PORTAL FLOW MODULATION IN LIVING DONOR LIVER TRANSPLANTATION

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Abstract

Background: Small-for-size syndrome is one of the major causes of graft dysfunction after living donor liver transplantation in adults. Excessive portal inflow leading to sinusoidal hyperperfusion and impaired graft function is the primary mechanism of this complication. Effective prevention requires not only morphometric evaluation of the graft but also strict control of portal hemodynamics. Aim of the study is evaluate the effectiveness of graft inflow modulation and determine the prognostic significance of graft-to-recipient weight ratio, spleen-to-graft volume ratio, portal venous flow, and portal venous pressure.

Materials and Methods: This study included adult patients who underwent living donor liver transplantation from 2011 to 2025. Portal hemodynamics was assessed intraoperatively. Graft inflow modulation was performed upon detection of portal hyperperfusion($p< 0.05$).

Results: Patients with small graft volume demonstrated elevated portal venous flow and pressure prior to intervention. Inflow modulation effectively reduced portal venous pressure to physiological levels and was associated with a lower incidence of small-for-size syndrome and reduced mortality. A spleen-to-graft volume ratio greater than 1.0 was linked to significant hyperperfusion and poorer clinical outcomes. Intraoperative modulation proved markedly more effective than delayed postoperative interventions, resulting in higher survival rates and an absence of severe graft dysfunction.

Conclusion: Excessive portal inflow is the key determinant of graft dysfunction in living donor liver transplantation. Timely intraoperative modulation of portal blood flow improves hemodynamic stability and enhances survival. A combined assessment of morphometric and hemodynamic parameters enables optimal prevention of small-for-size syndrome and supports a personalized transplantation approach.

Introduction

Living donor liver transplantation (LDLT) is one of the primary therapeutic approaches for end-stage chronic diffuse liver diseases and acute liver failure. However, the use of partial grafts, particularly in situations of graft-to-recipient size mismatch, is associated with the risk of developing small-for-size syndrome (SFSS)—a severe postoperative complication characterized by coagulopathy, cholestasis, ascites, and hepatic encephalopathy.[1,2,3]

The principal pathophysiological mechanism of SFSS is excessive portal inflow, which leads to graft overload, sinusoidal hyperperfusion, endothelial activation, and arterial vasoconstriction, ultimately resulting in impaired microcirculation and hepatocellular injury.[2,4]Elevated portal pressure and flow contribute to venous congestion, intrahepatic hemorrhages, and subsequent graft dysfunction.[5,6]

Post-transplant portal hypertension (PH) remains one of the most significant hemodynamic challenges following living donor liver transplantation (LDLT). Despite advancements in surgical techniques and improved donor selection, the risk of imbalance between portal inflow and the functional capacity of the graft persists in patients with a low graft-to-recipient weight ratio (GRWR < 0.8) and a high spleen-to-graft volume ratio (SVGVR > 1.0).[1,2,3]

Post-transplant portal hypertension may develop either as a consequence of excessive portal inflow in the setting of a small graft volume or due to persistent elevated splenorenal venous resistance in the recipient.[7,8]

Contemporary criteria for defining a small-for-size graft include a graft-to-recipient weight ratio (GRWR) of less than 0.8% or a graft volume-to-standard liver volume ratio (GV/SLV) of less than 40%.[3,9] However, numerous clinical observations indicate that the risk of SFSS is determined not only by graft size but also by portal hemodynamic characteristics and the efficiency of venous outflow.[4,10] Consequently, increasing attention has been directed toward the concept of "small-for-flow," which emphasizes that the key determinant is not the absolute graft size, but rather the balance between portal inflow and the functional capacity of the graft.[3,11]

Fernandes M. R. et al,[3] proposed revising the pathophysiological model by introducing the concept of "small-for-flow," which focuses not on the morphometric size of the graft but on the imbalance between portal inflow and the functional capacity of the transplanted liver. According to this concept, the key damaging factor is not the absolute graft mass but the excessive portal blood flow and pressure, which lead to sinusoidal hyperperfusion, endothelial injury, and subsequent arterial vasoconstriction (the hepatic arterial buffer response).[8,11]

Thus, even grafts with an adequate GRWR (>0.8) may develop hyperperfusion-related injury in the setting of excessive inflow from the splenoportal system—particularly in patients with pronounced splenomegaly and a high SVGVR (>1.0). [3,12]

The "small-for-flow" concept interprets SFSS as a consequence of a functional mismatch between portal hemodynamics and the sinusoidal perfusion reserve, rather than a purely "mass-related" problem. In this context, portal hyperperfusionis regarded as a "universal final pathway" of graft injury, regardless of graft size.[9]

Meta-analyses by *Law JH, et al* and *Gavriilidis P. et al.* have confirmed that portal pressure and flow parameters possess greater prognostic value for LDLT outcomes than GRWR, and that performing GIM even in the absence of overt hypertension reduces the risk of subclinical graft injury.[4,8]

Current strategies include both pharmacological (somatostatin) and surgical methods—ligation or embolization of the splenic artery (SAL, SAE), splenectomy, splenic devascularization, as well as shunting procedures.[12,13] Evidence from clinical studies indicates that timely portal inflow modulation contributes to reduced postoperative mortality, lower incidence of ascites, and accelerated functional recovery of the graft.[2,14]

A 2022 meta-analysis (25 studies) demonstrated that inflow modulation significantly reduces the incidence of SFSS and improves graft function.[8]

In the study by *Troisi RI. et al.,* the use of small grafts (GRWR < 0.8) combined with portal inflow modulation (splenectomy or splenic artery ligation) enabled outcomes comparable to those achieved with larger grafts.[15]

However, in a randomized trial by *Pamecha V, et al.*, splenic artery ligation did not demonstrate a statistically significant reduction in early graft dysfunction.[16]

Materials and Methods

This is an observational study with both prospective and retrospective components, including patients with end-stage liver disease who underwent treatment at the Department of Hepatopancreatobiliary Surgery and Liver Transplantation of the A.N. Syzganov National Scientific Center of Surgery over the period from 2011 to 2025.

From December 2011 to October 2025, a total of 342 liver transplantations were performed in adults and children at the A.N. Syzganov National Scientific Center of Surgery. Living donor liver transplantation was carried out in 311 patients (90.9%), including 51 pediatric recipients (16.3%), while deceased donor liver transplantation accounted for 31 cases (9.1%). The following graft types were utilized: right lobe — 237 (69.3%), left lobe — 27 (7.9%), posterior sector — 1 (0.3%), dual graft — 2 (0.6%), left lateral section — 44 (12.8%), whole liver — 30 (8.8%), and split transplantation — 1 (0.3%).

Portal inflow modulation during liv-

ing donor liver transplantation was performed in 33 cases (9.64%). Among them, intraoperative splenectomy was conducted in 9 patients (27.3%), postoperative splenectomy in 4 patients (12.1%), intraoperative splenic artery ligation in 19 patients (57.6%), and postoperative splenic artery embolization in 1 patient (3%). In patients who underwent portal inflow modulation, GRWR ranged from 0.5 to 1.1.

The aim of this study was to assess the effectiveness and indications for graft inflow modulation (GIM) in living donor liver transplantation, as well as to determine the impact of preoperative hemodynamic parameters (GRWR, SVGVR, MELD) on transplantation outcomes.

We analyzed the general clinical characteristics of the patients (age, sex, MELD-Na score, Child–Turcotte–Pugh class), operative parameters (graft weight, GRWR, SVGVR, portal venous flow volume, portometry results), and postoperative outcomes (bleeding and relaparotomy, length of hospital stay).

Inclusion criteria:

-Age 18 to 60 years

-Both male and female patients

-Undergoing portal inflow modulation

Exclusion criteria:

-Pediatric liver transplantation

-Deceased donor liver transplantation

Depending on morphometric and hemodynamic parameters, all patients were categorized into three main groups.

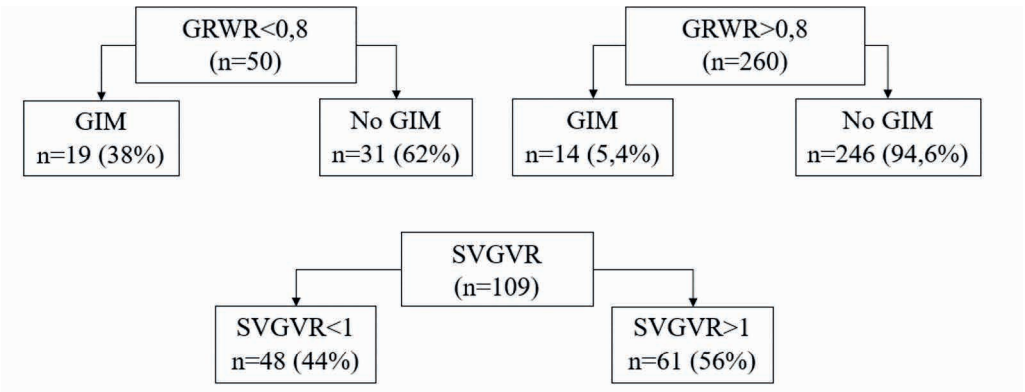

Figure 1.
Distribution of patients according to GRWR and SVGVR parameters

The first subgroup included recipients with a low graft-to-recipient weight ratio (GRWR < 0.8, n = 50). In this cohort, intraoperative graft inflow modulation (GIM) was performed in 19 patients (38%) to correct portal hyperperfusion and prevent small-for-size syndrome.

The second subgroup consisted of patients with an adequate graft-to-recipient weight ratio (GRWR > 0.8, n = 260). In this group, graft inflow modulation was also performed in 14 patients (5.4%) due to intraoperatively detected portal hypertension or elevated portal venous flow.

The third categorization was based on the spleen-to-graft volume ratio (SVGVR) and included 109 patients. Among them, 48 patients had SVGVR < 1, of whom 3 (6.3%) underwent GIM; and 61 patients had SVGVR > 1, where 19 patients (31.1%) required graft inflow modulation due to an increased risk of portal hyperperfusion.

This classification enabled a comparative analysis of the effects of morphometric parameters (GRWR, SVGVR) and the performance of GIM on hemodynamic characteristics and clinical outcomes of living donor liver transplantation (Figure 1).

Additionally, in three clinical cases, the need for graft inflow modulation arose during the postoperative period based on clinical and laboratory signs of portal hyperperfusion and graft dysfunction, manifested by increasing levels of hepatic transaminases, bilirubin, ascites formation, and impaired synthetic liver function.

In two cases, intraoperative splenic artery ligation (SAL) was performed, followed by early postoperative splenectomy due to persistent hyperperfusion and insufficient reduction of portal pressure after the primary procedure.

Portal venous flow was assessed intraoperatively using Doppler ultrasonographic portometry. Portal vein pressure was measured after graft reperfu-

sion and following the completion of GIM (when performed).

The graft inflow modulation (GIM) techniques applied in our study included:

- Splenicarteryligation (SAL)
- Splenectomy

Statistical analysis was performed using IBM SPSS Statistics version 26.0. Non-parametric tests (x^2 and Mann–Whitney) were used for group comparisons. A p-value ⩽ 0.05 wasconsidered-statistically significant.

Ethical approval: The clinical study protocol, the informed consent form,and the information sheet were approved by the Local Bioethics Committee of the A.N. Syzganov National Scientific Center of Surgery (Protocol of meeting №4. November 10, 2023).

Results

Table 1.
Hemodynamic parameters in patients with GRWR < 0.8 depending on GIM

GRWR<0.8			
Parameter	**GIM n = 19 (38%)**	**No GIM n = 31 (62%)**	**p-value**
Donorage, years	25.1 ± 4.3 (19–33)	25.0 ± 5.1 (18–36)	0.944
Recipientage, years	49.5 ± 8.2 (32–61)	50.1 ± 9.0 (30–65)	0.814
MELD	18.7 ± 3.2 (12–24)	17.9 ± 4.1 (11–25)	0.472
PVF before GIM (mL/min/100 g)	310 ± 58.4 (240–380)	221.5 ± 51.7 (150–290)	<0.0001*
PVP before GIM (mmHg)	20.3 ± 4.3 (15–26)	19.0 ± 3.8 (13–24)	0.269
PVF after GIM (mL/min/100 g)	237 ± 56.4 (170–310)	—	—
PVP after GIM (mmHg)	12 ± 2.5 (9–15)	—	—
SFSS, n (%)	1 (5.8%)	5 (17.9%)	0.783
Mortality, n (%)	1 (5.8%)	5 (17.9%)	0.783
* P value ⩽ 0.05 was considered statistically significant			

No significant differences were observed between the subgroups in donor and recipient age or in the severity of preoperative condition assessed by the MELD score (p > 0.05). This indicates that the study groups were comparable, with no preoperative bias that could influence the outcomes. The mean donor age was 25.1 ± 4.3 years in the GIM group and 25.0 ± 5.1 years in the non-GIM group, whereas the mean recipient age was 49.5 ± 8.2 years and 50.1 ± 9.0 years, respectively. The average MELD score in both subgroups ranged between 17 and 19 points, corresponding to moderate liver failure severity. (Table 1).

Before modulation, patients with GRWR < 0.8 in the GIM group demonstrated significantly higher portal venous flow (PVF)—310 ± 58.4 mL/min/100 g compared with 221.5 ± 51.7 mL/min/100 g in patients without modulation (p < 0.001). This difference reflects the presence of pronounced portal hyperperfusion caused by the mismatch between graft mass and portal venous inflow.

In the GIM group, significantly elevated portal venous flow (PVF before GIM) was recorded—310 ± 58.4 mL/min/100 g, which exceeded the values in the non-GIM group by nearly 40% (221.5 ± 51.7 mL/min/100 g; p < 0.001). This underscores the presence of pronounced portal hyperperfusion in patients with a "small graft."Following GIM, a marked reduction in portal hemodynamics was observed: PVF decreased to 237 ± 56.4 mL/min/100 g, and PVP decreased to 12 ± 2.5 mmH_2O, which corresponds to a physiological range for an adult liver graft.

After GIM:

- PVF decreased by 23.5%, reaching 237 ± 56.4 mL/min/100 g
- PVP decreased by 41%, to 12 ± 2.5 mmHg

Achieving a target PVP < 15 mmHg confirms the effectiveness of inflow modulation and meets international criteria for SFSS prevention.

The incidence of SFSS was:

- GIM group — 1 case (5.8%)
- Non-GIM group — 5 cases (17.9%)

Representing nearly a threefold reduction in complication risk (p = 0.24).

Mortality also demonstrated a favorable trend:

- GIM: 1 patient (5.8%)
- No GIM: 5 patients (17.9%)

Corresponding to a 67% reduction in mortality, although the difference has not yet reached statistical significance (p = 0.24).

Table 2.
Hemodynamic parameters in patients with GRWR > 0.8

GRWR>0.8			
Parameter	**GIM n = 14**	**No GIM n = 246**	**p-value**
Donorage, years	28.4 ± 6.8 (18–55)	28.4 ± 7.1 (18–55)	1.0
MELD	17.7 ± 5.2 (11–36)	17.1 ± 4.8 (6–36)	0.651
PVF before GIM (mL/min/100 g)	305.2 ± 80.7 (210–450)	233.6 ± 52.9 (150–330)	< 0.0001*
PVP before GIM (mmHg)	19 ± 4.2 (14–25)	12 ± 3.0 (8–19)	< 0.0001*
PVF after GIM (mL/min/100 g)	213.9 ± 31.8 (160–270)	—	—
PVP after GIM (mmHg)	12 ± 2.8 (9–15)	—	—
SVGVR	1.2 ± 0.4 (0.8–2.0)	1.0 ± 0.3 (0.6–1.6)	0.018*
SFSS, n (%)	1 (7.1 %)	-	-
Mean reduction values after GIM PVF — 22.1 ± 5.8%;and PVP — 7.0 ± 2.2 mmHg. * P value ⩽ 0.05 was considered statistically significant			

In the second group, the majority of recipients (n = 246, 94.6%) demonstrated portal venous flow (PVF) and pressure (PVP) values within the physiological range, which did not require inflow modulation. In this subgroup, no cases of SFSS or mortality were recorded, consistent with a stable hemodynamic profile typical for adequately sized grafts (table 2).

In contrast, 14 patients (5.4%) exhibited elevated portal hemodynamic parameters exceeding the critical thresholds of PVF > 250 mL/min/100 g and/or PVP > 15 mmHg, necessitating intraoperative graft inflow modulation (GIM). Following intervention, PVF decreased from 305.2 ± 80.7 to 213.9 ± 31.8 mL/min/100 g, and PVP decreased from 19 ± 4.2 to 12 ± 2.8 mmHg, indicating the achievement of hemodynamic balance.

Although the incidence of SFSS in this subgroup was 7.1% (1 case), the clinical course was mild, without mortality. This confirms the effectiveness of timely portal inflow modulation even in patients with an adequate GRWR when excessive portal hyperperfusion is present. Thus, even in recipients with GRWR > 0.8, in the presence of elevated portal inflow, GIM contributes to the reduction of portal pressure and improvement of microcirculation. These findings support the concept that the pathophysiological basis of SFSS is determined not by graft size, but by the "inflow–functional capacity" imbalance, which is consistent with the current "small-for-flow" paradigm.

Therefore, GIM should be considered not only as a corrective measure for small graft volume, but also as a strategy for the prevention of portal hyperdynamics in cases of sub- compensated portal hypertension in the recipient.

Table 3.
Analysis of patients according to SVGVR

Parameter	SVGVR < 1 n = 48 (44%)	SVGVR > 1 n = 61(56%)	p-value
GRWR	1.1 ± 0.2 (0.65–1.2)	0.9 ± 0.2 (0.52–0.91)	< 0.0001*
GIM performed, n (%)	3 (6.3%)	19 (31.1%)	0.384
PVF (mL/min/100 g)	207.8 ± 41.8 (160–320)	238.3 ± 40.9 (220–410)	< 0.0002*
PVP (mmHg)	14.2 ± 2.7 (10–18)	19.5 ± 3.8 (13–26)	< 0.0001*
SFSS, n (%)	1 (2.1%)	6 (9.8%)	0.815
Mortality, n (%)	0	6 (9.8%)	< 0.05*
* P value ⩽ 0.05 was considered statistically significant			

The retrospective analysis of 109 patients demonstrated that stratification based on the SVGVR index reveals fundamentally different hemodynamic and clinical profiles. The SVGVR < 1.0 group included 48 patients (44%), whereas SVGVR > 1.0 was observed in 61 patients (56%), meaning that the majority of patients exhibited a relative predominance of splenic volume over graft volume. (Table 3).

Portal venous flow (PVF) in patients with SVGVR < 1 was 207.8 ± 41.8 mL/min/100 g (160–320), while in those with SVGVR > 1 it reached 238.3 ± 40.9 mL/min/100 g (220–410), p < 0.05. Similarly, portal venous pressure (PVP) was significantly lower in the SVGVR < 1 group: 14.2 ± 2.7 mmHg (10–18) versus 19.5 ± 3.8 mmHg (13–26) in the SVGVR > 1 group (p < 0.05). Thus, a high SVGVR is clearly associated with functional portal hyperperfusion and elevated portal pressure, creating pathophysiological conditions for hyperperfusion-induced small graft injury.

These differences directly affect surgical tactics: intraoperative graft inflow modulation (GIM) was required in 3 patients (6.3%) with SVGVR < 1, whereas in the SVGVR > 1 group, the intervention was performed in 19 patients (31.1%); however, the difference did not reach statistical significance (0.384). In other words, nearly one-third of patients with an elevated SVGVR required inflow correction to achieve acceptable PVF and PVP levels, indicating that SVGVR > 1 is a practical marker of increased need for GIM.

Regarding SFSS incidence, a trend toward higher rates was observed in the SVGVR > 1 group (6 cases, 9.8%) compared with SVGVR < 1 (1 case, 2.1%); however, the difference did not reach statistical significance (0.815), likely due to sample size limitations. Nonetheless, the direction of the effect is physiologically plausible and aligns with the pathogenic model: the higher the portal inflow relative to graft capacity, the higher the risk of small-for-size graft dysfunction.

The strongest differences were observed in mortality. No deaths were reported in the SVGVR < 1 group, whereas 6 patients (9.8%) with SVGVR > 1 died, with the difference reaching statistical significance (p < 0.05). This supports SVGVR > 1 as an independent adverse prognostic factor associated with increased postoperative mortality risk.

Taken together, these findings confirm that SVGVR is not merely a morphometric parameter of the spleen, but an integrated hemodynamic marker that reflects the splenoportal load imposed on the graft. High SVGVR values (>1) are associated with a smaller GRWR, higher PVF and PVP, more frequent need for GIM, and significantly higher mortality. Therefore, incorporating SVGVR into the standard preoperative assessment protocol for both donors and recipients, as well as utilizing it in the decision-making algorithm for GIM, appears pathophysiologically justified and should be regarded as an important component of personalized planning in LDLT.

Of the 33 interventions, 28 (78.6%) were performed intraoperatively, and only 3 (21.4%) were carried out in the early postoperative period. In two of these cases, splenectomy was required postoperatively despite prior splenic artery ligation.

Parameter	Intraoperative (n = 28)	Postoperative (n = 5)	p-value
Reductionin PVF, %	25 ± 7	12 ± 5	0.0004*
Reductionin PVP, mmHg	8.5 ± 3.0	3.5 ± 1.2	0.001*
SFSS, n (%)	1 (3.6%)	5 (100%)	0.029*
Mortality, n (%)	1 (3.6%)	4 (80%)	0.201
* P value ⩽ 0.05 was considered statistically significant			

Table 4.
Effectiveness of GIM depending on the timing of intervention

The analysis demonstrated that the timing of graft inflow modulation (GIM) has a critical impact on both hemodynamic efficacy and clinical outcomes.

In the intraoperative GIM group (n = 28), the mean reduction in portal venous flow (PVF) was 25 ± 7%, whereas in the late postoperative intervention group (n = 5) it was only 12 ± 5% (p = 0.004). Similarly, the decrease in portal venous pressure (PVP) after intraoperative GIM averaged 8.5 ± 3.0 mmHg, compared with only 3.5 ± 1.2 mmHg in the postoperative group (p = 0.002). Thus, intraoperative GIM is nearly twice as effective in reducing both PVF and PVP.

These hemodynamic differences translated into fundamentally different clinical outcomes. In the intraoperative GIM group, small-for-size syndrome (SFSS) developed in only 1 of 28 patients (3.6%), whereas in the postoperative GIM group SFSS occurred in all 5 patients (100%) (p = 0.029). In other words, the incidence of SFSS was 27-fold higher when GIM was performed late.

Post-transplant GIM was performed as a rescue therapy after hyperperfusion-induced graft dysfunction had already developed. The high mortality rate (80%) in this subgroup is explained by late microcirculatory decompensation and the inability to achieve reversible restoration of hepatosinusoidal perfusion. These results are consistent with the findings of Troisi et al. (2017), which indicate that the optimal timing for GIM is no later than the reperfusion stage when portal hyperperfusionis first detected by portometry.

Mortality data further highlight this effect: in the intraoperative GIM group, 1 of 28 patients died (3.6%), whereas in the postoperative modulation group, 4 of 5 patients died (80%). (Table 4).

Comparison of intraoperative inflow modulation techniques: SAL vs. splenectomy

Parameter	SAL (n = 19)	Splenectomy (n = 9)	p-value
PVF before (mL/min/100 g)	305.4 ± 74.5 (210–430)	367.4 ± 62.4 (280–450)	0.040 *
PVF after (mL/min/100 g)	242.1 ± 53.4 (180–320)	230 ± 55.3 (170–310)	0.584
PVP before(mmHg)	19 ± 4.1 (14–25)	22 ± 6.6 (17–29)	0.151
PVP after (mmHg)	13.7 ± 3.3 (10–18)	14 ± 1.7 (12–16)	0.800
Reductionin PVF (%)	30 ± 8 (18–42)	37 ± 9.0 (25–49)	0.048*
Reductionin PVP (mmHg)	7.8 ± 2.6 (5–11)	8.0 ± 3.1 (5–13)	0.860
SFSS, n (%)	1 (4.5 %)	-	-
Mortality, n (%)	1 (4.5 %)	-	-
Mean PVF values after intervention: SAL – 242 mL/min/100 g; splenectomy – 230 mL/min/100 g.Mean reduction in PVP in both groups was approximately 8 mmHg. * P value ⩽ 0.05 was considered statistically significant			

Table 5.
Comparative effectiveness of SAL and splenectomy in portal inflow modulation

The choice of GIM technique was guided by intraoperative portometry results and the response to a trial clamping of the splenic artery (the so-called clamp test). When portal pressure decreased by more than 5 mmHg and portal flow dropped below 250 mL/min/100 g during the test, SAL was preferred as the first-line inflow modulation method. In cases of insufficient hemodynamic response or pronounced portal hyperperfusion (PVF > 500 mL/min/100 g), splenectomy was performed.

In our analysis, we compared two portal inflow modulation techniques: splenic artery ligation (SAL, n = 19) and splenectomy (n = 9). In the splenectomy group, baseline portal hyperperfusionwas more pronounced: the mean PVF was 367.4 mL/min/100 g versus 305.4 mL/min/100 g in the SAL group (p=0.040), and PVP was 22 mmHg versus 19 mmHg (p = 0.151), respectively, indicating that splenectomy was mostly used in more hemodynamically compromised patients. (Table 5).

Following intervention, both methods provided comparable portal system decompression: PVF decreased by approximately 30% after SAL and by 37% after splenectomy, while PVP decreased by approximately 40% in both groups, with target values achieved at ~230–240 mL/min/100 g(statistically significant p = 0.048*) and 13–14 mmHg (p = 0.860), respectively. SFSS occurred in 4.5% of patients (1/19) after SAL and in 0% after splenectomy, and mortality rates were also 4.5% versus 0% (p = 0.42). Thus, given the comparable clinical outcomes, SAL provides effective reduction of portal inflow and pressure by approximately 30–40% while remaining a less invasive approach, whereas splenectomy is justified in patients with more severe baseline portal hyperperfusion.

In the present study, SAL provided sufficient reduction in PVF and PVP to prevent SFSS with minimal surgical risk.

Discussion

Small-for-size syndrome (SFSS) remains one of the key limiting factors in living donor liver transplantation (LDLT), particularly when using partial grafts in adult recipients. Traditionally, a critical threshold has been defined as a GRWR <0.8% or GV/SLV <40%, which is associated with an increased risk of early graft dysfunction.[2,17,18] However, as demonstrated in the early works by *Kow AWC et al*, the clinical manifestation of SFSS correlates more closely with portal hyperperfusion and portal pressure than with graft morphometric parameters alone.[17] Subsequent reviews and meta-analyses have confirmed that portal hemodynamic parameters—pressure and flow—are of primary prognostic importance, rather than graft size alone.[2,3,4,5,9]

Our study reinforces that the key pathogenetic mechanism underlying SFSS after LDLT is excessive portal inflow to a small-volume graft. While the classic indicator remains a reduced graft-to-recipient weight ratio (GRWR <0.8%), [2,18] modern evidence emphasizes the importance of portal hemodynamic monitoring and inflow modulation.[17,19-21] The ILTS/iLDLT/LTSI consensus recommends maintaining PVP < 15 mmHg and/or PVF < 250 mL/min/100 g at reperfusion.[22]

When the functional capacity of the graft is insufficient to meet the metabolic requirements of the recipient, metabolic imbalance, cholestasis, hyperbilirubinemia, and reduced synthetic function occur. Yet, over the past decades, it has become clear that graft size alone does not determine outcomes.

Evidence from *Kamei H*, *et al., Troisi RI et al.,* as well as *Soin, A.S. et al.* supports the use of small grafts when strict portal inflow control is achieved: with GRWR < 0.8%, but with adequate inflow modulation (SAL, splenectomy, shunting), both early and long-term outcomes may become comparable to those observed with standard-size grafts.[15,18,20,21,23] Conversely, a randomized trial by *Pamecha, V. et al.* demonstrated that routine SAL without clear hemodynamic indications does not always reduce the incidence of early graft dysfunction, highlighting the importance of a personalized hemodynamic strategy.[16]

In our cohort, patients with GRWR < 0.8 indeed demonstrated an elevated risk of SFSS and mortality, especially when excessive portal inflow was present. The mean baseline PVF and PVP were 310 mL/min/100 g and 20 mmHg, respectively, indicating functional hyperperfusion rather than simply a deficit in graft mass.

A meta-analysis by *Gavriilidis P. et al* demonstrated that in patients with GRWR < 0.8, GIM reduced the incidence of SFSS nearly threefold, while 5-year graft survival became comparable to outcomes in those with GRWR > 0.8.[8] Thus, GRWR remains a fundamental morphometric parameter, yet its prognostic value is greatly strengthened when portal hemodynamics are accounted for.

A separate direction of research involves SVGVR (spleen-to-graft volume ratio) as an integrated marker of splenoportal load on the graft. Yao et al. demonstrated that SVGVR > 1.0 correlates with an increased risk of SFSS, early graft dysfunction, and reduced survival.[12] Subsequent studies by *Kishore G.S. Bharathy*, and colleagues confirmed that SVGVR reflects the actual "portal load per graft volume unit" and should be incorporated alongside GRWR for preoperative risk stratification.[3,12,13] High SVGVR indicates persistent splenomegaly, increased splenoportal resistance, and enlarged venous volume, creating conditions for hyperperfusion even when GRWR is normal.

Unlike GRWR, SVGVR does not directly reflect graft size but indicates the splenoportal venous volume that drives excessive portal inflow into small grafts.

Our results demonstrated that patients with SVGVR > 1.0 had markedly higher PVF (308 ± 54 mL/min/100 g) and PVP (19.5 ± 3.8 mmHg), indicating occult portal hyperperfusion despite the absence of clinically evident portal hypertension. Graft inflow modulation (GIM) was required approximately five times more frequently in this subgroup compared with those with SVGVR < 1.0 (31.1% vs. 6.3%), although without statistical significance (p < 0.384). A tendency toward increased rates of SFSS (9.8% vs. 2.1%) and mortality (13.1% vs. 2.1%) was also observed in patients with SVGVR > 1.0.

The combination of GRWR < 0.8 and SVGVR > 1.0 was associated with the poorest outcomes in our study. This identifies an additional risk factor—the splenic component—that reflects splenoportal hemodynamics. Literature reviews similarly emphasize that graft size is only one part of the equation, while the flow-to-mass mismatch is increasingly recognized as the main determinant.[19,24]In such scenarios, GIM (SAL, splenectomy) should be applied not as a treatment but as a preventive strategy designed to achieve hemodynamic balance at reperfusion.

Thus, GRWR reflects anatomical adequacy, whereas SVGVR reflects functional-hemodynamic load, and their interplay determines the clinical outcome.

This paradigm underlies the modern "small-for-flow" concept, which focuses on optimizing portal inflow through GIM rather than increasing graft volume.[4,8]

The pathophysiological mechanism of SFSS is well described: after reperfusion of a small graft under excessive inflow, sinusoidal hyperperfusion occurs, shear stress rises, endothelial activation develops, and hepatic arterial buffer response (HABR) is blunted — leading to ischemic and cholestatic hepatocyte injury.[7,20] In our analysis, baseline values in the high-risk group (~310 mL/min/100 g and ~20 mmHg) are consistent with thresholds proposed by *Kamei H, et al.* (PVP < 15 mmHg, PVF < 250 mL/min/100 g).[23]

An important aspect emphasized in international literature is the timing of GIM. Systematic reviews by *Rammohan et al.* and ILTS–iLDLT–LTSI guidelines demonstrate that intraoperative preventive modulation at the time of reperfusion significantly reduces SFSS and mortality, whereas delayed "rescue-GIM" in the postoperative setting after graft dysfunction has already developed is associated with a very poor prognosis.[22,24]

In our study, intraoperative GIM reduced PVF by ~24% and PVP by ~8 mmHg, leading to nearly a threefold reduction in SFSS and improved survival. These findings are consistent with results from other centers and meta-analyses demonstrating that inflow modulation (SAL, splenectomy, shunting) improves outcomes in SFSG.[18,24]

We also confirmed the importance of intervention timing: intraoperative GIM resulted in >96% survival without SFSS, whereas postoperative rescue modulation was associated with high mortality (~80%). These results support recommendations that GIM should be performed preventively at the reperfusion stage rather than as a late corrective measure.[22,24]

A comparison of GIM methods (SAL vs. splenectomy) showed that SAL is preferred as a less invasive first-line technique in moderate hyperperfusion, while splenectomy is reserved for severe portal inflow not controlled by SAL or for markedly elevated PVF/PVP.[11,14,15,18] Reports by *Su C.M., et al*, as well as *Yoshizumi T. et al.* indicate that concurrent splenectomy may improve outcomes in patients with severe splenomegaly and portal hypertension, but requires careful assessment of infection and thrombosis risks.[14,25]

Baseline hemodynamic parameters showed that PVF was higher in the splenectomy group (p = 0.040), and PVP was also elevated, although without statistical significance (p = 0.151), indicating that this intervention was used in more severe cases; however, after intervention, the outcomes became equivalent between groups (PVF ~230–242, PVP ~12–14 mmHg). Literature confirms that SAL remains less invasive and effective in moderate hyperperfusion, while splenectomy is justified as a secondary option in severe hyperinflow.[25,26]

Long-term outcomes further underline the clinical relevance of GIM: 5-year survival was ~86.6% with inflow modulation versus ~79% without (p = 0.001). These results are comparable to leading LDLT centers and demonstrate that, with adequate inflow adjustment, even small grafts can achieve near-standard outcomes.[18,21]

Ikegami T., et al. emphasize that GIM is becoming an essential part of LDLT protocols in high-volume centers, particularly in situations of portal hyperperfusion risk.[6]

Limitations. This cross-sectionalanalysis was conducted mainly based on the results of a retrospective analysis, however, a long-range analysis requires a wide coverage of patients before and after liver transplantation from a living donor for prospective material collection and data analysis.

What's known? Correction of portal hyperperfusion during living donor liver transplantation requires accurate hemodynamic assessment and timely surgical intervention. Portal inflow directly influences sinusoidal perfusion, hepatocellular integrity, and overall graft function. Adequate modulation of portal venous inflow determines the risk of small-for-size syndrome and the postoperative outcome of the liver transplant recipient.

What's new? This study identifies the combination of graft-to-recipient weight ratio <0.8 and spleen-to-graft volume ratio > 1.0 as the strongest predictor of small-for-size syndrome and postoperative mortality in living donor liver transplantation. It demonstrates that intraoperative graft inflow modulation is significantly more effective than delayed postoperative intervention, with superior hemodynamic correction and survival outcomes.It confirms that integrating morphometric and intraoperative hemodynamic parameters enables personalized surgical decision-making and improves long-term transplantation success, supporting the "small-for-flow" paradigm.

Conclusion

Portal hyperperfusion remains the leading pathophysiological factor contributing to small-for-size syndrome (SFSS) in living donor liver transplantation. The most unfavorable outcomes are observed in patients with a combination of GRWR < 0.8 and SVGVR > 1.0, indicating a mismatch between portal inflow and the functional capacity of the graft.Intraoperative graft inflow modulation effectively normalizes portal hemodynamics by reducing portal vein pressure to physiological levels (< 15 mmHg) and significantly improves 5-year patient survival.Among surgical approaches, splenic artery ligation is the preferred first-line technique for moderate hyperperfusion due to its high efficacy and low invasiveness, whereas splenectomy is justified in cases of severe splenic venous inflow or SAL failure.Integration of morphometric parameters (GRWR, SVGVR) with intraoperative hemodynamic monitoring (PVF, PVP) and targeted application of GIM forms the basis of the modern "small-for-flow" concept, aimed at maintaining a physiological balance between portal inflow and graft functional capacity. Such an individualized strategy should become the standard for SFSS prevention and for improving long-term outcomes in LDLT.

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