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ORIGINAL ARTICLE

Reliable Estimation of Preoperative Graft Volume in Living Donor Liver Transplantation

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ABSTRACT

Aims & Objectives: Corner stone in performing living donor liver transplant is to assess and predict the adequacy of the donated liver for recipient and remaining liver. Previously the conversion of liver volume to estimated weight is done by using unit to unit conversion with a factor of 1. We analyzed data of our institute to research the methodology and local applicability of the same.

Place and duration of study: Shaikh Zayed Hospital, Lahore. January 2011 to June 2017

Material & Methods: Retrospective data was collected for the first 115 recipients and donors. Their preoperative liver volumes calculated by C.T scan and post-operative graft harvested with weights were compared.

Results: The parameter of actual volume of right lobe averaged to 769.77 ± 12.73 gm varying with a quantum of 17.73% (426 – 1123 gm). Estimated volume of right lobe of liver varied 358 to 1218 ml (CV = 17.84%) with an average value of 798.96 ± 13.29 ml. Results of linear regression between estimated volume of right lobe and actual weight of the right lobe in gm was significantly linear ($r = 0.830$, $r^2 = 0.690$, adj. $r^2 = 0.689$ and $F = 250.98$, $p < 0.0001$), showing that volumetric assessment overestimated graft weight/volume. Following is equation generated from our data for graft weight estimation. Actual right lobe (g) = 134.004 + 0.796 (estimated right lobe volume (ml) ± 76.42.

Conclusion: Using one to one principle for volume estimation of healthy liver can be misleading and therefore we propose an equation to reach more accurate estimation of graft weight.

Keywords: living donor liver transplant, CT volumetry, graft to body weight ratio

INTRODUCTION

The first liver successful liver transplant was performed by Dr Thomas Starzl in 1967. Bismuth and Houssin reported the first reduced size liver graft in 1981, paving the path for living donor liver transplantation. Numerous advancements in surgical techniques and improvement in immunosuppressant drugs made it a treatment of choice in various liver related diseases.[1] Pakistan started its Liver Transplant Program in 2011-2012.[2] Unlike most of the developed nations, countries like Pakistan mostly rely on living donors as a source of grafts for transplantation rather on cadaveric supply. Initially there were many concerns about usefulness of living donor grafts as compared to cadaveric livers. Multiple studies have successfully addressed this issue of safety and effectiveness of taking smaller grafts from living donors for transplantation.[2,3,4]

The corner stone in performing living donor liver transplantation is to assess and predict the adequacy of the donated liver for recipient and remaining liver for the donor. The importance of this preoperative evaluation is highlighted by a study conducted by Hahn, which demonstrated that 66% of liver donor candidates were rejected for donation because of inadequate liver volumes.[5] CT volumetry with different softwares and MRI are the principal radiologic modalities used to assess liver volumes and anatomy.[6]

Traditionally, liver volume to estimated weight is measured by using unit to unit conversion with a factor of 1. This conversion rule was based on taking weights of cirrhotic liver.[7] However, some recent studies have revealed that 1gm/1ml conversion has a potential to overestimate graft weight of healthy livers. They have estimated that this factor is close to 0.82 in their studies.[8,9] We decided to analyse the data of our institute to review the methodology and local applicability of the graft weight/volume estimation techniques and attempt to formulate our own protocols which would lead to a more realistic graft weight/volume calculation.

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MATERIAL AND METHODS

It was an observational case series with purposive sampling technique. Ethical review was taken from Institutional review board of Shaikh Zayed Hospital, Lahore. Retrospective data was collected for the first 115 patients, who underwent liver transplantation in HPB and Liver Transplant center of Shaikh Zayed hospital from 2011 to June, 2017. All donors undergoing liver transplant included in the study were healthy individuals, their pre-operative computed tomography (C.T) scans to delineate the liver anatomy and volume were evaluated and recorded. During hepatectomy, cutting plane was guided by ischemia line after right pedicle clamping (i.e. right hepatic artery and right portal vein). Right hepatic graft, including partial middle hepatic vein, was used in all except 3 cases. After hepatectomy grafts were perfused via the right portal vein with cold UW (University of Wisconsin) solution and later solution was drained from the liver and pre-calibrated scale was used to define the actual graft weight.

Preoperative measurement of the liver volume Multidetector computed tomography (CT) images were obtained with CT ingenuity 128 slice (Philips Cleveland, USA). This data was used for CT volumetry measurements. The scanning parameters were as follows: 120 kV and mAs appropriate to body habitus. The right lobe graft volume (GV) was measured by tracing a line on the right of the middle hepatic vein, thus defining the virtual hepatectomy plane. The perimeters of the liver and the graft were outlined by hand tracing on each slice by an abdominal radiologist. The enclosed area was calculated with image analysis software (Itellispace Portal Radiology DICOM image processing application software version 8). The liver volume (in milliliters) was then obtained as the sum of all areas from the intervals of the serial CT slices (Fig-1), which was later used for comparison with actual graft weight obtained after graft harvesting and perfusion.

Statistical analysis: The volumetric data collected on 115 subjects was analysed for descriptive statistics following Zar (2010). The probability for test significance was $p < 0.05$. The correlation among the variables was determined by Spearman rank correlation. The regression between estimated and actual GRWR was performed to check isometricity between them. In this

allometric analysis, the slope of the fitted regression line was compared with the slope of the null line using following t-test formula (t = b - H / SEb; df = n-2; where n is the number of samples; b is the slope of the fitted line; SEb is the SE of b and H is the slope of the null line) (Underwood, 1977).

RESULTS

This study included 115 subjects out of which 88 were males (76.52%) and 27 were females (23.48%). BMI of the subjects ranged from 15.40 to 29.0 (CV = 13.0 %) and average BMI was 22.38 ± 0.2714. Around 58.3 % of the cases had BMI: 21.1 – 25.0. This parameter distributed normally (KS-z: 0.870, p < 0.435, NS).

The total volume of liver averaged to 1292.64 ± 20.36 ml. (varying from 920 to 1724 mL; CV: 16.89%). This parameter appeared to follow normal distribution as KS-z 0.930 (p < 0.352) was insignificant. The parameter of estimated volume of right lobe of liver varied from 358 to 1218 mL (CV = 17.84%) with an average value of 798.96 ± 13.29 ml. Insignificant value of Kolmogorov-Smirnoff z (KS-z: 0.971, p < 0.303, NS) indicated that estimated right lobe volumes of the subjects distributed normally (Fig-1). Around 87.8 % of the subjects had right lobe of liver falling in the range of 601 to 1000mL.

The parameter of actual volume of right lobe averaged to 769.77 ± 12.73 g varying with a quantum of 17.73% (426 – 1123 g) (Fig-2). This parameter also distributed normally (KS-z: 0.847, p < 0.470, NS). The magnitude of actual size of right lobe of liver (weight in gm) was, however, substantially lower than the estimated value of volume of the right lobe – the difference being significantly different at p < 0.0001as indicated by the paired t-test (Table-1). The parameters of estimated and actual GRWR (graft to recipient weight ratio) also behaved in manner as shown by the parameters of estimated volume of the right lobe and actual right lobe weight (grafted) in the subjects. Estimated and actual GRWRs averaged to 1.1706 ± 0.02159 and 1.0998 ± 0.02132, respectively. The size class of amplitude, 0.91 – 1.40, of actual GRWR associated with around 69.6% of the subject, which was substantially lower than the same size class of the Estimated GRWR (81.4 % of the subjects) by a quantum of 11.8%. Both parameters tended to deviate significantly from normal distribution although exhibited more or less similar variation in terms of coefficient of variation (Fig-3&4). Both parameters were significantly positively skewed. Average actual GRWR was significantly (p 0.0001) lower than the average estimated GRWR (Table-1).

The correlation amongst the volumetric parameters was determined by Spearman correlation Analysis and is presented in form of a matrix in (Table-2). There were some significant correlations amongst the parameters. There was highly significant positive association between Total volume of liver and the estimated volume of right lobe (ρ = 0.828, p < 0.0001), between estimated volume of right lobe and actual weight of the right lobe (ρ = 0.808, p < 0.0001).

The results of linear regression between estimated volume of right lobe in mL (X-axis) and actual weight of the right in g (Y-axis) is presented in (Fig-5). The relationship was highly significantly linear (r = 0.830, r^2 = 0.690, adj. r^2 = 0.689 and F = 250.98, p < 0.0001) with intercept = 134.0 and slope = 0.796 (standardized β = 0.830). The relationship was obviously not isometric as given below. In this equation neither intercept is equal to zero (t = 3.29, p < 0.0001) nor slope is equal to 1 (t = 4.08, p < 0.0001).

Actual right lobe (g) = 134.004 + 0.796 (estimated right lobe volume (mL) ± 76.42

Similarly, linear regression between estimated GRWR (X-axis) and actual GRWRs (Y-axis) (Fig-6) indicated a non-isometric linear highly significant relationship between them (r= 0.879, r^2 = 0.773, adj. r^2 = 0.771and F = 384.39, p < 0.0001) with intercept = 0.084 and slope = 0.868 (standardized β = 0.879).

Actual GRWR = 0.084 + 0.868 estimated GRWR ± 0.109

As regard to the Actual GRWR – EGRWR relations, it was evident that differences in magnitudes of these parameters revealed three situations –1) EGRWR < AGRWR in 25 cases, 2) EGRWR = AGRWR in 7 cases and 3) EGRWR > AGRWR in 83 cases. The estimated values were predominantly higher in majority of cases (Fig-7).

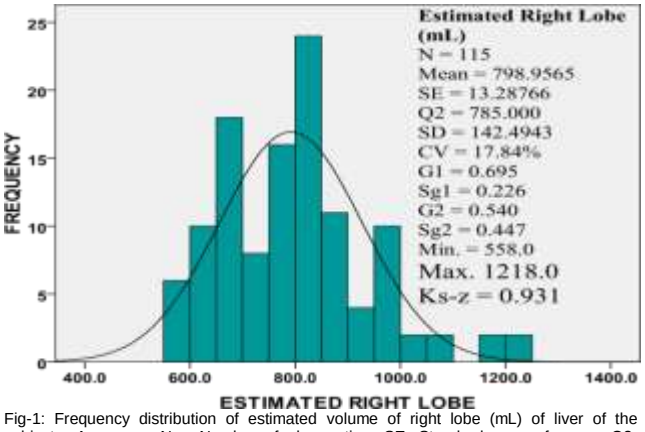

Fig-1: Frequency distribution of estimated volume of right lobe (mL) of liver of the subjects. Acronyms: N = Number of observation; SE, Standard error of mean; Q2, Median, SD = Standard deviation; CV = coefficient of variation (%); G1, skewness; Sg1 = Standard error of skewness; g2, kurtosis; Sg2 = Standard error of kurtosis; Min. = Minimum; Max. = Maximum; KS-z = Kolmogorov-Smirnoff z; p, probability.

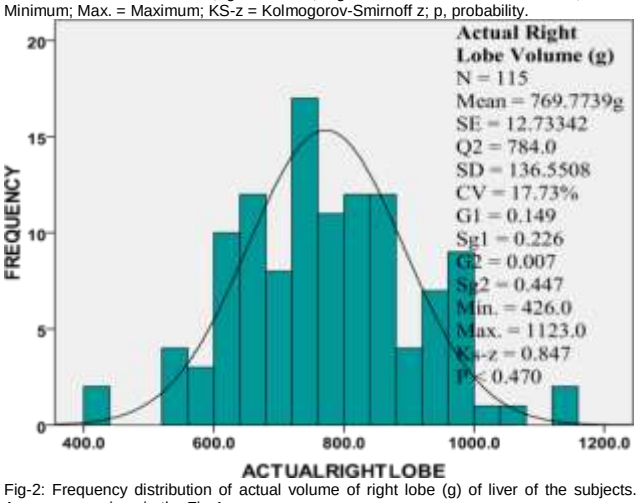

Fig-2: Frequency distribution of actual volume of right lobe (g) of liver of the subjects. Acronyms as given in the Fig-1.

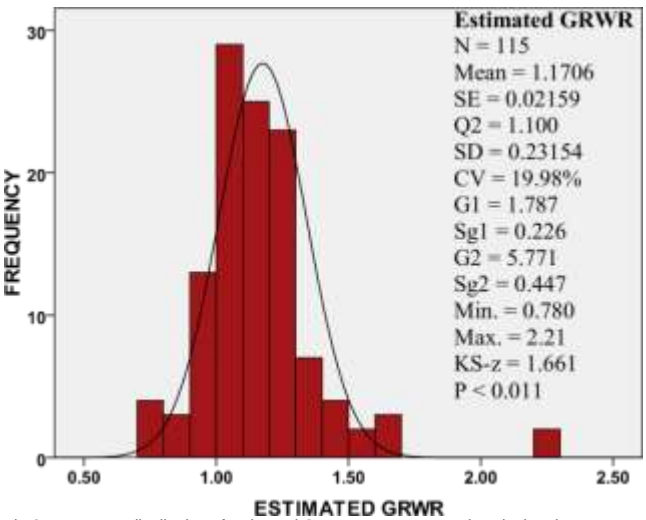

Fig-3: Frequency distribution of estimated GRWR. Acronyms as given in the Fig-1.

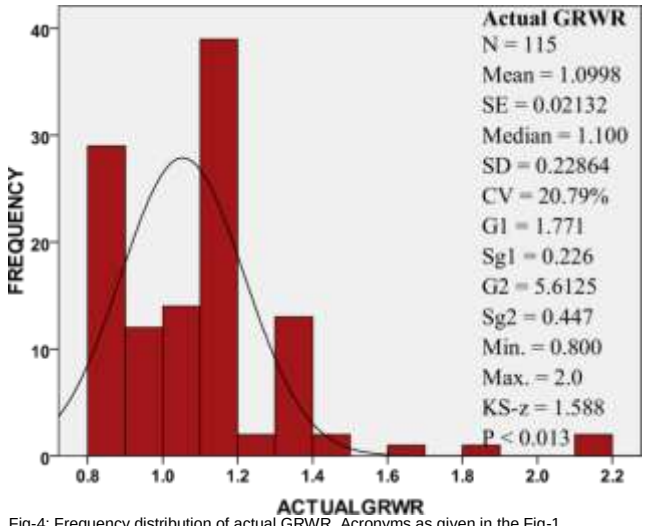

Fig-4: Frequency distribution of actual GRWR. Acronyms as given in the Fig-1.

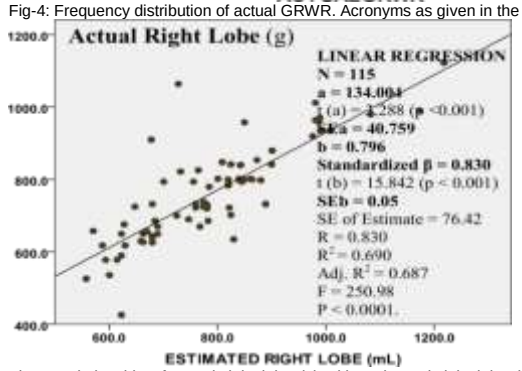

Fig-5: Relationship of actual right lobe (g) with estimated right lobe (mL) as given by linear regression. The relationship is not isometric

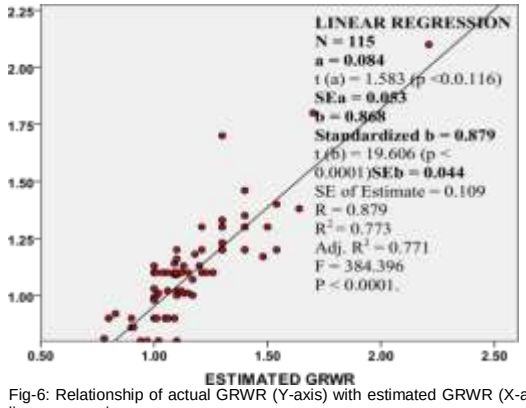

Fig-6: Relationship of actual GRWR (Y-axis) with estimated GRWR (X-axis) as given by linear regression.

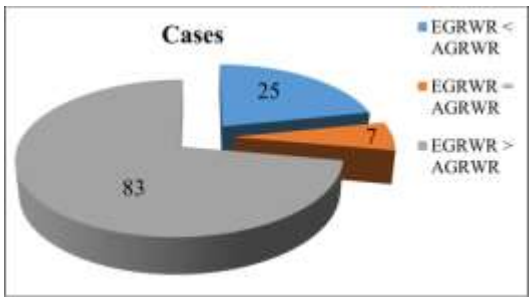

Fig-7: Number of cases falling in three categories i.e. EGRWR < AGRWR, EGRWR = AGRWR and EGRWR > AGWR. In most of the observations (72.20% of the cases), EGRWR was larger than AGRWR.

Table-1: Paired sample t-tests.

Variable Pairs	Paired Differences					t	df	Sig. (2-tailed)
	Mean	SD	SE Mean	95% Confidence Interval of the Difference				
				Lower	Upper			
Estimated Right Lobe (mL) – Actual right Lobe (g)	29.1826	81.46117	7.59629	14.13441	44.23081	3.842	114	0.000
Estimated GRWR – Actual GRWR	0.07078	0.11318	0.01055	0.04988	0.09169	6.707	114	0.000

Table-2: Spearman rank correlation (ρ) analysis among the volumetric parameters of liver.

AGE	AGE						
BMI	A 0.014	BMI					
	B 0.882						
TV	-0.132	0.4	TV				
	0.161	0.001					
ERL	-0.16	0.446	0.828	ERL			
	0.087	0.0001	0.0001				
ARL	-0.202	0.42	0.812	0.808	ARL		
	0.03	0.0001	0.0001	0.0001			
EGRWR	-0.233	0.053	0.34	0.374	0.306	EGRWR	
	0.012	0.577	0.0001	0.0001	0.0001		
AGRWR	-0.198	0.045	0.203	0.172	0.258	0.839	AGRWR
	0.034	0.636	0.03	0.066	0.005	0.0001	

Acronyms: BMI, Body mass index; TY, Total volume; ERL, Estimated Right Lobe (mL); ARL, Actual Right lobe (g); EGRWR, Estimated GRWR; AGRWR, Actual GRWR; a, magnitude of Spearman correlation; b, significance (p value).

DISCUSSION

Having established itself as a safe and effective alternative to cadaveric transplant, living donor liver transplant (LDLT) is the main transplant method used in countries where no cadaveric transplant system is organized and is contributing to fill the gap in demand vs. supply in those where such a system is established. The principal objective of performing living donor liver transplant (LDLT) is to ensure 30-40% of the liver remnant for donor functionality[9] and at least a graft recipient weight ratio (GRWR) of 0.8 for recipient.[6] GRWR < 0.8 has been reported to lead to less than desirable outcomes such as small for size syndrome (SFSS).[10,11]

Different techniques have been employed in order to provide a reliable and accurate prediction of liver mass available for transplantation. These include various computer programs,[12] decreasing CT slice thickness and different equations and formulas using patient's age, height, gender, body weight, BSA, and even maximal portal vein diameters.[8,13] It is however recognized that universal applicability of such proposed methods is questionable due to several factors.[14] Although CT scan with manual volumetry is gold standard for assessment of liver volumes, it overestimated the graft weight in most of the cases of our study. This is similar to a study conducted by Madbouly in 2021.[15] The reason for the discrepancy in the estimation and

actual weights of liver mass is because of the difference in the blood perfusion of the liver at times of assessment and then later intra-operatively during transplantation.[16] Other factors such as miss-match of actual surgical plane of transection to the radiological plane of liver parenchyma transection plane and graft dehydration by the University of Wisconsin solution due to its high osmolality have also been proposed.[9]

In our study we found that utilizing the CT volumetric method alone led to an accurate prediction of GRWR in only 7% of the cases. Overestimation was seen in 72.20% (Fig 7), this is a potentially dangerous situation as it has the chance of leading to transplants that might in effect lead to a transplant achieving GRWR less than 0.8.

The correlation coefficient for graft weight and GRWR in our study was 0.830 and 0.879 respectively. These values are very similar to those reported by Pinheiro[8] (0.82) and Yoneyama[17] (0.84 for right lobe and 0.85 for left lobe).

On the basis of our analysis we propose the following equation for estimation of graft weight

Actual right lobe (g) = 134.004 + 0.796 x (estimated right lobe volume (mL)

Our study has limitations as it is a single center study with limited number of subjects. Further validation of the formula, which we have proposed, can be achieved by larger number of patients with multicentre studies.

CONCLUSION

Using one to one principle for volume estimation of healthy liver can be misleading and therefore we propose an equation to reach more accurate estimation of graft weight.

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