SCIENTIFIC ARTICLE

# Comparing short-term outcomes after hepatic resection: is there a difference between then and now?

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**Keywords:** Hepatic resection; outcome; morbidity; mortality

**Abstract**

**Introduction**

Despite numerous advances, hepatic resection remains a challenging surgical procedure in developing countries. The objective of our study was to review the short term outcome of recent 75 cases of hepatic resection at our centre and compare the results with our previously published data.

**Methods**

All the patients who underwent a formal hepatic resection at Aga Khan University Hospital, Karachi between 2016 and 2018 were included in the current study. Group comparison was made between our previously published data [Group A] and the current results [Group B].

**Results**

The mean age of the patients in the current study was 54 years and there were 40 [53%] males. Hepatic resection was performed for hepatobiliary malignancies in 42, metastatic malignancy in 18 and symptomatic benign conditions in 15 patients. Major hepatic resection [>3 segments] was performed in 24 [32%] patients and the mean estimated blood loss was 643 millilitres. Post-operative complications were observed in 21 [28%] patients, while 30-day and 90-day mortality were 2.6% and 4%, respectively.

Group comparison with the previous data revealed that the estimated blood loss [$p < 0.048$] and transfusion requirements [$P < 0.000$] were significantly lower in group B. Group B also showed a trend towards lower postoperative complications, 30-day and 90-day mortality than Group A.

**Conclusions**

Despite small numbers in our study, there was a trend towards lower estimated blood loss, fewer transfusion requirements, and improved outcomes in the recent patients.

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## Introduction

Once considered a highly morbid procedure, hepatic resection has since been established as a curative procedure for primary hepatic malignancies and various metastatic liver tumours including colorectal metastases [1, 2]. Post resection outcomes have significantly evolved over the years and procedure-related mortality has improved from > 20% to < 5% in the experienced centres [3]. Morbidity from hepatic resections continues to be high, with data from the American College of Surgeons – National Surgical Quality Improvement Program [ACS – NSQIP] reporting overall morbidity rates for partial, hemi- and extended hepatic resections at 20.6%, 25.2% and 32.8%, respectively [4]. Despite the significant advances made in hepato-biliary surgery in the Western world, hepatic resections are yet to move under the 5% mortality rate mark in the developing world [5].

Very few centres in Pakistan perform hepatic resections, which translates to a low number of published reports demonstrating the various outcomes following hepatic resections in our country [6]. We published the short-term outcomes following hepatic resection of the first 75 cases over 8 years from 2008 to 2015 at our centre, which is a tertiary care hospital with no liver transplant facilities [7]. The next 75 cases were operated in a mere 3 years, from 2016 to 2018, depicting an increasing case volume trend at our facility.

The impact of hospital case volumes and surgeon's practical experience on the morbidity and mortality of a particular surgical procedure has been a much-debated issue and numerous studies have tried to explore this association for hepatic resections. A study from Taiwan with a large number of patients who underwent liver surgery for various benign and malignant pathologies over five years reported that the factors influencing the early outcome after surgery were largely related to hospital and surgeons' case volumes. The number of procedures performed by a particular surgeon influenced the patient mortality independent of the hospital volumes. The combination of high volume surgeons and high volume hospitals had the most beneficial outcome from the patients' perspective [8].

Despite being a low volume centre for liver surgery, we have performed progressively increasing numbers of hepatic resections at our hospital. The objectives of our study were to review the short-term outcomes of hepatic resections at Aga Khan University Hospital and to compare our recent results with the previously published study from our centre and evaluate any differences in trends of the outcomes.

**Materials and methods**

This was a retrospective chart review of 75 adult patients, in succession, who underwent elective hepatic resection at Aga Khan University Hospital from January 2016 onwards, while patients with liver resections secondary to trauma were excluded. All hepatic resections were performed by a single hepatobiliary surgeon who has experience of around 15 years now and the procedure as well as the perioperative care were standardized for all the patients. The basic resources and technical support for liver resection and post-surgical management, including a well-equipped intensive care unit [ICU], are available at our tertiary care university hospital.

The data for the study were collected from the patient charts, clinic notes, surgical operative notes and discharge summaries onto a structured questionnaire. The information gathered in the study included details about patient demographics [age, gender]; and the pre-operative assessments comprising of patient history and clinical examination findings and any known co-morbidities, the laboratory diagnostic tests including liver function tests and the calculated Child-Pugh scores, computerized tomography [CT] scan findings and the admitting diagnosis. The diagnosis of cirrhosis was based on a range of parameters including positive viral serology, Child-Pugh score, evidence of portal hypertension in terms of low platelets and/or endoscopic diagnosis of varices and imaging findings on ultrasound and CT scan. Fibro scan was performed in selected patients and liver biopsy was not routinely performed in our patients. The operative particulars included the indication[s] for surgery, the type of hepatic lesion [neoplastic versus non-neoplastic], the American Society of Anesthesiologist [ASA] score, the variant of liver resection, the duration of the procedure, estimated blood loss [EBL] during the procedure, the need for transfusion of blood products intraoperatively and any procedures additional to the primary surgery. Post-operative data comprised of all surgical complications [surgical site infections, bile-leaks, intra-abdominal collections and post-operative bleeding], systemic complications [liver decompensation and pulmonary infections], post-operative care and recovery, the total length of hospital stay [LOS] and 30-day and 90-day patient morbidity and mortality.

All patients undergoing hepatic resections received general anaesthesia with invasive monitoring intraoperatively and selective epidural analgesia for postoperative pain relief. An intraoperative low CVP was preferred with selective use of inotropes if required. The open approach was used for all patients with staging laparoscopy in selected cases only. Intraoperative ultrasound was routinely performed to detect intrahepatic metastasis / new lesions and to define the relationship of tumours with hepatic inflow pedicles and hepatic veins. Parenchymal transection was performed using a combination of a harmonic scalpel and cavitron ultrasonic surgical aspirator [CUSA]. Pringle manoeuvre was not used routinely and employed only when significant bleeding was encountered. After transection, bleeding and bile leak from the cut surface was repaired with fine sutures. Fibrin glue was used to seal the raw surface and drains were not routinely used. Postoperatively, patients were monitored in a high dependency unit and pain control was provided by epidural analgesia or patient-controlled analgesia. Oral feeding and mobilization were encouraged as early as possible. Patients were discharged once stable and were followed up in outpatient clinics. The same standardized protocol was used for all the patients over the years with minor variations based on the individual patient needs.

Statistical analysis was performed using the Statistical Package for the Social Sciences [SPSS] version 22. Mean and standard deviations were utilized to express categorical data and the Chi-square test or Fisher's exact test was run to compare the categorical variables. Frequencies were used to present quantitative data and the comparison of continuous variables was performed using a t-test when normally distributed. In all the tests, $p < 0.05$ was regarded as significant at a 95% confidence interval.

Information regarding the same variables was available from the previous study and the current results were compared with the results of the past study to determine any significant difference in outcomes. The previously published study at our institution had also investigated short-term outcomes following hepatic resections in 75 patients over 8 years, starting from January 2008 to December 2015 [6]. A comparison between the groups with the previously published data considered Group A and the current results labelled as Group B.

**Results**

Out of 75 patients from the recent data [Group B], 40 patients were males and the mean age of the study population was 54±15 years. Almost half [49.3%] of the patients had at least one comorbid condition and an American Society of Anesthesiology [ASA] score of III; hypertension [40%] was the most common comorbidity followed by diabetes mellitus [29%]. Seventeen [22.6%] patients had underlying liver cirrhosis, as shown in Table-1.

Common indications for resection included hepatobiliary malignancies and metastatic disease from various primary tumours. In addition, 15 patients [20%] underwent hepatic resections for various symptomatic benign conditions. Five patients with xanthogranulomatous cholecystitis presented with the features suggesting gallbladder malignancy with gallbladder mass. Three of the patients also had clinical features of obstructive jaundice and weight loss. Imaging features were strongly suggestive of gallbladder malignancy and the final histopathology was a diagnostic surprise. Similarly, two patients in each group had preoperative imaging suggestive of hepatocellular carcinoma and final histopathology revealed focal nodular hyperplasia. Details of indications are given in Table-2.

Major hepatic resections were performed in 24 [32%] patients while 51 [68%] patients underwent minor hepatic resections. The mean operating time was 264±97 minutes, estimated blood loss was 643±49 millilitres and 28 [37%] patients required perioperative packed cell volume blood transfusions. Details are shown in table 3. Postoperative complications were seen in 21 [28%] patients and more than half of the complications were classified as Clavien-Dindo class III. The mortality rate at 30 days was 2.7% while mortality at 90 days was 4% [Table-3 and 4].

All the relevant variables in our current data were compared with the previously published data [group A] [6] as shown in Tables 1 – 3. The two groups were comparable in terms of baseline parameters including demographics, comorbid conditions and laboratory parameters. Despite this, the overall distribution of primary and secondary hepatic malignancies was comparable in the two groups. The number of patients with underlying cirrhosis was significantly higher in group A [$p < 0.034$], but the proportion of patients with an ASA score of III was significantly higher in group B [$p < 0.012$]. The mean size of the resected lesion and the margin of resection at the histopathology report were comparable in the two groups.

Type of hepatic resection and the mean duration of surgery was comparable in the two groups, however, there were a significantly greater number of patients in group B undergoing procedures with operative time <300 minutes [$p < 0.009$]. Estimated blood loss during surgery [$p < 0.048$] and the number of intraoperative transfusions [$p < 0.000$] was significantly lower in group B. There was no statistically significant difference in the overall morbidity [$p = 0.168$], 30-day mortality [$p = 1.000$] and 90-day mortality [$p = 0.719$] in the two groups, but the absolute numbers reflected a downward trend in group B.

**Discussion**

Liver resection has become more prevalent over the past several decades due to progressive improvements in survival for primary hepatic malignancies and liver metastasis from various organs. Once considered a high-risk procedure, the outcomes after liver resection has dramatically improved over the years due to better patient selection, modern anaesthetic management and advancements in surgical techniques and post-operative care. A trend over time study by Cloyd et al [9] studied the impact of various factors on the complications and outcomes after liver surgery over three distinct periods. Their results indicated that there was a significant improvement in blood loss and transfusion requirements over time despite increasing volumes and complexity of the procedures. The overall number of complications remained high at 40%, but the overall mortality remained low at around 2% with a decreasing trend over time.

Despite consistently improving outcomes of liver surgery in the developed world and the Far Eastern region [8], the development of this speciality has been slow in developing countries. Low volumes due to poor referral systems, resource restrictions and scarcity of modern technology have contributed to high morbidity and mortality rates compared to high case volume centres of the developed world [5]. We are a tertiary care university hospital in Pakistan where liver surgery was formally initiated in 2008. Our audit of the first 75 cases performed over 8 years was published in 2017. The next 75 cases were operated on in only 3 years depicting the progressive increase in the numbers of patients seeking care for hepatic pathologies at our centre. Patient outcomes are linked to hospital patient volumes and published literature from both Western and Asian countries has proven a significant inverse relationship between hospital patient volumes and morbidity and mortality after hepatic resections [8,10,11,12].

In our study, there was no considerable difference in the baseline characteristics of the study population between the two groups [Group A and B]. There were significantly more patients in the recent study with an ASA score of III, stipulating that the anaesthetic management has improved over the years to optimize high-risk patients intraoperatively. Several documented anaesthetic techniques improve the outcomes of patients undergoing liver surgery including the use of anaesthetic drugs that do not alter the hepatic blood flow, reduction of central venous pressure to reduce intraoperative bleeding and use of vasoactive drugs to avoid hypotension [11]. This also explains the reduction in estimated blood loss and a decline in the need for intraoperative transfusions in group B. Although the overall

**Table 1.** Group Comparison* of Baseline Characteristics

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| **Demographics** | **Group A** | **Group B** | **p valve** |
|---|---|---|---|
| Male/Female(n) | 43/32 | 40/35 | 0.743 |
| Age (years, mean ± SD) | 52±14 | 54±15 | 0.653 |
| **Co-morbid Conditions** | 40(53.3%) | 37(49.3%) | 0.744 |
| Hypertension (n, %) | 31(41%) | 30((40%) | 1.000 |
| Diabetes Mellitus (n, %) | 23(31%) | 22(29.3%) | 1.000 |
| Pulmonary Disease (n, %) | 5(7%) | 6(8%) | 1.000 |
| ASA Level I/II/III | 6/47/22 | 7/31/37 | **< 0.028** |
| **Status of Disease and Liver** | | | |
| Number of lesions<br>❖ Single lesion<br>❖ More than one lesion | <br>63(84%)<br>12(16%) | <br>70(93.3%)<br>5(6.66%) | <br>0.120 |
| Mean size of lesion (cm, mean±SD) | 5.48±4.4 | 5.84±4.3 | 0.854 |
| Underlying Cirrhosis of Liver | 30(40%) | 17(22.6%) | **< 0.034** |

*Group A= 2008 – 2015; Group B = 2016 – 2018
ASA: American Society of Anesthesiology, SD: Standard Deviation

**Table 2.** Group Comparison - Indications for Surgery and Underlying Pathology

| | **Group A** | **Group B** | **p value** |
|---|---|---|---|
| Malignant Hepatic and Biliary Pathology (n, %) | 46(61.3%) | 42(56%) | 0.185 |
| Primary Hepatocellular Carcinoma | 37(49.3%) | 24(32%) | |
| Adenocarcinoma of Gallbladder | 6(8%) | 13(17.3%) | |
| Hilar Cholangiocarcinoma | 2(2.7%) | 5(6.6%) | |
| Embryonal Sarcoma | 1(1.3%) | 0 | |
| Sarcomatoid Carcinoma | 0 | 1(1.3%) | |
| Metastatic Malignancy (n, %) | 18(24%) | 18(24%) | 0.441 |
| Colorectal Malignancy | 10(13.3%) | 9(12%) | |
| Neuroendocrine Tumor | 2(2.7%) | 1(1.3%) | |
| Renal Cell Carcinoma | 2(2.7%) | 0 | |
| Ovarian Carcinoma | 0 | 3(4%) | |
| Others* | 4(5.3%) | 5(6.7%) | |
| Benign Diseases (n, %) | 11(14.6%) | 15(20%) | 0.931 |
| Focal Nodular Hyperplasia | 2(2.7%) | 2(2.7%) | |
| Giant Haemangioma | 2(2.7%) | 2(2.7%) | |
| Xanthogranulomatous Cholecystitis | 2(2.7%) | 3(4%) | |
| Hepatic Cystadenoma | 1(1.3%) | 3(4%) | |
| Primary Hepatic Adenoma | 1(1.3%) | 1(1.3%) | |
| Primary Paraganglioma of Liver | 1(1.3%) | 0 | |
| Hepatolithiasis | 1(1.3%) | 1(1.3%) | |
| Other benign conditions | 1(1.3%) | 3(2.7%) | |

*Others include metastatic breast cancer, adrenocortical carcinoma, endometrial carcinoma, germ cell tumor, gastric cancer and unknown primary

**Table 3.** Group Comparison – Intraoperative events

| Intraoperative Variables | Group A | Group B | p value |
|---|---|---|---|
| Major Hepatic Resections (≥ 3 segments) | 30(40%) | 24((32%) | 0.395 |
| Minor Hepatic Resections (≤2 segments) | 45(60%) | 51(68%) | |
| Additional procedures | 15(20%) | 17(22.6%) | |
| Operating time (minutes, mean ± SD) | 300±138 | 264±97 | 0.051 |
| Operating time<br>≤ 300mins<br>>300mins | <br>32(43%)<br>43(57%) | <br>49(65%)<br>26(34%) | < 0.009 |
| Estimated blood loss (ml, mean ± SD) | 665±580 | 643±494 | < 0.048 |
| Blood transfusion requirement | 45(60%) | 28(37%) | < 0.000 |
| Margin of resection on pathology (mm, mean+SD) | 13.48±15 | 12.89±23 | 0.628 |

**Table 4.** Postoperative outcomes

| | Group A | Group B | P value |
|---|---|---|---|
| Overall Morbidity (n, %) | 30(40%) | 21(28%) | 0.168 |
| Wound Infection | 12(16%) | 5(6.7%) | 0.120 |
| Intraabdominal collection | 8(10.6%) | 8(10.6%) | 1.000 |
| Pulmonary infection | 7(9.3%) | 8(10.6%) | 1.000 |
| Ascites | 5(6.7%) | 3(4%) | 0.719 |
| Bleeding | 2(2.7%) | 0 | 0.497 |
| Myocardial infarction | 1(1.3%) | 0 | 1.000 |
| Clavien-Dindo classification (I/II/III/IV/V) | 9/4/9/5/3 | 1/7/11/0/2 | |
| Length of hospital stay | 9.51±3.16 | 9.67±6.5 | 0.763 |
| 30-day Mortality | 3(4%) | 2(2.7%) | 1.000 |
| 90-day Mortality | 5(6.7%) | 3(4%) | 0.719 |

amount of blood loss in our recent data was still higher than that reported from the high volume centres of the developed world [9], the general trend in our study population reflects a significant improvement in this parameter. Progressive improvement in surgical techniques, the expertise of associated operating room staff, use of novel devices for parenchymal transection like Harmonic and Cavitron Ultrasonic Surgical Aspirator [CUSA] at our centre might be the other contributing factors to decreased the intraoperative blood loss and transfusion requirement in our recent patients.

Our overall morbidity rates have improved over the years. The morbidity rate has dropped down to 28% from 40% which is comparable to high volume centres in the developed world. There was a reduction in both the surgical and systemic complications associated with hepatic resection. One of the most important risk factors associated with morbidity after liver resection is cirrhosis [13] and its incidence in our recent study population was lower which has possibly contributed to the reduction in overall morbidity rates. A recent report from Japan suggests that the mortality rate after hepatic resection may be less than 1% in high volume centres, but rates of 3 to 4% have been reported at low volume centres [14]. We had a 30-day mortality of 4% [2008-2015] which has reduced to 2.7% [2016-2018], and 90-day mortality has reduced from 6.7% to 4%, respectively, which is comparable to low volume centres elsewhere [14].

Over the last two decades, technical innovations in liver surgery have shifted the paradigm towards a laparoscopic approach [15]. The Second International Experts' Consensus Conference in 2014, suggested that a laparoscopic approach is advantageous in terms of reduced blood loss, decreased postoperative morbidity and a shorter hospital stay [16], which has been further substantiated in the recent reviews [17,18, 19]. Improvement in overall outcomes of hepatic resection at our centre over time is encouraging enough for us to start exploring the laparoscopic approach for minor liver resections and develop expertise with time to undertake major liver resections with this approach.

In conclusion, despite the small number of total cases, an increase in the number of cases being operated has resulted in a trend towards lower estimated blood loss, fewer transfusion requirements, and overall improved morbidity and mortality in the recent patients.

All authors disclose no conflict of interest. The study was conducted in accordance with the ethical standards of the relevant institutional or national ethics committee and the Helsinki Declaration of 1975, as revised in 2000.

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