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Standard Formulae in Predicting Liver Volumes: A South East Asian Series of Adult Living Donors

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Abstract

Introduction

Historically Urata et al. first described a formula, based on donor biometrics, to predict total liver volumes. Many centres have shown that such formulae have different accuracy based on the population studied. To date, no such study has been carried out in a South East Asian population. Our primary aim was to study the accuracy of seven internationally recognized formula. Secondarily we aimed to derive a formula for caluculating the weight of a liver graft using CT derived volume.

Methods

A prospectively held database of adult living donor liver transplants between July 1996 and January 2015 was interrogated. Only entries with complete data were included. Donors' biometrics were tabulated with corresponding CT based volumetry and actual graft volumes and weight, using seven well recognized formulae derived from international centres. The accuracy of these formulae was compared to the CT generated volume. Finally a correlation formula between CT volume and actual graft weight was described.

Results

In the study period, 100 adult donors underwent donor hepatectomies for the purposes of living donation. 79 of these had complete data allowing downstream analysis. None of the seven formulae were accurate at predicting volume and were similar in accuracy. However, the estimated liver volumes using formulas by FuGui and A. Poovathumkavadil showed the same and closest correlation with CT predicted volumes (r^2 = 0.55). Finally, we derived a formula to calculate weight of the graft based on predicted CT volumetry (Weight (g) = 0.86 X Vol (cm^3) + 72.5) with good accuracy (r^2 = 0.9)

Conclusion

For the first time to date, we describe here the most reliable formula for predicting liver volume in a South East Asian population. Also, with good accuracy we propose a formula for calculating the weight of a liver graft based on CT volumetry.

Keywords: Formula; Liver volume; Living donor liver transplantation

Introduction

Liver volume is crucial to determine graft suitability for living donor liver transplantation (LDLT) and organ resectability [1,2]. The absolute necassity for success of an LDLT is the realization of adequate liver parenchyma for both the recipient and the donor. Liver remnant volume of 30% of the total liver volume is sufficient for the donor to survive, provided that the liver parenchyma is normal without evidence of disease such as steatosis. A small graft may cause dysfunction and may not be able to sustain adequate metabolic function in the recipient (small for size syndrome). On the other hand, a large graft can be associated with risk of graft compression and poor perfusion (large for size syndrome) or compromise donor safety. Therefore, accuracy of liver volumes is important to avoid donor-recipient volume mismatch [3].

Historically, in 1995, Urata et al. first described a formula, based on donor biometrics, to predict total liver volumes [4]. However in recent years; many centres have shown that such formulae have different accuracy based on the population studied. The other factors including race/ethnicity or more than a single body index could affect the estimation. Differences in population have implication on BMI and therefore calculated liver volume and further differences in the prevelance of steatosis. This has resulted in numerous formulae that are derived by different centres that are population specific [4,5-10]. Accurate estimation is crucial to avert graft size mismatch or post-hepatectomy liver failure, hence the importance to determine the most suitable formula for a patient group. The current gold-standard for calculating liver volume pre-operatively is CT volumetry. However this is dependent on CT facilities and software packages as well as demands on clinical time of radiologists and surgeons. The use of biometric data in accurately predicting liver volumes is potentially a non-invasive, cheaper with quicker throughout and therefore more universally applicable.

Further, while estimating volume based on patient biometrics may be worthwhile, the correlation between volume and weight of liver grafts is a further variable that has important clinical implications. The Graft to recipient weight ratio (GRWR) is crucial to the outcome of living donor liver transplantation. In European countries, liver volume is equated to the liver weight and is generally calculated the GRWR. The minimum graft volume for successful liver transplantation is

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controversial, and in living donors the GRWR is desired to be 1% or more [4,11] . However, successful results have even been reported with grafts having a GRWR less than 0.7% [12,13]. The relationship of weight and volume is related directly to density. Density of the liver is a directly related to steatosis and this can be population dependent. For reasons previously stated, a formula that can relate a biometric derived standard liver volume to weight would be clinically invaluable. To date, no such study has been carried out in a South East Asian population.

The National University of Hospital, Singapore is the largest adult donor liver transplant unit in South East Asian. While the experience in living donor liver transplantation is still early, these early results have formed the basis for the current study. The low incidence of obesity and non-alcoholic fatty liver disease in this population makes the estimation of such calculations in this population unique. Our primary aim was to study the accuracy of seven internationally recognized formulas to determine the best formula to be used in our population; with a secondary aim of determining a formula for calculating the weight of a liver graft using CT derived volume.

Methods

A prospectively held database of adult living donor liver transplants between July 1996 and Jan 2015 was interrogated. Only entries with complete data were included. Pre-transplant factors that may affect liver volume were measured, and included age, sex, body weight (BW) in kilograms, and body height (BH) in meters, body mass index (BMI) and body surface area (BSA). BMI was calculated as weight in kilograms divided by height in meters squared, and BSA was calculated using the Mosteller's formula ($BSA = \sqrt{[(\text{height[cm] x weight[kg]} / 3,600]}$).

CT volumetry was used to calculate standard liver volume (SLV). For this purpose, a triphasic CT scan was performed for each donor. Following this using the Syngo volume programme on a Leonardo work station (Siemens, Syngo MMWP VE 30A, syngo VE 32B, WinNT 5.2, Service Pack2, COEM), a liver transplant surgeon then reviewed each cross sectional image and marked the outline of the liver. For this portal and caval structures were excluded. Following this, a volume is generated of the standard liver volume for each donor. Subsequently, a measure of donor graft volume (GV) was performed. For this a similar method of marking the outline of the graft based on the planed transection line was undertaken. This resulted in graph volume for each donor. For the purposes of transplantation a conversion of 1 has historically been applied; where volume (mls) = weight (g). This was then used to calculate GRWR for pre-operative planning for LDLT.

For the purposes of this study, for each donor an estimated Standard liver volume (eSLV) was calculated using the seven well recognized formulae derived from international centres; Japan = 2, US = 1, China = 1, India = 1, Hong Kong = 1, Saudi Arabia = 1 (Table 1).

For each donor in turn, the SLV was compared against eSLV for each of the seven formulae. The SLV was compared against eSLV for all donors. The line of best fit was drawn using Microsoft Excel 2010. The accuracy of these formulae was compared to by calculating the correlation coefficient (r^2). By this method, the formula which most accurately estimated liver volume was determined.

To achieve our secondary aim, we plotted graft volume against actual weight of graft following resection. Using the formula for line of best fit a formula that correlates graft volume with actual graft weight was derived.

Source, Year	Country	Formula
Urata et al. [4]	Japan	705.2 x BSA + 2.4
Hashimoto et al. [5]	Japan	961.3 x BSA - 404.8
Vauthey et al. [6]	US	1267.28 x BSA - 794.41
Fu-Gui et al. [7]	China	11.508 x BW + 334.024
Chandramohan et al. [8]	India	874.461 x BSA - 204.09
Chan et al. [9]	Hong Kong	1.19 x (12.29 x BW + 218.32 [+ 50.74 if male])
A. Poovathumkadavil et al. [10]	Saudi Arabia	12.255 x BW + 555.65

Table 1: Seven formulae derived from international centres.

Results

During the study period, 100 adult donors underwent donor hepatectomies for the purposes of living donation. 79 of these had complete data allowing downstream analysis. The characteristics of the subjects are given in Table 2. There was an equal proportion of males and females with a median donor age of 34 with a median BMI of 24.

Table 3 showed the comparison of range and mean of standard liver volumes measured at computer tomography against the estimated standard liver volume using the seven internationally recognised formulas with the R2 values. Formulas by Urata, Hashimoto, Vauthey and Chandramohan predicted liver volumes using body surface area whereas formulas by formulas by Fu Gui, A. Poovathumkavadil and Chan predicted liver volumes using body weight. None of the seven formulae were accurate at predicting volume but all seven formulas showed very similar correlation (r = 0.53-0.55). However, the estimated liver volumes using formulas by FuGui et al. and A. Poovathumkavadil et al. showed the same and closest correlation with CT predicted volumes (r^2 = 0.55; Figure 1) [7,10]. The estimated liver volume using formula by Chan et al. showed the next closest correlation with r^2 of 0.54. The relatively low r^2 value demonstrated here reflects the inaccuracies in such formula in predicting liver volume [9].

In a measure to enhance the accuracy of predicting graft weight based on CT derived volumetry, we subsequently used a plot of actual graft weight versus CT estimated volume and the correlation equation and coefficient value (R2) was determined using Microsoft Excel. The formula that we have derived is used to estimate graft weight using CT volumetry: Graft Weight (g) = 0.86 X CT Volume (cm^3) + 72.5 and has good accuracy (r^2 = 0.9) (Figure 2).

Discussion

Living donor liver transplantation has been well established in major Asian transplant centers as a primary type of liver transplantation or as a complement to the markedly limited supply of cadaveric grafts. Due to historical, religious and cultural beliefs in some of these countries, organ transplantation from deceased has not been a widely accepted practice [14]. Although deceased donor organ transplantation was started relatively early in Asia, deceased donor organ rates in this region are among the lowest in the world [15]. Liver transplantation from living donors then emerged as an important option for many patients due to the constant undersupply of cadaveric grafts.

Accurate estimation of liver volume is vital prior to living donor liver transplant since small-for size graft has a significant impact on morbidity and mortality. Graft volume-to-SLV ratio of 30% of less

Variable	Value / Median
Sex (M, F)	41/38
Age, y	34 [22-57]
Body Height , m	1.65 [1.48-1.89]
Body Weight , kg	62 [39-117]
BMI, kg/m²	24 [15.23-36.05]
BSA, m²	1.7 [1.31-2.41]
BMI, body mass index; BSA, body surface index; BW, body weight	

Table 2: Characteristics of seventy adult living donors

Source, Year	Formula	Mean estimated volume ± Stardard deviation (cm³)	Range of Estimated volume (cm³)	R2 value
Urata et al. [4]	705.2 x BSA + 2.4	1221.56 ± 155.30	930.84-1706.59	0.53
Hashimoto et al. [5]	961.3 x BSA - 404.8	1257.13 ± 211.69	860.81-1918.29	0.53
Vauthey et al. [6]	1267.28 x BSA - 794.41	1396.51 ± 279.08	874.04-2268.11	0.53
Fu-Gui et al. [7]	11.508 x BW + 334.024	1087.92 ± 165.95	782.84-1678.16	0.55
Chandramohan et al. [8]	874.461 x BSA - 204.09	1307.71 ± 192.57	947.19-1909.14	0.53
Chan et al. [9]	1.19 x (12.29 x BW + 218.32 [+50.74 if male])	1248.47 ± 226.56	830.18-2028.39	0.54
A. Poovathumkadavil et al. [10]	12.255 x BW + 555.65	1358.48 ± 176.73	1033.60-1987.03	0.55
CT estimated volume		1274.07 ± 251.92	783.00-2006.00	

Table 3: Standard liver volume (SLV) measured at computed tomography and estimated standard liver volume (eSLV) using each formula from seven international centers with R2 value.

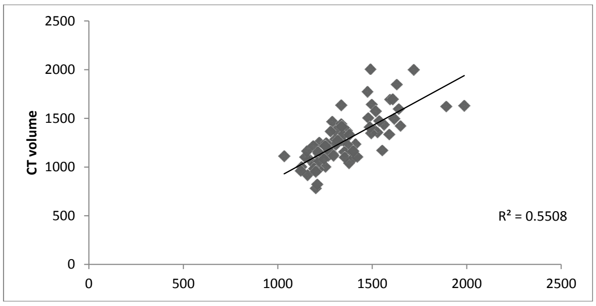

Figure 1: eSLV against SLV based on A. Poovathumkadavil et al. formula.

and graft-to-recipient body weight ratio of less than 0.8 are associated with increased morbidity and impaired graft and patient survival post-transplant [16,17]. In the setting of LDLT, volumes of donor grafts are largely based on CT volumetry, with all the inherent limitations to these technologies. From the CT volumetry an estimation of subsequent grafts weight and hence GRWR is a further crucial measure of outcome of transplantation; again based on a number of assumptions. While limited by its laborious and time consuming nature, CT volumetry also requires x-ray radiation of potential living donors and using a predictive formula based on donor biometrics could help screen potential recipients prior to work-up for donation. Again, the use of accurate formulae for calculation of volumes and weights remain crucial to outcomes of this surgery by helping define resectability.

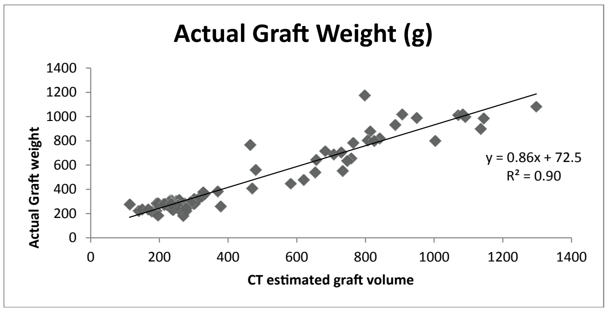

Figure 2: CT estimation of donor graft volume versus actual graft weight at backbench during transplant.

In 1995, Urata et al. [5] proposed a formula to estimate liver volume based on body surface area using computed tomographic imaging for three-dimensional reconstruction of the liver in 96 Japanese children and young adults. In the subsequent years, many centers have derived their formulas based on the population studied using different body indices including body weight, body surface area with arying levels of accuracy.

This study is the first study to attempt to identify the most accurate formula at predicting graft volume in a South East Asian population. In this study, we have found that the formula by Fu Gui et al. and A. Poovathumkadavil et al. are closest in estimation of standard liver volume in South East Asian adults [7,10]. However, the accuracy of estimation is limited likely due to the different body habitus of donors in the studied populations compared with our population.

Of note, these three formula estimate the liver volume using body weight, while the other four formulas (Urata, Hashimoto, Vauthey and Chandramohan) estimated the liver volume using body surface area. This implies that body weight may be a more important factor in predicting liver volume in this population. In fact, four of twelve reported studies showed that BW is more significant than BSA [6,7,9,18]. Body weight is preferred as a primary index, and is obtained by precise weighing measurement as opposed to BSA, which is a secondary index estimated using few possible formulas.

The GRWR has long been used as the gold standard of safety in LDLT. Presently, the volume derived preoperatively from CT volumetry in ml [19] is converted into grams for this estimation. Here we describe a correcting formula in determining the weight of the liver graft based on preoperative volumetry.

In summary, none of the seven formulas derived from international centers is accurate in estimating liver volumes in our population. For this reason, we feel it is important to develop a specific formula for SLV estimation in the South East Asian population. Hence, more studies need to be conducted in our population with larger numbers of subjects to predict a suitable formula to estimate liver volume with better accuracy. The formula that we have derived can be used to calculate graft weight based on CT volume with good accuracy. Currently, CT volumetry remains the most accurate manner to predict volume. Failing this facility, the formula by Fu Gui and A. Poovathumkadavil et al. [7,10] show best accuracy in this population. Finally, using volumetry, the predicted graft weight is calculated by a novel formula described here.

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