



Effect of donor graft hepatosteatosis on postoperative complications in adult living donor liver transplant recipients

Donör graft hepatosteatozunun yetişkin canlı donör karaciğer nakli alıcılarında ameliyat sonrası komplikasyonlara etkisi

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Background and Aims: Steatosis is one of today's important and common donor liver problems, affecting graft function to varying degrees and leading to marginal graft failure. We examined the effect of graft steatosis on postoperative complications, in our study. **Material and Methods:** One hundred forty eight donors and adult living donor liver transplant recipients who underwent transplantation were included in the study. The numbers and rates of perioperative blood product transfusion, postoperative biliary complications, hepatic vein thrombosis, portal vein thrombosis, postoperative bleeding, sepsis and primary graft dysfunction were analyzed statistically. **Results:** Early postoperative intra-abdominal bleeding was observed to be more common in fatty grafts, with a rate of 10.5%, than in non-fat grafts, with a rate of 4.5%. There was no statistically significant difference between those with and without donor graft steatosis. **Conclusion:** Although not statistically significant, the high rate of postoperative intra-abdominal bleeding in fatty grafts may be an important finding.

Key words: Liver, graft, steatozis, transplantation, donor

Giriş ve Amaç: Steatoz, greft fonksiyonunu değişen derecelerde etkileyen ve marjinal greft yetmezliğine neden olan günümüzün önemli ve yaygın donör karaciğer problemlerinden biridir. Çalışmamızda, greft steatozunun postoperatif komplikasyonlara etkisini inceledik. **Gereç ve Yöntem:** Çalışmaya 148 donör ve transplantasyon yapılan yetişkin canlı donör karaciğer nakli alıcısı dahil edildi. Perioperatif kan ürünü transfüzyonu, postoperatif safra komplikasyonları, hepatic ven trombozu, portal ven trombozu, postoperatif kanama, sepsis ve primer greft disfonksiyonu sayıları ve oranları istatistiksel olarak analiz edildi. **Bulgular:** Ameliyat sonrası erken dönemde intraabdominal kanamanın yağlı greftlerde oran olarak, yağsız greftlere göre daha sık olduğu görüldü. Donör greft steatozu olan ve olmayanlar arasında tüm parametreler açısından istatistiksel olarak anlamlı fark yoktu. **Sonuç:** İstatistiksel olarak anlamlı olmasa da yağlı greftlerde ameliyat sonrası intraabdominal kanama oranının yüksek olması önemli bir bulgu olabilir.

Anahtar kelimeler: Karaciğer, greft, steatoz, transplantasyon, donör

INTRODUCTION

Steatosis is one of today's important and common donor liver problems, affecting graft function to varying degrees and leading to marginal graft failure. The rate of graft steatosis can be classified as mild (5 - 10%), moderate (10 - 20%), and severe

(> 20%) (1). Hepatocyte necrosis and inflammation caused by steatosis in the donor liver may pose a risk for graft function in the recipient (2). Although the benefit from transplantation varies depending on the The Model for End-Stage Liver Disease

(MELD) score and ischemia times, post-transplantation outcomes may be worse in implanted grafts especially with > 30% steatosis (3).

Perioperative blood transfusion requirement in the recipient, postoperative vascular and biliary complications, and sepsis rates have been evaluated in many studies in terms of the effect of graft hepatosteatosis.

There is heterogeneity in both significant and insignificant results regarding the effect of a fatty graft on these complications and infections (1,4,5).

In our study, we examined the effect of graft steatosis on postoperative complications.

MATERIAL and METHODS

The data of the patients were examined retrospectively. The study included 197 donors and adult (18 years and older) living donor liver transplant recipients who underwent transplantation between July 2021 and July 2023. The operations were performed by a single surgical team. The graft steatosis rates of donors were calculated on routine non-contrast abdominal computed tomography (CT). The average age and gender characteristics of the recipients were examined as numbers and ratios. MELD and Child score averages and etiological factors were stated in the study. The numbers and rates of perioperative blood product transfusion, postoperative biliary complications (leak and stenosis), hepatic vein thrombosis (HVT), portal vein thrombosis (PVT), postoperative bleeding, sepsis and primary graft dysfunction (PGD) were analyzed.

These parameters were analyzed statistically between those with and without fat and then according to the rates of 5 - 10%, 10 - 20% and 20 - 30%, and > 30 graft fat.

Additionally, the effect of steatosis on graft survival was examined statistically. All procedures were

conducted in accordance with the ethical standards of the committees concerned with human experimentation (institutional and national) and the 1964 Declaration of Helsinki and its later editions. This study was approved by the İstanbul Aydın University Human Experiments Ethics Committee with an ethics committee decision number 2023/115 on the date 10.4.2023.

Determination of Hepatosteatosis Rate and Surgery Decision in Donors

The density measurement from the liver parenchyma, the difference between liver and spleen density, and the spleen-liver ratio were used to diagnose and grade liver steatosis in the non-contrast computer tomography (CT) examination. In the non-contrast CT examination, the density of the normal liver parenchyma was approximately 50 - 57 Hounsfield units (HU), and it was considered to be approximately 8 - 10 HU higher than the spleen density.

Those with a liver density below 50 HU in the non-contrast examination were considered to have a fatty liver. Those with a liver density of 48 - 50 HU were considered as 5% - 10%, those between 45 - 48 HU as 10 - 20%, those between 40 - 45 HU as 20 - 30%, those with < 40 HU as > 30%, those with 30 - 40 HU as approximately > 50% steatosis.

Additionally, a liver-spleen ratio below 1.1 or a difference of less than 10 HU between the liver and spleen was considered to be at least moderate steatosis (6,7).

Donors with up to 20% graft steatosis were taken into surgery. For donors with steatosis between 20% and 30%, a weight loss and diet program was implemented under the supervision of a dietitian, while those with over 30% steatosis underwent medical treatment, and at the end of the treatment, fat measurement was performed with CT. If the steatosis rate fell below 20% based on this measurement, they were taken into surgery. The transplant surgery was performed by the same team.

Statistical Analysis

Nominal and ordinal parameters were defined with frequency analysis, whereas scale parameters were defined with means and standard deviations. The Chi-Square Test and Chi-Square Likelihood tests were used for differences between categorical parameters. The Kolmogorov-Smirnov test was used for the normality of scale parameters. The Mann-Whitney U test was used for difference analysis, since distributions were non-normal. Spearman's rho correlation and Cox Regression tests were used for relational analysis. SPSS 17.0 for Windows was used at 95% Confidence Interval. When referring to SPSS versions prior to the IBM acquisition, authors should cite SPSS Statistics for Windows, version 17.0 (SPSS Inc., Chicago, 3., USA).

RESULTS

The number of patients with hepatosteatosis was 54 (%27). Among them, 39 (%72) patients had less than 10% steatosis, 9 (%17) patients had steatosis between 10 - 20%, and 6 patients (%11) had steatosis of between 20-30%.

The average age of all patients was 53.5 (range: 18 - 78). Forty-six percent of the patients were female, and 54% were male. Twenty-four percent of the patients were Child A, 47% were Child B, and 29% were Child C. The rate of implanting fatty grafts in Child A patients was 25%, in Child B patients was 45%, and in Child C patients was 30%. The average MELD score was 16.2. The average MELD score in fatty grafts was 16.1. Among the known etiological factors for all recipients, the most com-

Table 1 The demographic and clinical data in patients with hepatosteatosis

Hepatosteatosis	Donor No Steatosis (n: 143) % (n)	Donor Hepatosteatosis (n: 54) % (n)
Age	54.4	52.3
Gender		
• Female	%48 (68)	%27 (20)
• Male	%52 (75)	%63 (34)
MELD	16.3	16.1
Anhepatic phase [minute] (std. dev.)/(interval)	86.7 (+ 33.2) / (73.5 - 96.4)	82.9 (+ 35) / (78.6 - 88.1)
Cold ischemia time [minute] (std. dev.)/(interval)	58.7 (+ 24.2) / (50.2 - 61.2)	57.7 (+ 27.6) / (54.2 - 64.4)
Operation time [minute] (std. dev.)/(interval)	481.4 (+ 79.4) / (437 - 525)	480.6 (+ 78.4) / (450 - 515)
Child		
• A	%21 (31)	%25 (13)
• B	%51 (72)	%45 (24)
• C	%28 (40)	%30 (17)
Etiology		Total
• HBV		%22 (44)
• HCC		%18 (35)
• NASH		%15 (30)
• HBV+HDV		%4 (8)
• Budd-Chiari		%2 (4)
• Others		%16 (31)
• Cryptogenic		%23 (45)

Other etiologies: Autoimmune hepatitis, alcohol, familial cholestasis, primary hyperoxaluria, hemochromatosis, Wilson's disease, and Hepatitis C virus. HBV: Hepatitis B Virus; HCC: Hepatocellular carcinoma; NASH: Nonalcoholicsteatohepatitis; HDV: Hepatitis D virus.

mon was hepatitis B virus (HBV) with 22%, hepatocellular carcinoma (HCC) in second place with 18%, and nonalcoholic steatohepatitis (NASH) in third place with 15%. Autoimmune hepatitis rate was 6%, the alcohol-related cirrhosis rate was 5%, the HBV+hepatitis D virus (HDV) rate was 4%, and the Budd-Chiari rate was 2%. Other known etiological factors included familial cholestasis, primary hyperoxaluria, hemochromatosis, Wilson's disease, and hepatitis C virus (HCV) rate of 1%. Twenty three percent of patients had cryptogenic cirrhosis. The cold ischemia time averaged 69.7 minutes, and the anhepatic phase duration averaged 86.1 minutes. In grafts with all degrees of steatosis, the average cold ischemia time was

57.7 minutes, and the anhepatic phase duration averaged 82.9 minutes. The average duration of surgery was 481.4 minutes in patients without hepatic steatosis and 480.6 minutes in those with hepatic steatosis. In grafts with 5% steatosis, the cold ischemia time was 60 minutes, and the anhepatic phase duration was 86.3 minutes. For grafts with 10% steatosis, the cold ischemia time was 44 minutes, and the anhepatic phase duration was 76 minutes. Grafts with 20% or more steatosis had a cold ischemia time of 79 minutes and an anhepatic phase duration of 67 minutes. However, due to insufficient sample size, statistical evaluation could not be performed. The demographic data as well as clinical features have been shown in Table 1.

Table 2 Results of perioperative blood transfusion and postoperative complications in liver recipients in terms of donor hepatosteatozsis

	Donor No Steatosis %/n (n: 143)	Donor Hepatosteatozsis %/n (n: 54)	P Value
Peroperative blood transfusion			
• Yes	%18.9 (27)	%27 (14)	0.283
• No	%81.1 (116)	%73 (40)	
Postoperative bile complication (stricture/leakage)			
• Yes	%21.7 (28)	%17.7 (9)	0.824
• No	%79.3 (115)	%82.3 (45)	
Postoperative early intraabdominal bleeding			
• Yes	%4.5 (7)	%10.5 (6)	0.160
• No	%95.5 (136)	%89.5 (48)	
Postoperative PVT			
• Yes	%2.8 (4)	%0 (0)	0.227
• No	%97.2 (139)	%100 (54)	
Postoperative HVT			
• Yes	%2.8 (84)	%0 (0)	0.483
• No	%97.2 (139)	%100 (54)	
Postoperative Sepsis			
• Yes	%13.3 (19)	%7.7 (4)	0.341
• No	%86.7 (124)	%92.3 (50)	
PGD			
• Yes	%1.4 (2)	%0 (0)	0.396
• No	%98.6 (141)	%100 (54)	

PVT: Portal vein thrombosis; HVT: Hepatic vein thrombosis; PGD: Primary graft dysfunction.

There was no statistically significant difference in perioperative blood product transfusion ($p = 0.283$) between those with and without donor graft steatosis. No statistical difference was observed in terms of postoperative biliary complications ($p = 0.824$), portal vein thrombosis (PVT) ($p = 0.227$), hepatic vein thrombosis (HVT) ($p = 0.483$), early postoperative bleeding ($p = 0.160$), sepsis ($p = 0.341$) and primary graft dysfunction (PGD) ($p = 0.396$) (Table 2). No postoperative hepatic artery thrombosis or insufficiency was detected in recipients.

However, although not statistically significant, the early postoperative intra-abdominal bleeding rate showed a proportional difference of 10.5% in fatty grafts compared to 4.5% in non-fat grafts. The

average patient follow-up period was 15.3 months (range: 14.1 - 16.5 months). It was observed that donor graft steatosis did not statistically affect graft survival ($p = 0.636$). Therefore, different steatosis rates could not be compared statistically with patients without graft steatosis. However, no statistical difference was observed in terms of postoperative complications, PGD, graft and patient survival between 5%, 10 - 20% and 20 - 30% graft steatosis rates ($p > 0.05$) (Table 3).

DISCUSSION

The recipient problems caused by fatty grafts have been researched for many years and are a popular topic, with different results both perioperative-

Table 3 Rates of peroperative blood transfusion and postoperative complications in liver recipients in terms of donor hepatosteatosis grade

Hepatosteatosis Grade (n: 54)	%5-10 (n: 39) % (n)	%10 - 20 (n :9) % (n)	%20 - 30 (n: 6) % (n)	P Value	
Peroperative blood transfusion					
• Yes	%15 (6)	%44 (4)	%0 (0)	> 0.05	
• No	%85 (33)	%56 (5)	%100 (6)		
Postoperative bile complication (stricture/leakage)					
• Yes	%25 (10)	%0 (0)	%17 (1)		
• No	%75 (29)	%100 (9)	%83 (5)		
Postoperative early intraabdominal bleeding					
• Yes	%5 (2)	%22 (2)	%0 (0)		
• No	%95 (37)	%78 (7)	%100 (6)		
Postoperative PVT					
• Yes	%0 (0)	%0 (0)	%0 (0)		
• No	%100 (39)	%100 (9)	%100 (6)		
Postoperative HVT					
• Yes	%0 (0)	%0 (0)	%0 (0)		
• No	%100 (39)	%100 (9)	%100 (6)		
Postoperative Sepsis					
• Yes	%2 (1)	%22 (2)	%0 (0)		
• No	%98 (38)	%78 (7)	%100 (6)		
PGD					
• Yes	%0 (0)	%0 (0)	%0 (0)		
• No	%100 (39)	%100 (9)	%100 (6)		

PVT: Portal vein thrombosis; HVT: Hepatic vein thrombosis; PGD: Primary graft dysfunction.

ly and postoperatively (1,2,4). When we examine these results, while in some studies it was observed that PGD, hepatic artery thrombosis (HAT) and bile complication rates increased with graft steatosis (5,8), in another group of studies, it can be said that there is no relationship between donor hepatosteatosis and early postoperative bleeding, PVT, HAT and biliary complications (1,9-12).

In other studies examining different steatosis rates such as < 10% and 10% - 20%, apart from those with and without steatosis, no significant difference was observed between the two groups in terms of HAT, PVT, postoperative bleeding and sepsis, and biliary complications (13).

It can also be said that the need for blood transfusion does not change with increasing graft fat content (11-13) and that graft fat has no effect on recipient infections (9,12).

In our study, 5%, 10 - 20% and 20 - 30% graft steatosis rates were determined separately in terms of perioperative blood product transfusion, postoperative complications such as bleeding, PVT, HAT, HVT, bile stenosis, bile leaks and sepsis- and in two groups: those with and without fat. No statistical difference was observed in the results evaluated in case.

However, the rate of early postoperative intra-abdominal bleeding was observed to be higher in fatty grafts (10.5%) than in non-fat grafts (4.5%).

Although there are studies showing that there is no relationship between graft survival and primary graft dysfunction and steatosis (9,11,12,14); in

one study, patient and graft survival decreased at > 15% steatosis (15), in another group of studies, PGD increased and patient survival was shortened at > 25% steatosis (16,17), in yet another study, it has been shown that PGD increases in patients with > 30% steatosis, and that graft survival decreases at > 60% steatosis (18).

In addition, it should be taken into consideration that > 40% steatosis shortens survival (19), while > 50% increases PGD (20). In the statistical analysis of our study in which 5%, 10 - 20% and 20 - 30% graft steatosis rates were evaluated separately, no significant difference was observed in terms of PGD and graft/patient survival. However, when these groups with steatosis rates ranging from 10% to 20% and 20% to 30% were compared with those without graft steatosis, they could not be statistically interpreted due to the insufficient number of patients.

Although the fatty graft-related postoperative complications and survival results in our study were not statistically significant, postoperative problems related to fatty grafts and the shortening of graft survival have been demonstrated in many studies. It is important to examine these results well in order to maximize the recipient's benefit from the graft.

Ethics Committee: *This study was approved by the İstanbul Aydın University Human Experiments Ethics Committee with an ethics committee decision number 2023/115 on the date 10.4.2023.*

Conflict of Interest: *There is no conflict of interest with any institution or person. No financial support was received.*

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