# Strategies in management of small-for-size graft in recipients of right lobe graft in living donor liver transplantation: a retrospective study

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### Background

Liver transplantation is the only survival option for patients with end-stage liver disease. Therefore, candidates for liver transplant have been rapidly increasing, which in turn, has led to accepting borderline and small-size grafts to accommodate the demand.

# Patients and methods

Of 217 right lobe living donor liver transplant recipients, 18 got small-for-size grafts (SFSG) (graft-to-recipient weight ratios <0.8%) in the period between November 2016 and November 2021 in Ain Shams Center for Organ Transplantation. Intraoperatively, glypressin infusion was started empirically in cases with SFSG and portal pressure was measured. Cases were divided into pharmacological group, where glypressin infusion was kept solely according to their portal pressure (<20 mmHg), and surgical group, which had splenic artery ligation (SAL) according to their portal pressure (>20 mmHg). Splenectomy was done in cases with SFSGs with portal pressure more than 20 mmHg accompanied by huge splenomegaly or hypersplenism. The surgical group was further divided into two subgroups: SAL subgroup and splenectomy subgroup.

#### Results

Six recipients had terlipressin infusion solely as a pharmacological graft inflow modulation, whereas surgical graft inflow modulation was done in addition to terlipressin infusion in 12 recipients (nine with SAL and three with splenectomy). Total bilirubin in the surgical group was significantly lower than that in the pharmacological group in the first and third 5-day intervals (P=0.039 and 0.040, respectively). Portal vein flow velocity mean values of the third 5-day interval were significantly lower in the surgical group (P=0.011). In surgical subgroups, total bilirubin and international normalized ratio in the splenectomy subgroup were significantly lower than that in the SAL group by the fifth 5-day interval (P=0.019 and 0.020, respectively). Mortality in the pharmacological group was extremely higher than that in the surgical group (P=0.009).

#### Conclusion

Surgical inflow modulation in the form of SAL and more importantly splenectomy is more potent in controlling portal flow and carries better outcome in terms of avoiding the development of small-for-size syndrome.

#### Keywords:

living donor liver transplantation, right lobe graft, small-for-size graft syndrome

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# Introduction

Liver transplantation (LT) has emerged as the survival option for patients with end-stage liver disease (ESLD). The indications of LT have expanded generously to include severe acute hepatitis, advanced cirrhosis, and hepatocellular carcinoma. LT procedure showed striking improvements in postoperative results and survival. However, LT is still a challenging procedure, carrying both the preoperative and postoperative sequelae. Lack of organ availability represents one of the main significant issues that LT faces owing to the widening gap between the number of ESLD cases

waiting for transplant and the donor pool. Therefore, living donor liver transplantation (LDLT) has emerged as an acceptable option to overcome organ shortage [1].

Since the advent of LDLT in adults, obtaining a minimum graft size for a recipient has been the

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major issue, to maintain donor safety and achieve recipient survival [2].

The emergence of adult-to-adult living liver donation has helped in determining an adequate liver mass for LT. It is possible to determine a minimum liver volume needed to achieve satisfactory recipient survival after transplantation thanks to the excellent graft quality donated by living donors and the follow-up of recipients of these partial liver grafts [3].

The graft-to-recipient weight ratios (GRWR) should not be less than 0.8% to achieve graft and patient survival of 90% [4].

However, there are differences recognized between presumed and actual graft volume. Studies showed a trivial change in the ratio of liver weight in grams to liver volume in milliliters from 1.0 to 1.12 g/ml. In addition, concerning the liver volume during contrast computed tomography scan, it is found enlarged as much as 7% during the venous phase than the plain phase. Moreover, studies showed that LDLT actual graft volume from younger donors tends to be reduced by 14% than presumed graft volume, whereas actual graft volume from older donors may have 4.4% reduction than presumed graft volume [2].

Small-for-size grafts (SFSG) is defined as those with GRWR of less than 0.8% or those with graft volume to standard liver volume ratios of less than 30-40%. Small-for-size syndrome (SFSS) also depends on diverse factors other than the graft size, such as graft quality and recipient factors. Therefore, the minimum graft volume has been pursued and is different among transplant centers. SFSS is clinically characterized by prolonged coagulopathy, intractable cholestasis, ascites, and encephalopathy at the end of the first week after LDLT. Complications such as infection, rejection, or even technical should be excluded to establish the SFSS diagnosis [5].

Patients with SFSS are more prone to infection due to impaired acute-phase response, immunosuppressive therapy, and intestinal bacterial translocation that commonly end up with severe sepsis and usually encounter multisystemic comorbidities in the form of encephalopathy, reversible or irreversible renal failure, and higher risk of acute lung injury [6].

The occurrence of SFSS depend s on multiple factors like functional graft size, portal inflow, and hepatic veins outflow. Therefore, many strategies were applied in controlling portal inflow and establishing adequate hepatic veins outflow to guard against the occurrence of SFSS by surgical and nonsurgical means [7].

# Patients and methods

Approval of the ethical committee, written informed consent from each donor and each recipient, and approval from ethics and indications committees at our institution for each LDLT procedure and the principal committee of organ transplant, MOH, Egypt, were taken. A total of 217 LDLT operations were done between November 2016 and November 2021 in Ain Shams Center for Organ Transplantation (ASCOT), Ain Shams University. Our study is a retrospective review that included all the recipients who got SFSG and met the following inclusion criterion: adult recipients older than 18 years who got right lobe graft with GRWR less than 0.8%. A total of 18 patients were included. Adult recipients who got a graft with GRWR more than 0.8%, recipients who got left lobe LT, and pediatric recipients were excluded from our study.

## **Preoperative workup**

All the recipients were subjected to thorough preoperative full clinical and laboratory assessments and investigations, including abdominal duplex ultrasonography, spiral computed tomography abdomen for exclusion of any unrecognized diseases, arteriography, portography, and venography to assess arterial and venous anatomy. These were done to assess if there are more venous anastomosis beyond the right hepatic vein (RHV) by detecting any venous variability in the hepatic vasculature such as large V5, V8, and single or double inferior RHVs. In addition, upper and lower endoscopies and medical consultations including cardiological, chest, psychological, ENT, dental consultations, and gynecological consultation for female cases were done.

#### Intraoperative workup

It included graft weighting for assessing GRWR, number of veins that need reconstruction on the back table, portal pressure measurement in recipients who had SFSG by using 23-G catheter with direct puncture to the portal vein, intraoperative duplex after vascular anastomosis to assess both arterial and portal inflow and outflow through the graft, operation time, and operation cold and warm ischemic times of the graft.

# Procedure

After performing right hepatectomy in the donor, the right lobe procured graft was then transferred to the back table.

# Back-table stage - preparation of the graft

The graft was continuously irrigated until the effluent was clear. The graft was kept immersed in the HTK solution inside a plastic bag with underlying sterilized ice prepared in advance. The graft was assessed at the back table regarding the actual weight, the right hepatic artery stump, the right portal vein stump, the right hepatic duct, the RHV stump, and number of significant accessory hepatic veins to be anastomosed in the recipient according to their size. If V5 and/or V8 were found more than 4 mm, they were reconstructed accordingly using ePTFE synthetic grafts. V5 alone was anastomosed to inferior vena cava (IVC), whereas V8 alone was anastomosed to the Middle Hepatic Vein (MHV). In some cases, where both V5 and V8 were present, anastomosis was done through two separate grafts for each vein with an end-to-end anastomosis or through a single graft by end-to-side anastomosis for both veins.

# Recipient surgical procedure: hepatectomy stage

Basically, after establishing deep anesthesia, a right subcostal with midline extension laparotomy incision is performed to enter the abdomen. Suction of ascitic fluid if any found is performed, and identification of any portosystemic shunts is done. Proceeding with total hepatectomy is done by mobilization of the liver with utilizing piggyback technique without performing any venovenous bypass and preserving the retrohepatic IVC with RHV, and MHV and Left Hepatic Vein (LHV), common trunk.

Liver hilar dissection is performed by skeletonizing and separating the right and left hepatic arteries and portal vein along with the bile duct.

# Graft utilization

The graft was then inserted into the abdomen after being prepared for implantation on the back table to replace the removed native liver. Implantation was started by an end-to-end running anastomosis between the graft's RHV and the recipient's RHV using 4/0 prolene. In some occasions, inferior RHV were expected in the graft's cut surface, and they were anastomosed to IVC using 5/0 prolene. Then, the right portal vein of the graft was anastomosed to the recipient's portal vein by an endto-end running anastomosis using 6/0 prolene. The portal vein was then declamped allowing the graft to be flushed with portal blood. V5, if present, was anastomosed to IVC via synthetic graft, and V8 as well, if present, was anastomosed to MHV of the recipient via synthetic graft with prolene 5/0.

Right hepatic artery of the graft to recipient's right or left hepatic artery anastomosis was performed by an interrupted end-to-end fashion using 8/0 prolene with the aid of surgical loupes. Vascular clamp was removed from hepatic artery and intraoperative Doppler ultrasound was performed to ensure proper patency of the anastomoses and adequate flow. Portal pressure was measured in graft with GRWR less than 0.8%. At the end, reconstruction of the biliary tree was done using 6/0 PDS sutures with or without stent applied and intraoperative cholangiography was done to assess the patency of the biliary tree. Finally, anatomical closure of the abdominal was done after application of intraperitoneal drains at the Morrison pouch, hepatic pedicle, and left subdiaphragmatic space.

# Inflow modulation in small-for-size graft

Glypressin infusion was started empirically in cases with SFSG. Then, portal flow velocity and pressure were measured after completion of the anastomoses and declamping. In cases where their portal pressure was less than 20 mmHg, glypressin infusion was kept solely, whereas those with portal pressure more than 20 mmHg, splenic artery ligation (SAL) was done and portal pressure was reassessed. Splenectomy was done in cases with SFSG accompanied by huge splenomegaly or hypersplenism.

# Postoperative follow-up

Patients had postoperative follow-up period for a month of monitoring full blood laboratory tests, ultrasonography, and duplex study every day in the first week and every other day in the second week, then every 3 days in the third and fourth weeks. Duplex study was performed to assess portal venous inflow, hepatic venous outflow, and hepatic artery inflow to detect any postoperative vascular complications.

### Statistical analysis

The data were collected, tabulated, and statistically analyzed. Description of quantitative variable was done as mean and SD in data that had no clear outliers, and median was used in describing the data with skewed values. The results were considered significant (S) with P value less than 0.05 and highly significant (HS) with P value less than 0.01. P value more than or equal to 0.05 was considered nonsignificant (NS). Analysis of data was done using IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.

# Results

Of 217 right lobe LDLT recipients, 18 got SFSG (GRWR<0.8%) in the period between November 2016 and November 2021 in Ain Shams Center for Organ Transplantation and were included in our study.

Recipients included in our study were classified according to the portal inflow modulation technique used into the pharmacological group and the surgical group; the latter group was further divided into two subgroups (SAL subgroup and splenectomy subgroup). Intraoperative data and postoperative period follow-up of bilirubin, international normalized ratio (INR), and portal flow velocity were represented by median and mean values in 5-day interval till 25th postoperative day.

Recipients had an average age of 53 (SD=6.49) years, and most of them were men (88.9%). More than half of the recipients had diabetes mellitus (55.6%). Donors' mean age was 25.72±6.61 years. Recipients' median Model for End Stage Liver Disease (MELD) score was 14, with an interquartile range of 12–16, and according to Child Turcotte Pugh (CTP) classification, six recipients were CTP-A, five recipients were CTP-B, and seven recipients were CTP-C (Table 1).

Six recipients received terlipressin infusion solely for graft inflow modulation (GIM), whereas surgical GIM was done in addition to terlipressin infusion in 12 recipients (nine with SAL and three with splenectomy) owing to high portal pressure (>20 mmHg) (Table 2).

Although all recipients had right lobe grafts of GRWR less than 0.8%, the difference between the mean values of actual GRWR in both groups was insignificant. Operative time mean value in both groups was close to each other. Regarding accessory vein reconstruction, five of six recipients in the pharmacological GIM group did not need accessory vein reconstruction. Unlike in the surgical GIM group, only two of 12 recipients did

 Table 1 Demographic and clinical data of study population

| • •                     | 211              |            |  |  |  |
|-------------------------|------------------|------------|--|--|--|
| Data                    | Statistical unit | Value      |  |  |  |
| Recipients' age (years) | Mean±SD          | 53.11±6.49 |  |  |  |
|                         | Range            | 43–67      |  |  |  |
| Donors' age (years)     | Mean±SD          | 25.72±6.61 |  |  |  |
|                         | Range            | 19–40      |  |  |  |
| Sex                     |                  |            |  |  |  |
| Male                    | n (%)            | 16 (88.9)  |  |  |  |
| Female                  | n (%)            | 2 (11.1)   |  |  |  |
| HTN                     | n (%)            | 8 (44.4)   |  |  |  |
| DM                      | n (%)            | 10 (55.6)  |  |  |  |
| Classification          |                  |            |  |  |  |
| Child–Pugh              |                  |            |  |  |  |
| A                       | n (%)            | 6 (33.3)   |  |  |  |
| В                       | n (%)            | 5 (27.8)   |  |  |  |
| С                       | n (%)            | 7 (38.9%   |  |  |  |
| MELD score              | Median (IQR)     | 14 (12–16) |  |  |  |
|                         |                  |            |  |  |  |

DM, diabetes mellitus; HTN, hypertension; IQR, interquartile range.

not need accessory vein reconstruction (P=0.006). In the surgical GIM group patients who needed accessory vein reconstruction, V5 reconstruction was done the most. There was one recipient where Makuuchi vein was found along with V5 and V8, and they were reconstructed. Intraoperative portal vein flow velocity after the application of GIM technique was recorded. Mean value for portal flow velocity in the pharmacological GIM group was 74 and 84 cm/s in the surgical GIM group (Table 2).

Total bilirubin in the surgical GIM group was significantly lower than that in the pharmacological group in the first and third 5-day intervals (P=0.039 and 0.040, respectively). Notably, portal vein flow velocity mean values of the third 5-day interval were significantly lower in the surgical GIM group (P=0.011), as illustrated in Figs 1 and 2. INR was found to be insignificantly lower in the surgical group than in the pharmacological group (Fig. 3).

SAL was the favored surgical GIM technique in all recipients of surgical GIM, but the ones who had huge splenomegaly or hypersplenism, splenectomy was chosen over SAL. Only three recipients underwent splenectomy. The mean operative time in splenectomy group was noticed to be insignificantly higher than in the SAL group (Table 3).

In surgical GIM subgroups, although it is statistically insignificant, it is worth mentioning that we noticed the intraoperative mean value for portal flow velocity after the technique was done in the SAL subgroup was higher than in splenectomy subgroup (Fig. 4).

Total bilirubin and INR median and mean values in splenectomy group were noticed to be significantly lower than that of the SAL group by the fifth 5-day interval of the postoperative period as illustrated by Figs 5 and 6.

Four of the six recipients who received terlipressin infusion only as an inflow modulation died during the first month following LT resembling a highly significant mortality rate in comparison with surgical GIM, which recorded only one recipient death from 12 recipients (P=0.009) (Table 4). The only death recorded in surgical GIM was in the SAL subgroup; seventh day syndrome was the cause of death.

# Discussion

LDLT is the only possible and legally permissible way to perform LT in Egypt. Subsequently, the progressive

| Operative data                   | Pharmacological GIM (terlipressin infusion)<br><i>N</i> =6 | Surgical GIM<br><i>N</i> =12 | Test value                  | P value | Significance |
|----------------------------------|--|------------------------------|-----------------------------|---------|--------------|
| Actual graft weight (g)          |  |                              |                             |         |              |
| Mean±SD                          | 701.67±133.22  | 647.08±104.37                | 0.956•                      | 0.353   | NS           |
| Range                            | 540–945  | 480-800                      |                             |         |              |
| Actual (GRWR)                    |  |                              |                             |         |              |
| Mean±SD                          | 0.75±0.04  | 0.73±0.07                    | 0.700•                      | 0.494   | NS           |
| Range                            | 0.69–0.79  | 0.58-0.79                    |                             |         |              |
| Warm ischemia time (min)         |  |                              |                             |         |              |
| Mean±SD                          | 50.83±16.86  | 45.00±19.77                  | 0.617•                      | 0.546   | NS           |
| Range                            | 30–75  | 25-100                       |                             |         |              |
| Cold ischemia time (min)         |  |                              |                             |         |              |
| Mean±SD                          | 49.17±22.00  | 50.00±15.81                  | -0.093•                     | 0.927   | NS           |
| Range                            | 20-80  | 25-80                        |                             |         | _            |
| Operative time (min)             |  |                              |                             |         |              |
| Mean±SD                          | 588.33±105.91  | 548.33±101.88                | 0.776•                      | 0.449   | NS           |
| Range                            | 450–720  | 420–720                      |                             |         |              |
| Accessory veins reconstruction   |  |                              |                             |         |              |
| V5 to IVC                        | 1 (16.7)   | 5 (41.7)                     | 1.125*                      | 0.289   | NS           |
| V8 to MHV                        | 0  | 2 (16.7)                     | 1.125*                      | 0.289   | NS           |
| V5+V8                            | 0  | 2 (16.7)                     | 1.125*                      | 0.289   | NS           |
| Makuuchi (RIHV) to IVC           | 0  | 2 (16.7)                     | 1.125*                      | 0.289   | NS           |
| Intraoperative measurements      | -  | _ (,                         |                             |         |              |
| HARI                             |  |                              |                             |         |              |
| Mean±SD                          | 0.67±0.02  | 0.63±0.07                    | 1.284•                      | 0.217   | NS           |
| Range                            | 0.63–0.7   | 0.54-0.77                    | -                           |         | _            |
| Portal pressure (>20 mmHg        |  |                              |                             |         |              |
| No                               | 6 (100.0)  | 0                            | 18.000*                     | 0.000   | HS           |
| Yes                              | 0  | 12 (100.0)                   |                             |         |              |
| PV PSV intraoperative +9 (c      |  | (,                           |                             |         |              |
| Mean±SD                          | 74.5±10.37   | 84.5±29.67                   | -0.791•                     | 0.440   | NS           |
| Range                            | 65–90  | 50–150                       | 0.7013                      | 01110   |              |
| Significant postoperative follow |  |                              |                             |         |              |
| Total bilirubin (1–5)            |  |                              |                             |         |              |
| Median (IQR)                     | 3.85 (2.9–5.9)   | 1.95 (1.35–2.8)              | –2.064≠                     | 0.039   | S            |
| Range                            | 1.8–8.7  | 1–6.5                        | 2.001                       | 01000   | C C          |
| Total bilirubin (11–15)          |  |                              |                             |         |              |
| Median (IQR)                     | 1.25 (1.2–2)   | 1 (0.88–1.23)                | <i>–</i> 2.010 <sup>≠</sup> | 0.044   | S            |
| Range                            | 1.2–13   | 0.5–24.15                    | 2.0.0                       | 01011   | C C          |
| PV PSV (11–15)                   | 0  | 0.0 2 1.10                   |                             |         |              |
| Mean±SD                          | 78.5±15.28   | 56.4±14.03                   | 2.889•                      | 0.011   | S            |
| Range                            | 60.5–94  | 36.75–74.67                  | 2.0000                      | 0.011   | 0            |
| PV PSV (16–20)                   | 00.0 04  | 00.10 14.01                  |                             |         |              |
| Mean±SD                          | 78.67±13.04  | 58.46±12.18                  | 2.656•                      | 0.026   | S            |
| Range                            | 60–90  | 35.4–68.75                   |                             | 0.020   | 5            |

GIM, graft inflow modulation; GRWR, graft-to-recipient weight ratio; IQR, interquartile range; IVC, inferior vena cava; PV, portal vein. *P*-value > 0.05: Non-significant; *P*-value < 0.05: Significant; *P*-value < 0.01: Highly significant; •: Repeated Measures ANOVA test;

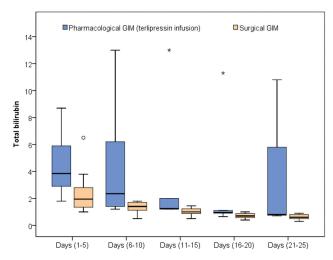
<sup>≠</sup>: Friedman test; \*: Chi-square test.

increase in patients with ESLD has made it challenging to find a suitable donor. As a result, borderline and small-sized grafts became widely accepted. Patients with ESLD in need for LT usually tend to have increased portal pressure that may increase portal flow after transplantation and jeopardize especially SFSG. Increased portal flow to a SFSG most likely will alter the function of the graft in the form of hyperbilirubinemia, coagulopathy, and production of large amount of ascites, a condition known as SFSS [2].

Thus, we confronted the unpleasant prognostic fact of using SFSG of GRWR less than 0.8% by considering portal inflow modulation pharmacologically and surgically. In this series, the mean age of the recipients was 53 years, which is higher than the smallsized graft group in the studies by Wahab *et al.* [8] and Shoreem *et al.* [7], which were 44 and 46 years, respectively. Overall, 88% of recipients in our work were men. The percentages were 90, 89, and 67% in Wahab *et al.* [8], Abdallah *et al.* [1], and Shoreem *et al.* [7], respectively.

Our study population's median MELD score was 14, whereas in he study by Abdallah *et al.* [1], it was 19. Of 18 recipients, 10 were diabetic in our study, whereas in Wahab *et al.* [8] and Abdallah *et al.* [1] were six and four, respectively [7].





Total bilirubin follow-up according to GIM technique. GIM, graft inflow modulation.

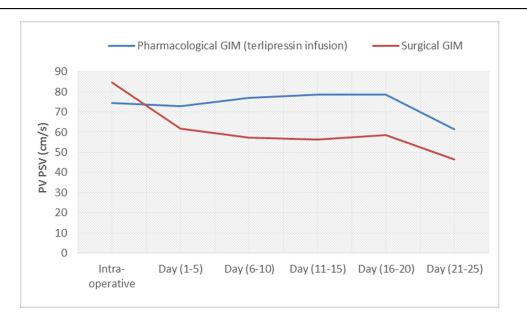
## Figure 2

We adopted the usage of the vasopressin analog 'terlipressin' as a pharmacological modulator of portal inflow and was recorded, and its outcome was analyzed as a single entity for efficacy in controlling portal flow. On the contrary, Emond *et al.* [9] mentioned vasopressin use as a standard anesthetic management and was not considered in their study analysis. However, our study results interestingly favor the surgical GIM over the usage of terlipressin only as an inflow modulator.

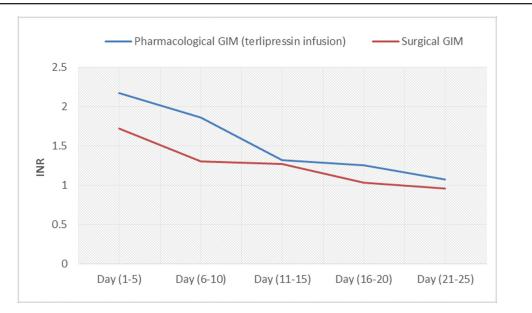
The mean age of donors was relatively young (25 years) in our series. A younger graft age enhances the graft function, and this is because older grafts lack the capacity of regeneration compared with younger ones. However, other several factors affect the outcome of graft regeneration and function as stated by Lué *et al.* [11]. In addition, the study by Li *et al.* [10] showed that donor age had an effect on the early outcome of the graft.

Many studies have favored the effect of surgically created portosystemic shunts as an approach to reduce excessive portal inflow, as firstly reported by Boillot *et al.* [12]. However, our center does not use surgical portosystemic shunts as an inflow modulator for many reasons – time consumption and most importantly the possible risk of developing portal flow steal phenomenon, as experienced by Ikegami *et al.* [2] and Elshawy *et al.* [13].

Our study also included recipients who had both splenectomy or SAL as a surgical inflow portal



Trend of portal vein velocity mean values along the postoperative period according to GIM technique. GIM, graft inflow modulation.



Trend of international normalized ratio (INR) mean values along the postoperative period according to GIM technique. GIM, graft inflow modulation.

| Table 3 ( | Operative d | lata in bot | h subgroups o | f the surgical | graft inflow | modulation group |
|-----------|-------------|-------------|---------------|----------------|--------------|------------------|
|-----------|-------------|-------------|---------------|----------------|--------------|------------------|

| Operative data                 | Terlipressin+SAL<br><i>N</i> =9 | Terlipressin+splenectomy<br><i>N</i> =3 | Test value | P value | Significance |
|--------------------------------|---------------------------------|---|------------|---------|--------------|
| Actual graft weight (g)        |                                 |   |            |         |              |
| Mean±SD                        | 638.89±117.09                   | 671.67±62.12                            |            |         |              |
| Range                          | 480-800                         | 600-710                                 | -0.454•    | 0.660   | NS           |
| Actual (GRWR)                  |                                 |   |            | 0.000   |              |
| Mean±SD                        | 0.72±0.07                       | 0.75±0.06                               |            |         |              |
| Range                          | 0.58-0.77                       | 0.69-0.79                               | -0.809•    | 0.437   | NS           |
| Warm ischemia time (min)       |                                 |   |            |         |              |
| Mean±SD                        | 47.22±22.38                     | 38.33±7.64                              |            |         |              |
| Range                          | 25–100                          | 30–45                                   | 0.657•     | 0.526   | NS           |
| Cold ischemia time (min)       |                                 |   |            |         |              |
| Mean±SD                        | 45.00±13.69                     | 65.00±13.23                             |            |         |              |
| Range                          | 25–70                           | 55–80                                   | -2.206•    | 0.052   | NS           |
| Operative time (mins)          |                                 |   |            |         |              |
| Mean±SD                        | 535.56±104.89                   | 586.67±100.66                           | -0.737•    | 0.478   | NS           |
| Range                          | 420-720                         | 480–680                                 |            |         |              |
| Accessory veins reconstruction | n [ <i>n</i> (%)]               |   |            |         |              |
| V5 to IVC                      | 4 (44.4)                        | 1 (33.3)                                | 0.114*     | 0.735   | NS           |
| V8 to MHV                      | 2 (22.2)                        | 0                                       | 0.800*     | 0.371   | NS           |
| V5+V8                          | 1 (11.1)                        | 1 (33.3)                                | 0.800*     | 0.371   | NS           |
| Makuuchi (RIHV) to IVC         | 2 (22.2)                        | 0                                       | 0.800*     | 0.371   | NS           |
| Intraoperative measurements    |                                 |   |            |         |              |
| HARI                           |                                 |   |            |         |              |
| Mean±SD                        | 0.63±0.07                       | 0.62±0.04                               | 0.318      | 0.757   | NS           |
| Range                          | 0.54-0.77                       | 0.59–0.67                               |            |         |              |
| Portal Pressure (>20 mmHg      | g) [ <i>n</i> (%)]              |   |            |         |              |
| No                             | 0                               | 0                                       | -          | -       | -            |
| Yes                            | 9 (100.0)                       | 3 (100.0)                               |            |         |              |
| PV PSV intraoperative (cm/s    | s)                              |   |            |         |              |
| Mean±SD                        | 91.56±30.77                     | 63.33±12.58                             | 1.507•     | 0.163   | NS           |
| Range                          | 65–90                           | 50–150                                  |            |         |              |

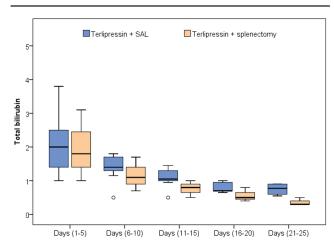
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#### Table 3 (Continued)

| Operative data                  | Terlipressin+SAL<br><i>N</i> =9 | Terlipressin+splenectomy<br><i>N</i> =3 | Test value          | P value | Significance |
|---------------------------------|---------------------------------|---|---------------------|---------|--------------|
| Significant postoperative follo | w-up 5-day interval             |   |                     |         |              |
| Total bilirubin (21–25)         |                                 |   |                     |         |              |
| Median (IQR)                    | 0.78(0.6-0.9)                   | 0.3(0.3–0.5)                            | –2.343 <sup>≠</sup> | 0.019   | S            |
| Range                           | 0.55-0.9                        | 0.3–0.5                                 |                     |         |              |
| INR (21–25)                     |                                 |   |                     |         |              |
| Mean±SD                         | 0.99±0.03                       | 0.9±0                                   | 3.386•              | 0.020   | S            |
| Range                           | 0.93–1                          | 0.9–0.9                                 |                     |         |              |

GRWR, graft-to-recipient weight ratio; INR, international normalized ratio; IVC, inferior vena cava; SAL, splenic artery ligation. *P*-value > 0.05: Non-significant; *P*-value < 0.05: Significant; *P*-value < 0.01: Highly significant; •: Repeated Measures ANOVA test;  $\neq$ : Friedman test; : Chi-square test.

Figure 4



Trend of portal vein velocity mean values along the postoperative period according to the surgical GIM subgroup. GIM, graft inflow modulation.

modulation. By observing the SAL subgroup's mean portal flow velocity through the postoperative period, we find a decline from 91 to 61 cm/s by postoperative day 5 and trending down reaching 46 cm/s by 25th postoperative day. Furthermore, there was a significant decline in portal flow velocity in the surgical GIM group when compared with the pharmacological group at postoperative day 15 (P=0.001), endorsing the effectiveness of SAL in controlling portal inflow. Umeda *et al.* [14] have praised splenic artery embolization or ligation for controlling portal inflow to SFSG.

Splenectomy has been raised to be beneficial for GIM by many studies. In our series, recipients who had splenectomy had a significant decline in total serum bilirubin and INR levels. Moreover, portal flow velocity postoperative follow-up showed a plateau

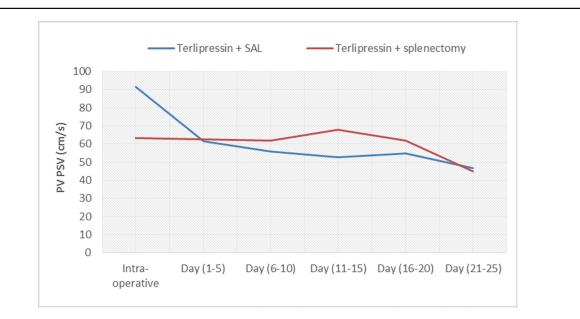
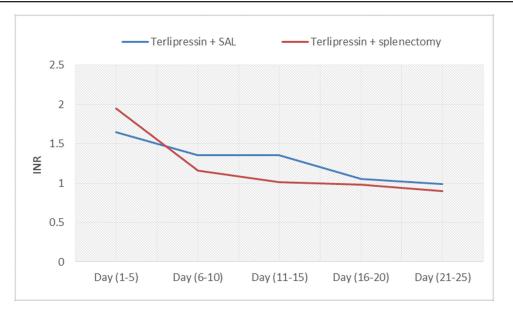


Figure 5

Total bilirubin follow-up according to the surgical GIM subgroup. GIM, graft inflow modulation.



Trend of international normalized ratio (INR) mean values along the postoperative period according to the surgical GIM subgroup. GIM, graft inflow modulation.

|   | Mortality [n (%)]  |           |                    |         |              |
|---|--------------------|-----------|--------------------|---------|--------------|
| Inflow modulation technique                 | No ( <i>N</i> =13) | Yes (N=5) | Test value         | P value | Significance |
| Pharmacological GIM (terlipressin infusion) | 2 (15.4)           | 4 (80.0)  | 6.785 <sup>*</sup> | 0.009   | HS           |
| Surgical GIM                                | 11 (84.6)          | 1 (20.0)  |                    |         |              |

GIM, graft inflow modulation.

pattern correspondingly. Results show the efficacy of splenectomy in GIM, as agreed by Yoshizumi and Mori [15]; they stated that splenectomy was favorable in overcoming SFSS and had better graft function when compared with SAL.

On the contrary, none of our cases that had splenectomy developed portal vein thrombosis. This is in contrast to findings *of* Kurata *et al.* [16], where 33% of their cases who had splenectomy developed postsplenectomy portal vein thrombosis.

Although it is statistically insignificant, it is worth mentioning that one recipient had reexploration for splenic bed hematoma after splenectomy out of three recipients, as Ito *et al.* [17] reported higher incidence of postoperative bleeding after splenectomy.

SAL was the first surgical technique of choice in our study. Splenectomy was performed only if splenomegaly or hypersplenism was found. We found that splenectomy is more potent in decreasing portal flow than SAL. This was reported by Su *et al.* [18] and Yoshizumi and Mori [15], who recommended simultaneous splenectomy in SFSG and portal hypertension for better outcome.

Overall, 80% of the mortality in our study (four recipients out of five) was among the terlipressin infusion group, which is a highly significant mortality rate when compared with the surgical GIM group. The only death recorded in the surgical GIM group was from the SAL subgroup. Emond *et al.* [9] also recorded only one death among the SAL recipients and zero deaths among recipients who had splenectomy. Although Su *et al.* [18] recorded only one death in their surgical GIM group, it was among the splenectomy subgroup.

# Conclusion

LT has been introduced as the only life-saving treatment for patients with ESLD. With the emergence of LDLT over the last decade, SFSS has become a well-recognized complication. As donor safety is the basic principle in LDLT, recipients are more prone to have SFSGs, which in turn, increases the risk of developing SFSS. However, it became evident that SFSS occurrence is multifactorial and not dependent on graft size. Further understanding of pathogenesis helped in better donor-recipient match selection and thus, achieving better recipient outcomes in managing SFSS. GIM techniques have been evolving and being tested over decades.

Despite the fact that our study gives us the opportunity to recommend surgical strategies over terlipressin infusion in controlling portal inflow and shows better outcome in performing splenectomy over SAL in maintaining controlled portal inflow, a larger sample size study should be conducted in the future to endorse the results.

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Conflicts of interest

There are no conflicts of interest.

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