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Factors Affecting Difference between EGW and AGW in Liver Transplantation

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ABSTRACT
Background: An accurate preoperative estimate of the graft weight and remnant liver volume is vital to avoid small-for-size syndrome(SFSS) in the recipient and ensure donor safety after Living donor liver transplantation (LDLT). CT has been widely used as a method for the preoperative volumetric assessment of the liver transplantation. The graft size as measured from preoperative imaging which is often different from the actual weight of the liver graft as obtained by the donor hepatectomy.
The difference between preoperative volumetry and Actual graft weight (AGW) was graded into minimal difference (≤15%) and big difference (>15%).
Aim of The Work: This study was conducted to assess different preoperative factors that might affect the difference between estimated graft weight and actual graft weight in liver transplantation.
Patients And Methods: This single center retrospective study was conducted on 86 cases who have been subjected to donation for liver transplantation in Ain Shams Center of organ transplantation.**Donors were divided into two groups:**
Group (A): formed of 33 donors who showed minimal difference (≤15 %) between EGV and AGW.
Group (B): formed of 53 donors who showed big difference (>15 %) between EGV and AGW.
Each donor data was examined for: Age, Sex: male or female, Body mass index (BMI), Lipid profile (positive / negative) Type of hepatectomy (Rt lobe / Lt lobe), AGW.Estimated graft weight (EGW), Total liver volume, Liver biopsy: Fibrosis (positive/ negative), Steatosis: Negative: (0%) and Positive: (5% or 10%).
Results: EGW of 903 gm was identified as cutoff point of the best specificity with the best sensitivity showing 60.4 % and 60.6% for sensitivity and specificity, respectively. At this cutoff point, 47.7% of cases (n=41) showed EGW < 903 gm, while 52.3% of cases (n=45) showed EGW ≥ 903 gm. Thus, it can be said that cases showed EGW ≥ 903 gm have a probability of 71.1% to have big difference between EGW and AGW (≥15%).
EGW of 1069 gm was identified as another cutoff point of a better specificity on ROC curve showing 32.1% and 93.9% for sensitivity and specificity, respectively, on ROC curve. At this cutoff point, 77.9% of cases (n=67) showed EGW < 1069 gm, while 22.1% of cases (n=19) showed EGW ≥ 1069 gm. Thus, it can be said that cases showed EGW ≥1069 gm have a probability of 89.5% to have big difference between EGW and AGW (≥15%).
TLW of 1587 gm was identified as cutoff point of the best specificity with the best sensitivity and specificity on ROC curve showing 56.6% and 60.6% for sensitivity and specificity, respectively, on ROC curve. At this cutoff point, 50% of cases (n=43) showed TLW < 1587 gm, while 50% of cases (n=43) showed TLW ≥ 1587 gm.
Thus, it can be said that cases showed TLW ≥1587 gm have a probability of 69.8% to have big difference between EGW and AGW (≥15%).
TLW of 1807 gm was identified as another cutoff point of better specificity on ROC curve showing 18.9% and 93.9% for sensitivity and specificity, respectively, on ROC curve. At this cutoff point, 86% of cases (n=74) showed TLW < 1807 gm, while 14% of cases (n=12) showed TLW ≥ 1807 gm. Thus, it can be said that cases showed TLW ≥1807 gm have a probability of 83.3% to have big difference between EGW and AGW (≥15%).
Conclusion: TLV and EGV in CT volumetry are most reliable preoperative factors that can predict big difference between EGW and AGW. Re-evaluation of CT volumetry protocol is recommended for better prediction.
Keywords: AGW: EGW. EGW: EGW. LDLT: Living donor liver transplantation. SLV: standard liver volume. TLV: total liver volume.

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INTRODUCTION

The first human orthotopic liver transplantation (LT) in Europe was performed by Sir Roy Calne in Cambridge in 1968, only one year after the first successful human liver transplantation reported by Thomas Starzl in the United States which was operated in 1967. Then liver transplantation has evolved rapidly, becoming the standard therapy for acute and chronic liver failure of all etiologies due to introduction of new immunosuppressive agents and preservation solution improvements in surgical techniques and due to the early diagnosis and management of complications after liver transplantation. Survival rate has improved significantly in the last 25 years, achieving rate of 71% at 10 years after liver transplantation[(1)].

LDLT using left-lobe grafts was introduced for adult recipients in 1993, in order to overcome the inadequate graft volume encountered with left-lobe grafts, transplantation with right-lobe liver grafts was introduced for adult recipients in 1996[(2)].

In liver transplantation, it is generally accepted that the ratio of the graft volume to standard liver volume (SLV) needs to be at least 30% to 40% to fit the hepatic metabolic demands of the recipient[(3)]. The graft-to-recipient weight ratio (GRWR) is an important selection criterion for LDLT. The generally accepted threshold is known to be 0.8%[(4)].

An accurate preoperative estimate of the graft weight and remnant liver volume is vital to avoid small-for-size syndrome in the recipient and ensure donor safety after LDLT[(5)]. CT has been widely used as a method for the preoperative volumetric assessment of the liver transplantation[(6)].The graft size as measured from preoperative imaging which is often different from the actual weight of the liver graft as obtained by the donor hepatectomy[(7)].

The difference between preoperative volumetry and AGW was graded into minimal difference (≤15%) and big difference (>15%)[(8)].

AIM OF THE WORK

This study was conducted to assess different preoperative factors that might affect the difference between estimated graft weight and actual graft weight in liver transplantation.

PATIENTS AND METHODS

This single center retrospective study was conducted on cases who have been subjected to donation for liver transplantation in Ain Shams Center of organ transplantation.

The study was approved by the Ethics Board of Ain Shams University.

Donors were divided into two groups:

Group (A): formed of 33 donors who showed minimal difference (≤15 %) between EGV and AGW.

Group (B): formed of 53 donors who showed big difference (>15 %) between EGV and AGW.

Patient selection:

Data of 112 donors could be identified to be subjected to live donation, during the period between January 2015 and August 2017 in Ain Shams center of organ transplantation.

Each donor data was examined for:

Age, Sex: male or female, BMI, Lipid profile (positive / negative) Type of hepatectomy (Rt lobe / Lt lobe), AGW. EGW, Total liver volume(TLV), Liver biopsy: Fibrosis (positive/ negative), Steatosis: Negative: (0%) and Positive: (5% or 10%).

Twenty six cases were excluded due to missed data. So, 86 cases, who fulfilled the required data, were included in the study.

Statistical Analysis

Descriptive statistics were calculated and data expressed as means ± SD for age (year), mass index (kg/m2), estimated graft weight (gm), Total liver weight (gm). Then, data was analyzed using multivariate methods to detect correlation between each variable and difference between estimated graft weight and actual graft weight . linear regression analysis was done and ROC curve was used to determine possible cutoff points, then crosstabs test was done to detect predictive value of cutoff points.

P value considered staticaslly significant if P value < 0.05.

RESULTS

Distribution of different variables among both groups (group A and group B) was summarized in table 1, 2:

Table (1): Distribution of variables of positive/negative values.

		Difference between est. & actual graft size < 15% N (%)		Difference between est. & actual graft size > 15% N (%)		P
x	male	11	33.3%	13	24.5%	.376
	ale	22	66.7%	40	75.5%	
story of drug take	gative	30	90.9%	52	98.1%	.123
	sitive	3	9.1%	1	1.9%	
pid profile	gative	24	72.7%	44	83.0%	.254
	sitive	9	27.3%	9	17.0%	
brosis	gative	13	39.4%	26	49.1%	.381
	sitive	20	60.6%	27	50.9%	
eatosis (level)	%	18	54.5%	24	45.3%	.689
	%	12	36.4%	24	45.3%	
	%	3	9.1%	5	9.4%	
eatosis (-ve, +ve)	gative	18	54.5%	24	45.3%	.403
	sitive	15	45.5%	29	54.7%	
lobe or Lt lobe	lobe	0	0.0%	4	7.5%	.106
	lobe	33	100.0%	49	92.5%	

Table (2): Distribution of variables of numerical values.

	difference between est. & actual graft size < 15% Mean ± SD (min – max)	difference between est. & actual graft size > 15% Mean ± SD (min – max)	P
e	30.4 ± 8.0 (18.0-47.0)	26.5 ± 5.9 (17.0-42.0)	.017*
II	24.2 ± 2.6 (18.0-27.0)	24.4 ± 2.5 (20.0-29.0)	.752
W	864.7 ± 150.6 (554.0-1150.0)	972.5 ± 178.8 (509.0-1416.0)	.005*
W	1486.5 ± 245.5 (938.0-2050.0)	1628.3 ± 232.9 (1250.0-2208.0)	.009*

Table (3): Summarize correlations between different variables and each others.

		Age	BMI	EGW	TLW	Difference between estimated & actual graft Wt (%)
Age	R	1				
	P					
BMI	R	.126	1			
	P	.247				
EGW	R	-.013	.203	1		
	P	.902	.061			
TLW	R	-.019	.221*	.865**	1	
	P	.864	.041	.000		
Difference between estimated& actual graft Wt (%)	R	-.187	.148	.267*	.308	1
	P	.085	.173	.013	.004	

Table (4): Linear regression analysis for different variables

Model Summary				
Model	**R**	**R Square**	**Adjusted R Square**	**Std. Error of the Estimate**
1	.975[a]	.950	.943	2.5497

	Unstandardized Coefficients		Standardized Coefficients	t	P	95.0% Confidence Interval for B	
	B	Std. Error	Beta			Lower Bound	Upper Bound
(Constant)	20.802	3.318		6.269	.000*	14.191	27.412
Age	-.028	.044	-.018	-.642	.523	-.115	.059
Sex	-.272	.773	-.011	-.351	.726	-1.811	1.268
History of drug intake	.279	1.501	.006	.186	.853	-2.712	3.270
BMI	.103	.127	.024	.812	.419	-.150	.356
Lipid profile	.325	.741	.012	.438	.662	-1.152	1.801
Fibrosis	.171	.586	.008	.292	.771	-.996	1.338
steatosis (-ve, +ve)	-.113	.593	-.005	-.190	.849	-1.295	1.069
Rt / Lt lobe	-4.400	1.396	-.087	-3.152	.002*	-7.181	-1.619
Estimated graft weight	.083	.003	1.369	30.618	.000*	.078	.089

ROC curve test for both age and BMI revealed P value of age and BMI equal 0.033 and 0.947, respectively, but still low AUC for both age and BMI: 0.363 and 0.504, respectively.

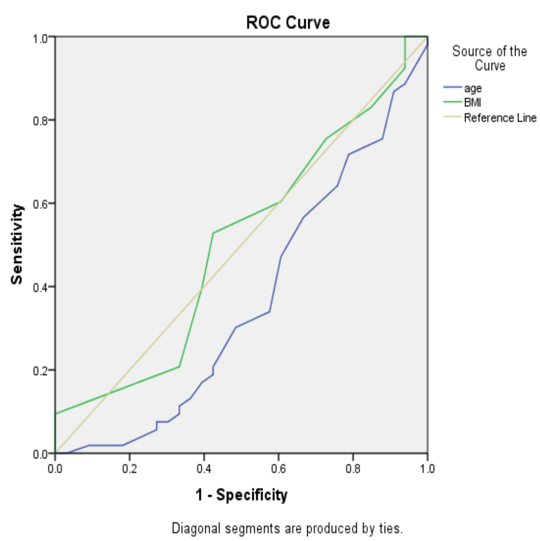

Figure (1): ROC curve for age and BMI.

Table (5): Data of ROC curve for age and BMI

est Result Variable(s)	Area Under the Curve	P	95% Confidence Interval	
			Lower Bound	Upper Bound
Age	.363	.033*	.238	.487
BMI	.504	.947	.377	.632

ROC curve test was used to detect cutoff points for estimated graft weight and total liver weight.

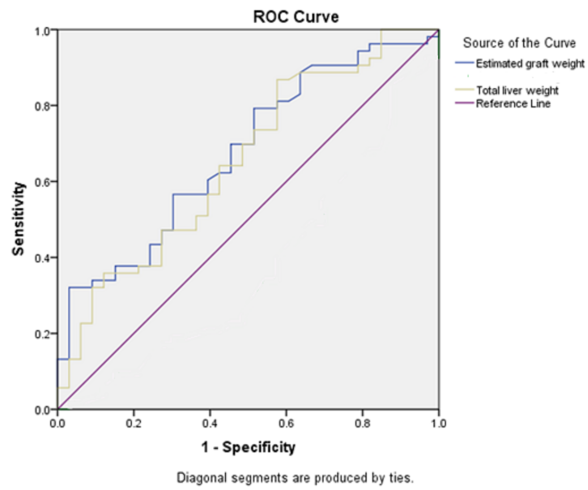

Figure (2): ROC curve for EGW and TLV.

Table (1): Data of ROC curve for EGW and TLW

Test Result Variable(s)	Area Under the Curve	P	95% Confidence Interval	
			Lower Bound	Upper Bound
Estimated graft weight	.676	.006*	.561	.790
Total liver weight	.652	.018*	.533	.772

Cutoff points for EGW

EGW of 903 gm was identified as cutoff point of the best specificity with the best sensitivity showing 60.4 % and 60.6% for sensitivity and specificity, respectively. At this cutoff point, 47.7% of cases (n=41) showed EGW < 903 gm, while 52.3% of cases (n=45) showed EGW ≥ 903 gm. Thus, it can be said that cases showed EGW ≥ 903 gm have a probability of 71.1% to have big difference between EGW and AGW (≥15%).

EGW of 1069 gm was identified as another cutoff point of a better specificity on ROC curve showing 32.1% and 93.9% for sensitivity and specificity, respectively, on ROC curve. At this cutoff point, 77.9% of cases (n=67) showed EGW < 1069 gm, while 22.1% of cases (n=19) showed EGW ≥ 1069 gm. Thus, it can be said that cases showed EGW ≥1069 gm have a probability of 89.5% to have big difference between EGW and AGW (≥15%).

Cutoff points for TLW:

TLW of 1587 gm was identified as cutoff point of the best specificity with the best sensitivity and specificity on ROC curve showing 56.6% and 60.6% for sensitivity and specificity, respectively, on ROC curve. At this cutoff point, 50% of cases (n=43) showed TLW < 1587 gm, while 50% of cases (n=43) showed TLW ≥ 1587 gm.Thus, it can be said that cases showed TLW ≥1587 gm have a probability of 69.8% to have big difference between EGW and AGW (≥15%).

TLW of 1807 gm was identified as another cutoff point of better specificity on ROC curve showing 18.9% and 93.9% for sensitivity and specificity, respectively, on ROC curve. At this cutoff point, 86% of cases (n=74) showed TLW < 1807 gm, while 14% of cases (n=12) showed TLW ≥ 1807 gm. Thus, it can be said that cases showed TLW ≥1807 gm have a probability of 83.3% to have big difference between EGW and AGW (≥15%).

DISCUSSION

In this study, 61.6% of donors (n=53) showed big difference between estimated and AGW while 38.4% of donors (n=33) showed minimal difference between estimated and AGW. This result is worse than that of **Mussin *et al.***[8] study, conducted to 215 donors, and showed that big differences between estimated and AGW were 44.9% and 30.6% using Rapidia software and Dr. Liver software, respectively.

Findings in this study suggest that donors with EGW ≥ 903 gm have the probability of 71.7% to show big difference between EGW and AGW (≥15%), and those who have EGW ≥ 1069 gm have the probability of 89.5% to show big difference between estimate and AGW. Also this study revealed that donors with TLW ≥ 1587 gm have the probability of 69.8% to show big difference between EGW and AGW, and those who have TLW ≥ 1807 gm have the probability of 83.3% to show big difference between estimate and AGW.

These findings could be helpful to decrease incidence of big difference between EGW and AGW in LDLT, through helping in decision making about the suitable graft volume for LDLT.

Other preoperative variables including, age, sex, BMI, history of drug intake, liver fibrosis and steatosis could not show real correlation in making big difference between estimated and AGW. Weak negative correlation could be observed between age and difference between estimated and AGW, as Mean of age was 30.4 $\pm$ 8.0 in group A of minimal difference between EGW and AGW, while mean was age 26.5 $\pm$ 5.9 in group B of big difference between EGW and AGW, but area under curve (AUC) in ROC curve was 0.363 which is too small to put it in consideration**.**

Choukèr *et al*. revealed that liver weight (LW) was best predicted in younger people (16–50 years) by body weight, age, and gender. In contrast, in elderly people (51–70 years) LW was best predicted by BW and age only. Gender was not a significant factor[9]**.**

In this study the upper limit of age did not exceed 47 years. Correlation between age and difference between estimated and AGW showed weak negative slope. The prediction of difference between EGW, using CT volumetry, and AGW was slightly better at the age of 30.4 $\pm$ 8.0 with P value= 0.017. However this good predictive value of age was missed on analysis of data using multivariate methods: P value = 0.523 on using multiple linear regression test.

Sex and BMI could not show any role in prediction of difference between EGW and AGW. P value of sex was 0.376 and 1.268 on using descriptive and multiple linear regression analyses, respectively. P value of BMI was 0.752 and 0.356 on using descriptive and multiple linear regression analyses, respectively. The same is history of drug intake did not give any help in prediction of difference between EGW and AGW, with P value equals 0.123 and 3.270 on using descriptive and multiple linear regression analyses, respectively.

Findings of this study show that the presence and degree of hepatic steatosis does not in practice affect the accuracy with which CT volume measurements estimate graft weight. This outcome is similar to that of the study of ***Siriwardana et al*** **,** revealed that the pattern of estimation errors was independent on the extent of steatosis [10]. Also, similar to that of the study of Yeonjung Ha et al., who revealed that CT volumetric measurement is an accurate and reliable tool for preoperative estimation of hepatic weight in surgical candidates for liver donation or resection, regardless of steatosis grade.[11] Our results show that CT-based volume measurement is accurate and reliable regardless of the severity of the hepatic steatosis.

Claire *et al*. concluded to Liver volume assessed by CT did not correspond to real Liver Weight. Liver density changed according to the aetiology and severity of liver disease in cirrhotic liver and commonly used formulae did not accurately assess Liver volume [12]. But, it was found, in this study, that there is no evidence that fibrosis has a role in disparities between estimated and AGW. This could be due to the fact that fibrosis in donors of our study was minimal to mild, microscopic, not distorting the hepatic architechure, unlike the liver cirrhosis which is gross and distorts the hepatic architecture and intrahepatic circulation. Both EGW and TLW showed good correlation to big difference between estimated and AGW. EGW showed P value =0.005 at descriptive analysis, p value = 0.013 on multivariate methods and p value = 0.006 with AUC = 0.676 on ROC curve. TLW showed good correlation to big difference between estimated and AGW. EGW showed P value =0.009 at descriptive analysis, p value = 0.004 on multivariate methods and p value = 0.018 with AUC= 0.652 on ROC curve.

CONCLUSION

TLV and EGV in CT volumetry are most reliable preoperative factors that can predict big difference between EGW and AGW. Re-evaluation of CT volumetry protocol is recommended for better prediction.

REFERENCES

1. Patrizia B, Andrew B, Ivo G *et al.* (2015): EASL Clinical Practice Guidelines: Liver transplantation. Journal of Hepatology, 64 (2):433-485.

2. Lee SG (2010): Living-donor liver transplantation in adults. Br Med Bull., 94 (1): 33-48.

3. Hee J, Choong Y, Young H *et al*. (2013): Comparison of remnant to total functional liver volume ratio and remnant to standard liver volume ratio as a predictor of postoperative liver function after liver resection. Korean J Hepatobiliary Pancreat Surg. , 17(4): 143–151.

4. Alim A, Erdogan Y, Yuzer Y *et al.* (2010): Graft-to-recipient weight ratio threshold adjusted to the model for end-stage liver disease score for living donor liver transplantation. Liver Transpl., 22: 1643–1648.

5. Wang F, Pan KT, Chu SY *et al.* (2011): Preoperative estimation of the liver graft weight in adult right lobe living donor liver transplantation using maximal portal vein diameters, Liver Transpl., 17: 373–380.

6. Lim MC, Tan CH, Caib J *et al.* (2014): CT volumetry of the liver: Where does it stand in clinical practice?.Clinical Radiology,69: 887-895.

7. Chan C, Lo CM, Chok KS *et al.* (2011): Validation of graft and standard liver size predictions in right liver living donor liver transplantation, Hepatology International, 5 (4): 913–917.

8. Mussin N, Sumo M, Lee K-W *et al*. (2017): The correlation between preoperative volumetry and real graft weight: comparison of two volumetry programs. Ann Surg Treat Res., 92(4):214-220.

9. Choukèr A, Martignoni A, Dugas M *et al.* (2004): Estimation of liver size for liver transplantation: The impact of age and gender. Liver Transpl., 10: 678–685.

10. Siriwardana RC, Chan SC, Chok KS *et al*. (2011): Effects of the liver volume and donor steatosis on errors in the estimated standard liver volume. Liver Transpl.,17(12):1437-1442.

11. Yeonjung Ha, Shim J H, Song G-W *et al.* (2017): Role of Computed Tomography Volumetry in Estimating Liver Weights in Surgical Patients with Hepatic Steatosis. Experimental and Clinical Transplantation, 2: 196-202

12. Goumard C, Perdigao F, Cazejustet J *et al*. (2014): Is computed tomography volumetric assessment of the liver reliable in patients with cirrhosis? HPB (Oxford), 16(2): 188–194.