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CT evaluation of living liver donor

Can 100-kVp plus iterative reconstruction protocol provide accurate liver volume and vascular anatomy for liver transplantation with reduced radiation and contrast dose?

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Abstract

We evaluated whether donor computed tomography (CT) with a combined technique of lower tube voltage and iterative reconstruction (IR) can provide sufficient preoperative information for liver transplantation.

We retrospectively reviewed CT of 113 liver donor candidates. Dynamic contrast-enhanced CT of the liver was performed on the following protocol: protocol A (n=70), 120-kVp with filtered back projection (FBP); protocol B (n=43), 100-kVp with IR. To equalize the background covariates, one-to-one propensity-matched analysis was used. We visually compared the score of the hepatic artery (A-score), portal vein (P-score), and hepatic vein (V-score) of the 2 protocols and quantitatively correlated the graft volume obtained by CT volumetry (graft-CTv) under the 2 protocols with the actual graft weight.

In total, 39 protocol-A and protocol-B candidates showed comparable preoperative clinical characteristics with propensity matching. For protocols A and B, the A-score was 3.87 ± 0.73 and 4.51 ± 0.56 (*P* < .01), the P-score was 4.92 ± 0.27 and 5.0 ± 0.0 (*P* = .07), and the V-score was 4.23 ± 0.78 and 4.82 ± 0.39 (*P* < .01), respectively. Correlations between the actual graft weight and graft-CTv of protocols A and B were 0.97 and 0.96, respectively.

Liver-donor CT imaging under 100-kVp plus IR protocol provides better visualization for vascular structures than that under 120-kVp plus FBP protocol with comparable accuracy for graft-CTv, while lowering radiation exposure by more than 40% and reducing contrast-medium dose by 20%.

Abbreviations: CE-CT = contrast-enhanced computed tomography, CT = computed tomography, CTDIvol = volume CT dose index, FBP = filtered back projection, CTv = CT volumetry, IR = iterative reconstruction, LDLT = living donor liver transplantation, SD = standard deviation.

Keywords: image enhancement, iterative reconstruction, living liver transplantation, multidetector computed tomography, radiation dosage

1. Introduction

Living donor liver transplantation (LDLT) has increasingly been accepted as a therapeutic strategy in the management of the patients with end-stage liver failure. Important aspects of the preoperative donor evaluation include clear visualization of the intrahepatic vascular anatomy for the determination of the resection line and accurate estimation of the donor's liver volume and intended liver graft size.[1,2] Correct and appropriate therapeutic planning by radiologists and surgeons for both the donor and recipient is imperative for successful LDLT. For ensuring the donor's safety, calculating the accurate remnant volume of the liver is critically important to preserve sufficient postoperative, metabolic, and synthetic capacity.[3] For avoiding small-for-size syndrome in the recipient, more than 0.8% of graft-to-recipient body weight ratio is needed.[4] Therefore, an accurate preoperative estimate of graft volume and weight is important for the success of LDTL.

Dynamic contrast-enhanced computed tomography (CE-CT) that is simple, reproducible, and of high spatial resolution facilitates detection of the edge of the liver parenchyma and hepatic vessels. Therefore, computed tomography (CT) volumetry (CTv) of the donor's liver using abdominal CE-CT imaging is widely accepted as a standard method for preoperative estimation.[5] Many software-aided methods have been developed in the past decade for the measurement of the liver volume.[6,7] According to previous studies,[8] the correlation between CTv and actual liver volume/weight is substantial. Dynamic CE-CT is also useful in determining the resection line because it clearly shows the venous and arterial anatomy of the liver.

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On the other hand, radiation exposure for liver donors should be as low as possible because they tend to be healthy and nonelderly. Reduced contrast-medium dose is also desirable because contrast-medium-induced nephropathy has been reported.[9] Lower tube voltage CT can reduce not only radiation dose but also contrast-medium dose because iodine attenuation increases as the tube voltage decreases due to the energy shift of the x-ray beam to the k-absorption edge of iodine. However, lower tube voltage scan suffers from increased image noise.[10,11] Previous studies demonstrated that iterative reconstruction (IR) technique can reduce image noise without image-quality deterioration. We hypothesized that lower tube voltage scan with IR technique may preserve CT image quality of the liver parenchyma and vascular anatomy with reduced radiation and contrast dose, leading to appropriate pre-LDLT planning and accurate CTv estimates. Thus, we compared the image quality of dynamic CE-CT under 100 kVp plus IR protocol with that under 120 kVp plus filtered back projection (FBP), and correlated the CTv results of these protocols with the actual resected liver volume.

2. Methods

2.1. Study population

This retrospective study received institutional review board approval; written informed consent was obtained.

We retrospectively reviewed the database of donor candidates who had undergone liver-donor CT between October 2011 and December 2014 at the Department of Transplantation and Pediatric Surgery of our hospital. We evaluated the CE-CT images of 113 donor candidates (58 men and 55 women; mean age, 42.8 ± 13.1 years). Of the 113 donor candidates, 86 underwent hepatectomy.

2.2. CT protocols

Until February 2014, donor candidates (n = 70) were scanned at 120 kVp on a multidetector CT (MDCT) instrument (Brilliant 64; Philips Medical Systems, Cleveland, OH); the contrast dose was 600 mgI/kg (protocol A). From March to December 2014, donor candidates (n = 43) underwent scanning at 100 kVp on an MDCT instrument (Aquilion ONE ViSION; Toshiba, Otawara, Japan) using a contrast dose of 480 mgI/kg (protocol B). In protocol B, a 20% reduction in the contrast dose was chosen for 100 kVp scan based on a previous study by Itatani et al.[12]

Both CT scan protocols were performed with breath holding at inspiration. After obtaining the noncontrast CT scan, nonionic contrast material (Iopamiron 370, Bayer HealthCare, Osaka, Japan) was administrated at a flow rate of 3 mL/s using an automated power injector (Autoenhance A-250; Nemoto Kyorindo, Tokyo, Japan), following a 3-phasic dynamic CT scanning during hepatic arterial, portal, and venous phases. A bolus-tracking method was used to determine the start of scanning in each phase after contrast material injection. The anatomical level for monitoring was set in the descending aorta at Th10 level. The trigger threshold was set at 150 Hounsfield units (HU). Eight seconds after the trigger, the CT scanning was started.

The parameters for protocol A were detector configuration (64 × 0.625 mm) (detector collimation), slice thickness (0.625 mm), section interval (0.3 mm), and gantry rotation time (0.4 seconds), 200 effective mAs, and 120 kVp, all of which were determined as described by Nakayama et al.[6] The tube potential and tube current were determined with automatic exposure control (DoseRight, Philips Medical Systems) on the basis of x-ray attenuation on the anterior, posterior, and lateral scout images and on the reconstruction kernel.

The parameters for protocol B were detector configuration (320 × 0.5 mm) (detector collimation), slice thickness (0.5 mm), section interval (0.25 mm), and gantry rotation time (0.275 seconds). The tube voltage was 100 kVp, and the tube current was determined with automatic exposure control (SURE Exposure 3D; Toshiba, Otawara, Japan), on the basis of x-ray attenuation on the anterior, posterior, and lateral scout images and on the reconstruction kernel. The CT images obtained with protocol B were reconstructed with the adaptive IR technique (AIDR 3D; Toshiba, Otawara, Japan), using a standard kernel.

2.3. Quantitative evaluation of liver-donor CT imaging

For evaluating the image quality of dynamic CE-CT images, we calculated the contrast and contrast-to-noise ratio (CNR) of the liver in the portal and venous phases. In the portal phase, mean and standard deviation (SD) of CT numbers in HU for the portal vein of S8 subsegmental branch and perivascular liver parenchyma were measured in all patients on a monitor by placement of a circular region of interest by a board-certified radiologist of 11-year experience. In venous phase, mean and SD of CT numbers for the middle hepatic vein and perivascular liver parenchyma were also measured.

The formula of calculating contrast and CNR was as follows:

$\text{contrast}_{\text{portal}}$ = mean CT number of portal vein − mean CT number of the liver parenchyma

$\text{contrast}_{\text{vein}}$ = mean CT number of hepatic vein − mean CT number of the liver parenchyma

$\text{CNR}_{\text{portal}} = \text{contrast}_{\text{portal}}$/((SD of portal vein + SD of the liver parenchyma)/2)

$\text{CNR}_{\text{vein}} = \text{contrast}_{\text{vein}}$/((SD of hepatic vein + SD of the liver parenchyma)/2)

2.4. Visual evaluation of liver-donor CT imaging

All CT images were consensually reviewed and graded by 2 board-certified radiologists, according to a 5-point scale for the visualization of vascular structures that is necessary for preoperative surgical planning (a score of the hepatic artery: A-score, of the portal vein: P-score, and of the hepatic vein: V-score). The 5-point scores were as follows: 5 (excellent) = hepatic vascular structures of the subsegmental branches are clearly visualized, sufficient information; 4 (good) = hepatic vascular structures of the both segmental and subsegmental branches can be identified, useful information; 3 (fair) = hepatic vascular structures of the segmental branches are visualized but those of the subsegmental branches are difficult to be identified, acceptable information; 2 (unacceptable) = hepatic vascular structures of the segmental branches are visualized but are not clear, inadequate information; and 1 (poor) = vascular structures are unclear, no information.

2.5. CT volumetry for graft

CT images were imported into a workstation (ZioStation2; Ziosoft, Tokyo, Japan) (Fig. 1). We performed the CTv using the following steps. First, we used the automated volumetry system based on the density and enhancement pattern and measured the

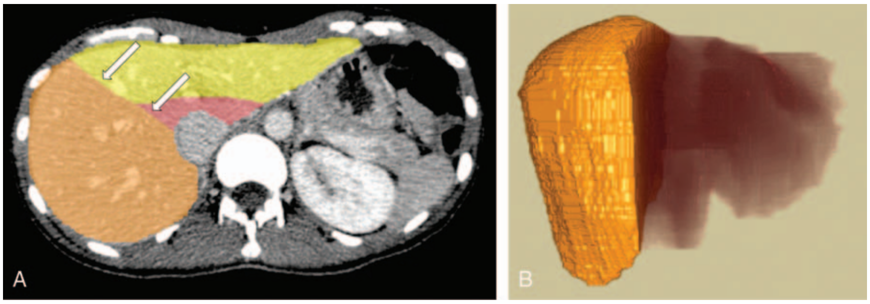

Figure 1. Computed tomography (CT) volumetry for the liver graft. The graft is traced with the cutting line along the middle hepatic vein (arrows) on the axial CT image in the venous phase (A). Volume-rendering 3D image (B) shows the total volume of the graft (637 mL). The accurate graft weight was 590 g.

whole liver volume. Second, we manually excluded the retro vena cava, gallbladder, and extra-hepatic structures attached to the liver (such as the kidney, spleen, and stomach). Third, we manually corrected the region of interest of the entire liver. The time required for measuring the entire liver volume was approximately 10 minutes. The model for the entire liver was then subjected to virtual hepatic resection based on the type of hepatectomy planned; the volume of the simulated graft was then measured. We repeated volumetric analysis based on the actual surgical procedure at instances where the preoperatively planned resection and actual type of resection were different.

2.6. Comparison between CTv and actual explanted liver weight

In living donor surgery, hepatectomy was performed according to the cutting plane that was preoperatively imaged. The explanted liver was immediately flushed with histidine–tryptophan-–ketoglutarate solution or University of Wisconsin solution at 4 °C. After the solution was completely drained from the liver, the actual graft weight was measured in grams by an automatic weighing machine.[8] In 86 of the 113 candidates who had undergone hepatectomy, the liver volume with CTv was compared with the actual volume of the explanted liver.

2.7. Radiation dose by CE-CT imaging

From the database of the Department of Radiology, we obtained the volume CT dose index (CTDIvol) displayed on the CT console, which was measured by the manufacture on a 32-cm polymethyl-methacrylate phantom. We used the CTDIvol of the arterial, portal venous, and venous phases as the donor's radiation exposure and calculated the radiation dose reduction rate using the following formula:

Radiation dose reduction rate #1 = (1 − CTDI of protocol B/CTDI of protocol A) × 100 (%)

In our study, different CT machines were used for the 2 protocols (protocol A with Philips, protocol B with Toshiba). The accuracy of CTDIvol values could be different depending on the venders, and therefore we also estimated the radiation dose reduction rate by another method (radiation dose reduction rate #2). The image noise is inversely proportional to the square root of the CTDI.[13] CT scanning at Aquilion ViSION with AIDR 3D standard setting was performed with reduced tube current (25% mA) compared with FBP. Then, we measured the image noise of the portal vein in the portal venous phase under each protocol, and calculated the radiation dose reduction rate #2 by following formulas:

Noise ratio = noise of protocol A of portal vein/(noise of protocol B of portal vein $\times \sqrt{0.25^{-1}}$)

Radiation dose reduction rate #2 = (1 − Noise ratio) × 100 (%)

2.8. Statistical analysis

Values were expressed as mean ± SD (range). We used one-to-one propensity-matched analysis to equalize background covariates. The propensity matching was calculated using logistic regression, and donor candidate protocol A was matched with protocol B, using the nearest neighbor technique with a predefined caliper of 0.2.

The Student *t* test was used to compare continuous, parametric values between the groups. The Mann–Whitney *U* test was used to compare nonparametric values between the groups. Correlation was analyzed by standard Pearson correlation analysis.

Statistical analysis was performed using statistical software package (JMP, version 12; SAS, Cary, NC). A *P* value of <.05 was considered statistically significant.

3. Results

3.1. Characteristics of donor candidates

Characteristics of overall donor candidates and those used for propensity-score matching are shown in Table 1. No significant differences between variables in the groups were observed.

3.2. Differences of radiation exposure between 2 protocols

After propensity matching, the arterial phase, portal phase, and venous phase of CTDIvol values of protocol A (120 kVp) were 12.7 ± 4.3, 13.6 ± 4.5, and 13.6 ± 3.6 mGy, respectively. The corresponding CTDIvol values of protocol B (100 kVp) were 6.3 ± 4.3, 6.5 ± 2.5, and 6.5 ± 2.2 mGy, respectively. The radiation dose of arterial, portal venous, and venous phase of protocol B was significantly lower than that of protocol A (arterial: $P < .001$, portal venous: $P < .001$, and venous: $P < .001$). The radiation dose reduction rate #1 of arterial, portal venous, and venous phase were 50.4%, 52.2%, and 52.2%, respectively. The radiation dose reduction rate #2 was 42.7%.

3.3. Quantitative evaluation

The $\text{contrast}_{\text{portal}}$ and $\text{CNR}_{\text{portal}}$ of protocol B were significantly higher than those of protocol A (Table 2). The $\text{contrast}_{\text{vein}}$ and CNR_{vein} of protocol B were also significantly higher than those of protocol A (Table 2).

Table 1

Characteristics of donors.

	Overall donor cohort (n=113)			Propensity-matched donor (n=78)		
	Protocol A (n=70)	Protocol B (n=43)	*P*	Protocol A (n=39)	Protocol B (n=39)	*P*
Age, y	42.8±13.8	42.8±12.2	.97	45.0±14.4	43.1±12.5	.54
Gender (male)	35	20	.72	21	21	1.0
Body weight, kg	60.4±11.1	61.7±13.1	.58	60.8±10.0	60.4±10.6	.86
Surgical procedure	62	24	.78	35	22	.55
Lateral sectionectomy	18	7	–	13	6	–
Posterior sectionectomy	2	2		1	1	
Left hepatectomy	20	8		7	8	
Right hepatectomy	22	7		14	7	

3.4. Visual evaluation

After propensity matching, the mean A-scores of protocol A and B were 3.87±0.73 and 4.51±0.56, respectively; the difference was statistically significant ($P<.001$). Inappropriate visualization of the hepatic artery (score 3 or lower) was observed in 13 patients under protocol A (1 and 10 for scores 2 and 3, respectively) and in 1 patient under protocol B (score 2); the differences were statistically significant ($P<.01$).

After propensity matching, the mean P-scores of protocols A and B were 4.92±0.27 and 5.0±0.0, respectively; the difference was not statistically significant ($P=.07$). No images were assigned a score of 3 or less on both protocols.

After propensity matching, the mean V-scores of protocols A and B were 4.23±0.78 and 4.82±0.39, respectively; the difference was statistically significant ($P<.001$). Inappropriate visualization for the hepatic vein (score 3 or lower) was observed in 5 patients under protocol A (1 and 4 patients for scores 2 and 3, respectively) and in no patient under protocol B; the difference was statistically significant ($P<.01$).

3.5. Correlation between preoperative CTv and actual weight of liver graft

Sixty two donor candidates with protocol A and 24 candidates with protocol B underwent donor hepatectomy. After propensity matching, 35 of 39 candidates of protocol A and 22 of 39 candidates of protocol B underwent hepatectomy. The correlation coefficients between CTv and the actual liver weight of both protocols were high (protocol A: $r=0.97$, $P<.001$, bias=−79.6, 95% CI=−59.6 to −99.7, protocol B: $r=0.96$, $P<.001$, bias=−101.4, 95% CI=−46.7 to −156.0).

4. Discussion

Safe donor hepatectomy requires meticulous preoperative evaluation on the liver CE-CT images. Accurate volume of the resected and remnant liver and detailed information on the intrahepatic vascular anatomy can be obtained on preoperative donor CT scans.[14–16] In this study, the lower tube voltage plus IR (AIDR3D) protocol (100-kVp) yielded statistically better visualization of hepatic vascular structures than the standard protocol (120-kVp and FBP reconstruction). Iodine attenuation increases as the tube voltage decreases because the mean photon energy in the x-ray beam moves closer to the K-absorption edge of iodine. This movement of mean photon energy increases the photoelectric effect and decreases Compton scattering, and in effect, translates into higher mean iodine attenuation.[17] In addition, the IR technique has the ability to decrease the image noise while keeping the spatial resolution.[18]

Table 2

Contrast and contrast-to-noise ratio (CNR) of portal vein and hepatic vein in each protocol.

	Protocol A	Protocol B	*P*
Contrast$_{\text{portal}}$	82.8±27.9	103.7±30.8	<.01
CNR$_{\text{portal}}$	4.2±1.7	6.4±1.8	<.001
Contrast$_{\text{vein}}$	61.3±21.7	81.9±20.3	<.001
CNR$_{\text{vein}}$	3.2±1.3	4.7±1.2	<.001

With respect to preoperative simulation, the 100-kVp plus IR technique showed advantages for assessment of hepatic vascular anatomy. Although the segmentation of the liver is determined by the portal vein tributary, the cutting line is determined by the hepatic vein. Moreover, the clear information of the hepatic artery is needed for the hepatic artery reconstruction before operation.[19] From our results, the 100-kVp plus IR technique was useful for preoperative simulation because the protocol provided better visualization of hepatic vascular structures and better contrast between the liver parenchyma and hepatic vascular structures than standard protocol (Figs. 2 and 3). Our results are consistent with previous studies.[18,20,21]

Our study demonstrated that the liver volume of 100-kVp plus IR technique had good correlation with the actual liver weight ($R=0.96$, $P<.001$). To the best of our knowledge, our study is the first to correlate low-dose CTv findings with the actual volume of the resected liver. Li et al[22] reported that the graft volume preoperatively calculated by the standard-dose CT using a 64-row machine showed good correlation with the actual liver graft weight ($R=0.86$, $P<.001$). Our results employing low tube voltage and IR showed better correlation than theirs; this may be because of the better visualization of hepatic vascular structures. The experience of the radiologist in the measurement might partially affect the results.

Although correlation coefficients of low-dose and standard-dose protocols were comparable, we believe that the lower tube voltage plus IR technique offered an advantage over the standard technique in CTv; this technique clearly identifies the liver contour and hepatic cutting line based on the hepatic vein due to the higher contrast of hepatic vasculature.[6] We performed CTv by a combined automated and manual technique. Suzuki et al[7] reported the automated CTv alone accurately estimated the liver volume, but the noise reduction technique was needed for automated CTv system. Therefore, reduced-image noise could be achieved using IR, and it was of use to the automated CTv system,

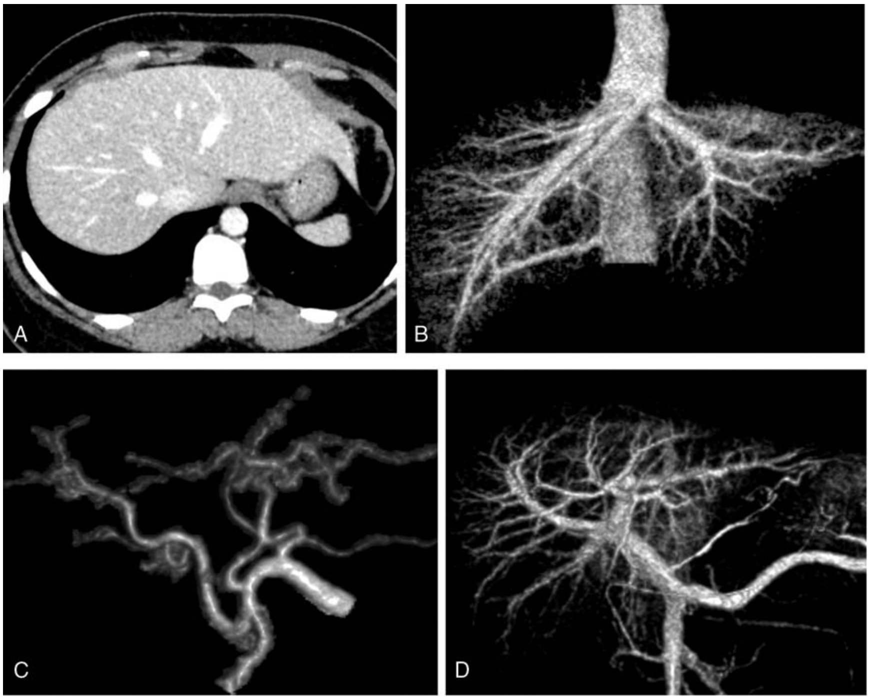

Figure 2. Thirty-year-old male donor candidate undergoing CT imaging under 100-kVp with IR (protocol B). Hepatic vein is clearly identified on the axial CT (A) and volume-rendering 3D images (B), providing helpful information for surgery. The hepatic artery and portal vein are also clearly visualized on volume-rendering 3D images (C and D, respectively). Each visual score (hepatic artery, hepatic vein, and portal vein) is excellent (score 5). CT = computed tomography, IR = iterative reconstruction.

leading to an accurate preoperative CT analysis with high reproducibility. Assessment of the accuracy of automated CTv with a low-dose and IR protocol is underway in our laboratory.

Because liver donors are usually healthy individuals, their exposure to radiation must be kept as low as possible. For the reduction of radiation exposure, several methods have been reported.[11,23–26] In this study, our low tube voltage protocol (protocol B) had the capability to reduce the radiation dose by 43% (radiation dose reduction rate #2) to 52% (radiation dose reduction rate #1) and contrast dose by 20%. The accuracy of CTDI reported on CT console is generally different among the different vendors' CT machines, but we did not have direct measurement data of radiation dose of the patients undergoing CT scanning on each scanner. Therefore, we additionally estimated the radiation dose reduction rate #2 based on the image noise in the portal vein (portal venous phase) to correct the errors due to the different machines, and the rate was calculated as 43.2%. The radiation dose reduction rate #2 was slightly lower than radiation dose reduction rate #1, but our protocol B can reduce the radiation dose by more than 40%. We posit that the combination of low-dose CT imaging at 100-kVp setting, automatic tube current modulation scanning, and hybrid-type IR is an effective and appropriate method for reducing the radiation exposure on liver donors.

Nakamoto et al[27] reported that at least 50% radiation dose would be needed to maintain the visual image quality using IR. We believe that our radiation dose reduction will be appropriate with respect to maintaining qualitative and quantitative image quality. On the other hand, 80-kVp and high-level IR may be potentially applicable in slim patients (eg, those with a body mass

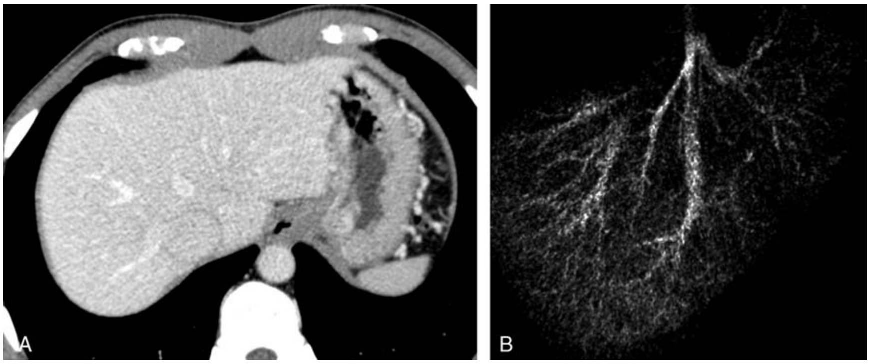

Figure 3. A 40-year-old female donor candidate undergoing computed tomography (CT) imaging under 120-kVp with filtered back projection (protocol A). Hepatic vein is identified but partially unclear on the axial CT (A) and volume-rendering 3D images (B). The visual score for hepatic vein was fair (score 3).

index of 22 kg/m^2 or less), leading to more contrast dose reduction.[11] Although the main objectives of the donor CE-CT are assessment of the hepatic vascular structure and liver volume, presurgical screening of other-organ diseases, such as malignant tumors, is also important. The image quality obtained at 80-kVp may be compromised particularly in the pelvic space because of the increased image noise attributable to radiation scattering and absorption, and the texture of the image may appear over-smoothing, such as plastic, when a high-level IR algorithm is applied. We believe that 100-kVp plus moderate-level IR technique may be generally suitable for the preoperative CT evaluation of living liver donors. Future studies evaluating the effects of 80-kVp with high-level IR on liver transplantation CT analysis should be performed.

Our study has 4 limitations. First, subjects were recruited from a small population in a single center. Although large-scale studies are preferable, the number of hospitals in which LDLT can be performed is limited. Second, we did not address potential difficulties encountered with liver CTv (eg, the time required for 3-dimensional-image reconstruction and the measurements). Third, because of the retrospective nature of our study, our 2 protocols were used on different CT scanners. Fourth, we did not evaluate the effects of the advanced type of IR (full IR) because it was not available for the Toshiba scanner used in the study. We speculate that the full IR technique may potentially lower radiation exposure and reduce contrast-medium dose to a greater level than that used in the present study; however, this speculation should be verified in future studies.

In conclusion, the technique that combines 100-kVp scanning and IR provides better visualization of hepatic vascular structures than 120-kVp plus FBP with accurate donor CTv of the liver while lowering radiation exposure by more than 40% and reducing contrast-medium dose by 20%. We suggest that 100-kVp plus IR technique is sufficiently informative for a preoperative CT evaluation of LDLT.

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