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Hepatic hemodynamics and portal flow modulation: The A2ALL experience

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Abstract

Objective—A principal aim of the Adult-to-Adult Living Donor Liver Transplantation Cohort Study was to study hepatic blood flow and effect of portal flow modulation on graft outcomes in the setting of increasing use of smaller and left lobe grafts.

Methods—Recipients of 274 living donor liver transplant were enrolled in A2ALL-2, including 233 (85.0%) right lobes, 40 (14.6%) left lobes, and 1 (0.5%) left lateral section. Hepatic hemodynamics were recorded after reperfusion. A total of 57 portal flow modulations were performed on 52 subjects.

Results—Modulation lowered portal pressure in 68% of subjects with inconsistent effects on hepatic arterial and portal flow. A higher rate of graft dysfunction was observed in modulated vs. unmodulated subjects (31% vs. 18%; $p=0.03$); however, graft survival in modulated subjects was not different from unmodulated subjects at 3 years.

Conclusions—These results suggest the need for a study using a prespecified portal flow modulation protocol with defined indications to better define the effects of these interventions.

INTRODUCTION

Despite excellent clinical outcomes, the use of living donor liver transplantation (LDLT) has been limited in North America and Europe, in contrast to Asian countries where LDLT is the principal liver transplant procedure¹. In the first phase of the Adult-to-Adult Living Donor Liver Transplantation Cohort Study (A2ALL-1, 2003–2010), the U.S. National Institutes of Health (NIH) funded a consortium of 9 North American LDLT transplant centers that demonstrated that LDLT offered superior outcomes for candidates for liver transplantation^{2,3}. Donor-recipient size matching is critical in LDLT due to the need for adequate functional liver mass in the recipient; a ratio of 0.8% ($100\% \times \text{graft weight(g)}/\text{recipient weight(g)}$) (GW/RW) has been posited as a safe lower limit for the recipient^{4–8}. Graft size at or below that threshold occurs in right lobe donation when the recipient is larger than the donor or when the left lobe or left lateral section is used as the graft for an adult recipient. Although lesser hepatectomies are thought to improve donor outcomes^{9,10}, a graft smaller than 0.8% has been associated with an increased risk of morbidity and graft loss^{4,11–14}. Functional failure of the small graft is manifested by impaired coagulation, cholestasis and ascites^{4,15}, and has been termed “small for size syndrome” (SFSS) and attributed to excess portal blood flow⁴. Based on this hypothesis, several investigators^{14,16–18} have demonstrated that a variety of techniques for portal modulation (reduction of excess portal blood flow) can improve outcomes in LDLT when a small graft is used.

Considering the scientific rationale and a growing body of clinical work establishing the ability of smaller grafts to be used successfully, a principal aim of A2ALL-2 (2011–2014) was to study hepatic hemodynamics and portal modulation prospectively in the multi-center consortium. The aims of this study were to measure hepatic hemodynamics in LDLT and describe the use of flow modulation in our centers. We sought to determine the effects of portal modulation on hepatic hemodynamics and clinical outcomes. Because of continued uncertainty about the optimal parameters for portal flow reduction, the study design was observational, considering variation among local center practices.

METHODS

Patient population

The A2ALL-2 study prospectively enrolled 274 recipients of LDLT between February 2011 and January 2014 from 9 North American transplant centers (6 continuing from A2ALL-1). All patients were enrolled at the time the donor was accepted for transplantation; donors were also offered enrollment. Baseline demographic and clinical data were collected at the time of enrollment. Detailed clinical data were collected prior to transplant, perioperatively and postoperatively with follow-up continuing through August 1, 2014.

Intraoperative data collection

In addition to variables related to graft and recipient anatomy and surgical technique, intraoperative hepatic hemodynamics were collected during the dissection on the native liver, after reperfusion upon completion of the portal vein and hepatic artery anastomoses, and following each surgical modulation. Portal pressures were measured with a needle inserted directly in the portal vein, and the trans-hepatic pressure gradient was derived from the difference between the free portal pressure and the central venous pressure at each time point. Portal and arterial flows were quantified using electro-magnetic flowmeters (Transonics system) applied to the vessels simultaneously and recorded with a 2-channel display. After application of the probes, flows were observed for several minutes until appropriate apposition of the vessel to the detector was assured and observed flows were seen to stabilize. After this point, standard 15-second paper recordings were saved with auto-calculation of min/max and mean flow rates for each channel. Measurements were repeated after each modulation.

Modulation interventions

Portal flow modulations were performed either before or after reperfusion based on local clinical practice. Three main surgical modulations were performed in the study. Splenic artery ligation (SAL) was performed as described by Troisi¹⁶ with a proximal ligation in the lesser sac. Splenectomy was performed when the effect of SAL was deemed insufficient. Portal-systemic shunts were performed in a side to side fashion using grafts between the portal vein and the vena cava as needed to optimize flow as described by Botha¹⁸. While most modulations were performed after reperfusion of the graft, prereperfusion modulations were performed in 19 subjects. The use of vasopressin or octreotide infusions was standard anesthetic management in most A2ALL centers, and was recorded but not considered in the analysis. Baseline use of these agents during anesthesia was not changed during the flow

measurements therefore, the changes in the recorded hemodynamics reflected the mechanical modulations only.

Clinical Outcome Measures

Clinical outcomes evaluated included early graft function, graft failure, and mortality. The occurrence of graft dysfunction was defined using criteria previously reported¹⁹ derived from A2ALL-1 data based on postoperative day 7 lab values. Graft failure was defined as the earlier of retransplant or death.

Analytical and statistical methods

Study subjects were followed from the time of transplant until death or last available follow-up. Descriptive statistics are given as mean and standard deviation (SD) or median, and interquartile range for continuous variables or as proportions for categorical variables. Comparisons were made between groups using t-tests and chi-squared tests for continuous and categorical variables, respectively.

We examined potential predictors of surgical modulation using logistic regression models. The outcome was the use of surgical modulation, and potential predictors included: left vs. right lobe graft, graft weight, GW/RW, pretransplant spleen volume, Model for End-stage Liver Disease (MELD) at transplant, recipient age, sex, race, and ethnicity, and donor age, sex, race, and ethnicity.

Changes in pressure and flow variables before and after postreperfusion surgical modulation were examined graphically and tested with paired t tests. Because of very high correlation between unclamped portal pressure and portal gradient ($r=0.77$, $p<0.001$), portal pressure was used for all analyses.

Unadjusted graft and patient survival were displayed using Kaplan-Meier survival curves comparing outcomes for patients with and without modulation. Differences in survival were tested using log-rank tests.

Statistical analyses were carried out using SAS version 9.4 (SAS Institute; Cary, NC). Results with a 2-sided p value ≤ 0.05 were considered statistically significant.

RESULTS

Description of the study population (Table 1)

Demographic and clinical data of the study population are presented in Table 1 grouped by whether a modulation was performed. Recipients had an average age of 52 (SD=12) years and 101/274 (37%) were female. Thirty-one percent of the recipients had hepatitis C virus infection and 23% had hepatocellular carcinoma. The mean lab MELD score was 16 (SD=6) with an interquartile range of 12–19. Of the 274 transplants, 233 (85%) used right lobes, 40 (15%) used left lobes, and 1 used a left lateral segment (<1%).

Portal flow modulations: (Table 2)

The series included 57 modulation procedures in 52 subjects. Of the 52 modulated subjects, 17 (33%) had modulation prior to reperfusion, 33 (63%) had modulation after reperfusion, and 2 (4%) had a modulation before and after reperfusion. The modulations included 34 SALs, 14 shunts, 8 splenectomies, and 1 collateral vein ligation. We collected reasons for performing modulation to examine clinical decision-making, with the option to select more than 1 reason. For all modulated subjects, the most common reason for modulation was elevated portal pressure reported in 56% of cases, followed by elevated portal flow in 42%. Portal gradient (21%), graft size (15%), and decreased arterial flow (8%) were less frequent indications for modulation.

Figure 1 demonstrates the utilization of grafts and modulation among the 9 A2ALL centers. The great variability of center-based practice patterns is illustrated by the variation in the use of left lobes, grafts less than 0.8% GW/RW and modulation. For example, 2 centers account for the great majority of left lobe grafts (76%) and grafts below 0.8% GW/RW (45%). Three centers performed no left lobes, and 27 of the 52 subjects (52%) who received modulation had GW/RW greater than 0.8%. Modulations were performed in 31 right lobe recipients (13%) and 21 left lobes (51%). In Figure 1A, cases are grouped by graft size (GW/BW). The 2 centers that used most of the left lobe grafts show most clearly the use of modulation is predominant in grafts below 0.8 GW/BW. However, many grafts in that size were not modulated. When plotted against hepatic artery flow, portal flow, or portal pressure (Figure 1B,C and D), no discernible pattern emerges distinguishing modulated subjects from the rest.

Portal hemodynamics before and after reperfusion

Scatterplots demonstrate the dramatic alterations in arterial flow, portal flow, and portal pressure that are observed before and after reperfusion (Figure 2). In general, the native cirrhotic liver has high arterial flow, relatively low portal flow, and high portal pressure, when compared to the graft postreperfusion. Postreperfusion, the soft graft accepts a much higher portal flow due to high compliance leading much lower hepatic artery flow consistent with the arterial buffer response²⁰. Postreperfusion hepatic arterial flow was lower than baseline in 90% of subjects (Figure 2; panel A). Consistent with the arterial buffer hypothesis, a strong inverse relationship was observed for portal vein flow, which increased markedly after reperfusion in the majority of subjects (Figure 2; panel B). In contrast, portal vein pressure was noted to fall markedly after reperfusion in most recipients (Figure 2; panel C), suggesting markedly higher compliance of the transplanted liver.

Comparison of portal and systemic hemodynamics in modulated and unmodulated subjects

Postreperfusion median hepatic arterial flow was significantly lower in modulated subjects compared to nonmodulated subjects (Table 3). Median portal vein flow was similar in unmodulated and modulated subjects. Portal vein pressure was lowest in unmodulated subjects and comparable in subjects modulated prior to reperfusion. Portal vein pressure was much higher in subjects in whom postreperfusion modulation was subsequently performed. No significant differences in systemic hemodynamics were observed among subject groups.

Effect of modulation on portal hemodynamics

The 4 panels of Figure 3 demonstrate the effect of modulation on portal hemodynamics for the subset of subjects for whom both pre and postmodulation measurements were obtained (n=23 modulations). In panel A, the expected postmodulation increase in hepatic arterial flow was observed in about 1/2 of the subjects. Portal vein flow decreased in 61% of subjects after modulation, but the most consistent changes were observed in portal vein pressure; all but 3 subjects had unchanged or lower portal vein pressure after modulation. Individual patient patterns for those with at least 2 measurements are depicted as hepatic arterial flow (panel B), portal vein flow (panel C), and portal vein pressure (panel D).

Effect of modulation type on hemodynamics, function and survival: (Table 4)

A description of effects by modulation type is presented though the numbers are too small for statistical comparison. Patients with SAL and splenectomy had comparable reductions in portal pressure ($-2.4/2.5$) while portal pressure was increased in the 2 subjects with repeated measures. Final portal flow was highest in the splenectomy patients and lowest in the shunt patients.

Graft dysfunction was most common in the SAL patients (42%) and occurred in a single splenectomy patient (13%). In contrast, mortality was 3% in SAL, 8% in shunt patients, and 0% in the splenectomy cases.

Factors predictive of modulation

Among all modulated subjects, left lobe graft, smaller GW/RW, higher spleen volume, and female donor were associated with the decision to perform modulation (Table 5). For those who underwent modulation after reperfusion, small GW/RW and higher portal pressure were significantly predictive.

Graft function and survival

A higher percentage of the modulated subjects experienced graft dysfunction compared to unmodulated subjects (31% vs. 18%, $p=0.03$). The increased incidence of graft dysfunction did not result in an increase in graft loss for the modulation group. Graft survival for the 2 groups is depicted in Figure 4. Survival at 2 years posttransplant was 90% for the modulated subjects and 81% for the unmodulated subjects ($p=.19$ by log rank test).

DISCUSSION

We present here the only multi-center study of hepatic hemodynamics and portal flow modulation for LDLT with the largest number of subjects in a single study. Our study design was observational and surgeon preference determined the timing and indication for modulation. Measurements of hepatic hemodynamics before and after reperfusion showed highly consistent results demonstrating low portal flow in cirrhosis and the effect of the arterial buffer response after reperfusion. Despite variability in center practice, portal flow, graft size, and use of the left lobe were significant predictors for the use of modulation among the sites. For subjects who were modulated based on pressure and flow parameters, portal pressure was lowered in 65% of subjects, with less consistent effects on portal and

arterial flow. Clinical outcomes were excellent with an overall graft survival of 90% observed among the modulated subjects at 2 years from transplant. While most of the modulation occurred in subjects below 0.8% GW/RW, several investigators modulated larger grafts, and there was substantial variability of practice among investigators in the approach in the face of abnormal portal perfusion. Although variability of practice was a limitation, our multicenter experience is more reflective of real-world experience than single center reports.

In the setting of portal overflow, adaptive responses in the liver lead to vasoconstriction of the hepatic artery, termed the “arterial buffer response”²⁰. While portal overflow injures the liver directly through nutrient excess,^{17,21,22} endothelial activation²¹, and sinusoidal shear stress^{19,23,24}, arterial vasoconstriction introduces secondary ischemic damage^{25,26}. Several lines of work indicate that these insults are attenuated by reduction of portal flow. Converse to the ischemic responses, attenuating portal flow increases arterial flow leading to improved graft function (our unpublished observations). Based on this research Boillot¹⁴, Troisi¹⁶ and others introduced portal flow reduction in clinical LDLT with improvement in clinical outcomes in small series of patients. In addition to removing these toxic effects, reduction of the portal flow results in increased arterial flow based on the arterial buffer response in the liver described by Lauth et al,²⁷ and observed clinically by Chan et al.²⁸ It is possible that portal overflow contributes to a paradoxical ischemic injury to the small liver ie, decreasing effective tissue perfusion despite the excess of sinusoidal flow. In any case, a wide variety of experimental work underlies the approach to portal modulation that has been accepted among those who are pursuing transplantation with smaller grafts.

The increased use of smaller grafts was a major aim in A2ALL-2, and the study of portal modulation was explicit in the design of the protocol. This required standardized monitoring of hepatic hemodynamics in the data collection protocol. In the early part of data collection, portal pressure and flow, and arterial flows were measured in the donor after graft dissection, and in the recipients during the dissection and after reperfusion. Arterial and portal flows were measured using electromagnetic probes that have been well validated in previous work^{29,30} including our own studies in portal hypertension³¹. Several limitations of this technology have been observed. First, there is inherent variability in the accuracy of the measurements, some due to the normal physiology of portal flow that may vary widely during the transplant surgery and is affected by local and systemic factors. Secondly, the instruments are sensitive to apposition of the detector to the vessel and the fluctuation of diameter of the vessels during the cardiac cycle, and due to the manipulations required to position the probes. In the current study, we used the newer detector that auto-calculates an integrated summation of flows over time rather than averaging single time points. Measurements were not possible in many subjects in the face of surgical challenges and patient instability in some of the cases. In 19 of the 52 subjects, the modulation was performed prior to implanting the graft to prevent any period of hyperperfusion after reperfusion. This approach precluded the ability to make baseline postreperfusion observations prior to modulation. Our data evaluating the effect of modulation is limited to 23 cases with measurements made both before and after modulation.

In the protocol design, we recognized that there was no consensus in the literature about indications for modulation and we observed variable responses to the hepatic hemodynamic measurements after reperfusion. Published portal pressure triggers for modulation range from 15 to 25 mmHg or else use a portal vein gradient greater than 15 mmHg^{32–34}. Other authors have emphasized portal flow; a cutoff of 250cc/min/100g of liver was proposed by Vasavada et al, in a recent publication³⁵. Alternatively, Sainz-Barriga et al, has proposed a subtler algorithm that considers portal and arterial flows, as well as systemic hemodynamics that might be factored into an overall interpretation of the hepatic stress in small for size grafting³³. Kaido et al, demonstrated improved outcomes in subjects in whom the pressure could be lowered to <15mmhg, advocating that target to optimize outcomes of smaller grafts³⁶. In a recent study of 649 recipients of LDLT, Alim et al, identified 43 subjects who received grafts with GW/BW<.0837. Using SAL in 5 subjects they achieved a 93% patient survival in that subset. It is likely that a multidimensional algorithm would be optimal but it will be hard to power such a model based on current data.

Though we did not have sufficient numbers to quantify center differences, center practices were examined (Figure 1), 2 main observations stood out. First, there was a variable use of left lobe grafts; only 2 centers transplanted a substantial proportion of left lobe grafts and 3 centers performed none. Three centers performed 66% of 76 grafts under 0.8% GW/RW. Center practice ranged from modulation of many large right lobe grafts (mostly prereperfusion) to selective modulation of even very small grafts. When we modeled the decision to modulate, we found that left lobe, graft size, and female gender were predictive of any modulation, while portal pressure and GW/BW were predictive of postreperfusion modulation. This is consistent with the idea that postreperfusion modulation is carried out based on operative findings and measurements, while prereperfusion modulations are based on surgical judgment and preconceived expectations of the surgeon regarding portal pressure.

There were substantial differences between baseline hepatic hemodynamic measurements in the cirrhotic liver and those obtained after reperfusion (Figure 2). In the cirrhotic liver, hepatic arterial flow is very high, while portal flow is impaired. Normal portal flow in the noncirrhotic liver is about 100cc/min/100gm of liver, while in our subjects, portal flows of as much as 4 liters per minute were recorded in the smallest grafts as small as 500gm. Overall, the findings are consistent with the arterial buffer hypothesis that there is an inverse relationship between portal and arterial flow. We were unable to replicate the relatively consistent effects of modulation on portal pressure, portal flow, and arterial flow described in previous single center reports. This is certainly due, in some measure, to variability of practice among A2ALL centers but also reflects the remarkable diversity of portal flow between subjects, even with comparable graft size or GW/RW. MELD and the severity of baseline portal hypertension have been proposed as predictors of the need for modulation but we did not observe this effect, however, it is possible that the subjects receiving prereperfusion modulations due to the surgeon's clinical impression of severe portal hypertension obscured this effect. Overall, the impact of portal modulation was most profound when portal pressure was used as the endpoint (Figure 3). We were unable to detect a differential effect of porto-systemic shunt vs. SAL and thus analyzed these together.

As noted earlier, pharmacologic reduction of portal flow during LDLT was used nearly routinely as an adjunctive therapy, and was not analyzed in this study.

When we examined the effects of modulation on the incidence of graft dysfunction (using the A2ALL definition¹⁹), we noted that the modulated livers had an increased incidence of graft dysfunction consistent with the high frequency of left lobes and small grafts in the modulated population. A predictive model for the development of graft dysfunction identified modulation, left lobe, bilirubin, and donor age as predictors. Our data do not exclude the possibility that modulation could be harmful in some or all subjects and that this could account for the increased rate of graft dysfunction although the graft survival was excellent with an overall graft survival of 90% at 2 years in the modulated cohort. Among the subset with GW/RW<0.8, graft survival at 2 years was 79% compared to 85% for those >0.8 (p=0.22). When compared by lobe, 2-year graft survival was 86% for left lobes and 82% for right lobes (p=0.56).

In summary, the A2ALL experience with modulation in a multi-center study demonstrates the wide variability of practice associated with the use of smaller grafts and the application of modulation. Consistent with predicted physiologic effects, modulation lowered portal pressure in nearly all subjects with reduction of portal flow in 63% of cases. Certainly, the increased risk of graft failure in the modulated subjects is of concern, yet this experience indicates that this phenomenon is transient and not associated with graft loss. Regrettably, the observational study design and the small sample of subjects with pre and postintervention measurements did not enable us to define the best approach for modulation, or the cutoff values for safe hepatic hemodynamics. The next step will require a cohort study testing the use of a defined modulation protocol in a series of small grafts to clarify the impact of hepatic hemodynamics at the limits of graft size.

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ABBREVIATIONS

A2ALL	Adult-to-Adult Living Donor Liver Transplantation
GW/RW	Graft weight(g)/recipient weight
LDLT	Living donor liver transplantation
MELD	Model for End-stage Liver Disease
NIH	National Institutes of Health
SAL	Splenic artery ligation
SD	Standard deviation
SFSS	Small for size syndrome

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Figure 1.

Use of modulation by center, lobe and: (A) graft to recipient weight ratio, (B) hepatic artery flow, (C) portal vein flow, (D) unclamped portal pressure. (Mod=portal flow modulation).

Figure 2.
Relationship between pre and postreperfusion hemodynamics by use of surgical modulation.
(A) hepatic artery flow measurements (B) portal vein flow measurements (C) portal vein pressure (unclamped) measurements.

Figure 3.

Effects of modulations on portal hemodynamics. In the bar graph (A) each bar represents the change in flow or pressure before and after a surgical modulation. Bars are ordered by the amount of change. The line graphs show the flow and pressure values for subjects across modulations for: hepatic artery flow (B), portal vein flow (C) and unclamped portal vein pressure (D).

Figure 4.
Graft survival by use of surgical modulation.

Table 1

Characteristics of study cohort

	No surgical modulation (n=222) Mean (s.d.) or n (%)	Surgical modulation (n=52) Mean (s.d.) or n (%)	p value
Recipient age	51.8 (11.4)	51.9 (14.2)	0.96
Recipient gender			0.49
Male	138 (62.1%)	35 (67.3%)	
Female	84 (37.8%)	17 (32.6%)	
Recipient race			0.25
Asian	11 (4.9%)	0 (0%)	
Black or African American	6 (2.7%)	0 (0%)	
White	200 (90.0%)	51 (98.0%)	
Multiracial	3 (1.3%)	0 (0%)	
Unknown	2 (0.9%)	1 (1.9%)	
Recipient ethnicity			0.76
Hispanic/Latino	14 (6.3%)	4 (7.6%)	
Nonhispanic/nonlatino	206 (92.7%)	47 (90.3%)	
Unknown	2 (0.9%)	1 (1.9%)	
Recipient height (m)	1.72 (0.10)	1.70 (0.12)	0.72
Recipient weight (kg)	78.2 (17.3)	80.0 (21.8)	0.57
HCV Diagnosis	71 (31.9%)	13 (25.0%)	0.33
HCC Diagnosis	54 (24.3%)	9 (17.3%)	0.28
Lab MELD	15.9 (6.2)	15.3 (5.5)	0.54
Donor age	36.0 (10.3)	37.7 (11.3)	0.31
Donor gender			0.007
Male	99 (44.5%)	13 (25.0%)	
Female	111 (50.0%)	37 (71.1%)	
Missing	12 (5.4%)	2 (3.8%)	
Donor race			0.70
American Indian	1 (0.4%)	. (.)	
Asian	7 (3.1%)	. (.)	
Black or African American	5 (2.2%)	1 (1.9%)	
White	185 (83.3%)	47 (90.3%)	
Multiracial	6 (2.7%)	2 (3.8%)	
Unknown	18 (8.1%)	2 (3.8%)	
Donor ethnicity			0.74
Hispanic/Latino	14 (6.3%)	4 (7.6%)	

	No surgical modulation (n=222) Mean (s.d.) or n (%)	Surgical modulation (n=52) Mean (s.d.) or n (%)	p value
Nonhispanic/nonlatino	192 (86.4%)	45 (86.5%)	
Unknown	16 (7.2%)	3 (5.7%)	
Donor height (m)	1.72 (0.20)	1.68 (0.10)	0.03
Donor weight (kg)	77.4 (15.0)	73.3 (11.7)	0.04
Graft type			<0.001
Right lobe	202 (90.9%)	31 (59.6%)	
Left lobe	19 (8.5%)	21 (40.3%)	
Left lateral segment	1 (0.4%)	. (.)	
Graft weight (gm)	782.4 (192.2)	636.9 (187.2)	<0.001
Graft to recipient weight ratio (%)	1.030 (0.288)	0.828 (0.274)	<0.001
Graft to recipient weight ratio <0.8%	51 (22.9%)	25 (48.0%)	<0.001
Use of vasopressin or octreotide	134 (60.3%)	36 (69.2%)	0.24

HCV = hepatitis C virus; HCC = hepatocellular carcinoma; MELD = model for end-stage liver disease.

Table 2

Details on surgical modulations (n=52 recipients with 57 surgical modulations)

Characteristic	n (%)
Number of subjects with modulation	52
Number of surgical modulations per subject	
1	47 (90.4%)
2	5 (9.6%)
Timing of surgical portal flow modulation(s)	
Prereperfusion only	17 (32.6%)
Pre and postreperfusion	2 (3.8%)
Postreperfusion only	33 (63.4%)
Type of surgical modulation performed	
Portocaval shunt	14 (26.9%)
Splenectomy	8 (15.3%)
Splenic artery ligation	34 (65.4%)
Collateral vein ligation	1 (1.9%)
Reason listed by investigator for performing surgical modulation *	
Graft size	8 (15.4%)
Portal pressure	29 (55.8%)
Gradient (portal pressure minus CVP)	11 (21.2%)
Portal flow	22 (42.3%)
Artery flow	4 (7.7%)

* More than 1 reason for modulation could be given so percentages add to more than 100%

Table 3

Postreperfusion portal and systemic hemodynamics by modulation status

Characteristic	Statistic	No modulation (n=222)	Prereperfusion modulation performed prior to measurement (n=17)	Postreperfusion modulation performed after measurement (n=35)	p value [*]
Hepatic artery flow (ml/min)	n	200	14	30	0.03
	Median (Q1–Q3)	123.0 (77.7–183.0)	71.8 (40.0–210.0)	82.0 (64.4–124.0)	
Portal vein flow (ml/min)	n	199	15	30	0.73
	Median (Q1–Q3)	1232.0 (840.0–1904.0)	1374.0 (1106.0–1994.0)	1193.0 (940.0–1884.0)	
Unclamped portal pressure (mmHg)	n	162	15	26	<0.001
	Median (Q1–Q3)	13.0 (10.0–16.0)	15.0 (10.0–18.0)	20.5 (15.0–24.0)	
Mean arterial pressure (mmHg)	n	214	17	34	0.77
	Median (Q1–Q3)	72.2 (66.0–79.0)	75.0 (66.0–77.0)	73.0 (65.0–76.0)	
Central venous pressure (mmHg)	n	215	17	34	0.18
	Median (Q1–Q3)	8.0 (6.0–11.0)	9.0 (9.0–12.0)	9.5 (6.0–11.0)	
Cardiac output (L/min)	n	161	13	20	0.14
	Median (Q1–Q3)	9.40 (8.00–11.50)	10.70 (9.90–14.20)	11.00 (7.05–12.90)	

* Nonparametric Kruskal–Wallis test for differences among the 3 modulation groups.

Table 4

Outcome measurements by surgical portal flow modulation type *

Result **		Splenic artery ligation (n=31)	Portocaval shunt (n=12)	Splenectomy (n=8)
Final portal pressure (open)	n	16	3	4
	Mean (std.)	16.3 (5.7)	21.7 (7.6)	12.3 (2.6)
Final portal flow	n	16	2	4
	Mean (std.)	1185 (525)	496 (93)	2045 (618)
Final arterial flow	n	16	2	3
	Mean (std.)	99 (80)	77 (3)	69 (64)
Change in portal pressure (open) ***	n	12	3	4
	Mean (std.)	-2.4 (3.6)	1.7 (4.5)	-2.5 (2.4)
Change in portal flow ***	n	15	2	4
	Mean (std.)	-259 (360)	238 (322)	51 (832)
Change in arterial flow ***	n	16	2	3
	Mean (std.)	22 (70)	-90 (34)	-12 (61)
GW/RW (%)	n	31	12	8
	Mean (std.)	0.8 (0.2)	0.7 (0.2)	0.9 (0.4)
Early allograft dysfunction	n (%)	13 (42%)	2 (17%)	1 (13%)
Graft failure within 90 days	n (%) ⁺	3 (10%)	1 (8%)	0 (0%)
Death within 90 days	n (%) ⁺	1 (3%)	1 (8%)	0 (0%)

* n=1 collateral vein ligation not included in table

** Results are for last modulation only in subjects with more than 1 modulation

*** For subjects with pre and postmodulation measurements

⁺ Based on Kaplan-Meier estimate

Table 5

Logistic models predicting portal vein modulation.

Model 1 uses any modulation as the outcome and baseline characteristics as covariates.

Model 2 uses postreperfusion modulation as the outcome and includes intraoperative measures and baseline characteristics as covariates. Covariate selection was informed by the method of best subsets.

Parameter	Estimate	Odds ratio	p value	95% Confidence interval
Model 1. Any modulation (pre or postreperfusion) (n=243, number of modulations=46)				
Left lobe or segment	1.59	4.9	0.001	1.8 – 13.1
GW/RW (per 1% increase)	−0.14	0.87	0.10	0.73 – 1.03
Female donor	1.27	3.6	0.003	1.6 – 8.1
Spleen volume (per 100cc)	0.10	1.11	0.004	1.03 – 1.18
Model 2. Postreperfusion modulation (n=203, number of modulations=26)				
Immediate postreperfusion unclamped portal pressure (per 1 mmHg increase)	0.16	1.18	<0.001	1.08 – 1.29
GW/RW (per 1% increase)	−0.42	0.66	<0.001	0.52 – 0.84

GW/RW = Graft weight (g) to recipient weight (g) ratio ($\times 100\%$)