Evaluation of the difference between preoperative estimated liver volume and intraoperative actual graft volume in living donor liver transplantation and its effect on the recipient

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Background
Living donor liver transplantation (LDLT) is the only treatment for patients with end-stage liver diseases and liver tumors in Egypt, although in LDLT, there are two paradoxical concerns of adult LDLT: one is the size of liver remnant for the donor, and another is the minimum graft size for the recipient, in considering living donor safety and recipients' prognosis.

Objective
In this retrospective study, we evaluated the difference between the preoperative estimated liver volume and the actual intraoperative graft volume in donors who underwent right hepatectomies and analyzed the effect of age, BMI, and sex on this difference and its effect on the recipient regarding small-for-size syndrome (SFSS).

Patients and methods
Our study was conducted on 200 donors who underwent right hepatectomies performed at Ain Shams Center for Organ Transplantation in Cairo between 2016 and 2020. We evaluated the preoperative liver graft volume by computed tomography volumetry and the actual graft volume intraoperatively and following up the recipient to detect the effect of graft volume difference (delta volume) on the recipient in regard to SFSS and factors affecting it.

Results
The mean preoperatively estimated graft volume was 922.52±157.53 g, and the mean intraoperatively measured actual graft volume was 796.15±147.28 g. There was a statistically significant difference (*P*=0.000). Age of the donor had a significant effect on the discrepancy between the predicted and actual graft volume, whereas sex and BMI did not. The higher the BMI of the recipient, the more was the incidence of SFSS. Glypressin with or without splenectomy decreases SFSS manifestation after LDLT in patients diagnosed with SFSS.

Conclusion
Proper preoperative selection of the donor and estimation of graft volume should be performed accurately to prevent donor morbidity and mortality and to decrease the incidence of SFSS in recipients. We should put into consideration that there is a difference of 13.7% between the predicted and the actual graft volume that is usually encountered. Administration of glypressin with or without splenectomy is effective in the management of patients with SFSS. Decreasing BMI of the recipient plays a role in decreasing the incidence of SFSS and its manifestations.

Keywords:
computed tomography volumetry, liver volume, living donor liver transplantation

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Introduction

Living donor liver transplantation (LDLT) is a successful treatment for patients with end-stage liver illness; this procedure is possible because of the anatomical structure of the liver and the regeneration potential of the remnant parts [1].

In Egypt, the use of deceased organ donors is still not allowed, and as a result, some patients seek liver transplant abroad. Thus, LDLT is the only possible option for patients with end-stage liver disease in Egypt [2].

In July 1989, Strong *et al.* [3] performed the first successful transplantation of a liver graft from a living

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related donor; the donor was a 29-year-old woman, and the recipient was her 17-month-old son.

LDLT using left-lobe grafts was introduced to adult recipients in 1993. However, this procedure did not become widespread owing to the inability of these relatively small-sized grafts to meet the metabolic demands of all adult recipients. To overcome the problem of inadequate graft volume encountered by left-lobe grafts, transplantation with right lobe liver grafts was introduced to adult recipients in 1996 [4].

Given the potential risks to the living donor, only recipients with a reasonably favorable posttransplant outcome should be considered for LDLT. Thus, before proceeding to work up any potential donor, the recipient candidate should first be deemed suitable for the LDLT operation both medically as well as surgically [5].

Accurate preoperative prediction of functional donor and remnant hemiliver volumes in LDLT is essential in preventing postoperative liver failure and optimizing safety. Regardless of the benefit that LDLT offers to the critically ill patients with end-stage liver disease, donor safety is a prime concern [6].

Two formulas are used to assess graft size adequacy: (a) graft–recipient body weight ratio (GRBWR) and (b) graft weight (GW) as a percentage of standard liver mass. There is an excellent linear correlation between the two, and either is acceptable. It probably is reasonable to correct the GRBWR for steatosis by subtracting the percentage of steatosis noted on liver biopsy from the functional hepatic mass [7].

Resection should not exceed 70% of the total liver volume, that is, the donor should be left with at least 30% of the measured total liver volume. Liver failure has been reported after donation, with at least one donor requiring an urgent liver transplant because of liver failure after donation. As a result, LDLT has limited applicability in many patients because of the inability to identify a suitable donor [8].

A GRBWR of 1% is approximately equal to 50% of standard liver mass. The consensus is that the GRBWR should be equal or greater than 0.8% (equivalent to about 40% of the standard liver volume). It should be stressed, however, that these values are based upon LDLT performed in noncritically ill patients [9].

Small-for-size syndrome (SFSS) was initially described as a number of clinical manifestations resulting from the use of small-for-size grafts (SFSGs). SFSS is characterized by persistent hyperbilirubinemia, coagulopathy, intractable ascites, and encephalopathy; however, the definition varies among centers. It was considered to occur because of reduced metabolic and synthetic capacity, causing delayed recovery of bilirubin clearance and prothrombin time, and putting recipients at a higher risk for surgical and/or septic complications. Dahm and colleagues defined SFSS as a dysfunction of a partial liver graft [graft-to-recipient weight ratio (GRWR)<0.8%] based on the presence of two of the following three criteria on three consecutive days during the first postoperative week, after the exclusion of other causes: (a) total bilirubin greater than 5.8 mg/dl, (b) prothrombin international normalized ratio greater than 2, and (c) encephalopathy grade greater than 3 [10].

In LDLT, the preoperative donor graft volume is often calculated using computed tomography (CT) and automatic volume calculation programs. However, despite technological developments, discrepancies between the preoperative and intraoperative volume measurements are seen [11].

Preoperative radiological evaluation of liver volume is the standard method for donor evaluation, aiming minimization of unnecessary risks. Therefore, accurate assessment of the volume of the liver and its lobes before surgery is mandatory. CT volumetry is a useful tool for predicting GW for LDLT [12].

Patients and methods

Our study was conducted on 200 adult patients who underwent right lobe graft LDLT and their demographic data and estimated GRWR at Ain Shams Center for Organ Transplantation (ASCOT) in the period from January 2016 to December 2020. We calculated the preoperative estimated GRWR and estimated graft volume and compared them with actual GRWR and actual graft volume. Moreover, we calculated the difference between them and the effect of this difference on the recipient and the relation of age, BMI, and sex to this difference and SFSS. The difference between the preoperative calculations and the intraoperative volumetric measurements is known as the delta (Δ) volume, and according to the incidence of SFSS, we divided the patients into two groups: patients with or without SFSS for better understanding of the factors affecting it.

We used CT volumetry to evaluate the preoperative liver volume and graft by automatic volume calculation. Our protocol was the same for all patients of our study in which precontrast thin-slice scanning was done and dynamic phases with contrast including arterial, portal, and venous phases were done, and then virtual hepatectomy line was drawn to the right of the middle hepatic vein. We assumed that the mean liver density equals 1 g/ml (the calculated volumes equal their respective weights), considering estimated GRWR not to be less than 0.8.

IBM SPSS Statistics for Windows, version 23.0, Armonk, NY: IBM Corp, software was used for the statistical analysis. The quantitative data were presented as mean, SD, and ranges when parametric and median and interquartile range when data were found nonparametric. Moreover, qualitative variables were presented as number and percentages. χ^2 test, Fisher exact test, independent *t* test, Mann–Whitney test, paired *t* test, and Spearman correlation coefficients were used. A *P* value less than 0.05 was accepted as the level of statistical significance.

Results

At ASCOT in the period from January 2016 to December 2020, our study included 200 adult patients who underwent right lobe graft LDLT, and their demographic data were evaluated.

Of 200 liver donors, 148 were male and 52 were female. The median age was 28.04 years, the median BMI was 24.26 kg/m^2, and the median preoperative liver volume calculated was 922.52 g, whereas the volume measured intraoperatively was 796.15 g. The demographic data are shown in Table 1.

The difference between the mean preoperative liver graft volume value and the volume measured intraoperatively was 126.37 ± 9.45 g, with *P* value less than 0.001.

The difference calculated between the estimated liver volume and the volume of the extracted liver graft intraoperatively increased with the increase in age (*P*=0.007) (Fig. 1).

No significant difference was seen in the analysis of volume values based on sex (*P*=0.085) or BMI of the donor (*P*=0.271).

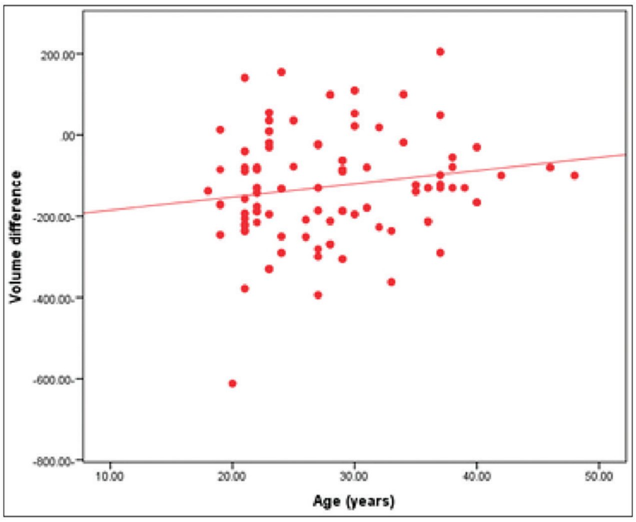
Table 2 and Fig. 2 show that the difference between estimated liver graft volume and actual volume among patients with SFSS was a mean of 159.52 g, an underestimation fallacy, with *P* value less than 0.001. However, among patients without SFSS, the mean was 121.29 g, with *P* value less than 0.001, which was statistically significant.

Table 1 Demographic data of the patients and early postoperative mortality

	N=200
Donor age (years)	
Mean±SD	28.04 ± 6.85
Range	18–48
Donor sex [*n* (%)]	
Females	52 (26.0)
Males	148 (74.0)
Donor BMI (kg/m^2)	
Mean±SD	24.26 ± 3.43
Range	15.8–38
Donor-estimated graft volume (g)	
Mean±SD	922.52 ± 157.53
Range	653–1272
Donor-estimated GRWR [*n* (%)]	
Mean±SD	1.20 ± 0.25
Range	0.83–2.07
Actual GRWR%	
Mean±SD	1.03 ± 0.22
Range	0.6–1.9
Intraoperative graft volume (g)	
Mean±SD	796.15 ± 147.28
Range	480–1160
Difference in graft volume (g)	
Mean±SE	126.37 ± 9.45
Early postoperative mortality within 1 month of the recipients [*n* (%)]	
No	194 (97.0)
Yes	6 (3.0)

GRWR, graft-to-recipient weight ratio.

Figure 1



Scatter plot diagram showing correlation between delta volume and age.

The difference in graft volume is higher in patients with SFSS, with *P* value less than 0.001.

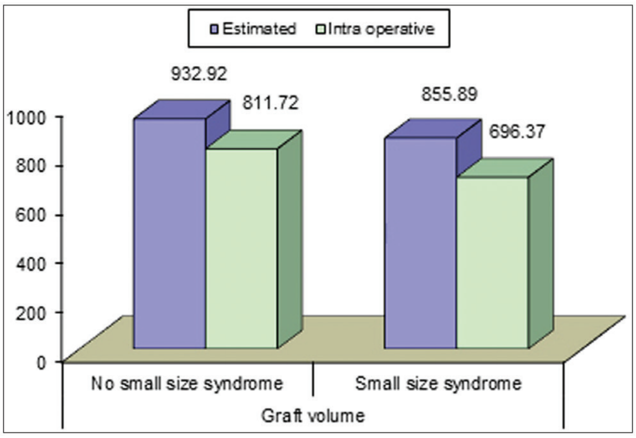
Tables 1 and 3 show that the 27 (13.5%) recipients were diagnosed as having SFSS. They all received glypressin, and of them, five recipients went for splenectomy. One

Table 2 The difference between preoperative estimated liver graft volume and graft-to-recipient weight ratio and intraoperative actual graft volume and graft-to-recipient weight ratio regarding small-for-size syndrome

	Estimated	Intraoperative	Difference	Test value	*P* value	Significance
Graft volume						
No small-for-size syndrome	932.92 ± 153.34	811.72 ± 147.74	121.2 ± 127.11	12.541	<0.001	HS
Small-for-size syndrome	855.89 ± 170.45	696.37 ± 98.37	159.52 ± 169.6	4.887	<0.001	HS
GRWR %						
No small size syndrome	1.23 ± 0.24	1.07 ± 0.21	0.16 ± 0.01	11.250	<0.001	HS
Small size syndrome	1.02 ± 0.18	0.79 ± 0.12	0.23 ± 0.16	7.588	<0.001	HS

GRWR, graft-to-recipient weight ratio; HS, highly significant.

Figure 2



The difference between preoperative estimated graft volume and intraoperative actual graft volume regarding SFSS. SFSS, small-for-size syndrome.

of them died after 1 week of the operation, and the other one from who were diagnosed with SFSS died due to insufficient metabolic need and small graft. There were other four deaths in our study but due to other causes other than SFSS: two owing to sepsis, and other two due to Disturbed Conscious Level (DCL) and chest infection as the total deaths were six (3%) patients out of 200 recipients.

Discussion

Liver transplantation is currently considered the salvage treatment for otherwise fatal liver illnesses, and LDLT solves the problem of donor shortage and significantly reduces the waiting time for such surgery.

The problem of graft size is one of the critical factors limiting the expansion of adult-to-adult LDLT. GRWR greater than 0.8% is perceived as the critical graft size to meet the metabolic demand of the recipient [13].

SFSG is the graft with GRWR less than 0.8 and when its unable to meet the recipients metabolic demands, SFSS occurs which is clinically characterized by a postoperative prolonged hyperbilirubinemia, presence of severe ascites, prolonged coagulopathy, and encephalopathy (grade 3 or 4), which would result in poor postoperative outcomes. In fact, there was evidence showing that SFSG resulted in significantly worse graft survival [14].

We carefully left 30% of the total liver volume in the donor and to obtain a graft/weight ratio for the recipient of 0.8. The scenario of lower GRWR in LDLT occurs more by accident than by intent, as CT volumetry overestimated the GRWR as compared with the actual GRWR.

Our study included 200 adult patients who underwent right lobe graft LDLT and their donors' demographic data and estimated the GRWR at ASCOT in the period from January 2016 to December 2020. We calculated the preoperative estimated GRWR and estimated graft volume compared with the actual GRWR and actual graft volume and the difference between them and the effect of this difference on the recipient and the relation of age, sex, and BMI to this difference and SFSS.

According to the incidence of SFSS, we divided the patients into two groups (patients with or without SFSS) for better understanding of the factors affecting it.

Most transplant centers regard 1 cm^3 of liver on preoperative volumetry to be equal to 1 g of liver, with the assumption that the mean density of healthy liver tissue is 1.00 g/ml [15].

So, preoperatively calculated volume of right liver lobe graft have been equated with their respective weights.

In our study, we found that there was a statistically significant difference between the preoperative estimated liver graft volume and intraoperative actual graft volume with mean difference of 126.37 g with *P* value of 0.000, with nearly 13.7% discrepancy demonstrated as an overestimation of the graft volume, which was an important factor in our study that led to SFSS.

Similar to our study, Li *et al.* [16] reported a mean deviation in delta volume of 13.81 ± 8.12% .

Table 3 Comparison between patients with small-for-size syndrome and those without regarding intraoperative and postoperative management and the effect of BMI on small-for-size syndrome

Recipient	Small-for-size syndrome		Test value*	*P* value	Significance
	No (*N*=173)	Yes (*N*= 27)			
Splenectomy [*n* (%)]					
No	173 (100.0)	22 (81.5)	32.858	0.000	HS
Yes	0	5 (18.5)			
Glypressin [*n* (%)]					
No	173 (100.0)	0	200.000	0.000	HS
Yes	0	27 (100.0)			
BMI (kg/m^2)					
Mean±SD	26.73±4.01	28.52±4.03	−2.164•	0.032	S
Range	17–35	21.22–39			

HS, highly significant; S, significant. *χ^2 test. •Independent *t*-test. *P* value greater than 0.05, nonsignificant. *P* value less than 0.05, significant. *P* value greater than 0.01, highly significant.

However, in a study by Salvalaggio *et al.*[17], a 20% discrepancy was demonstrated between estimated liver volume and intraoperative measurement of the extracted liver .

Moreover, we found that the higher the difference (delta volume), the higher the incidence of SFSS.

We realized that the incidence of SFSS increased with GRWR less than equal to 0.8, which results from GW overestimation in the donor by CT volumetry.

Shoreem *et al.* [18], in a recent 10-year retrospective cohort study on 174 cases of adult-to-adult LDLT demonstrated that a lower GRWR was linked to an increased risk of SFSS, and SFSG is the independent and main factor for occurrence of SFSS after Adult Living Donor Liver Transplantation (A-ALDLT) leading to poor outcome.

In our analysis, the graft volume difference increased with age, and similar to our study, Baskiran and colleagues found that the delta volume increased with age, which was consistent with other published study results. The primary reason is that as a result of alterations in liver parenchyma with aging, the demarcation line on the liver made during the CT scan cannot be done as accurately, which affects the volumetric analysis, and in contrast to our study, they found that the difference between the mean preoperative volume value of 800±112 g and the volume measured intraoperatively of 750±131 g was calculated (*P*=0.003). A greater difference was observed between the estimated liver volume and the volume of the extracted liver measured intraoperatively in parallel with an increase in BMI of the donor [19], but in our study, there was no effect of BMI nor sex on this difference.

There was a statistically significant difference between patients with SFSS and those without, as the incidence of SFSS increases with the increase of BMI of the recipient.

Of a total number of 27 patients diagnosed as having SFSS, five of them went for splenectomy intraoperatively, which was an effective method for portal flow modulation and decreasing postoperative SFSS manifestations on the recipient and better graft survival.

Similar to our study, an experimental study by Athanasiou *et al.* [20] indicated that perioperative portal modulation can successfully prevent the manifestation of SFSS. Therefore, by focusing on 'flow' rather than on 'size,' researchers may understand better the pathophysiology of this syndrome.

We found that glypressin administration is effective in intraoperative and postoperative continuation for enhancement and improving portal flow and better graft survival in recipients diagnosed with SFSS.

Similar to our study, terlipressin (glypressin) rapidly modulated excessive portal pressure in the early postoperative period after extensive hepatectomy in a large animal model. Consequently, the modulated portal pressure could optimize the liver regeneration process, resulting in reduced liver injury and improved survival [21].

There was no statistically significant difference between recipients postoperative follow-up in regard to increase level of bilirubin nor postoperative ascites that is due to portal flow modulation by glypressin with or without splenectomy that improved postoperative liver function tests and better graft survival and regeneration, whereas there was a statistically significant difference in increase of international normalized ratio value greater than 2 during first week after transplantation and encephalopathy even with portal flow modulation.

There was no statistically difference between patients with SFSS and patients without regarding postoperative sepsis.

Regarding the outcome, in our study, we found that there is a significant correlation between SFSS and early postoperative mortality, which was higher in patients with SFSS than in those without SFSS, with percentages of 14.8 and 1.2%, respectively. Similar to our study, the study by Sanefuji *et al*. [22] included 172 patients who underwent Living Aonor for Adult liver transplantation (LDALT) for chronic liver disease and reported that SFSS is associated with poor postoperative outcome as 1-year survival in patients with SFSS was 71% compared with 87% in patients without SFSS. Moreover, the study by Soejima *et al*. [23] reported that recipients who developed SFSS had inferior patient survival.

Conclusion

Proper preoperative evaluation of the donor graft volume should be performed to prevent donor morbidity and mortality as well as SFSS in the recipient. Physicians working in the field of transplantation should be aware of the fact that a difference of 13.7% between the predicted and the actual graft volume is usually encountered. Moreover, if SFSS is encountered, glypressin with or without splenectomy has an important role in portal flow modulation to decrease SFSS manifestations and better graft survival on basis to our study. Moreover, age had a significant effect on the discrepancy between the predicted and actual graft volume, whereas sex and BMI did not. Decreasing BMI of the recipient plays a role in decreasing the incidence of SFSS and its manifestations. According to our study results, we think that we can use smaller liver graft with GRWR up to 0.6 with age less than 48 years and portal flow modulation. For further evaluation, a study on a larger group of patients may be needed for validation.

Declaration of patient consent

Patients are freely giving fully informed consent to participate. Participant's confidentiality and data security are guaranteed. Participants should be able to withdraw from the research process at any time, they also should be able to withdraw their data if it is identifiable for them and should be told when this will be no longer be possible. We describe any expected benefits for the research participants, also any possible risk to them.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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