Comparison of Patients With and Without Anterior Sector Venous Drainage in Right Lobe Liver Transplantation From Live Donors in Terms of Complications, Rejections, and Graft Survival: Single-Center Experience

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ABSTRACT

Aim. The issue of performing an anastomosis of the anterior sector veins to the vena cava in living donor liver transplantation is still controversial. We aimed to research whether there was any difference in terms of complications, rejections, and graft survival between patients with and without anterior sector venous drainage to the vena cava.

Patients and Methods. Patients were retrospectively investigated for demographic data and ratio of graft needed to available graft weight. Donors had volumetric calculations and middle hepatic vein anterior sector drainage documented in detail.

Results. Seventy-three donors with middle hepatic vein drainage were included. Thirty-five had anterior sector venous drainage performed and 38 patients did not have drainage procedures performed. The incidence of general complications was higher in the group without anterior sector drainage (78.3% and $P = .002$). Biloma linked to bile leaks were observed in 8 patients without drainage (72.8%) and 3 patients with drainage (27.2%). Late acute rejection occurring during follow up after transplantation was identified in 28 patients (11.6%). Of these, 1 (14.3%) had anterior sector drainage and 6 (85.7%) were in the patient group without drainage ($P = .067$).

Conclusion. As a result of this study, for patients with grafts at the volume limit (graft weight to receiver weight ratio <0.8) and with congestion observed in the anterior sector after liver implantation and for patients with outflow problems identified on Doppler ultrasonography, anterior sector veins >5 mm should definitely be drained into the vena cava. Hence, both complication and rejection rates will reduce, and we can lengthen the graft, and thus patient, survival.

BECAUSE of cadaver limitations, in recent years the increase in living donor liver transplantation (LDLT) globally has reached noteworthy dimensions. Due to this, LDLTs have very difficult surgical margins for both the receiver and donor. This situation also leads to complications that may occur because of the use of small grafts. Along with the difficult surgical indications, some complications are unavoidable for both receiver and donor.

For receiver candidates, especially those with a high body mass index, it may not always be possible to find an appropriate donor with sufficient right liver graft volume (graft weight to receiver weight ratio >0.8). At this point, we need to be very careful when transplanting grafts with marginal volume. After implantation of liver grafts with this

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volume problem, it is necessary to ensure very good venous drainage. This is because even the smallest venous drainage disorder is known to cause small-for-size syndrome (SFSS) [1–7].

As a result, using computed tomography (CT) angiography taken of the donor in the preoperative period, transplant surgeons must determine in detail whether there are anterior sector veins emptying into the middle hepatic vein (MHV), and if present, how many and with what diameters. The surgeon must be prepared to drain these, otherwise catastrophic outcomes may be unavoidable.

In the literature, the necessity for anterior sector drainage in live right liver transplantation is well defined [8–10]. Lee et al [11] indicated that reconstruction is necessary when segment 5 or 8 veins are larger than 5 mm in diameter but also took into consideration liver graft size, congestion volume, and the technical feasibility of the reconstruction.

In our study, we aimed to compare complications, rejections, and graft survival for patient groups with and without anterior sector venous drainage during live right liver transplantation.

PATIENTS AND METHODS

The study included 240 patients older than 18 years with at least 6 months survival post-transplantation with LDLTs performed from June 2000 to June 2017 at Dokuz Eylül University, Faculty of Medicine, Department of General Surgery, Hepatopancreatobiliary Surgery and Liver Transplantation Unit. Patient files were retrospectively investigated. Transplant patients were investigated for age, sex, body mass index, underlying liver diseases, Child-Turcotte-Pugh score and model for end-stage liver disease scores, graft weight to standard liver volume ratio, cold ischemia duration, and the biochemical parameters of serum creatinine, sodium, total bilirubin, international normalized ratio (INR), and albumin levels before transplantation. All patients had hepatic artery anastomoses performed with the end-to-end anastomosis technique. Bile duct anastomosis was performed with duct-to-duct or Roux-en-Y hepaticojejunostomy. For immunosuppressive treatment, patients used tacrolimus and mycophenolate mofetil or cyclosporine and mycophenolate mofetil.

Our study retrospectively documented anterior sector veins draining to the MHV, their sizes, number, and diameters on CT angiography taken for appropriate graft and volumetry of donors.

After appropriate donors were found, during donor surgery, we determined the liver resection line so that the MHV remained in the donor. With CT we performed anterior sector venous drainage procedures for anterior sector veins with a diameter of 5 mm or larger draining to the MHV if the graft volume (graft weight to receiver weight <0.8) was marginal. In this way, anterior sector drainage requirements were noted in patients with marginal graft volume and preparations were made before surgery for materials to be used for drainage. Liver grafts without volume problems had vascular clamps placed on the anterior sector veins draining into the MHV and were examined to see if congestion on the liver surface formed or not. If congestion areas did not form or veins were <5 mm, drainage procedures were not performed.

Of 240 transplant patients, anterior sector drainage was performed for 35 patients and not performed for 38 patients. Cases that were decided to require anterior sector venous drainage for the right liver grafts had the anterior sector veins to be implanted joined with material of appropriate diameter and length on the back table (Fig 1). Later, after completing receiver hepatectomy, the liver surface was checked with Doppler ultrasonography (US) to determine whether there were congestion areas in the anterior sector after implantation of the graft liver into the receiver. If congested parenchymal areas were observed on the graft or if SFSS was possible, anterior sector drainage to the vena cava was performed immediately.

In the literature, many methods and materials are recommended for drainage of these veins [12–18]. For venous drainage, autologous, homologous, or synthetic material may be chosen [19]. At our center, for anterior sector vein implantations, composite grafts between the liver and vena cava using expanded polytetrafluoroethylene (ePTFE) (GORE-TEX, W.L. Gore & Associates Inc., Newark, DE, United States) stretch vascular graft or cadaveric iliac vein grafts, if available, for interposition with 6-0 prolene (Ethicon PROLENE, Antrim, UK) sutures were performed end-to-end and continuously (Fig 2). After vascular implantation, graft patency was assessed with intraoperative Doppler US (Fig 3). Because the graft opening remained open for the first 2 postoperative weeks to ensure sufficient liver growth, the receiver passed this critical period in a more reliable fashion. For this, postoperative graft patency was checked every day for the first week with Doppler US. All receiver patient groups using venous implantation for the graft were administered intraoperative 5000 IU heparin and then 2 weeks of daily low molecular weight heparin (Clexane 1 mg/kg twice per day). After transplantation, all receivers were discharged using antiplatelet treatment (aspirin 75 mg per day) for 3 months.

Statistical Analysis

Statistical analysis used SPSS 22.0 (IBM, Armonk, NY, United States) program for Windows. According to distribution of data with properties determined with measurable variables in the groups, median, minimum-maximum, mean, and standard deviation are presented. Countable variables were analyzed with the χ^2 test, while measurable variables were analyzed with the *t*-test if they had normal distribution and with the Mann-Whitney *U* statistic if they had non-normal distribution. Advanced analyses created a logistic regression model. Significance level was accepted as $P < .05$.

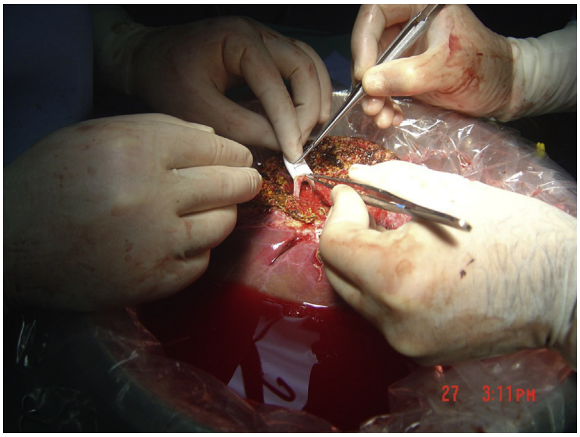

Fig 1. Joining anterior sector veins on the back table with appropriate diameter and length of ePTFE (GORE-TEX stretch vascular graft) material.

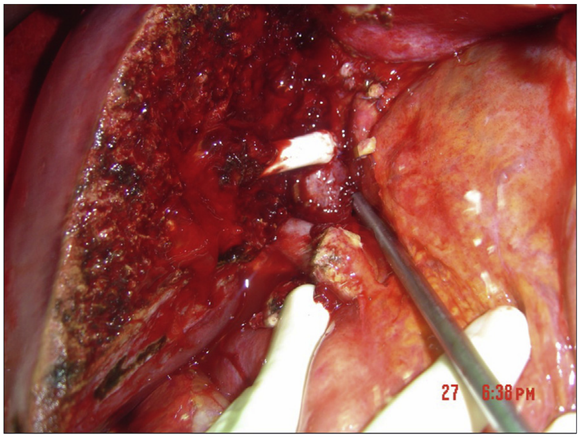

Fig 2. Implantation of anterior sector veins with ePTFE (GORE-TEX stretch vascular) graft and 6-0 prolene sutures to vena cava.

RESULTS

From June 2000 to June 2017, 580 liver transplants were performed in Dokuz Eylül University, Faculty of Medicine, Department of General Surgery, Hepatopancreatobiliary Surgery and Liver Transplantation Unit. Data from 240 patients with LDLT abiding by the inclusion criteria for the study (169 men [70.4%], 71 women [29.6%]) were included in the assessment. Mean age was 47.04 years (18–66 years), mean body mass index was 26.2 kg/m^2 (19.1–39.3 kg/m^2), mean graft weight was 782 g (552–1315 g), mean cold ischemia duration was 98.4 minutes (32–760 minutes), and mean follow-up duration was 3056 days (184–4877 days).

After investigating CT for radiologic and intraoperative assessment of 240 donors included in the study, 73 patients (30.41%) were observed to have anterior sector venous drainage into the MHV. During these 73 liver graft implantations, 35 patients with areas of congestion observed on the liver surface (47.9%) had anterior sector venous drainage to the vena cava performed (on reconstruction, 12 patients had cadaveric iliac vein grafts and 23 patients had 6–8 mm diameter ringed GORE-TEX vascular grafts used). The other 38 patients (52.1%) had both sufficient graft volume and anterior sector vein diameters <5 mm and did not have areas of congestion observed in the liver parenchyma during implantation, so anterior sector drainage procedures were not performed.

The incidence rate for general complications was higher in the group without anterior sector venous drainage to the vena cava (18 patients, 78.3%) compared with the group with venous drainage performed (5 patients, 21.7%). Biloma formation due to bile leak was observed at higher rates in the transplant patient group without drainage (72.8%). Late acute rejections occurring during follow up after transplantation was found in 6 patients without anterior sector drainage (85.7%) and in 1 patient with drainage performed ($P = .067$). Of those with ePTFE graft used for reconstruction, 1 patient had thrombosis on the second day with another having thrombosis on the sixth day. Graft survival was 92.62 months in the patient group with drainage and 83.61 months in the group without drainage ($P = .322$). The demographic data of transplant patients with and without anterior sector drainage performed are summarized in Table 1.

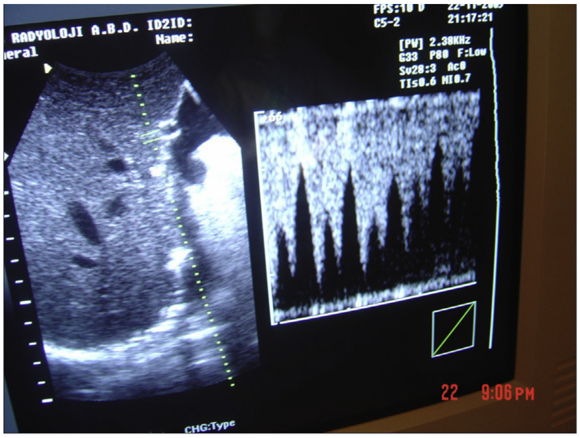

Fig 3. Graft patency assessment with intraoperative Doppler ultrasonography after vascular implantation.

DISCUSSION

In adult LDLT, right lobe grafts are usually used without the MHV for donor safety [20]. However, a right lobe graft without MHV may be associated with severe congestion, which may result in hepatic dysfunction and serious complications, including liver failure and sepsis [1].

The reasons anterior sector venous drainage is mandatory in right liver transplants from living donors when the MHV is left in the donor are, first, because the graft volume is marginal and, second, because a visible congestion area in the implanted liver graft and an outflow problem are identified with intraoperative Doppler US. Especially for the receiver, the importance of the necessity to perform anterior sector drainage for small-for-size grafts is increasing every day. In these patients, anterior sector venous drainage procedures prevent graft congestion and hence resolve dysfunction and allow more reliable use of grafts with marginal volumes. In these critical situations, anterior sector venous drainage into the MHV ensures drainage of the transplanted liver and allows more rapid regeneration of the graft in the critical early period after transplantation [4,12,16,21,22].

In the literature, there are many methods and grafts for anterior sector venous drainage. These are allogenic (autologous and homologous) or synthetic grafts. Autologous grafts may include the portal vein from the liver of the receiver (with the condition that hepatocellular carcinoma is not in the etiology of the receiver), saphenous vein, recanalized umbilical vein, internal jugular vein, omental vein, or any widened collateral vein. Homologous grafts are the internal jugular vein, ovarian vein, or inferior mesenteric vein taken from the same donor. Synthetic vascular grafts

Table 1. Demographic Data of Patients

	Anterior Sector Drainage (+) n = 35 (47.9%)	Anterior Sector Drainage (-) n = 38 (52.1%)	*P* Value
Age, mean ± SD, y	47.77 ± 12.11	46.36 ± 11.76	.614
Sex, No. (%)			
Male	25 (56.8)	19 (43.2)	.051
Female	10 (34.5)	19 (65.5)	
Complications, No. (%)	5 (21.7)	18 (78.3)	.002
Biloma	3 (27.2)	8 (72.8)	.122
Pneumonia	0 (0)	2 (100)	
Wound site infection	0 (0)	1 (100)	.067
Vascular complication (graft thrombosis)	2 (100)	0 (0)	
Late acute rejection	1 (14.3)	6 (85.7)	
Graft to recipient weight ratio <0.8, No. (%)	4 (66.6)	2 (33.4)	
Graft survival duration, mean ± SD, mo	92.62 ± 42.31	83.61 ± 35.37	.322
Ideal liver volume, mean ± SD, g	1.13 ± 0.29	1.09 ± 0.24	.608
Graft weight, mean ± SD, g	782.62 ± 162.45	785.78 ± 152.86	.601
Body mass index, mean ± SD, kg/m^2	25.47 ± 3.88	26.87 ± 4.17	.142
Etiology, No. (%)			
Hepatitis B	3 (60)	2 (40)	
Hepatitis B + hepatitis D	8 (40)	12 (60)	
Hepatitis C	3 (50)	3 (50)	
Hepatitis B + hepatitis D + hepatocellular carcinoma	2 (33.3)	4 (66.7)	
Hepatitis B + hepatocellular carcinoma	6 (54.5)	5 (45.5)	
Hepatitis C + hepatocellular carcinoma	4 (80)	1 (20)	
Cryptogenic	7 (44)	9 (56)	
Ethylism	1 (50)	1 (50)	
Fulminant hepatitis	0 (0)	1 (100)	
Wilson disease	1 (100)	0 (0)	
Child-Turcotte-Pugh score, No. (%)			
A	0 (0)	0 (0)	
B	4 (30.7)	9 (69.3)	
C	31 (51.6)	29 (48.4)	
MELD score, mean ± SD	15.17 ± 5.01	14.84 ± 6.5	
Acid, No. (%)			.409
None	9 (50)	9 (50)	
Controlled with medical treatment	8 (36.4)	14 (63.6)	
Present	18 (54.5)	15 (45.5)	
Preoperative laboratory values, mean ± SD			
Creatinine, mg/dL	0.82 ± 0.24	0.74 ± 0.20	
Total bilirubin, mg/dL	3.34 ± 3.6	3.89 ± 5.7	
INR	1.64 ± 0.44	1.66 ± 0.54	
Sodium, mmol/L	136.98 ± 4.46	135.6 ± 5.64	
Albumin, g/dL	2.95 ± 0.69	2.84 ± 0.61	

Abbreviations: INR, international normalized ratio; MELD, Model for End-Stage Liver Disease; SD, standard deviation.

include ePTFE graft (stretch vascular graft) or Dacron [23–32]. Chia-Yu et al [33] identified no significant differences among reconstruction procedures with these 3 materials in their study. We did not choose homologous grafts from the donors as donor safety is always the first priority for living donor right liver transplantation. If necessary during transplant and if cadaveric iliac vein graft was present in our cold storage, we primarily chose these every time. The cadaveric iliac vein grafts with a Y shape are more appropriate anatomically for patients with both segment 5 and segment 8 drainage required. Two veins can be joined to the vena cava with a single anastomosis (Fig 1). However, if there was no cadaveric graft, in spite of knowing the higher risk of thrombosis tendency [34], we chose to use ringed 6–8 mm diameter GORE-TEX grafts.

The selection of a graft material depends mainly on patency, especially short-term patency. Considering that rapid graft regeneration occurs during the first month, a patency duration of 2 weeks is enough for intrahepatic venous channels to open, thus avoiding critical congestion and achieving adequate graft function [35,36]. In accordance with the literature, we believe that if these reconstructions remain open for 1 to 2 weeks after the drainage procedure, this duration is long enough to complete sufficient and reliable regeneration of the transplanted liver graft [36].

In our study, we identified 73 patients that were emptying into the MHV on donor CT angiography. After implantation of the liver graft into the receiver, anterior sector venous drainage to the vena cava was performed for 35 patients (47.9%) with outflow problems identified on intraoperative Doppler US or with a visible congestion area in the liver parenchyma (for reconstruction, 12 patients had cadaveric iliac vein grafts and 23 patients had 6–8 mm diameter GORE-TEX vascular grafts). For the other 38 patients (52.1%), because both graft volume was sufficient and vein diameters were <5 mm and there were no congestion areas observed on the liver parenchyma during implantation, anterior sector venous drainage procedures were not performed.

The ideal liver graft weight ratio is accepted as >0.8 for LDLT (graft weight to receiver weight) [37–39]. If this is not the case, it is not surprising over time to encounter disruption of liver functions, development of SFSS, late acute rejections, graft loss, and even complications leading to loss of the receiver. As a result, especially in situations with marginal liver volumes, if there are anterior sector veins draining into the MHV, performing vena cava drainage significantly affects receiver survival. In our study, we performed anterior sector venous drainage in 4 of the 6 patients with graft weight to receiving weight <0.8 volume and did not encounter any complications during follow up. Of the other 2 patients without anterior sector drainage, 1 developed SFSS (INR elevated >3.3). The hospital stay for this patient after transplant was lengthened. The other patient developed biloma. Biloma was treated with drainage and antibiotic treatment. In accordance with the literature [38,39], the most important result obtained was that for patients with ideal graft weight ratio <0.8, drainage of anterior sector veins >5 mm should definitely be performed.

Some complications are unavoidable for grafts using anterior sector drainage. The most common graft complications are intraoperative hemorrhage, postoperative hematoma, seroma and biloma formation, thrombosis of the graft in the early period, and infections [40].

In our study, the most common complication was biloma in 11 patients (15%). The most common causes of biloma are bile leaks from the bile duct anastomosis or from the cut surface of the liver. When we assessed biloma formation in patient groups with and without anterior sector drainage, it appeared to occur at higher rates in patients without anterior sector drainage (72.8%), in accordance with the literature [7]. The most important cause is that there is congestion of the liver graft and development of dysfunction due to anterior sector veins without drainage. In both patient groups, patients with biloma development were treated with percutaneous drainage and discharged without problems. During follow-up, none of these 11 patients had recurrent bilomas, and none had bile anastomosis problems. These results show that bilomas occurring in our study have a higher possibility of being linked to bile leaks from the cut surface of the graft. Additionally, it must be stated that there were no features of the bile anastomosis in the 11 patients developing biloma. Of the 3 patients with anterior sector drainage, 2 had Roux-en-Y and 1 had duct-to-duct, while for the 8 patients without drainage, 6 had duct-to-duct and 2 had Roux-en-Y.

Two patients with anterior sector drainage had thrombosis of the graft used for reconstruction in the early period. Daily Doppler US checks of receivers after transplantation identified thrombosis of the grafts. There was no additional treatment intervention for graft thrombosis occurring on the second and sixth days. In both patients, 8 mm diameter ringed GORE-TEX grafts were used. The first patient with graft thrombosis on the second day had minimal elevation of liver function tests in the first 10 postoperative days. Marginal SFSS developed (INR elevated to 1.8). Additionally, during follow-up, this patient had increased liver function tests in the sixth month, and Tru-Cut biopsy was performed, and late acute rejection diagnosis was made. The patient was admitted to the hospital for rejection treatment. After 2 weeks of rejection treatment, the patient was discharged without problems. The second patient had graft thrombosis identified on a routine Doppler US check on the sixth day. The patient had a marginal elevation in the liver function tests during follow up; however, later these normalized, and the patient was discharged without problems.

As we all know, one of the most significant causes of mortality and morbidity in the long term after liver transplantation is late acute rejection. Late acute rejection is a clinical status with high morbidity and mortality, showing different histopathologic features compared with acute rejection and occurring after the sixth month with LDLT [41–44]. The incidence of late acute rejection observed more than 6 months after liver transplant is reported as 7% to 23% in the literature [45,46]. Acute rejection occurring in the late period is a clinical situation which is more difficult to treat because of delayed diagnosis compared with acute rejection and is linked to irregular routine checkups after liver transplantation. The most common causes of late acute rejection are insufficient immunosuppression treatment during the long-term follow up and lack of good regulation of immunosuppression treatment in infectious situations. In situations where infection forms in transplant patients, the patients should be closely monitored and even admitted to the hospital for treatment. Removal of the cause of infection or appropriate antibiotic selection for the vector has an important place in this process. If peritonitis or biloma due to intraabdominal bile leak are present in the transplant patient, antibiotic treatment alone may not be sufficient. It is necessary to perform drainage or reoperation procedures to remove the cause. In our study, 7 of 73 patients (9.5%) developed late acute rejection. Only 1 of these was in the group with anterior sector drainage, while 6 patients (85.7%) were in the group without drainage. Our rejection treatment protocol for patients developing late acute rejection is that the patient is isolated after admission to the hospital with pulse methylprednisolone administered for the first 2 days (15 mg/kg/day), 100 mg/day methylprednisolone begun on the third day, and this dose reduced every day by 10 mg to complete the rejection treatment process.

In LDLT, there are many factors affecting survival of liver grafts. Leading these are selection of appropriate graft with sufficient volume, good anesthesia and surgical technique, sufficient immunosuppression in the postoperative period, close patient surveillance, and good management and treatment of complications that occur.

In accordance with the literature [6], when liver graft survival was investigated in our study, it was longer in the transplant group with anterior sector venous drainage compared with the group without drainage (92.62 months and 83.61 months, respectively) ($P = .322$).

CONCLUSION

As a result of this study, for patients with marginal volume grafts (graft weight to receiver weight ratio <0.8) and with congestion areas observed in the anterior sector after liver implantation and outflow problems identified with Doppler US, anterior sector veins >5 mm should definitely be drained into the vena cava. Hence, both complication and rejection rates will reduce, and this will contribute to both graft and patient survival.

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