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Analysis of patients with acute liver failure after liver surgery: Single center experience

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Abstract

Liver transplantation is the lifesaving treatment option for rare acute liver failure that develops due to iatrogenic bile duct injuries or after major hepatectomy. The aim of the study is to analyze patients with acute liver failure due to iatrogenic bile duct injury or major hepatectomy on the waiting list for emergency liver transplantation. Between the years 2011-2020, 9 patients (5 female/4 male; median age: 30 years old, (range:4-63 years)) with acute liver failure related to bile duct injury or major hepatectomy for whom urgent liver transplantation was planned were included in this study. Eight patients were accepted for urgent liver transplantation. Acute liver failure developed in 6 patients due to hepatoduodenal ligament injury during cholecystectomy, and in 3 patients due to major hepatectomy. The patients were listed for urgent transplantation within the mean of 1.5 days (range:0-3 days) after acute liver failure. Two patients had living donor and 1 patient had cadaveric liver transplantation. Acute hepatic failure, especially after iatrogenic bile duct injuries associated with vascular injuries, seems to be more fatal than post hepatectomy liver failure. In these cases of acute liver failure, which is a difficult situation to decide, emergency liver transplantation should be kept in mind as the treatment option.

Keywords: Post-hepatectomy liver failure, bile duct injury, liver transplantation

Introduction

Liver transplantation is the only curative treatment for end stage liver disease and is a life-saving treatment in acute liver failure, which presents with deterioration in liver function and change in mental status [1]. Iatrogenic bile duct injury and hepatic insufficiency following major hepatectomy are rare causes of acute liver failure [2,3]. Injury to the biliary system is being frequently encountered in the era of laparoscopic cholecystectomy. It is frequently associated with concomitant complex vascular injuries. The decision for emergency liver transplantation due to major bile duct injury or hepatic insufficiency of the remnant liver following major hepatectomy is very challenging for physicians.

In this rare patient group, liver transplantation should be kept in mind as the last resort treatment modality where other therapeutic modalities have failed.

The aim of the study is to analyze patients with acute liver failure due to iatrogenic bile duct injury or major hepatectomy that have been enlisted for emergency liver transplantation.

Materials and Methods

Study population

512 patients were enlisted for emergency liver transplantation between 2011 and 2020 in Inonu university liver transplantation institute. Among these patients, 6 patients developed acute liver failure due to hepatoduodenal ligament injury during cholecystectomy and 3 patients (two with Echinococcus alveolaris and one with trauma) who developed acute liver after major hepatectomy were included in the present study.

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Study parameters

The demographic and clinical data of the patients were retrospectively analyzed from the prospective database of our institution. The patients who were transplanted or recovered and patients who died during the follow-up period were investigated. Ethical committee approval was obtained from the local ethical committee (2022/2931).

Patients with iatrogenic bile duct injury and post-hepatectomy liver failure

After the patients were admitted to intensive care, liver function tests, coagulation parameters, kidney function tests, ammonia and lactate levels were evaluated primarily. Multidetector computerized tomography (MDCT) was performed to evaluate the vascular and structures in our patients with normal renal functions, whose general condition was stable. If the general condition of the patients was poor and there was an acute liver failure, liver supporting systems such as plasmapheresis, Molecular Adsorbent Recirculating System™(MARS™), the Single-Pass Albumin Dialysis system and the Fractionated Plasma Separation and Adsorption system (Prometheus™) were used. King's College Criteria and Bilirubin – Lactate- Etiology (BiLE) Score were used to determine the degree of hepatic failure [4,5]. Transplantation decision was made for patients who did not respond despite the treatments and encephalopathy worsened.

Patients that require major hepatectomy undergo a thorough investigation including an assessment of the future remnant liver volume by abdominal MDCT. The main goal is to obtain a future remnant liver volume (FRLV) >40%. However, any borderline cases that include an FLRV between 25-40% require the preparation of a living donor (if present) for a potential to develop remnant liver failure.

In patients with liver failure after hepatectomy, supportive therapy was considered the first-line therapy. Liver supporting systems includes plasmapheresis, MARS and Prometheus. For reducing portal flow diuretics and beta-blockers were used. Indocyanine green test was performed to evaluate the liver parenchyma. Only after the failure of the supportive therapy, a decision is made to proceed with liver transplantation as the last resort treatment to save the patient's life.

Statistical analysis

Since the cohort is very small, we only performed the descriptive statistical analysis. The continuous data are expressed as median and range. The categorical data are expressed as the number of affected patients and the percentage of the study population. All statistical analyses were performed on Microsoft Excel v.2016 (Microsoft, USA) and Statistics Software Package for Social Sciences SPSS v 26 (IBM, USA)

Results

General demographic and clinical characteristics of patients

Between 2011-2020, 9 patients (5 female/4 male) with a median age of 30 years old (range:4-63 years) were listed for emergency liver transplantation due to acute liver failure at our liver transplantation

institute. Six patients (66.6%) had hepatoduodenal ligament injury during cholecystectomy, and all were referred from other centers. Two patients (22.2%) that had undergone major hepatectomy in our institute and 1 patient were admitted from a different hospital, were enlisted for emergency liver transplantation for remnant liver failure (Table 1). The patients were listed for urgent transplantation within a mean of 1.5 days (range:0-3 days) after acute liver failure.

Table 1. Summary of the demographic and clinical characteristics of the all patients

Total patients' number	9
Female/Male	5/4
Age (median)	30 years (range: 4-63)
Etiology of liver failure	
Biliary injury	6 patients
Post hepatectomy failure	3 patients
Waiting time in transplantation list (median)	1.5 days (range 0-3)
Liver transplantation number	
Biliary injury	1/6 (16.6 %)
Post hepatectomy failure	2/3 (66.6 %)
Mortality	
Biliary Injury	4/6 (66.6 %)
Post hepatectomy failure	1/3 (33.3 %)

From a total of 9 patients, 8 were evaluated for emergency liver transplantation. Two patients had living donor and 1 patient had cadaveric liver transplantation. The remaining patient underwent hepaticojejunostomy for isolated bile duct injury and was not transplanted.

Patients who were enlisted for emergency liver transplantation due to iatrogenic bile duct injury

Six patients with iatrogenic injury of the hepatoduodenal ligament during cholecystectomy led to acute liver failure. Five of the six patients (83.3%) had the accompanying major vascular injury. Four (66.6%) died during the waiting period before any transplantation could be performed. Three of these patients had acute liver failure and 1 had multiple organ dysfunction syndrome (MODS). Two patients (33.3%) survived; one of these patients received a living donor liver transplantation and the other had isolated bile duct injury and a hepaticojejunostomy was performed. The data are summarized in Table-2.

Patients who were enlisted for emergency liver transplantation due to remnant liver dysfunction following major hepatectomy

The characteristics of the patients with post-hepatectomy liver failure are summarized in Table-2. Emergency liver transplantation was performed for 2 of 3 patients (66.6%) with acute liver failure due to major hepatectomy. The indications for major hepatectomy were blunt trauma in a 4-year-old boy and echinococcus alveolaris in the remaining two patients.

The pediatric patient with blunt trauma received emergency right hepatectomy and portal vein thrombosis had developed in the remnant liver. He was transplanted 24 hours after the index operation due to acute liver failure. He survived for 10 months after the operation but died due to chronic rejection due to non-compliance with the immunosuppressive medication.

In the remaining two patients with *Echinococcus alveolaris* (ages: 52 and 27 years) planned liver resections were performed. In a 52-year-old female patient, an extended right hepatectomy was performed and she developed post-hepatectomy liver failure and

received a living donor liver transplantation on postoperative third day. The patient survived and still alive without any complications. In a 27-year-old male patient, right hepatectomy was performed for *Echinococcus alveolaris*. A portal vein thrombosis of the remnant liver developed on the postoperative early period. The patient was reoperated and portal thrombectomy was performed. This patient was referred to us from another center. The condition of patient was poor at the admission. Although necessary preparations for liver transplantation were made, the patient died due to MODS. The data are summarized in Table-3.

Table 2. Summary of the demographic and clinical characteristics of the patients with iatrogenic hepatoduodenal ligament injury during cholecystectomy

m	Age (years)	Gender	Height (cm)	Weight (kg)	Disease	Primary procedure	Complications	Hannover Classification (12)	Interval from index operation (days)	Second operation	Survival (months)
Patient 1	30	F	155	45	Cholelithiasis	Laparoscopic cholecystectomy	Common bile duct injury	D3	1	Hepaticojejunostomy	109
Patient 2	48	F	160	80	Cholelithiasis	Laparoscopic cholecystectomy	Portal vein, right hepatic artery, common bile duct injury	D3dpv	0	Eksploration	exitus
Patient 3	17	M	180	75	Cholelithiasis	Laparoscopic cholecystectomy	Common bile duct, right hepatic artery injury	D3d	0	No operation	exitus
Patient 4	63	F	165	80	Cholelithiasis	Laparoscopic cholecystectomy	Right portal vein injury	D1pv	2	Right hepatectomy	exitus
Patient 5	41	F	162	70	Cholelithiasis	Laparoscopic cholecystectomy	Right hepatic artery injury	D1d	NA	No operation	exitus
Patient 6	26	M	162	50	Cholelithiasis	Laparoscopic cholecystectomy	Right portal vein, right hepatic artery, common bile duct injury	D3dpv	2	Living donor liver transplantation	2

F=Female, M=Male, NA= Not available

Table 3. The demographic and clinical characteristics of patients with post hepatectomy liver failure

	Age (years)	Gender	Height (cm)	Weight (kg)	Disease	Primary procedure	Complications	Interval from index operation (days)	Second operation	Survival (months)
Patient 1	4	M	120	20	Blunt trauma (liver laseration)	Right hepatectomy	Left portal vein thrombosis,	1	Cadaveric liver transplantation	10
Patient 2	52	F	160	75	<i>Echinococcus alveolaris</i>	Extended right hepatectomy	Post hepatectomy liver failure,	3	Living donor liver transplantation	36
Patient 3	27	M	177	80	<i>Echinococcus alveolaris</i>	Right hepatectomy	Portal vein thrombosis, Post hepatectomy liver failure	NA	Portal vein thrombectomy	exitus

F=Female, M=Male, NA= Not available

Discussion

In this study, we analyzed the results of patients who developed acute liver failure related to iatrogenic bile duct injury or major hepatectomy and were listed for urgent liver transplantation. According to our results 16.6% of patients with acute liver failure after iatrogenic biliary injury, and 66.6% of patients with post hepatic insufficiency after major hepatectomy overcome acute liver failure with liver transplantation. Vascular injuries accompanying biliary injuries have a poor prognosis when compared to acute liver failure after major hepatectomy. The reason for this, major hepatectomies are planned procedures and in a tertiary liver

transplantation center, necessary preparations are performed on every patient with a borderline remnant liver volume (25-40%) who are planned to undergo major hepatectomy. Iatrogenic hepatoduodenal injuries are complex problems that affect multiple components of the liver. On the other hand, remnant liver failure is related to the loss of functional capacity of the liver. In fact, one of our patients who underwent right hepatectomy died due to the development of vascular complications that lead to liver failure and MODS. This supports our theory for unexpected complications that affect more than one component in the liver are highly mortal events.

The incidence of iatrogenic bile duct injuries has increased to 0.6% as laparoscopic cholecystectomies were popularized [6,7,8]. The rate of vascular injuries accompanying injuries to the biliary system range between 16.7% to 47% and the most common type is right hepatic artery injury [9]. Deterioration in liver function tests, development of acute liver failure and unrepairable injuries are urgent liver transplantation indications in patients with iatrogenic biliary injuries [9]. Most of these patients lose their lives in the waiting list due to severe sepsis [9,10]. Morbidity and survival rates of patients who underwent liver transplantation due to biliary injury are between 52-100 % and 60-75 %, respectively [9]. Parilla et al. reported that, from 7 urgent liver transplantations performed because of biliary injury, 2 died on the waiting list and 90% of 5 liver transplanted patients died within the first 30 days of operation [11]. All our biliary injury patients had referred us from other centers. The condition of the patients who came to our clinic was poor. From 5 patients with accompanying vascular injury; four died on the waiting list because of severe sepsis accompanied by MODS and acute liver failure. One patient had a living donor liver transplantation and is still alive and in good condition. The patient without accompanying vascular injury, underwent hepaticojejunostomy and was discharged without any complications.

The gold standard treatment of *Echinococcus alveolaris* is resection or transplantation. Residue intact liver volume determines the success rate of resection. Normally, if the liver tissue is healthy, a remnant liver volume of 25-40% is enough [12]. However, remnant liver failure may develop due to operative stress and vascular complications that develop in the postoperative period. The findings of liver failure are hyperbilirubinemia, coagulopathy, ascites and even encephalopathy. The incidence of acute liver failure is between 2-30 % and depends on the quality of remnant liver parenchyma [12]. According to Egeli T. et al. study, the post-operative liver failure rate was 9.7% in healthy donors [13].

If supportive therapy fails, the mortality rate ranges between 0-8%, and liver transplantation is the last resort treatment [12]. In this study, liver transplantation was performed in 2 of 3 patients not responding to support. These patients were discharged without any complications. The third patient with major hepatectomy developed acute liver failure due to portal vein thrombosis and he was listed for emergency transplantation however the patient died on a waiting list. As in acute liver failure, it is difficult to make a decision for liver transplantation in patients with acute liver failure after hepatectomy. The demand for organs and limited donor pool is raised is a major problem in many Asian countries and in Turkey as well. Living donor liver transplantation is currently the only option to increase the donor pool and provide the necessary liver grafts to these patients that are in need for emergency liver transplantations.

Conclusion

Acute liver failure due to iatrogenic hepatoduodenal ligament injury has a poorer prognosis when compared to post-hepatectomy remnant liver failure. The main reason for this is because the latter is a planned surgery with necessary precautions which is generally performed in tertiary referral centers, however, the first is a

catastrophic event that has a sudden impact on the condition of the patient also is encountered during laparoscopic cholecystectomy which performed in many hospitals. Each surgeon performing hepatobiliary surgery, even if only performing cholecystectomy, should be aware of this condition and should take maximum care.

Conflict of interests

The authors declare that there is no conflict of interest in the study.

Financial Disclosure

The authors declare that they have received no financial support for the study.

Ethical approval

Ethical committee approval was obtained from local ethical committee (2022/2931).

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