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ABDOMINAL IMAGING

ORIGINAL ARTICLE

Manual and semi-automated computed tomography volumetry significantly overestimates the right liver lobe graft weight: a single-center study with adult living liver donors

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PURPOSE

Preoperative evaluation of donor liver volume is indispensable in living donor liver transplantation to ensure sufficient residual liver and graft-to-recipient weight ratio. This study aims to evaluate the accuracy of two computed tomography (CT) volumetry programs, an interactive manual and a semi-automated one, in the preoperative estimation of the right lobe graft weight.

METHODS

One hundred and nine right liver lobe living donors between January 2008 and January 2020 were enrolled in this retrospective study. Two radiologists measured the liver graft volumes independently using manual and semi-automated CT volumetry, and the interaction time was recorded. Actual graft weight (AGW) measured intraoperatively served as the reference standard. The paired samples t-test was used to compare the estimated graft weight (EGW) and the AGW. Inter-user and inter-method agreements were assessed with Bland–Altman plots.

RESULTS

Both manual and semi-automated CT volumetry significantly overestimated the graft weight (EGW manual: 893 ± 155 mL vs. AGW manual: 787 ± 128 g, $P < 0.001$, EGW semi-automated: 879 ± 143 mL vs. AGW semi-automated, $P < 0.001$). The junior radiologist measured higher volumes than the senior radiologist with either method ($P < 0.001$). The Bland–Altman analysis revealed mean difference and standard deviation for inter-method agreement of 7 ± 48 cc for the senior radiologist, and 34 ± 54 cc for the junior radiologist. The mean difference and standard deviation for inter-method agreement was 63 ± 59 cc in manual volumetry and 22 ± 38 cc in semi-automated volumetry. The mean interaction time was 27.3 ± 14.2 min for manual volumetry and 6.8 ± 1.4 min for semi-automated volumetry ($P < 0.001$).

CONCLUSION

Both manual and semi-automated CT volumetry significantly overestimated the right liver graft weight, while semi-automated volumetry significantly reduced the interaction time.

KEYWORDS

Liver, living donor liver transplantation, manual CT volumetry, semi-automated CT volumetry, transplantation

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Owing to technical improvements and the standardization of the operation, living donor liver transplantation (LDLT) has become as effective as cadaveric liver transplantation. The right hepatic lobe, which includes segments V, VI, VII, and VIII according to the Couinaud classification, is routinely used for adult-to-adult LDLT.[1] An acceptable graft-to-recipient weight ratio (GRWR) and donor safety with sufficient remnant are the most important concerns in LDLT. Inadequate liver volume is among the most common causes of imaging-based donor exclusion.[2] A residual liver of at least 30% of the initial volume should be

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left for the safety of the donor, while a minimum of 40% of standard liver volume (SLV) or GRWR ≥0.8 is required for the recipient.[3,4] Hence, a precise preoperative volumetric evaluation of the living donor liver is of great importance.[3,5] Although conventional manual segmentation is the gold standard, its use is limited due to the lengthy and tedious process.[6] Automated and semi-automated software developed for liver volume calculation has made volumetric evaluation less time-consuming.[7] Estimated graft volume (EGV) measured by computed tomography (CT) volumetry programs in many studies revealed admissible accuracy in estimating the actual graft weight (AGW), although they still need validation in clinical use.[6,8-10] The aim of this study is to analyze the difference between the estimated and actual right liver lobe graft weights to determine the accuracy of manual and semi-automated CT volumetry programs used in the authors' center.

Methods

Preoperative donor evaluation

Living liver donor evaluation included medical and psychiatric/social assessment, biochemistry and serology tests, and imaging studies. Eligible donors underwent imaging studies, including chest X-ray, abdominal ultrasound, and magnetic resonance imaging, to exclude any unknown disease. Living donors needed to be first, second, third, or fourth-degree relatives of the recipient. Spouses and others were approved by the Dokuz Eylül University Non-invasive Research Ethics Committee (decision/protocol number: 2019/11–11; date of the approval: 24.04.2019), and informed written consent was obtained from all donors. Other eligibility criteria for living donors included an age of 18–65 years, negative serology for hepatitis B and C, normal renal hepatic and hematological functions, and ABO blood group compatibility.

All living donors who underwent the right hemihepatectomy procedure between January 2008 and January 2020 were retrieved from the hospital database. Patients who underwent contrast-enhanced multi-phase CT angiography of the abdomen during donor candidacy selection for LDLT were included, and 11 patients without preoperative CT were excluded. Figure 1 summarizes the patient accrual.

Computed tomography imaging

CT examinations were performed with a 64-slice spiral CT (Philips Brilliance 64, Philips Healthcare, Netherlands) using a triple-phase CT protocol. Initially, a non-contrast scan was performed to exclude severe hepatic steatosis as it was associated with a poor graft outcome.[11] The hepatic arterial and portal venous phases were assessed for the identification of anatomical variations that might be surgically significant, while all three phases were evaluated for the detection and characterization of hepatic lesions. One hundred mL of iodinated contrast medium (Omnipaque 350, GE Healthcare, Shanghai, China) was administered intravenously at a flow rate of 3–5 mL/sec using an automatic injector, followed by a bolus of 50 mL of saline at the same rate. CT scans included the area from the right dome of the diaphragm to the lower pole of the kidneys. Table 1 summarizes the CT triple-phase liver protocol.

Computed tomography volumetry

Volume measurements of the right liver lobes were performed by two radiologists (a senior radiologist with 13 years of experience and a junior radiologist with 3 years of expe-

Main points

- Both manual and semi-automated computed tomography (CT) volumetry significantly overestimated the right liver graft weight.
- Semi-automated volumetry provided a strong agreement with manual volumetry with experienced users while significantly shortening the user time.
- Less experienced users tended to measure higher graft volumes with both CT volumetry methods.
- A higher graft-to-recipient weight can be applied to prevent small-for-size syndrome when evaluating the liver graft with CT volumetry.

Table 1. Computed tomography protocol used in potential living liver donors

Phase	Tube voltage (kV)	Tube current (mAs)	Rotation time (sec)	Pitch	Collimation	Slice thickness (mm)	Slice increment	Delay (sec)
Non-enhanced	120	220	0.75	1.178	64 × 0.625	2	1	NA
Hepatic arterial	120	250	0.5	0.91	64 × 0.625	0.9	0.45	15–25
Portal venous	120	250	0.75	1.178	64 × 0.625	2	1	40–60

NA, non-applicable.

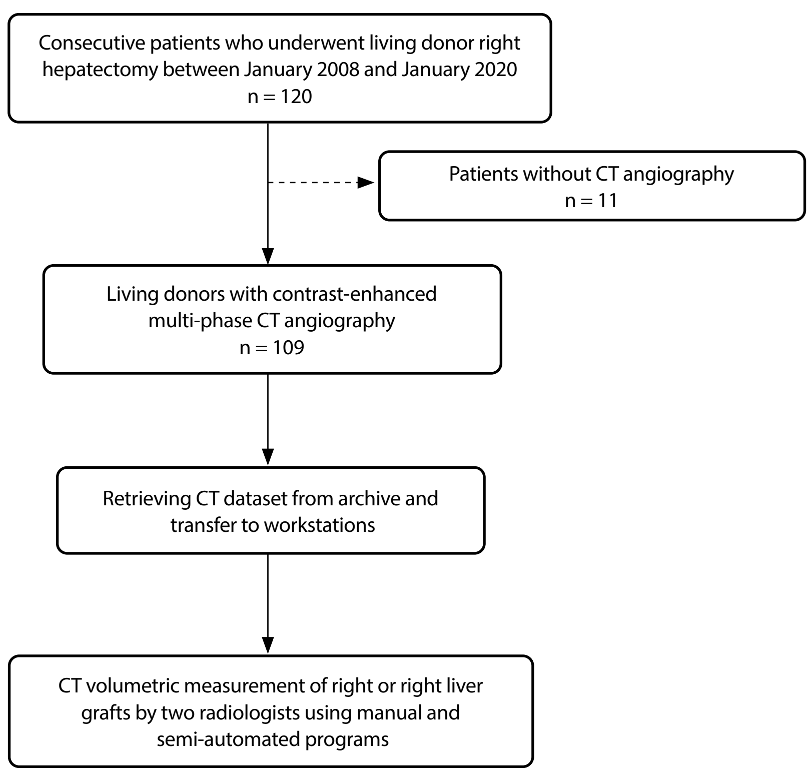

Figure 1. Flowchart summarizing patient accrual. CT, computed tomography.

rience in CT volumetry of the liver) using axial portal venous phase images. The archived CT data set was transferred to the relevant workstations for CT volumetry analysis.

First, the radiologists measured the right liver lobe volumes using the interactive manual program (Advanced Vascular Analysis, Philips Healthcare). Users selected one of three different volume sizes (low, medium, and high; 400, 1.500, and 4.000 voxels, respectively), then moved the pointer to paint the entire liver area on the transverse CT image. The users painted every 5–20 slices, depending on the parenchymal homogeneity and the volume size chosen. When the users painted an area outside the liver contours, that part could be removed using a spheric eraser tool with three diameter options: small, medium, and large, 5, 10, and 30 voxels, respectively. Consistent with the current standard approach,[12] volumetric measurements included intrahepatic vessels but excluded large vessels. A transection line was drawn along the middle hepatic vein (MHV) to determine the right and left liver lobe volumes. To measure the volume of the right liver lobe, users removed painted parenchyma to the left of the MHV and the MHV itself with the eraser tool. This removal could also be done on the three-dimensional volumetric image. The resulting volume of the right liver lobe was displayed in cubic centimeters (cc) (Figure 2).

The semi-automated software (CT Liver Analysis, Philips Healthcare) used in this study was developed for liver segmentation only. As a first step, the liver was identified on axial CT images and the total liver volume was automatically determined. Liver borders could be corrected manually if necessary. The vessels were then automatically detected and grouped as portal, hepatic, or unclassified vessels and included in the total liver volume. The users delineated the transection plane by setting two points (the vena cava inferior and the MHV) to measure the volumes of the right and left liver lobes semi-automatically (Figure 3).

The time needed to complete each CT volumetric measurement was recorded for each user. The time required to load the digital imaging and communications in medicine images on the workstation was not included in the user time.

Intraoperative data acquisition

Soon after the resection, the graft was flushed with histidine-tryptophan-ketoglutarate (HTK) solution (Dr. Franz Köhler Chemie GmbH, Alsbach-Hähnlein, Germany) containing 2.000 units of unfractionated heparin through the open ends of the main branches of the main hepatic artery and the portal vein, until the outflow from the hepatic veins was completely cleared. After flushing, the graft weight was measured using an electronic laboratory scale on the back table. The intraoperative graft weights were also considered actual graft volumes, as the mean density of the healthy liver tissue was assumed to be 1.00 g/mL.[13]

Statistical analysis

Descriptive analysis of the quantitative data was expressed as means and standard deviations. The paired samples t-test was used to compare the mean of the graft volumes calculated by the two radiologists using manual and semi-automated CT volumetry programs. A Bland–Altman analysis was used to evaluate the level of agreement between the observers and between the CT volumetry programs. The preoperatively calculated right lobe graft volume was converted to a graft weight with a conversion ratio of one (1 mL = 1 g).[13] A P value of < 0.05 was considered significant. Statistical analysis was performed with SPSS version 18.0 (SPSS Inc. Released 2009. PASW Statistics for Windows, version 18.0. Chicago: SPSS Inc.) and

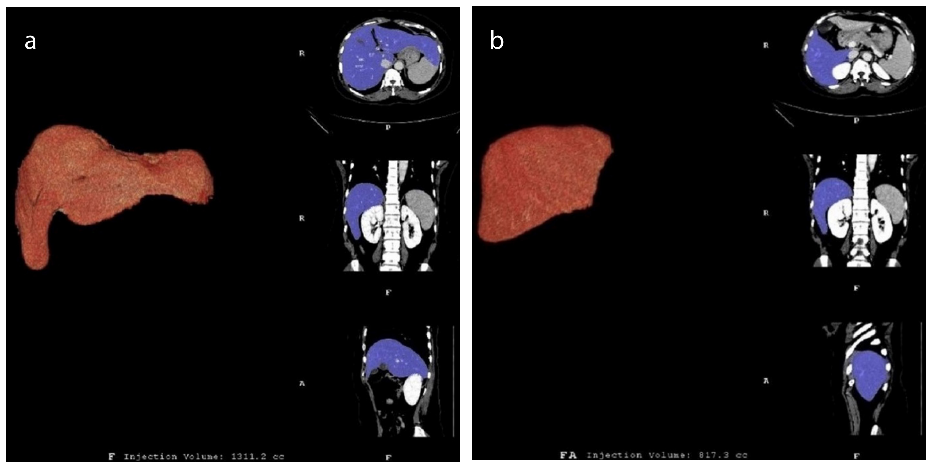

Figure 2. Interactive manual computed tomography (CT) volumetry (Volume Tracing in Advanced Vessel Analysis, Philips Healthcare). Three-dimensional rendered images representing the painted liver parenchyma on CT images: whole liver **(a)** and right liver lobe **(b)**.

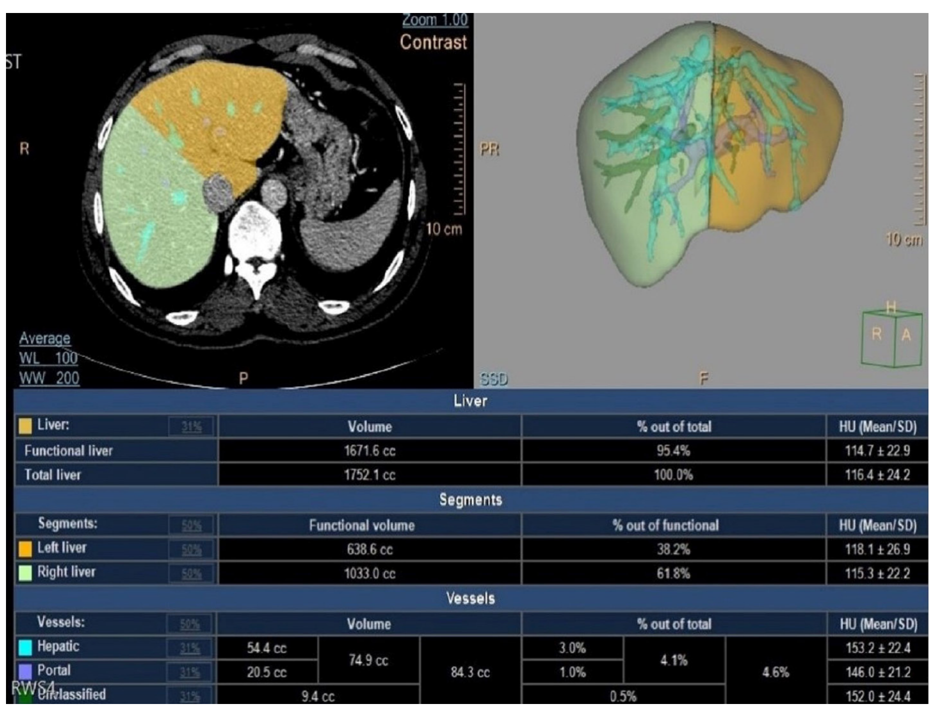

Figure 3. Semi-automated computed tomography (CT) volumetry (CT Liver Analysis, Philips Healthcare). The liver was automatically identified on CT images, and total liver volume was obtained. The volumes of each liver lobe were calculated semi-automatically after placing the landmark points on the middle hepatic vein and the inferior vena cava.

MedCalc version 18.9.1 (MedCalc Software, Mariakerke, Belgium).

Results

Of the 109 liver donors included in this study, 37/109 (34%) were female, and 72/109 (66%) were male, with a mean age of 31.4 ± 11.3 years (range 18–50). Table 2 presents the baseline demographics of the living liver donors.

Both manual and semi-automated CT volumetry significantly overestimated the AGWs (P < 0.001 for both methods). There was no significant difference between the interactive manual and the semi-automated volumetric measurements of the senior radiologist, however, the junior radiologist measured higher volumes using the manual program (P < 0.001). The Bland–Altman graphs showed that the 95% limits of agreement between the CT volumetry programs ranged from –79 to 65 cc with a mean difference of 7 ± 48 cc for the senior radiologist and –48 to +116 cc with a mean difference of 34 ± 54 cc for the junior radiologist (Figure 4). The junior radiologist calculated significantly higher volumes with both CT volumetry methods than the senior radiologist (P < 0.001 for both methods). The Bland–Altman plots revealed that the inter-observer variation tended to be greater in interactive manual volumetry. The 95% limits of agreement between the observers ranged from –54 to 179 cc with a mean difference of 63 ± 59 cc in manual volumetry and –20 to 64 cc with a mean difference of 22 ± 38 cc in semi-automated volumetry (Figure 5). The mean difference between the AGW and the EGV was 13.5% in the manual program and 11.7% in the semi-automated program. Table 3 summarizes the mean values of all measured volumes and the AGWs.

The required mean time to determine the volume of the right liver lobe with the manual method was 27.3 ± 14.2 min/case and 6.8 ± 1.4 min/case for the semi-automated volumetry (P < 0.001). There was no significant difference between the user times in both CT volumetry programs.

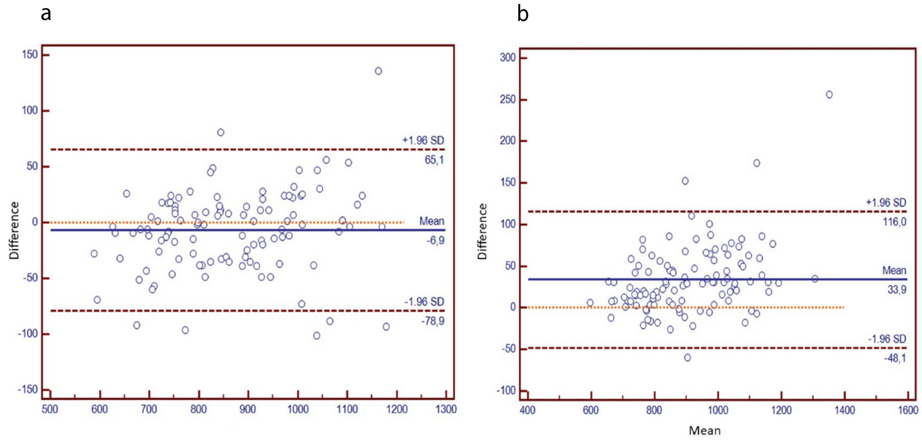

Figure 4. The Bland–Altman plots of the volume difference between the semi-automated software and the manual volumetry: senior radiologist **(a)** and junior radiologist **(b)**. The mean difference was demonstrated with a solid line and 95% limits of agreement with dashed lines.

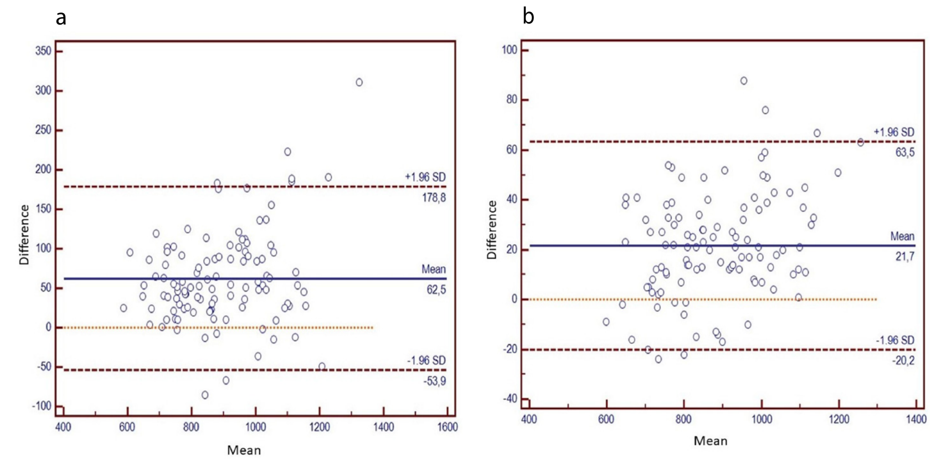

Figure 5. The Bland–Altman plots of the volume difference between the measurements of the junior radiologist and the senior radiologist: manual volumetry **(a)** and semi-automated volumetry **(b)**. The mean difference was demonstrated with a solid line and 95% limits of agreement with dashed lines.

Table 2. Baseline demographics of living liver donors

Age (year)	31.4 ± 11.3
Sex	
Male	72 (66%)
Female	37 (34%)
Body mass index (kg/m²)	
Mean ± standard deviation	26.7 ± 8.9
Smoking history*	26 (24%)

*Both current and former smokers.

Table 3. Liver graft volume measurements (mean ± standard deviation)

	Junior radiologist	Senior radiologist	Mean value of two observers
Manual CT volumetry	924 ± 163 cc	861 ± 147 cc	893 ± 155 cc
Semi-automated CT volumetry	890 ± 146 cc	868 ± 139 cc	879 ± 143 cc
Actual graft weight			787 ± 128 gr

CT, computed tomography.

Discussion

Automated and interactive CT volumetry programs provide an acceptable measurement and decrease the time needed for volumetric evaluation. Nevertheless, these volumetry programs tend to reveal more discrepancies than conventional segmentation methods.[6,14] Considering that optimal GRWR ≥0.8 is essential for a good prognosis in LDLT, an overestimated graft weight may create a risk of the small-for-size syndrome, particularly in cases with borderline GRWR.

The present study showed that right liver graft volumes measured using both interactive manual and semi-automated CT volumetry were significantly higher than the AGWs. Lemke et al.[15] concluded that intraoperative graft weight could be accurately predicted by reducing the preoperatively measured graft weight with a rectification factor of 0.75. Niehues et al.[16] found a 13% overestimation of in vivo volumes in an animal model. Another study revealed a 20.5% overestimation of the right liver lobe volumes using a non-commercial self-developed image postprocessing software.[10]

There are various factors that may explain the overestimation of graft volumes by CT volumetry, although intraoperative blood loss is considered the main reason.[17] Blood within the intrahepatic vasculature during imaging largely explains the overestimation of the graft volume compared to the actual blood-free liver graft measured after resection. Preoperative CT examination represents the "*in situ*" state in which the liver is exposed to physiological perfusion. However, the condition of the graft after resection during liver transplantation is not physiological. Fluids, such as blood, bile, and lymph, flow out of the vascular structures that have not yet been anastomosed with the recipient, and accordingly, the liver graft shrinks.[10,18] As a consequence, a fair amount of intraoperative volume loss is inevitable in the graft after resection.[10] In the present study, the right liver lobe grafts resected from the living donors were weighed in *ex vivo* conditions without blood after flushing with HTK solution. In a study, the preoperatively measured graft volume using CT volumetry was approximately 20% greater than the intraoperatively measured volume of the drained graft, while this difference was only 4% for the blood-filled graft.[18] Hwang et al.[17] revealed a rectification factor of 1.22 between the blood-free graft weight and the *in vivo* graft volume. Lemke et al.[15] revealed that the AGW could be calculated with sufficient accuracy by reducing the preoperatively estimated volume of the right hepatic lobe by a correction factor of 0.75. However, using a specified rectification factor may cause erroneous calculations as there may be inter-individual variations.

Transplant centers generally accept the mean density of healthy liver tissue as 1.00 g/mL and therefore assume that 1 g of liver tissue equals 1 cc of the liver in preoperative volumetry measurements.[15,19] Based on this fact, it can be assumed that the volume of the right hepatic lobe is equal to the respective weight. In this study, the conversion factor between the preoperatively measured graft volumes in milliliters and the graft weight in grams was also accepted as "1". However, Lemke et al.[10] found that the physical density of the right liver lobe grafts was 1.1172 ± 0.1015 g/mL, ranging between 1.00 and 1.33 g/mL. Therefore, it should be kept in mind that there may be a negligible level of inter-individual differences in the physical densities of transplanted liver lobes.

A virtual resection line that is misidentified on CT images and does not match the actual surgical resection line may cause a mismatch between the EGV and the AGW.[20] Intraoperative resection planes may differ from the lines separating the Couinaud segments. The Couinaud classification divides the liver into eight segments in straight lines along the hepatic and portal veins, but these vessels are usually not straight. Intraoperative dehydration of the graft by the hyperosmolar HTK solution may be considered as another factor that may contribute to the overestimation of the preoperative graft volume.[21]

Accurate and rapid calculation of the liver volumes to be resected and left in the donor in the LDLT is extremely important in transplantation clinics. In the authors' study, both the interactive manual and the semi-automated program significantly reduced the time required for volumetric evaluation compared with conventional segmentation methods, while the semi-automated software was even four times faster than the interactive manual method. In the current study, CT volumetric measurements were performed by two radiologists with different levels of experience. The authors found that the less experienced observer measured higher graft volumes using both methods, resulting in higher differences between the AGW and the EGV. However, the inter-observer difference was less in the semi-automated volumetry compared with the manual volumetry. Similarly, in another study, the less experienced users measured higher volumes in both the manual and the semi-automated volumetry, and the inter-observer difference was less in the semi-automated volumetry.[22] The fact that the experienced observers measured the liver graft volumes more accurately shows that there is still a need for new volumetry software that offers better inter-user agreement. Volume measurement should be performed by specialists who can accurately determine the hepatectomy plane to reduce potential errors and maximize the accuracy of volumetric estimates.

Excluding intrahepatic vascular volume can improve the performance of volumetry programs.[23] Additionally, by using equations developed from the data obtained in previous CT volumetry studies, anticipated intraoperative graft weight can be determined more accurately.[23,24] In a study, the following formula was developed to calculate the SLV by measuring the thoracoabdominal circumference (TAC) of the body at the level of the liver dome, especially in patients with potentially small grafts: SLV = (TAC × 3.58) – (age × 3.98) – (sex × 109.74) – 934.59.[23]

This study has some limitations. In this study, the water displacement method could not be used for intraoperative volume measurement of the liver graft. Although intrahepatic vascular volume can be obtained in the semi-automated program, it was not excluded from the graft volumes to avoid a methodological difference between the volumetry programs. Intra-observer agreement was not investigated to assess the repeatability of these programs. Last, the semi-automated software has some extra features that were not tested in the current study but could be used in other future studies, such as preprocedural planning of radiofrequency ablation.

In conclusion, the authors' study suggests that both manual and semi-automated CT volumetry significantly overestimates the AGW. Semi-automated CT volumetry significantly shortens the user time and provides strong agreement with the manual program if the user is sufficiently experienced. A higher GRWR can be applied to prevent small-for-size syndrome when evaluating the liver graft with these CT volumetry programs.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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