

Outcomes of Early Liver Retransplantation

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Abstract

Introduction: Early liver retransplantation can be defined as the one that takes place within 30 days after primary transplantation, and, traditionally, it has been associated with poor outcomes in terms of morbidity and survival.

The present study aims to identify the factors that adversely affect survival outcomes in these patients.

Methods: A retrospective analysis of the early liver retransplantations performed in a Spanish tertiary care center between 2007 and 2017 was conducted. The variables analyzed were demographics, causes of first transplantation and retransplantation, and mortality resulting from the latter.

Results: 30 early retransplantations were performed during this period, 19 men and 11 women, of a mean age of 52.2 years. The main precipitants of retransplantation were hepatic artery thrombosis (60%) and primary graft failure (13.3%). Perioperative death occurred in 5 recipients (16.7%), most commonly caused by cardiorespiratory arrest (40%). There were not differences between the patients that died and those who lived in terms of MELD score, average age donor or HCV presence. The 1-, 2- and 5-year survival rates were 83.3%, 76.7% and 59.9%, respectively.

Conclusion: in our study we were not able to discern the risk factors that contributed to perioperative death in recipients of early retransplantations. Nevertheless, survival rates among these patients were favorable, almost reaching those reported in global series of liver transplantation.

Keywords: Liver retransplantation, Early liver retransplantation

Introduction

The well-documented poor morbidity outcomes of liver retransplantation are the main reason why the need for its performance is commonly subdue to an intense clinical debate, specially, in late-elective settings.

Nevertheless, this decision-making is "easier" in some scenarios, in which the condition of the recipient is so severe that there is no room left for hesitation. This kind of situation calls for an early liver retransplantation, which is performed in a time lapse of 30 days after the original transplantation. This early retransplantation can be classified as urgent (when it is performed within 7 postoperative days) and early-elective (when it takes place between the 8th and 30th postoperative days) [1].

The two major causes of early liver retransplantation are artery thrombosis and primary graft failure [2], both of them resulting in an acute hepatic failure so severe that immensely jeopardizes the vital prognosis of the patient.

With the present study, we aim to describe the causes and outcomes of early liver retransplantations, and to identify the risk factors that affected survival in these recipients.

Methods

We carried out a retrospective analysis based on the data of 698 patients who underwent liver transplantation in a Spanish tertiary care center between 2007 and 2017, including 67 retransplantation recipients and selecting those 30 that could be considered as early retransplantations, that is to say, those that were performed within the first month after the original transplantation.

The first part of the analysis was dedicated to demographic, clinical, operative and death related data of all recipients of early retransplantation, as well as donors related data. For the second part, analysis was dedicated to identify the factors that negatively affected perioperative death.

Data sources included an internal scientific registry and digital patient charts from the Andalusian Health System.

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IBM ® SPSS ® Statistics 25.0 version was used for the statistical analysis. Survival estimation was performed using the Kaplan-Meier model.

Results

Global series

698 liver retransplantations were performed during this 11-year period of time in our center, including, among those, 67 retransplantations (9.6%). Regarding the latter, only 30 of them (4.3%) were considered as early retransplantations (26 urgent and 4 early-elective).

63.3% of recipients of early retransplantations were male and 36.7% were female, of a mean age of 52.2 (± 10.8 SD) years old.

In these recipients, the most common causes of liver transplantation were hepatocellular carcinoma (HCC, 46.7%), non-cholestatic chronic liver disease [30% (mostly alcoholic and/or HCV cirrhosis)] and metabolic liver disease [13.3% (familial amyloid neuropathy)].

The patients were included in the transplantation waiting list with an average MELD score of 12.6 (± 7.1 SD) and a Child-Pugh score of 7.2 (± 2.4 SD).

First and second donors were the same age (58.2 \pm 16.4SD years and 56.3 \pm 16.4SD years-old, respectively) ($p=0.6$), and so was their type [mostly DBD (Donation after Brainstem Death), 86.7 and 96.7% respectively].

Piggy-back technique was the standard approach for recipient hepatectomy, allowing anastomosis between suprahepatic veins of recipient and donor. Portaportal anastomosis was performed in all patients. Artery anastomosis varied due to the common presence of vascular anomalies in grafts (21.7%), although the preferred one was effectuated between common or proper hepatic artery of donor and recipient (50%). End to end biliary anastomosis was executed in 93.3% of recipients.

Table 1: Causes of Replantation

Cause of retransplantation	n	%
Hepatic artery thrombosis	18	60
Primary graft failure	4	13.3
Portal thrombosis	3	10
Arterial ischemia	3	10
Acute Budd-Chiari syndrome	1	3.3
Acute rejection	1	3.3

Replantation was needed most frequently because of hepatic artery thrombosis (18 cases, despite previously performing a surgical thrombectomy in 8 of them) and primary graft failure (4 cases) (Table 1). Reoperation rate among the group reached 16.7%, distributed as 1 minor and 4 major surgeries

Perioperative death occurred in 5 patients (16.7%), although mortality rates stabilized with time. Mean patient survival after retransplantation was 56.3 \pm 39.7 SD months (55.6 \pm 38.5 SD in the urgent retransplantation group and 60.5 \pm 53.2 SD in the early-elective retransplantation group, without differences between the groups). This way, early-retransplantation survival rates reached 83.3%, 76.7% and 59.9%, in the 1-,2- and 5-years follow-up, respectively.

Survivors vs dead recipients (Table 2)

Perioperative death occurred in 5 patients (16.7%), 3 men and 2 women. Although the mean age of recipients seemed to be greater in the group of patients who died (57.6 \pm 6.8 SD) than in the group of the survivors (51.2 \pm 11.2 SD), the differences were not statistically significant ($p=0.23$).

In the same way as the global series, in the recipients who died, the main precipitant of liver transplantation was hepatocellular carcinoma (60%), followed by primary biliary cirrhosis (20%) and familial amyloid neuropathy (20%).

Prevalence of hepatocellular carcinoma was similar between the survivors (40%) and dead recipients (60%) ($p=0.63$). Parallely, the prevalence of HCV was also similar in both groups (20% in survivors and 40% in dead recipients) ($p=0.57$).

In the patients who died, retransplantation was motivated because of arterial ischemic issues in 80% of the cases, meanwhile primary graft failure was responsible for the remaining 20%.

The new retransplantation MELD score was similar in the recipients who lived and those who died (18.7 \pm 7.5SD and 19 \pm 10.7, respectively) ($p=0.93$).

There were also no differences in the average time in which retransplantation was performed between the recipients that survived (4.4 \pm 6.3 SD postoperative days) and the patients who suffered a perioperative death (3.7 \pm 3.1 SD postoperative days) ($p=0.85$).

Average age donor seemed slightly greater in the group of survivors in both first transplantation (59.4 \pm 18 SD years in survivors and 52.6 \pm 10.2 SD in dead recipients) ($p=0.44$) and retransplantation (57.6 \pm 15.7 SD and 49.6 \pm 19.9 SD, respectively) ($p=0.33$).

Table 2: Summary results (survivors vs death recipients)

Main variables	Survivors	Dead recipients
Sex (male:female)	16:9	3:2
Age (years)	51.2 \pm 11.2 SD	57.6 \pm 6.8 SD
Main indication for transplantation	HCC	HCC
MELD	13.2 \pm 7.7	9.6 \pm 2.1
HCV presence	20%	40%
Age of first donor (years)	59.4 \pm 18 SD	52.6 \pm 10.2 SD
Main cause of retransplantation	Hepatic artery thrombosis	Hepatic artery thrombosis
Priority (urgent:early-elective)	22:3	4:1
Time until retransplantation (days)	4.4 \pm 6.3 SD	3.7 \pm 3.1 SD
Age of second donor (years)	57.6 \pm 15.7 SD	49.6 \pm 19.9 SD
Reoperation rate	8%	60%

Type of donor did not differ between both groups, 100% were DBD for both first and second transplantations.

There were not statistically significant differences between venous ischemic time in primary transplantation (385.5 ±115.3 SD minutes in survivors and 382 ±121.7 SD minutes in death recipients) (p=0.95). Arterial ischemic time seemed longer in dead recipients (447 ± 113.3 SD minutes) than in the group of survivors (424.6 ±109.8 SD), without statistically significant differences.

During retransplantation, average venous and arterial ischemic times appeared to be longer in the group of patients who suffered perioperative deaths (426.3 ±115.1 SD minutes and 448.75 ± 116.6 SD, respectively), although not statistically different, than those in the group of survivors (367.5 ±94.8 SD minutes and 395 ±94.8 SD, respectively).

Vascular anomalies were more common in first transplantation (10 cases, only 1 in the group of dead recipients) than in retransplantation (3 cases, 2 of them in dead recipients), again with no statistically significant differences.

Reoperation was necessary in 3 patients belonging in the group of dead recipients (60%). Surgery was performed because of hemoperitoneum (1 patient), dehiscence of biliary-enteric anastomosis (1 patient) and 1 biliary leakage (1 patient).

Out of the 5 patients that died in the perioperative time lapse, the most common cause of death was cardiorespiratory arrest (2 patients). The other 3 patients died because of subarachnoid hemorrhage (1 patient), rupture of hepatic artery pseudoaneurysm (1 patient), and massive hemoperitoneum (1 patient). There were not sepsis related deaths.

Although perioperative mortality rate may seem higher in the group of urgent retransplantation (4 cases) than in the early-elective group (only 1 case), not statistically significant differences were found (p=0.3).

Discussion

Early liver retransplantation is a tough choice to make for the surgeon who is faced with a fatally ill recipient presenting with a severe hepatic failure in the first postoperative days after transplantation. This critical situation is, most of the times, a consequence of hepatic artery thrombosis or primary graft failure [2], as it was confirmed by our series (60% and 13.3%, respectively).

Even though its outcomes have improved over time, it continues to be associated with worse general outcomes and a higher perioperative death rate (16.7% in our study) when compared to late-elective retransplantations [3]. This fact can be partially explained because of the critical condition of the recipient and its technical complexity.

Aside from these, other factors negatively affecting the outcomes of early retransplantation have been reported in literature over the years, such as an age donor over 60 years or a higher MELD score [3]. Nevertheless, our findings could

not confirm these as risk factors, as there were not differences regarding those aspects between the patients that suffered a premature death and those who survived in the long-term.

It is worth to notice that, even though the differences were not statistically significant, the average age of the recipient and ischemia times during retransplantation appeared to be longer in the patients who died, which suggest that both factors may have had a negative impact in survival rates [4].

On the other hand, average time interval for retransplantation was short and very similar in survivors and dead recipients (3-4 days), possibly a consequence of an increasing pool of donors, supposedly with a poorer quality of the graft, after applying the extended criteria donor as it is usually done in our country [4-6]. Despite this fact, this was not a problem that compromised our series, due to the fact that donors were DBD of a relatively young age.

The main cause of death was cardiorespiratory arrest (40%), and, despite sepsis being usually reported as the main cause of postoperative death among retransplantation recipients in general [7], it was absent in our series.

As it has been brought to attention before, even though perioperative death rate was initially high, it stabilized with time, showing promising results. This way, 5 year-estimated survival was almost 60%, well above the estimated 45% reported by the European Liver Transplant Registry [4,8].

Conclusion

Perioperative death among early retransplantations recipients seems to be a result of the combination of patient, operative and donor related factors. Unfortunately, this study failed to identify the precise risk factors that would allow us to predict and to try to avoid this tragic outcome.

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