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Preoperative Volume Prediction in Adult Live Donor Liver Transplantation: 3-D CT Volumetry Approach to Prevent Miscalculations*

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Abstract
Background: The precise preoperative calculation of functional liver volumes for both donor and recipient is a crucial part of the evaluation process in adult living donor liver transplantation. The purpose of this study was to describe and validate our modus 3-D CT volumetry.
Patients and Methods: Native (unenhanced), arterial, and venous phase CT images from 62 consecutive live liver donors were subjected to 3-D CT liver volume calculations and virtual 3-D liver partitioning. *Graft*-volume estimates based on our modus 3-D volumetry, which subtracted intrahepatic vascular volume from the "smallest" (native) unenhanced CT phase, were subsequently compared to the intraoperative *graft*-weights obtained in all 62 cases. Calculated (preoperative) liver-volume-body-weight-ratios and measured (intraoperative) liver-weight-body-weight-ratios of liver grafts were analyzed.
Results: Preoperative calculations of *graft*-volume according to our modus 3-D CT volumetry did not yield statistically significant over- or under-estimations when compared to the intraoperative findings independent of their age or gender.
Conclusion: Our modus 3-D volumetry, when based on the "smallest" (native) unenhanced CT phase, accurately accounted for intrahepatic vascular volumes and offered a precise virtual model of individualized operative conditions for each potential live liver donor.

Key words: Liver surgery; living donor liver transplantation; liver volume; surgery planning in LDLT; 3-dimensional reconstruction; liver imaging

Abbreviations: 3-D: three dimensional; Phase: CT image phase: native = unenhanced (N), arterial (HA), venous (V); ALDLT: adult living donor liver transplantation; CT: computed tomography; LVBWR: liver volume body weight ratio; LWBWR: liver weight body weight ratio; MHV: middle hepatic vein; MRI: magnetic resonance imaging; SD: standard deviation; SFS: Small for size; TLV: total liver volume

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Introduction

Accurate preoperative prediction of functional graft and remnant volumes in adult live donor liver transplantation (ALDLT) is essential in ensuring donor safety and preventing postoperative graft failure. Two-dimensional CT or MRI imaging has become the "current standard" for total liver volume (TLV) and graft/remnant volume estimations [1-3]. However, it is well known that computer systems overestimate real *graft*-volumes, and have an error ratio when compared to the actual graft weight obtained at the time of surgery [2-7]. The marked discrepancies in graft volumes among pre- and intra- operative values urged many groups to introduce "conversion" factors [8] or modified formula-derived estimates [4, 9-10].

The purpose of this study was to describe and validate our modus 3-Dimensional CT volumetry

Patients and Methods

1. Study Population

Between January 2003 and June 2006, sixty two (f:m = 29:33) of the 103 potential donors evaluated according to our routine protocol [11-13] ultimately underwent graft hepatectomy for transplantation. Mean age was 36 ± 10 years. Forty nine of the 62 grafts obtained were right lobes that included the middle hepatic vein (MHV). Of the remaining thirteen grafts, 6 were right lobes without MHV and 7 were left grafts that included the MHV. Biopsy results in all resected donors showed less than 10% steatosis and no evidence of histopathologic changes.

2. Study Design

Multiphasic CT image data from 62 consequtive live liver donors were prospectively analyzed by 3-D CT for graft and remnant liver volume calculations, by utilising the software assistant HepaVision (MeVis,

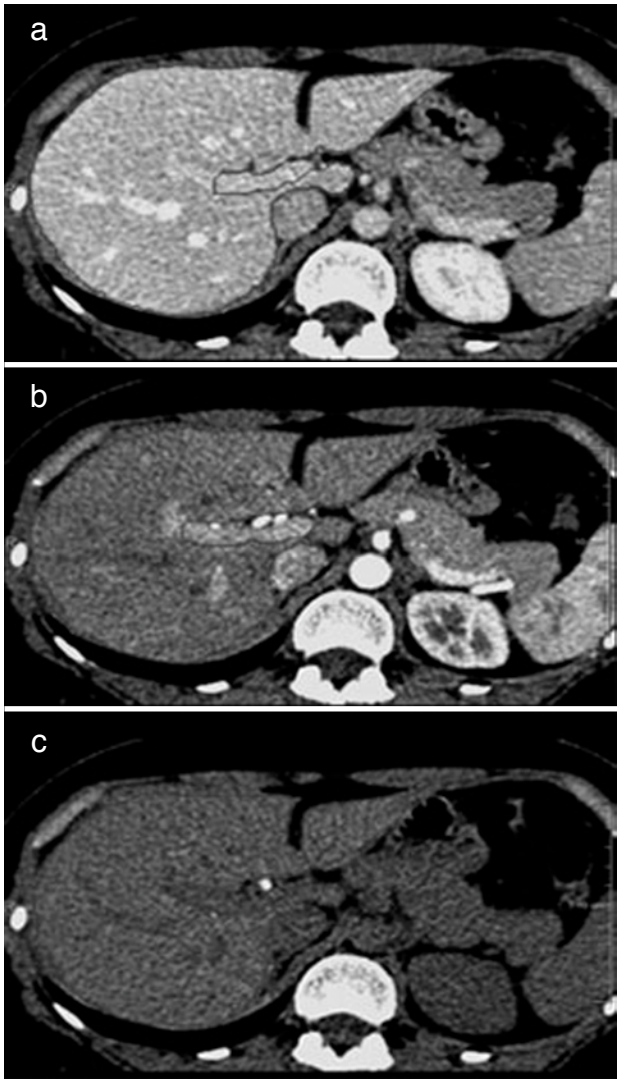

Fig. 1a-c. Assessment of total liver volume (TLV). Liver contours were traced with a modified live-wire, semi-automated, contour-finding algorithm approach. The live-wire contours were independently obtained from venous (a), arterial (b) and native = unenhanced (c) phase 3-mm, axial, 2-D CT images.

Germany), and subject to virtual 3-D liver partitions by two expert surgeons (A.R. and M.M.) and an experienced radiologist (T.S.).

Step one: The calculation of total liver volume (TLV) was carried out in a stepwise analysis. *Liver parenchymal segmentation* was evaluated independently in three separate axial 2-D CT imaging phases: phase N (native = unenhanced), phase HA (arterial), and phase V (venous). The data obtained enabled a multiphasic CT imaging comparison of TLV-estimates for each individual donor candidate (Fig. 1a-c). The volume of the intrahepatic vascular tree was calculated after the *segmentation of hepatic vessels* phase.

Step two: A virtual 3-D liver partition simulating the "carving" technique, which exactly follows the course of middle hepatic vein (MHV), routinely employed at our institution [14]. This calculation was performed in all cases using CT phase V images, usually considered the "standard" CT imaging for donor evaluation in LDLT [3, 14] (Fig. 2a-b). This step allowed for an initial estimation of graft- and remnant- liver volumes.

Step three: Subsequently the TLV was calculated according to our modus 3-D volumetry, by subtracting the intrahepatic vascular volume from the "smallest" TLV (derived from the "smallest" CT phase). The "smallest" TLV constituted the baseline for the additional estimation of "smallest" graft/remnant volumes, which were calculated based on the volume percentage values for graft- and remnant livers obtained during virtual 3-D liver partition for "standard" CT phase V (step two). Finally the definitive preoperative -graft- and remnant-LVBWRs for each live liver donor candidate were calculated.

Step four: The intraoperative graft weight was measured in 62 live liver donors who underwent graft hepatectomy. All resections were performed according to the "carving" transection of the virtual 3-D preoperative simulation.

The exact transposition of the virtual transection plane onto the operative field was confirmed in all cases by photographic documentation and doppler-scanning (presenting the MHV and it`s tributaries on the resection surface). This allowed for the retrospective calculation of "actual" intraoperative *graft*-liver-weight-body weight- ratios (LWBWR`s).

3. CT Protocol

CT imaging as originally published by Schroeder et al. [3, 15] was performed using a 16-row-Multidetector-CT-Scanner (Sensation16®, Siemens, Germany) using the following parameters: kVp 120, mAs 140-170, slice collimation 0.75mm, feed/rotation 12mm, and rotation time 0.5 sec. Reconstruction increments were 1mm for the native = unenhanced, arterial and venous scans.

4. Image Analysis and Virtual Resection

CT images were analyzed with the non-commercial software assistant HepaVision (MeVis, Germany). This software allows for the calculation of 1) total liver volume together with *graft*- and *remnant*- liver volumes as well as 2) volume of the intrahepatic vascular tree.

Liver parenchyma imaging was derived from CT data in a semi-automatic way. *Segmentation of liver parenchyma* was performed on axial slices with a modified live-wire algorithm. With this approach, contours between user-defined boundary points were determined automatically based on CT values and gradients during user-interaction. Parameters of the algorithm were adapted to each CT phase, and manual correction of the automatic delineation contours as well as manual drawing of contour parts was undertaken to ensure accurate liver segmentation. The live-wire contours were interactively determined on 3 mm axial 2-D CT slices during venous (V), arterial (HA) and native = unenhanced (N) phases. The contours of intermediate slices were automatically interpolated and optimised initially by the software and ultimately by the operator, summarizing all segmented areas and yielding volumetric calculations in milliliters (ml). All surrounding structures, including major extrahepatic vessels (portal vein, hepatic artery, inferior vena cava) and gallbladder fossa, were excluded.

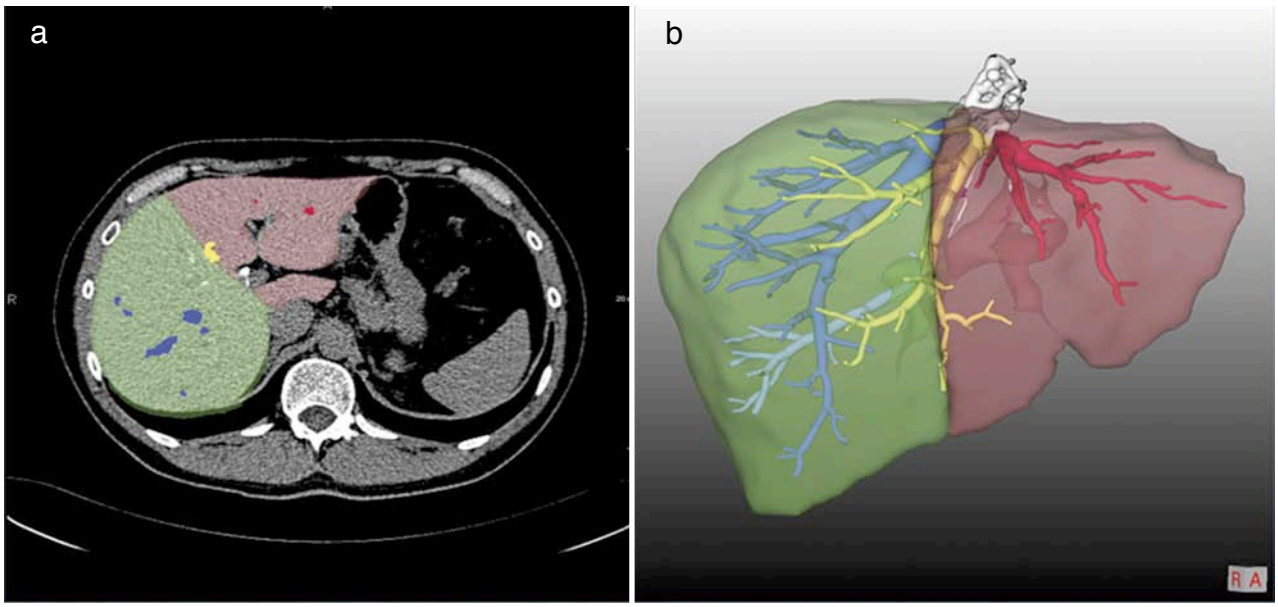

Fig. 2a-b. Donor virtual hepatectomy. Malagó partition ("carving technique"). The plane of transection runs along the course of the MHV – 2D view (2a). The MHV is "carved" out of the surrounding hepatic parenchyma – 3D cranial view (2b). RHV (blue), MHV (yellow), LHV (red), right graft (green), left liver remnant (brown).

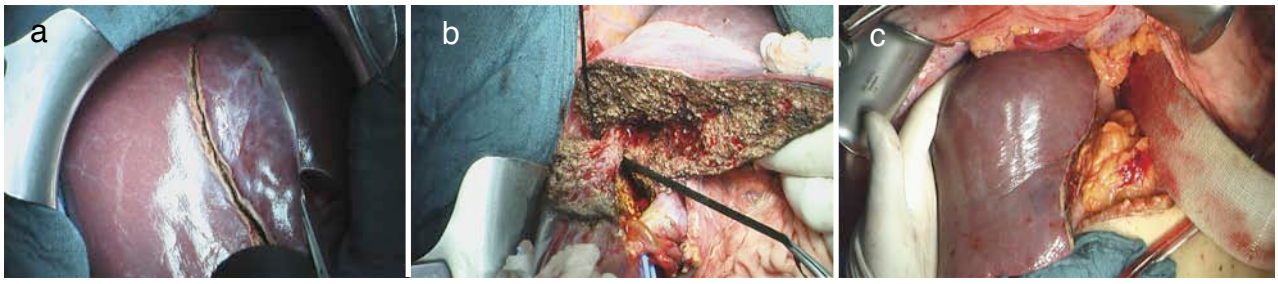

Fig. 3a-c. Malagó partition ("carving technique"), intraoperative view. The transaction line on the liver surface follows the course of MHV (a). Left remnant liver with the "MHV groove" on the transaction surface (b). Right liver graft including the MHV (c).

During the *segmentation of hepatic vessels*, arterial, portal and hepatic venous systems were extracted from the image data by using a filter for noise reduction and background compensation and a region-growing algorithm [16]. Intrahepatic vessels were automatically analysed and transferred into a hierarchical graph depicting dependencies between branches and direction of blood flow. Relevant branches of subtrees were labelled during exploration of the 3-D venous graph [17].

Virtual resections were performed in the resulting individual 3-D liver model that allowed optional display of vascular trees and territories. The volume arising from the manually (surgeon line) defined grafts and remnants was automatically calculated.

5. Liver Partition

The plane of transection in the liver partition (Fig. 3a-c) follows the course of the MHV ("carving technique") [14]. In nearly most cases, the MHV remained with the graft during the procuring resection. In each instance the MHV was initially identified by intra-operative ultrasound examination and subsequently "carved" out of the surrounding remnant liver parenchyma. The transection plane lied exactly over the MHV, leaving its left-or right-sided border exposed on the transection surface of the graft. The level of division of the MHV trunc depended on its anatomical relationship with tributaries from segments IVa and VIII and the size of their drainage territories.

6. Intraoperative Findings and Statistical Analysis

All 62 recipients of the live donor grafts underwent venous outflow tract reconstruction by means of our "blanket" technique [18]. Each liver graft was weighed immediately after retrieval. Comparisons between preoperatively calculated volumes and intraoperatively measured weights were performed by considering a specific weight of healthy liver parenchyma of 1 gm/ml [19]. Calculations of *graft*-LVBWR/LWBWR followed previously described formulas [11, 13, 20].

Table 1. Comparison of cases with over-estimated, under-estimated, and identical results from our 3-D CT volumetry with respect to intra-operative values for graft-volume and graft-LVBWR.

n = 62	Our modus 3-D CT volumetry	
	Graft-volume	*Graft*-LVBWR
Cases of overestimation	38 (61%)	26 (42%)
Cases of underestimation	9 (15%)	4 (6%)
Cases with identical values	15 (24%)	32 (52%)

Our-modus: native = unenhanced-phase CT volume (intrahepatic vessel volume subtracted); LVBWR: liver volume body weight ratio; identical: ≤1% deviation from intraoperative findings.

Results were expressed as mean volume percentage (%) ± standard deviation (SD) values. Continuous variables were analyzed by one-way analysis of variance and t-test when normal distribution was given. Univariate and multivariate designs analyzed by factorial Anova examined relations between gender and/or age (as categorized or continuous variable) and graft volume error ratio or graft to GVBWR error ratio. P-values of 0.05 or less were considered significant.

The error ratio (%) was calculated as [E-A] /A x 100, where E was the estimated volume (ml) and A was the actual weight (gm) as described by Hiroshige et al. [21].

Preoperative volume- / LVBWR- values with deviations of less than ≤ 1% from intraoperative values were denoted as "identical".

Major postoperative morbidity was defined as all life threatening events requiring invasive procedures, re-operations, hospital stays longer than 30 days, and re-hospitalizations.

Results

1. Total Liver Volume (TLV) Calculation: Comparison among Different CT Phases

Among the 62 live liver donors prospectively evaluated, the largest mean TLV (1596 ± 212ml) was obtained with the venous (V) CT phase measurements. The smallest mean TLV (1456 ± 196ml) was obtained in the native = unenhanced (N) CT phase in 61(98%) cases and in the arterial (HA) CT phase in n = 1(2%) of livers, respectively. The mean difference between largest (phase V) and smallest (phases: N or HA) TLV was 142 ± 78ml ($p<0.001$).

The calculated mean intrahepatic vascular volume for all 62 live liver donors, who underwent graft hepatectomy was 88 ± 17ml.

2. Virtual Liver Partition: Graft- vs. Remnant- Volume Percentages

There were 62 donors who underwent resection for live donation. Based on the 3-D virtual liver partition derived from the CT phase V, the mean right and left hemiliver volumes were 63 ± 8% and 37 ± 8% of the TLV.

3. Inaccuracy Incidences for Over- vs. Under-estimated Graft-volumes and -LVBWRs: 3-D CT Volumetry versus Intraoperative Data

Table 1 outlines in detail the incidence of the over- vs. under-estimated *graft*-volumes and -LVBWRs when comparing data derived from our -modus 3-D volumetry and the intraoperative findings in the transplanted subgroup (n = 62).

The *graft*-volume calculations based on 3-D CT volumetry yielded an overestimation in 61% of instances. *Graft*-LVBWR was overestimated in 42% of cases. In 24% (n = 15) of cases, an identical *graft*-volume, when compared to the intraoperative *graft*-weight, was predicted. A *graft*-LVBWR identical to the intraoperative *graft*-LWBWR value was calculated in over half (52%) of all transplants. There were 9 underestimations (15%) in the *graft*-volume, and n = 4 (6%) in the *graft*-LVBWR, respectively (Table 1).

When addressing the subgroup of 7 *graft* livers with "real" intraoperative LWBWR between 0.9 and 0.8, and an additional 6 recipients with a "real" *graft*-LWBWR < 0.8, our 3-D CT volumetry overestimated *graft*-LVBWR values in 6 (46%) of them. There were no underestimations of *graft*-LVBWR seen in these n = 13 live liver donors.

4. Overestimation Errors of *Graft*-volume and *Graft*-LVBWR: 3-D CT Calculation versus Intraoperative Data

Our- modus 3-D CT volumetry provided mean graft volumes of 847±187ml for the 62 cases who underwent donor hepatectomy. This did not represent significant overestimations (p = 0.229) with respect to the intraoperative mean actual graft weights of 808 ± 169gm as shown in Table 2. There was a mean overestimation error of 7% with our 3-D CT volumerty for *graft*-volumes, although in 5% (n = 3) of live liver donors the overestimation error was higher than 25%. We did not observe any statistically significant differences (p = 0.287) among virtually calculated *graft*-LVBWR and intraoperatively obtained *graft*-LWBWR values as delineated in Table 2. There was only a 6% mean overcalculation error with our 3-D volumetry

Table 2. Comparison of CT-derived and intra-operatively obtained graft-volume and graft-LVBWR values.

		Our modus 3-D CTvolumetry versus intra-OP values	
n = 62	overestimation error (%)	Our-modus	OP
Graft volume / weight	mean 7%	mean 847±187	mean 808±169
		p = 0.229	
Graft LVBWR / LWBWR	mean 6%	mean 1.16±0.3	mean 1.12±0.03
		p = 0.287	

Our-modus: smallest CT volume (intrahepatic vessel volume subtracted); OP: weight obtained intraoperatively ; LVBWR: liver volume body weight ratio; LWBWR: liver weight body weight ratio.

for *graft*-LVBWR, although an overcalculation higher than 15% was seen in 5% (n = 3) of our live liver donors.

5. Overestimation Error of Virtual *Graft*-volume and -LVBWR Calculations: Analysis in Relation to the Donor Age and Gender

Seventy four percent (n = 46) of the live liver donors (f:m = 22:24), who underwent graft hepatectomy had a less than 10% overestimation error for *graft*-volume and –LVBWR when compared to the "actual" intraoperative *graft*-weight and –LWBWR values. Five percent (n = 3) of donors had a greater than 20% overestimation error for *graft*-volume and –LVBWR when compared to the intraoperative calculations, including 2 females and one male. In these 3 cases, the "real" intraoperative *graft*-LWBWRs were of: 0.79, 0.83, and 1.04, respectively. Despite low "real" *graft*-LWBWR values, there was no evidence of postoperative small for size (SFS) syndrome in these 3 graft recipients.

5a. Age correlation test

Neither univariate nor multivariate designs analyzed by factorial Anova, disclosed any statistically significant differences considering relations between age (as categorized or continuous variable) and graft volume error ratio or graft to GVBWR error ratio (p = 0.4075).

5b. Donor subgroup: females versus males

Twenty nine (33.2%) live liver donor candidates who underwent graft hepatectomy were females. Among them, there was a mean overestimation error of 8.17% (range: 0.1-29%) and 6.75% (range: 0-28%) for *graft*-volume and –LVBWR, respectively, when compared to intraoperative values. Thirty three (46.8%) live liver donors who underwent resection were males. In these cases, the mean overestimation errors for *graft*-volume and –LVBWR were 6.12 % (range: 0-27.3%) and 5.51% (range: 0-19.1%), respectively. Neither univariate nor multivariate designs analyzed by factorial Anova, disclosed any statistically significant differences considering relations between age (as categorized or continuous variable) and graft volume error ratio or graft to GVBWR error ratio (p = 0.4679).

6. 3-D CT Volumetry: Analysis of Underestimation-rate and -Error for *Graft*-Volume and -LVBWR

There were underestimations for *graft*-volume in nine (15%) recipients, and for graft- LVBWR in four (6%) cases. However, we did not observe any significant differences (p = 0.526) between their virtually calculated mean *graft*-volume of 771 ± 158ml and the mean "actual" intraoperative graft-weight of 822 ± 156ml. The mean underestimation error for *graft*-volume was 7.8%. The difference between the preoperatively calculated mean *graft*-LVBWR of 1.2 and the mean "real" intraoperative *graft*-LWBWR value of 1.29 was not significant (p = 0.172). The mean underestimation error for *graft*-LVBWR was 7.65%.

7. Donor and Recipient Outcome after 62 LDLTs during a Mean Follow up Period of 21 ± 12 Months

7a. Donor subgroup

There were no donor deaths. In 16% (n = 10) of donors the retrospectively calculated "intraoperative" LWBWR for the remnant liver was >0.8, while in 37% (n = 23) of cases a LWBWR value between 0.8 and 0.7 was calculated, respectively. The remaining 29 (47%) donors had a LWBWR value of less than 0.7. We did not experience postoperative liver insufficiency associated with SFS remnants in any of the 33 operated donors who had "intraoperative" LWBWR values ≥0.7. One of these 33 donors developed a subphrenic abscess due to a bile leak early after a right graft hepatectomy including MHV. He was successfully reoperated without further morbidity. One donor, who had "intraoperative" LWBWR of 0.5, developed a transient SFS syndrome manifested by cholestasis (peak total serum bilirubin of 21mg/dl) and coagulopathy (drop in thrombine time to 23%). He recovered spontaneously and was discharged from the hospital on postoperative day 27. There were no late vascular or biliary complications within 3-6 months after LDLT in any of the 62 donors. Recovery time ranged from 9-12 weeks, after which all donors resumed their preoperative occupational activities.

7b. Recipient subgroup

The overall perioperative (30 days) recipient mortality was 10% (6/62). In 79% (n = 49) of recipients, the "real" intraoperative LWBWR for the graft liver was > 0.9, in 11% (n = 7) between 0.8 and 0.9, and in 10% (n = 6) less than 0.8. Lethal SFS syndrome was seen in all of the *graft*-LWBWR categories: <0.8 (n = 2), 0.8-0.9 (n = 1) and >0.9 (n = 1), respectively. Two further recipients of right grafts with MHV who had *graft*-LWBWR of 0.78 and 0.99, respectively, sustained transient SFS syndrome, that were successfully reverted with plasmapheresis. The existence of unusually severe preoperative portal hypertension was believed to be implicated in all of these cases.

Discussion

Insufficient graft and remnant liver volumes are major reasons for donor refusal in ALDLT. Although all-in-one protocols using multiphasic CT and MRI have markedly simplified the donor evaluation process, the preoperative estimation of graft and remnant liver volumes remains inaccurate and is usually associated with overestimation errors [2-7, 22-24]. The potential sources of such inaccuracy in radiologically-derived volume assessment are probably multifactorial.

In the current study we describe a significant difference between the "largest" and the "smallest" TLV in 62 prospectively evaluated live liver donors, who underwent graft hepatectomy. In a previous study, we discussed the potential factors responsible for the changes in hepatic volume during the extremely short time of performance of the multiphasic CT scanning [25]. However, both "liver compliance" as well as the "osmotic" or "vasoactive" effects of contrast agents used in CT imaging are at best speculations, and require extended clinical scrutiny and more basic research [26-27]. Yonemura et al. found significantly higher volume overestimation rates for donors less than 30 years of age in their series [7]. However, this finding was not validated in the present study.

The main purpose of this prospective study was to describe our concept of liver volume prediction by virtual 3-D CT based liver partitioning, and to test our modus of 3-D CT liver volumetry by comparing it to the intraoperative findings. The conceptual frame of our strategy was based on the calculation of total liver-, graft-, and remnant- volumes derived from the smallest CT phase, with the additional subtraction of intrahepatic vascular volume. Prior observations had determined that blood circulating in the intrahepatic vasculature at the time of imaging studies is associated with graft-volume overestimations when compared to actual blood-drained grafts measured intra-operatively at the back table [28]. The difficulty to exactly recreate the preoperatively planned liver partitioning at the time of the actual liver transection is also believed to be a contributor to such discrepancies [7].

Our modus 3-D CT volumetry allowed us to build a precise virtual liver reconstruction of each potential live donor's liver. This 3-D visualisation permitted a better understanding of the liver anatomy as well as a more precise and individualized interpretation of the classic 2-D mode. Hiroshige et al. recently analysed the accuracy of preoperative estimation of graft volume by 2-D and 3-D CT with respect to actual graft weight. In their series, the 3-D image error ratio of 12.8±8.3% compared favourably with the 19.4 ± 9.9% error ratio of 2-D CT imaging [21]. Finally, the software allowed for the accurate conceptualization of the MHV procurement together with the graft by means of the "carving" transection technique (both developed by our group) [14].

The "mismatch" of the virtual transection- and intraoperative surgical- planes at the time of the donor hepatectomy constitutes one of most troublesome sources of error [7, 29]. The virtual construction of the transection plane requires reproducible liver partition models and anatomical landmarks that can be easily identified. Cantlie's line, a landmark determined by both anatomical and physiological parameters, which has become the standard at most transplant centres, is extremely difficult to follow, especially on 2-D images. In contrast, the "carving" technique along the plane of the MHV can be easily identified.

Our data from 62 live liver donors who underwent graft hepatectomy validated the clinical usefulness of our modus 3-D CT volumetry by reliably predicting *graft*-volumes without the need for "conversion" factors [8]. Our data showed a mean overestimation incidence of 61% and 42% for virtual *graft*-volume and *graft*-LVBWR calculations respectively, with a mean overestimation error of 6-7%. We did not observe any statistically significant differences between the "virtual" *graft*-volume and -LVBWR estimates and "actual" intraoperative *graft*-weight and- LWBWR measurements. Similarly, there were no significant differences when donor age and gender were considered. Preoperative calculations in 24% of virtual *graft*-volumes and 52% of *graft*-LVBWR showed "identical" values in relation to the intraoperative findings.

In 15% of liver grafts there was a slight to moderate *graft*-volume underestimation, while a slight undercalculation of *graft*-LVBWR occurred in 6% of cases. The respective mean underestimation errors ranged between 7.7-7.8%. These results are comparable with those reported in the literature [4, 6-7, 21-24].

In the subgroup of n = 13 graft recipients who had calculated "real" intraoperative *graft*-LWBWR lower than 0.9 and 0.8, our modus 3-D volumetry overcalculated *graft*-LVBWR in 3/13 cases. However, these overcalculations only slightly exceeded the "actual" 0.8 and 0.9 values.

The clinical data from this study also indicated that the risk for postoperative liver failure increased with decreasing liver size. Live liver donors with remnant-LWBWR <0.7 and recipients of grafts with LWBWR < 0.8 were at extreme postoperative risk of lethal SFS syndrome. We believe that in order to optimize safety and outcomes, an appropriate donor / recipient match regarding not only the "liver volumes" but also scrutinising the recipients' condition in particular the severity of their portal hypertention is the most crucial aspect in the planning of ALDLT.

Based on the data analyzed, we were able to conclude that donor age and gender were not associated with statistically significant disparity between the preoperatively calculated *graft*-volume, and *graft*-GVBWR

and the intraoperative *graft*-weight and *graft*-GWB-WR. We also determined that our-modus 3-D volumetry, when based on the "smallest" (native = unenhanced) CT phase, accurately accounted for intrahepatic vascular volumes and offered a precise virtual model of individualized operative conditions for each potential live liver donor.

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