İzmir Tıp Fakültesi Dergisi
Journal of İzmir Faculty of Medicine

İzmir Tıp Fak Derg. 2025;4(2):39-46.

Klinik Araştırma
DOI: 10.57221/izmirtip.1654369

Cost Analysis of Acute Rejection in Liver Transplanted Patients

Karaciğer Nakilli Hastalarda Akut Rejeksiyon Maliyet Analizi

Funda Uğur Kantar[1] Gözde Derviş Hakim[2-3] Mesut Akarsu[4], Tarkan Unek[5], Mücahit Özbilgin[5], Tufan Egeli[5], İbrahim Astarcıoğlu[6]

[1]Bakırcay University, Faculty of Medicine, Department of Gastroenterology, Izmir, Turkey
[2]University of Health Sciences, Turkey, Izmir Tepecik Education and Research Hospital, Clinic of Gastroenterology, Izmir, Turkey
[3]University of Health Sciences, Turkey, Izmir Faculty of Medicine, Department of Gastroenterology, Izmir, Turkey
[4]Dokuz Eylul University, Faculty of Medicine Department of Gastroenterology, Izmir, Turkey
[5]Dokuz Eylul University, Faculty of Medicine Department of General Surgery, Izmir, Turkey
[6]Memorial Hospital,Department of General Surgery, Istanbul, Turkey

Abstract

Aim: Liver transplantation is the only definitive treatment for end-stage liver disease. Graft rejection is also an important complication of LT due to its high economic burden. In this descriptive study, we aimed to evaluate clinical characteristics of liver transplanted patients, economic impact of acute graft rejection and identify factors associated with this complication

Materials and Methods: A total of 455 liver transplantations were performed between 1998 and 2016 in a University Hospital, in Turkey. Among these 455 patients, 43 patients with acute graft rejection which were documented histologically by using Banff Schema were selected for this study. The cost of hospitalization during graft rejection period were recorded as specific cost associated factors such as intensive care unit, dialysis, blood bank, laboratory, radiology, medications and medical equipment.

Results: The mean cost of acute graft rejection was 12423.74 USD (315.00-61236.94 USD). Most important components of the total cost were medications, laboratory and medical equipment. The cost of acute rejection was independent of United Network for Organ Share (UNOS) (p=0.928), Model for End-stage Liver Disease (MELD) (p=0.935) scores, type of donation (p=0.976), age (p=0.464) and gender (p=0.584) of the patient.

Conclusion: The cost of acute graft rejection is independent of the patients' characteristics and commonly used prognostic scores. The importance of this study is that it is the first study of cost analysis among liver transplanted patients with acute rejection in Turkey which are very rare studies throughout the world

Keywords: Liver transplantation; rejection; cost analysis

Öz

Amaç: Greft rejeksiyonu, yüksek ekonomik yükü nedeniyle karaciğer naklinin önemli bir komplikasyonudur. Bu çalışmada, karaciğer nakli yapılan hastaların klinik özelliklerini, akut greft reddinin ekonomik etkisini değerlendirmeyi ve bu komplikasyonla ilişkili faktörleri belirlemeyi amaçladık.

Gereç ve Yöntemler: 1998-2016 yılları arasında Türkiye'deki bir üniversite hastanesinde karaciğer nakli gerçekleştirilen 455 hasta arasından, Banff Şeması kullanılarak histolojik olarak belgelenmiş akut greft rejeksiyonu raporlanan 43 hasta retrospektif olarak değerlendirildi. Greft rejeksiyonu dönemindeki hastane yatış maliyeti; yoğun bakım ünitesi, diyaliz, kan bankası, laboratuvar, radyoloji, ilaçlar ve tıbbi malzemeler gibi spesifik maliyet faktörleri dikkate alınarak kaydedildi.

Bulgular: Akut greft rejeksiyonunun ortalama maliyeti 12423.74 USD (315.00-61.236.94 USD) olarak hesaplandı. Toplam maliyetin en önemli bileşenleri ilaçlar, laboratuvar hizmetleri ve tıbbi malzemelerdi. Akut rejeksiyon maliyeti, Birleşik Organ Paylaşım Ağı (UNOS) skoru (p=0.928), Son Dönem Karaciğer Hastalığı Modeli (MELD) skoru (p=0.935), donör tipi (p=0.976), hasta yaşı (p=0.464) ve cinsiyetinden (p=0.584) bağımsız bulundu.

Sonuç: Akut greft rejeksiyon maliyeti, hastaların demografik özelliklerinden ve sık kullanılan prognostik skorlardan bağımsızdır. Bu çalışmanın önemi, Türkiye'de akut karaciğer rejeksiyonu olan karaciğer nakilli hastalar arasında maliyet analizi yapan ilk çalışma olmasıdır. Dünyada da bu alandaki çalışmalar oldukça sınırlıdır.

Anahtar sözcükler: Karaciğer nakli; rejeksiyon; maliyet analizi

Corresponding Author: Funda Uğur Kantar
Bakırcay University, Faculty of Medicine, Department of Gastroenterology, Izmir, Turkey
E-mail: fundaugurkantar@yahoo.com
Geliş ve Kabul Tarihi: 10.03.2025/24.05.2025

INTRODUCTION

Liver transplantation (LT) is the only definitive treatment for end-stage liver disease. LT does not only provide long-term survival but it also increases the quality of life. One year survival rate is %85-90 and the 5-year survival rate is %70-80 (1). Despite improvements in immunosuppressive treatments, hepatic allograft rejection remains an important cause of morbidity and graft loss. Graft rejection is also an important complication of LT due to its high economic burden.

The cost of liver transplantation and its complications has been analyzed in different studies from different countries as economic issues are becoming more and more important in today's health care policy (2). But there are limited number of studies about acute graft rejection and cost analysis (3).

Acute graft rejection is still common after liver transplantation and the incidence ranges between 30-70% in different studies (4). Pathogenesis of acute rejection is not fully understood but it's believed to be due to recognition of donor alloantigen by recipient T lymphocytes. After this recognition and activation, T lymphocytes trigger a series of immune responses. At present, The Banff schema is accepted as diagnostic criteria, which is morphologically characterized by lymphocyte infiltration of portal tracts, bile duct damage and venous endothelial inflammation in portal and hepatic venules (5).

The diagnosis of allograft rejection requires evidence of graft dysfunction that is followed by allograft biopsy. Although liver histology remains the gold standard for diagnosis of graft rejection, there are some studies to find out simpler and faster ways to determine rejection without the need for liver biopsy. Serum concentrations of IL-9 (6), blood eosinophil count (7), pretransplant lymphocyte cross-matching results (8), vascular endothelial growth factor (9), recipient IL-28B polymorphism (10) and ingraft CXCL9 mRNA levels (11) have been suggested as indicators of hepatic allograft rejection with different results, but none of them suffice alone.

Several risk factors associated with graft rejection have also been evaluated and lower recipient age, fewer HLA-DR matches, cold ischemia time of at least 15 hours, transplantation due to autoimmune disease were found to be an important factor in development of graft rejection (12,13,14).

In this study, 43 patients who had acute graft rejection were enrolled. We aimed to evaluate clinical characteristics of liver transplanted patients, economic impact of acute graft rejection and identify factors associated with this complication

MATERIAL and METHODS

Ethical approval was obtained from the local ethics committee (21.09.2020-631). A total of 455 liver transplantations were performed between 1998 and 2016. Among these 455 patients, the ones with an episode of acute graft rejection which were documented histologically by using Rejection Activity Index by Banff Schema were selected for this retrospective study (15).

Age, gender, operation date, pre-operative creatinine values, United Network for Organ Share (UNOS), Child and Model for End-stage Liver Disease (MELD) scores before the operation were recorded. The etiology of liver disease, donor age, graft cold ischemia time and donation source either living or cadaveric were also involved.

The etiology of liver disease in these graft- rejection cases were recorded as hepatitis B virus (HBV), hepatitis D virus (HDV), hepatitis C virus (HCV), hepatocellular carcinoma (HCC), alcoholic cirrhosis, cryptogenic cirrhosis, fulminant liver failure, autoimmune hepatitis, Wilson's disease, Budd-Chiari, primary biliary cholangitis (PBC) and primary sclerosing cholangitis (PSC) and others.

Economic analysis: The economic analysis was performed by using data from the official medical cost chart system. The cost of the hospitalization during graft rejection period were recorded as specific cost associated factors such as intensive care unit, dialysis, blood bank, laboratory, radiology, medications and medical equipment. The physician discharges were not involved in the analysis. All charges determined were converted from TL to USD based on the exchange rate of that day.

Statistical analysis: All statistical analyses were conducted by Statistical Package for Social Sciences 23.0 (SPSS 23.0, Chicago, IL, USA) statistical package program. Descriptive statistics were represented by frequencies and percentages for categorical variables, by means and standard deviations for continuous variables.

Median values and inter quartile ranges were calculated for hospital stay days, and the medians were compared by non-parametric tests (Kruskal-Wallis test).

Multivariate analysis of cost factors was calculated with regression analysis. "P" value less than 0.05 was considered statistically significant.

RESULTS

Demographic Data of All Transplanted Patients: Between 1998 and 2016, 455 patients had liver transplantation. The mean age of the patients was 44.03±13.41 years (2-66 years).

The number of female and male patients were 142 and 313 (31.2 %; 68.8 %) respectively. The number of cadaveric transplantations was 206 (45.3%), and living donor transplantation was 249 (54.7%)

The indications for orthotopic liver transplantation (OLT) were HBV (n=85; 18.6%), HDV (n=90; 19,7%), HCV (n=43; 9,4%), alcohol related cirrhosis (n=40;8,7%), autoimmune hepatitis (n=14; 3.1%), hepatocellular carcinoma (n=82; 18%), Wilson's disease (n=11; 2.4%), PBC and PSC (n=14; 3.1%), cryptogenic cirrhosis (n=39; 8.5%), fulminant liver failure (n=14; 3.1%), Budd-Chiarri (n=5; 1.1%), and others (n=18; 3.95%).

The mean MELD score was 16.11 ± 6,270 and Child score was 8,99 ± 2,172. The first, second- and third-year patient survival rates were 83.07%, 81.09% and 79.7% respectively. Most important factors for mortality were infections (38.3%), vascular complications (22.4%), biliary complications (3.7%), recurrent disease (10.3%) and others.

Post-transplant complications were also enrolled in this study. Most important complications were infections (n=63, 13.9%), allograft rejection (n=43, 9.5%), vascular problems (n=26, 5.7%), gastrointestinal bleeding (n=10, 2.2%), biliary stricture (n=28, 6.3%), biliary leakage (n=13, 2.8%) and others.

Patients with Allograft Rejection: Among the 455 patients, 43 experienced acute graft rejection as a complication following liver transplantation. Notably, three of these patients underwent re-transplantation and developed acute graft rejection after each procedure.

As a result, a total of 46 episodes of acute graft rejection were included in the study. These patients were evaluated according to their disease activity before transplantation.

The indication of liver transplantation in these patients were HBV (n=4), HCV (n=7), HDV (n=9), alcohol related cirrhosis (n=5), cryptogenic (n=3), fulminant (n=4), autoimmune (n=1), Budd-Chiari (n=3), PSC (n=3) and the others (n=7) (Table 1).

UNOS scores of these patients were 1 in 4 patients (8.7%), 2 in 8 patients (17.4%), 3 in 34 patients (73.9%). 6 patients were Child A (13%), 22 patients were Child B (47.8%), 18 patients were Child C (39.1%). The mean MELD score was 17.58±8.3 (range 4-41) (Table-2).

The mean age of the patients was 43,71±15,41 (range 7-64) including 15 male (32,6%) and 31 female (67.4%). 27 patients (58.7%) had living donor liver transplantation whereas 19 (41.3%) had deceased liver transplantation. The length of hospital stay during the rejection period was 24.58 ± 30.17; 16 (1–154) (Table 2).

Table 1. Indications of liver transplantation in patients with graft rejection

Etiology	Liver Transplanted n (%)
HBV	4 (8.69%)
HCV	7 (15.21%)
HBV + HDV	9 (19.56%)
Cryptogenic	3 (6.52%)
Fulminant	4 (8.69%)
Autoimmune	1 (2.17%)
Budd-Chiari	3 (6.52%)
PSC Alcohol related cirrhosis	3 (6.52%) 5 (10.86%)
Others	
Hepatic arterial trombosis	2 (4.34%)
HBV+HCV	1 (2.17%)
Hemochromatosis	1 (2.17%)
Wilson	1 (2.17%)
HCC + HCV	1 (2.17%)
Cystic Fibrosis	1 (2.17%)
Total	46 (100%)

HBV: Hepatitis B Virus, HCV: Hepatitis C Virus, HDV: Hepatitis D Virus, PSC: Primary sclerosing cholangitis, HCC: Hepatocellular cancer

Table 2. The demographic and laboratory characteristics of the patients with graft rejection

Variables	Patients with Graft Rejection n=46
Age, Years	43.71 ± 15.41; 48 (7 – 64)
Female / Male	31/15
Length of hospital stay	24.58 ± 30.17; 16 (1 – 154)
MELD	17.58 ± 8.35; 16 (4 – 41)
Child-Pugh Score	
Class A	6 (13)
Class B	22 (47.8)
Class C	18 (39.1)
UNOS	
A	4 (8.7)
B	8 (17.4)
C	34 (73.9)
Donor age	36.06 ± 14.73; 33 (9 – 71)
Living donor / Cadaveric donor	27(58.7)/19 (41.3)
Ex / Alive	7 (15.2) / 39 (84.8)
Cost of rejection (American Dollars)	12423.74 (315.00 - 61236.94)

UNOS: United Network for Organ Share, MELD: Model for End-Stage Liver Disease Scores

We could not find any association between the duration of hospitalization and UNOS, CHILD, MELD, type of donation and time of transplantation (Table 3).

Among these patients, 7 patients died during follow up (3 of the patients died in the first year after transplantation and 4 after three years). We could not find any relation between mortalities and MELD scores (p=0.43), Child Pugh Scores (p=0.10), UNOS (p=0.713), cold ischemia time (p=0.052), age (p=0.99), and gender (p=0.54) of the patients.

Table 3. Length of hospital stay during rejection period according to clinical characteristics

	Hospital Stays (Days)			
	n	Median	IQR	p
UNOS				0.059
1	4	11.0	35.8	
2	8	26.5	14.8	
3	34	15.0	29.0	
Child Pugh Score				0.611
A	6	10.0	33.3	
B	22	14.5	29.0	
C	18	18.5	23.3	
MELD Score				0.779
0-10	6	13.5	29.8	
11-20	29	16.0	27.5	
21-30	6	27.0	25.5	
>30	5	7.0	35.5	
Donation				0.804
Live donor	27	16.0	24.0	
Cadaveric	19	15.0	27.0	

UNOS: United Network for Organ Share, MELD: Model for End-stage Liver Disease scores

Economic analysis: The mean cost of acute graft rejection was 12423.74 USD (Range 315.00-61236.94 USD). The most important components of the total cost were medications, laboratory and medical equipment (Table 4).

Table 4. Components of cost of rejection

	Cost (American Dollars)	%
Medications	116039.90	30.7
Laboratory	92798.09	24.5
Medical equipment	51665.92	13.7
Hospitalisation	32671.86	8.6
Blood products	24975.22	6.6
Radiology	24505.83	6.5
General expenses	17342.03	4.6
Intensive care	12370.06	3.3
Patology	5610.22	1.5
Total cost	377979.20	100

The cost of acute rejection was independent of UNOS (p:0.928), MELD (p:0.935) scores, type of donation (p:0.976), age (p:0.464) and gender (p:0.584) of the patient (Table 5).

Table 5. Factors affecting the cost of rejection (MELD, UNOS, Operation year, donation type, age, gender)

	β	95% CI		*p*
		Lower	Upper	
Variables				
MELD	202.03	-444179.10	47911.27	0.935
UNOS	-462.35	-10780.18	9855.48	0.928
Donation type	253.99	-16504.55	17012.53	0.976
Age	145.22	-252.17	542.62	0.464
Gender	3246.57	-8654.85	15148.00	0.584

Multiple linear regression analysis was used. β: Unstandardized regression coefficient; CI: Confidence interval; A *P* value of <0.05 was considered significant).

DISCUSSION

In this retrospective study, we evaluated the clinical characteristics of patients and economic impact of acute graft rejection in liver transplanted patients. Among 455 patients, 46 episodes of acute graft rejection were included in the study. Most of the studies in literature have addressed the overall cost of liver transplantation and found different contributing clinical factors.

In a study of Akarsu et al, cost of liver transplantation in Turkey was evaluated. All costs during the period of hospitalization were involved in the study except for the physician charges (16). The mean cost reached about 30823.61 USD. The highest expenses were for medications, medical equipment and laboratories like in our study. The patients with HBV and HCC, child B cirrhosis and living donor transplantation patients showed significantly higher cost than the others. When compared with the cost of liver transplantation in other countries, this cost is quite low, which may be attributed to the health policy of each country.

Another study from Japan investigated the cost of adult living donor liver transplantation (LDLT) in Japan and identified the factors associated with high cost. The median direct total cost for LDLT was 82,017 USD. The donor age, acute renal failure, post-transplant plasma exchange was found to be independent risk factors for the cost of LDLT (17). Oostenbrink et al. found that the mean cost of liver transplantation is 141510 Euro in Netherlands (18). In another study from Japan, the mean cost of liver transplantation was 97901 USD, and there was a significant correlation between MELD scores and medical expenses as well as length of stay in intensive care unit (19). Earl showed that the median overall cost of liver transplantation was 82936 USD. In addition to MELD, pretransplant intensive care unit hospitalization, age and BMI were other variables correlated with post-transplant cost (20).

Prolonged length of stay (PLOS) and its effect on cost of liver transplantation was also evaluated by Smith et al. and found out that PLOS following OLT was associated with significant decrease in survival and a marked increase in cost and resource utilization. Donor age, primary diagnosis of hepatitis C virus, in-hospital post-OLT bacterial infections and cardiac complications were associated with increased 1-year mortality (21). Advanced liver disease, post-operative cytomegalovirus (CMV infections, the requirement for additional operative procedures and biliary complications were other factors associated with the high cost of liver transplantation (22). Jay et.al. found an increased cost of deceased-donor transplantation due to the

increased rate of re-transplantation and reduced 3-year patient survival (23). One- and three-year survival was 82% and 71% for DCD (donation after cardiac death) compared to 86% and 77% for DBD (donation after brain death) recipients. They found that DCD recipients required re-transplantation more frequently (DCD14.7% versus DBD 6.8%, $p<0.001$), and re-transplantation survival was markedly inferior to survival after primary transplant irrespective of graft type (23). The major cause of morbidity in deceased donor transplants was found to be increased frequency of biliary complications, particularly ischemic cholangiopathy (24).

There are also some ways to reduce the cost of liver transplantation. Leong et al. searched for the CMV prophylaxis either with oral acyclovir or ganciclovir in terms of cost-effectiveness and found out that acyclovir was better than ganciclovir (25). Shimoda et al. analyzed cost effectiveness of biliary anastomosis with or without T-tube after orthotopic liver transplantation. The study suggested that choledochocholedochostomy without T-tube reconstruction was the preferred strategy for biliary reconstruction in orthotropic liver transplantation, since this method was associated with fewer biliary complications and lower cost (26).

The complications of liver transplantation have been studied in a limited number of studies. One of them is a study of Ammori et al, who reviewed the medical and financial records of 214 adult liver transplant recipients and evaluated the cost of complications. The infections (55%) and biliary complications (33%) were the most widely seen complications. Hospital costs were independently associated with MELD scores and the presence of pneumonia (27). In another study from a German Transplant center, specific cost drivers among 96 liver transplantation were explored. The median cost of orthotropic liver transplantation was 30,120 Euro. They showed that post-transplantation complications significantly raised the cost, with an increase of 62% by vascular complications, 175% by renal failure, 207% by biliary leakage, 227% by graft failure and 234% by sepsis. The additional cost of graft failure was 105,911Euro, which was the major cost-determining factor (28). In our study, we found that infections, biliary complications and graft failure were most widely seen complications after liver transplantation, which was compatible with the literature.

As seen in the previous study, graft failure is one of the post-transplantation complications with a very high economic burden. On the other hand, graft failure is becoming a more and more important issue due to the shortage of organ donors which do not meet the growing demand for liver transplantation. Our study did not find any significant relation between cost of acute rejection and common prognostic scores such as MELD, Child-Pugh, and UNOS scores, nor with demographic factors such as age, donor type and gender. This suggests that economic burden of rejection is not affected by baseline clinical parameters but rather by intensity of medical interventions. The median hospital stay during rejection period was 16 days, but we could not find a statistically significant relation between duration of hospitalization and transplantation related factors.

There are only a few studies evaluating cost of graft rejection in the literature. Most studies are about predictive factors or risk factors for acute rejection. In a study of Marzano, the average lifetime healthcare cost of LT for HBV-related disease was €395,986. The average cost of liver rejection was € 234 (€ 223-€ 243), which was only 0.1% of total cost. In this study, risk factors for rejection were not evaluated (29). Alves et al. showed that MELD score >18 and small graft size were important predictive factors for graft failure (30). Mugaanyi evaluated 27 patients with acute graft rejection after liver transplantation and found that warm ischemia time, cold ischemia time and chronic liver failure were potential risk factors for acute rejection (31). Preexisting diabetes has also been shown to reduce the post-liver transplant survival (32). Skaro et al. showed that recipients of DCD livers had a 2.1 times greater risk of graft failure, a 2.5 times greater risk of re-listing, and a 3.2 times greater risk of re-transplantation compared to DBD recipients (33).

What will be the cost of re-transplantation? Re-transplant patients have significantly longer hospital and intensive care unit stays with higher total hospital charges than those receiving only one transplant. Since long term survival rate is revealed to be significantly lower in re-transplanted patients compared with the survival rate following first transplantation, re-transplantation should be avoided in subgroups of patients who have little chance of success (34).

In our study, we did not find any factor increasing the risk of rejection. We also studied relation between the cost of rejection and the MELD score, UNOS, type of donation, age and sex of the patients, but we did not find any statistical association. The importance of our study is it is the first study from Turkey about cost analysis of graft rejection after liver transplantation.

Our study has several limitations. Firstly, our study is a single center retrospective study with limited number of acute graft rejection episodes.

Second, the study period is between 1998 to 2016, which may encompass different immune suppressive protocols. This heterojenity may affect both the incidence and cost of rejection. Third, the presence of comorbidities is not evaluated in the study. We evaluated the cost of rejection after liver transplantation and the factors affecting the cost. We could not identify any predictive factor correlated with cost of rejection. In our study, mean cost of acute graft rejection was 12423.74 USD, and mostly associated with medications, laboratory and medical equipments.

Our study highlights the need for preventive strategies, early detection and management methods in both clinical and financial consequences.

CONCLUSION

Future prospective multicenter studies with higher number of patients are needed for better understanding the predictors and economic impact of graft rejection, utilise the donor sources correctly, find and improve the factors increasing the graft survival and decrease the graft rejection rates.

Author's Contribution

The authors declare no conflict of interest.

The authors disclose that no grants or support resources were used.

All authors declared their contribution to the study at all stages and approved the final version of the manuscript.

All authors declared that this manuscript has not been published before and is not currently being considered for publication elsewhere.

REFERENCES

1. Verdonk RC, Van der Berg AP, Slooff MJ, Porte RJ, Haagsma EB. Liver transplantation: an update. Neth J Med. 2007;65:372-80.
2. Altınörs N, Haberal M. The economics of organ transplantation. Exp Clin Transplant. 2018;Suppl 1:108-11.
3. Martin JE, Fleck P, Schroeder TJ, Whiting JF, Hanto DW. The cost of rejection in liver allograft recipients. Transplant Proc. 1998;30:1500-1.
4. Cheng L, Tian F, Tang L, Wang S, Chen G, Duan G, et al. Local distribution analysis of cytotoxic molecules in liver allograft is helpful for the diagnosis of acute cellular rejection after orthotopic liver transplantation. Diagn Pathol. 2012;7:148.
5. Ormonde DG, de Boer WB, Kierath A, Bell R, Shilkin KB, House AK, et al. Acute rejection after liver transplantation: diagnostic use of histopathology. Liver Transpl Surg. 1999;5:261-8.
6. Fábrega E, López-Hoyos M, San Segundo D, Casafont F, Mieses MA, Sampedro B, et al. Serum levels of interleukin-9 during acute rejection in liver transplantation. Transplant Proc. 2012;44:1533-5.
7. Rodríguez-Perálvarez M, Germani G, Tsochatzis E, Rolando N, Luong TV, Dhillon AP, et al. Predicting severity and clinical course of acute rejection after liver transplantation using blood eosinophil count. Transpl Int. 2012;25:555-63.
8. Joo DJ, Ju MK, Huh KH, Kim MS, Choi GH, Choi JS, et al. Does lymphocyte cross-matching predict acute rejection and graft survival in liver transplantation? Transplant Proc. 2012;44:418-20.
9. Zhou TB, Yang GS. Roles of vascular endothelial growth factor in acute rejection reaction following liver transplantation. Transpl Immunol. 2011;25:207-9.
10. Bitetto D, Fabris C, Falleti E, Fornasiere E, Avellini C, Cmet S, et al. Recipient interleukin-28B Rs12979860 C/T polymorphism and acute cellular rejection after liver transplantation: the role of calcineurin inhibitor used. Transplantation. 2012;93:1038-44.
11. Asaoka T, Marubashi S, Kobayashi S, Hama N, Eguchi H, Takeda Y, et al. Ingraft transcriptome level of CXCL9 as biomarker of acute cellular rejection after liver transplantation. J Surg Res. 2012;178:1003-14.
12. Wang YC, Wu TJ, Wu TH, Lee CF, Chou HS, Chan KM, et al. The risk factors to predict acute rejection in liver transplantation. Transplant Proc. 2012;44:526-8.
13. Wiesner RH, Demetris AJ, Belle SH, Seaberg EC, Lake JR, Zetterman RK, et al. Acute hepatic allograft rejection: incidence, risk factors, and impact on outcome. Hepatology. 1998;28:638-45.
14. Neuberger J, Adams DH. What is the significance of acute liver allograft rejection? J Hepatol. 1998;29:143-50.
15. Demetris A, Batts K, Dhillon A, Wight D, Williams J, Yamabe H. Banff schema for grading liver allograft rejection: an international consensus document. Hepatology. 1997;25:658-63.
16. Akarsu M, Matur M, Karademir S, Unek T, Astarcıoğlu I. Cost analysis of liver transplantation in Turkey. Transplant Proc. 2011;43:3783-8.

17. Sakata H, Tamura S, Sugawara Y, Kokudo N. Cost analysis of adult-adult living donor liver transplantation in Tokyo University Hospital. J Hepatobiliary Pancreat Sci. 2011;18:184-9.
18. Oostenbrink JB, Kok ET, Verheul RM. A comparative study of resource use and costs of renal, liver and heart transplantation. Transpl Int. 2005;18:437-43.
19. Kogure T, Ueno Y, Kawagishi N, Kanno N, Yamagiwa Y, Fukushima K, et al. The model for end-stage liver disease score is useful for predicting economic outcomes in adult cases of living donor liver transplantation. J Gastroenterol. 2006;41:1005-10.
20. Earl TM, Cooil B, Rubin JE, Chari RS. Cost prediction in liver transplantation using pretransplant donor and recipient characteristics. Transplantation. 2008;86:238-44.
21. Smith JO, Shiffman ML, Behnke M, Stravitz RT, Luketic VA, Sanyal AJ, et al. Incidence of prolonged length of stay after orthotopic liver transplantation and its influence on outcomes. Liver Transpl. 2009;15:273-9.
22. Taylor MC, Greig PD, Detsky AS, McLeod RS, Abdoh A, Krahn MD. Factors associated with the high cost of liver transplantation in adults. Can J Surg. 2002;45:425-34.
23. Jay C, Ladner D, Wang E, Lyuksemburg V, Kang R, Chang Y, et al. A comprehensive risk assessment of mortality following donation after cardiac death liver transplant: an analysis of the national registry. J Hepatol. 2011;55:808-13.
24. Jay CL, Lyuksemburg V, Kang R, Preczewski L, Stroupe K, Holl JR, et al. The increased costs of donation after cardiac death liver transplantation: caveat emptor. Ann Surg. 2010;251:743-8.
25. Leong RW, Smith DW, Garas G, Beaman JM, Mitchell AW, Heath DI, et al. Aciclovir or ganciclovir universal prophylaxis of cytomegalovirus infection in liver transplantation: an economic analysis. Intern Med J. 2004;34:410-5.
26. Shimoda M, Saab S, Morrisey M, Ghobrial RM, Farmer DG, Chen P, et al. A cost-effectiveness analysis of biliary anastomosis with or without T-tube after orthotopic liver transplantation. Am J Transplant. 2001;1:157-61.
27. Ammori JB, Pelletier SJ, Lynch R, Cohn J, Ads Y, Campbell DA, et al. Incremental costs of post-liver transplantation complications. J Am Coll Surg. 2008;206:89-95.
28. Lock J, Reinhold T, Bloch A, Malinowski M, Schmidt SC, Neuhaus P, et al. The cost of graft failure and other severe complications after liver transplantation: experience from a German Transplant Center. Ann Transplant. 2010;15:11-8.
29. Marzano A, Canali B, De Carlis L, De Simone P, Fiorentino F, Rendina M, et al. Estimation of lifetime costs for patients receiving a transplant: the case of liver transplantation related to hepatitis B in Italy. Front Public Health. 2024;12:1328782.
30. Alves RC, Fonseca EA, Mattos CA, Abdalla S, Gonçalves JE, Waisberg J. Predictive factors of early graft loss in living donor liver transplantation. Arq Gastroenterol. 2012;49: 157-61.
31. Mugaanyi J, Tong J, Lu C, Mao S, Huang J, Lu C. Risk factors for acute rejection in liver transplantation and its impact on the outcomes of recipients. Transpl Immunol. 2023;76: 101767.
32. Yoo HY, Thuluvath PJ. The effect of insulin-dependent diabetes mellitus on outcome of liver transplantation. Transplantation. 2002;74: 1007-12.
33. Skaro AI, Jay CL, Baker TB, Wang E, Pasricha S, Lyuksemburg V, et al. The impact of ischemic cholangiopathy in liver transplantation using donors after cardiac death: the untold story. Surgery. 2009;146:543-52.
34. Azoulay D, Linhares MM, Huguet E, Delvart V, Castaing D, Adam R, et al. Decision for retransplantation of the liver: an experience and cost-based analysis. Ann Surg. 2002;236:713-21.