the major cause for increased morbidity, mortality and prolonged hospital stay. The reported incidence varies from 1% to 30%, and depends on the extent of liver resection, condition of liver, quality and quantity of the remnant liver and the intraoperative factors [6,17]. The PHLF increases in the presence of major hepatectomy in jaundiced patient, presence of portal hypertension (quantified by Child-pugh score and platelet count), associated comorbidity (diabetes mellitus) and increased intraoperative blood loss [18,19]. In the present study, there were no such complications, as none of the patients were having features suggestive of portal hypertension (low platelet count) affecting liver regeneration and all the patients were in child pugh Class A or early B. Moreover, the remnant volume was adequate for the proposed major hepatectomy, based on gross remnant liver volume on CT/MRI, BMI of the patient and associated comorbidity. Indeed it was the team proper patient selection, experience and "gut feeling" of probably patient not going to PHLF after the major resection [20].

The impact of volume-outcome effect has long been highlighted by Birkmeyer JD et al., for many surgical procedures [21]. The outcome of complex visceral procedures (pancreas, oesophagus, liver, lung and aorta) undergoing in high volume centre have been better than the low-volume procedures. However, recently, more and more studies have shown, almost similar outcome in low volume centre, compared to the high volume centre [9,22]. The improvement in mortality and morbidity cannot only be attributed to the volume effect. This has now been attenuated by the proper patient selection, surgeon experience, improvement in the perioperative and anaesthetic care, better understanding of the liver anatomy and establishment of separate skilled hepatobiliary surgical team [18,23]. Moreover, the mortality after major hepatectomy has also been due to "Failure To Rescue" (FTR) the major complication after surgery, a new metrics to assess the quality work at the institute

[24]. A recent study by Ghaferi AA et al., from the University of Michigan, excellently depicted that the differences in mortality between high and low-volume centres are not associated with large differences in complication rates. Instead, these differences seemed to be associated with the ability of a hospital to effectively rescue patients from complications [24,25]. The present study institute is a low-volume, academic institute with a dedicated surgical team and the system, where the residents, nurses and surgeons team are well versed with early detection and management of the complication, hence, mitigating the FTR and preventing the mortality.

LIMITATION

The major limitation of the studies was small sample size, failure to derive statistical influences and survival outcome.

CONCLUSION

Major hepatectomy is a safe and feasible option at our centre (BP Koirala Institute of Health Sciences) despite limited resources and low-volume set-up. The results in terms of morbidity and mortality were comparable to other larger series from international centres. However, further care should be taken to note the increased bile leak in the present study.

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