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FULL PAPER

Pre-operative volume rather than area of skeletal muscle is a better predictor for post-operative risks for respiratory complications in living-donor liver transplantation

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Objective: To demonstrate the superiority of total psoas volume (TPV) over total psoas area (TPA) in terms of predicting post-operative complications in living-donor liver transplantation (LDLT).

Methods: The TPA and TPV were assessed in 32 recipients who underwent CT before LDLT. The TPA was measured using an axial CT image at the level of the upper margin of the fourth lumbar vertebral body. The TPV was calculated using all the CT images from the muscle origin through the level of the pubic symphysis. Patients were divided into a sarcopenia group and no-sarcopenia group based on the medians of normalized TPA (nTPA) and normalized TPV (nTPV). We calculated the odds ratio (OR) of post-operative respiratory complications in relation to nTPA and nTPV, respectively.

Results: Out of 32 recipients, 17 recipients experienced at least 1 post-operative respiratory complication. The OR for males according to nTPV [OR = 15.00, 95% confidence interval (CI) = 1.03–218.31; $p = 0.031$] was higher than that for nTPA (OR = 3.33, 95% CI = 0.36–30.70; $p = 0.280$). The OR for females according to nTPV (OR = 4.00, 95% CI = 0.56–28.40; $p = 0.16$) was the same as that for nTPA (OR = 4.00, 95% CI = 0.56–28.40; $p = 0.16$).

Conclusion: Pre-operative volume of the skeletal muscle might be a better predictor for post-operative risks in LDLT recipients than pre-operative area of the skeletal muscle.

Advances in knowledge: Post-operative risks for respiratory complications in LDLT recipients might be evaluated more accurately by using TPV instead of TPA.

INTRODUCTION

Living-donor liver transplantation (LDLT) is a life-saving intervention for many patients with end-stage liver diseases such as cirrhosis, decompensated disease, acute liver failure and hepatocellular cancer.^{1,2} LDLT recipients are likely to have complications such as post-operative infections and death due to the complexity of the surgical procedure.^{3–5} It is therefore critical to identify LDLT recipients with increased risks at the pre-operative stage.⁶

Recent evidence has shown that sarcopenia may identify LDLT recipients with increased risks for post-operative infections, complications and death.^{6,7} Sarcopenia is defined as the loss of skeletal muscle mass caused by aging, chronic medical illness and malnutrition and has been postulated to be a major factor for decline in strength.^{8,9} In

previous studies, sarcopenia has been assessed by total psoas area (TPA), which is the sum of the area of bilateral psoas major muscles calculated by a single axial cross-sectional image.^{7,8} Only a few studies have assessed sarcopenia by using total psoas volume (TPV), which is the sum of the volume of bilateral psoas major muscles calculated utilizing volume data.^{5,10} Furthermore, to the best of our knowledge, there is no article which shows TPV to be more useful than TPA in relation to evaluating post-operative risks of LDLT patients.

The aim of this study is to demonstrate the superiority of TPV over TPA based on the idea that TPV may be able to measure skeletal muscle mass more accurately by expanding measuring range and decreasing statistical error. We measured both pre-operative TPA and pre-operative

TPV of living-donor liver transplantation (LDLT) recipients and compared TPV with TPA using the odds ratio (OR) of post-operative respiratory complications of LDLT.

METHODS AND MATERIALS

Patients

32 consecutive recipients (14 males and 18 females) who underwent LDLT at a university hospital between January 2009 and December 2013 were retrospectively investigated. For all of the recipients, pre-operative abdominal CT images (*i.e.* within 3 months before surgery) were available. Standard demographic and clinical data were collected including data on sex, age, height, weight, body mass index (BMI) and existence of respiratory complications. In this study, respiratory complications were defined as applying to one or more of the following items: contracting pneumonia within 30 days after surgery, tracheotomy after surgery or more than 8 days with artificial respirator. 17 out of 32 recipients were classified as having respiratory complications. This study was conducted in accordance with the Declaration of Helsinki and its updates and was approved by the local ethics committee. Informed consent was obtained from all patients.

Image analysis

Sarcopenia was assessed by measuring the cross-sectional area of the right and left psoas muscles (total psoas muscle area = TPA) and the volume of the right and left psoas muscles (total psoas muscle volume = TPV). Equilibrium phase images of abdominal CT, covering the whole abdomen and pelvis were utilized in this study after administration of contrast at a dose of 650 mg I kg^{-1} of body weight over 30 s. All the images were taken within 3 months before LDLT. The tube voltage was set at 120 kVp with slice thickness of 5 mm in all cases. The tube current was not constant because automatic exposure control was applied. CT units used in this study consisted of the following 3 models: 64-detector-row Aquilion™ (Toshiba Medical Systems, Otawara, Tochigi, Japan) in 20 cases; 64-detector-row LightSpeed VCT® (GE Healthcare, Milwaukee, WI) in 7 cases; and 320-detector-row Aquilion One™ (Toshiba Medical Systems) in 5 cases. All images were analyzed using the workstation SYNAPSE VINCENT (Fujifilm Corporation, Tokyo, Japan). The measurements of TPA and TPV were performed with an automated analysis program installed in the workstation (Figure 1). The TPA was

measured using axial CT images at the level of the upper edge of the fourth lumbar vertebral body according to a previous study.⁶ The TPV was calculated for psoas major muscles using all the CT images from the muscle origin through the level of the pubic symphysis. Displacements of muscle region used to calculate TPA and TPV caused by segmentation error were manually modified by an operator and verified by a radiologist. The measured TPA and TPV were then normalized for square of height according to a previous study¹⁰ and renamed as normalized TPA (nTPA) and normalized TPV (nTPV), respectively.

Statistical analysis

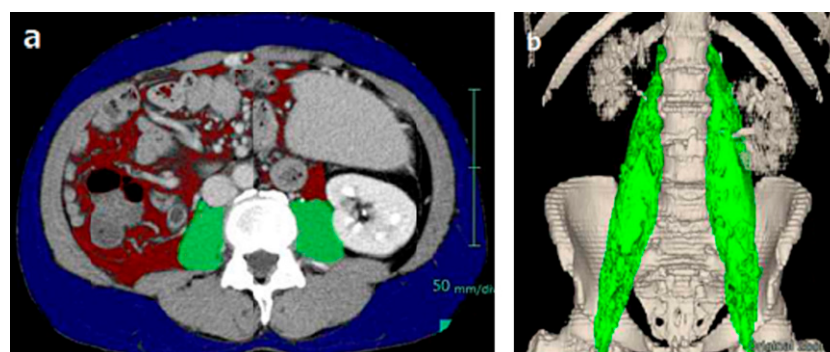
The data were presented as mean $\pm$ standard deviation for all continuous variables and as number (percentage) for all categorical variables. The correlation between nTPA and nTPV was evaluated by Pearson's correlation coefficient. We separated patients into males and females and tested the difference between these groups for all continuous variables using the Mann-Whitney *U* test. Each group was then divided into a sarcopenia group and no-sarcopenia group based on the medians of nTPA and nTPV, and the impact of sarcopenia on post-operative respiratory complications was examined using the OR in the males group and females groups with nTPA and nTPV, respectively. A *p*-value of <0.05 was considered statistically significant. All statistical analyses were performed with SPSS® v. 22 (IBM Corp., New York, NY; formerly SPSS Inc., Chicago, IL).

RESULTS

Patient characteristics

The demographic and clinical characteristics of the 32 patients included in the study are outlined in Table 1. There were 14 (43.75%) males and 18 (56.25%) females in the study population. The mean age was 54.0 ± 9.6 years. The number of patients who were classified as Child-Turcotte-Pugh Class A, B and C were 4, 6 and 22, respectively. Indications for LDLT were cirrhosis ($n = 12$), primary biliary cirrhosis ($n = 4$), hepatocellular carcinoma ($n = 2$), fulminant hepatitis ($n = 1$), primary sclerosing cholangitis ($n = 1$), familial amyloid polyneuropathy ($n = 1$), autoimmune hepatitis ($n = 1$), polycystic kidney and liver disease ($n = 1$), both cirrhosis and hepatocellular carcinoma ($n = 7$), both fulminant hepatitis and autoimmune hepatitis ($n = 1$) and unknown ($n = 1$).

Figure 1. Sarcopenia measurement using (a) total psoas area at the level of the upper edge of the fourth lumbar vertebral body and (b) total psoas volume.



Differences in psoas major muscle mass between the sexes

The average nTPA was $633.3 \pm 202.0 \text{ mm}^2 \text{ m}^{-2}$ and the average nTPV was $111.6 \pm 39.0 \text{ cm}^3 \text{ m}^{-2}$ after normalizing for patient height (Table 2). The mean nTPA was lower for females than for males (506.8 ± 146.4 vs $796.0 \pm 136.6 \text{ mm}^2 \text{ m}^{-2}$, $p < 0.001$) (Figure 2a). Similar to nTPA, the mean nTPV was lower among females than among males (84.2 ± 23.4 vs $146.9 \pm 23.8 \text{ cm}^3 \text{ m}^{-2}$, $p < 0.001$) (Figure 2b). There were significant differences between the sexes of both nTPA and nTPV. Pearson's correlation coefficients evaluating the correlation between nTPA and nTPV were 0.77 in males and 0.89 in females.

Impact of sarcopenia on post-operative respiratory complications

Out of the 32 patients who underwent LDLT, 17 experienced at least 1 post-operative respiratory complication with a morbidity of 53.1%. Morbidity for post-operative respiratory complications after LDLT included pneumonia ($n = 5$), tracheotomy ($n = 2$) and extubation delay ($n = 14$). Males were

divided into a sarcopenia group ($n = 7$) and no-sarcopenia group ($n = 7$) based on a median nTPA of $791.6 \text{ mm}^2 \text{ m}^{-2}$. Females were divided into a sarcopenia group ($n = 9$) and no-sarcopenia group ($n = 9$) based on a median nTPA of $488.8 \text{ mm}^2 \text{ m}^{-2}$. Similarly, males were divided into a sarcopenia group ($n = 7$) and no-sarcopenia group ($n = 7$) based on a median nTPV of $149.0 \text{ cm}^3 \text{ m}^{-2}$. Females were divided into a sarcopenia group ($n = 9$) and no-sarcopenia group ($n = 9$) based on a median nTPV of $83.3 \text{ cm}^3 \text{ m}^{-2}$. Patients who were classified as sarcopenia according to TPA had a higher risk of post-operative respiratory complications than those who were not classified as sarcopenia [males: OR = 3.33, 95% confidence interval (CI) = 0.36–30.70; $p = 0.28$; and females: OR = 4.00, 95% CI = 0.56–28.40; $p = 0.16$] (Table 3). In the same way as TPA, patients who were classified as sarcopenia according to TPV also had higher risk of post-operative respiratory complications than patients who were not classified as sarcopenia (males: OR = 15.00, 95% CI = 1.03–218.31; $p = 0.031$; and females: OR = 4.00, 95% CI = 0.56–28.40; $p = 0.16$) (Table 3).

Table 1. Clinical characteristics of patients who underwent living-donor liver transplantation

Characteristics	All ($n = 32$)	Males ($n = 14$)	Females ($n = 18$)
Cirrhosis [n (%)]	12 (37.5)	5 (35.7)	7 (38.9)
PBC [n (%)]	4 (12.5)	1 (7.1)	3 (16.7)
HCC [n (%)]	2 (6.3)	2 (14.3)	0 (0.0)
FH [n (%)]	1 (3.1)	1 (7.1)	0 (0.0)
PSC [n (%)]	1 (3.1)	0 (0.0)	1 (5.6)
FAP [n (%)]	1 (3.1)	1 (7.1)	0 (0.0)
AH [n (%)]	1 (3.1)	0 (0.0)	1 (5.6)
PCKLD [n (%)]	1 (3.1)	0 (0.0)	1 (5.6)
Both cirrhosis and HCC [n (%)]	7 (21.9)	4 (28.6)	3 (16.7)
Both FH and AH [n (%)]	1 (3.1)	0 (0.0)	1 (5.6)
Unknown [n (%)]	1 (3.1)	0 (0.0)	1 (5.6)
Child–Turcotte–Pugh class			
A (5–6 points) [n (%)]	4 (12.5)	3 (21.4)	1 (5.6)
B (7–9 points) [n (%)]	6 (18.8)	2 (14.3)	4 (22.2)
C (10–15 points) [n (%)]	22 (68.8)	9 (64.3)	13 (72.2)
Post-operative respiratory CC [n (%)]	17 (53.1)	8 (57.1)	9 (50.0)
Only pneumonia [n (%)]	3 (9.4)	2 (14.3)	1 (5.6)
Only tracheotomy [n (%)]	0 (0.0)	0 (0.0)	0 (0.0)
Only extubation delay [n (%)]	10 (31.3)	5 (35.7)	5 (27.8)
Pneumonia and tracheotomy [n (%)]	0 (0.0)	0 (0.0)	0 (0.0)
Pneumonia and extubation delay [n (%)]	2 (6.3)	0 (0.0)	2 (11.1)
Tracheotomy and extubation delay [n (%)]	2 (6.3)	1 (7.1)	1 (5.6)
Pneumonia, tracheotomy and extubation delay [n (%)]	0 (0.0)	0 (0.0)	0 (0.0)

AH, autoimmune hepatitis; CC, complications; FAP, familial amyloid polyneuropathy; FH, fulminant hepatitis; HCC, hepatocellular carcinoma; PBC, primary biliary cirrhosis; PCKLD, polycystic kidney and liver disease; PSC, primary sclerosing cholangitis.

Table 2. Demographic, total psoas area (TPA) and total psoas volume (TPV) data of patients who underwent living-donor liver transplantation

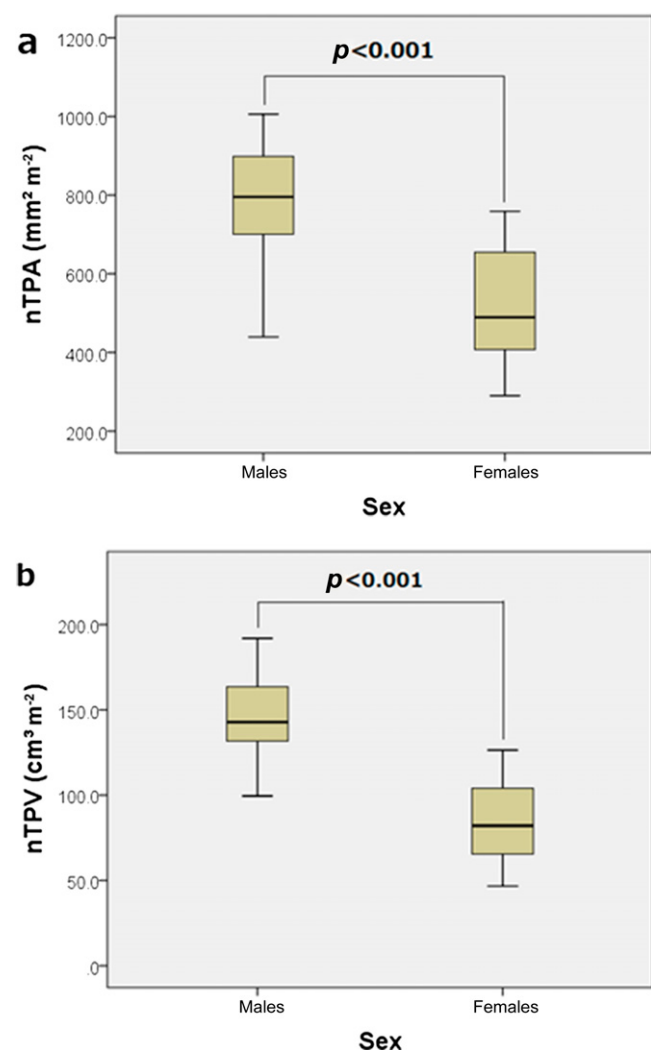
Characteristics	All (<i>n</i> = 32)	Males (<i>n</i> = 14)	Females (<i>n</i> = 18)	<i>p</i> -value
Age (years)	54.0 ± 9.6	49.5 ± 11.0	57.5 ± 6.6	0.037
nTPA (mm ² m ⁻²)	633.3 ± 202.0	796.0 ± 136.6	506.8 ± 146.4	<0.001
nTPV (cm ³ m ⁻²)	111.6 ± 39.0	146.9 ± 23.8	84.2 ± 23.4	<0.001
Height (cm)	160.1 ± 10.0	169.8 ± 5.4	153.6 ± 6.4	<0.001
Weight (kg)	62.7 ± 12.9	71.6 ± 11.7	55.7 ± 8.9	0.001
BMI (kg m ⁻²)	24.2 ± 3.9	24.8 ± 3.6	23.7 ± 4.0	0.403

BMI, body mass index; nTPA, normalized TPA; nTPV, normalized TPV.

DISCUSSION

Prior works have documented the correlation between increasing risks for recipients in liver transplantation and sarcopenia. In the first place, the reason that sarcopenia

Figure 2. The difference of (a) normalized total psoas area (nTPA) and (b) normalized total psoas volume (nTPV) between males and females.



correlates with increasing risks for liver transplantation is that sarcopenia reflects poor nutritional status, which deteriorates prognosis.^{11–13} In a previous study, sarcopenia was evaluated by TPA and was shown to negatively impact morbidity and mortality after liver transplantation.^{7,8} A few studies have been conducted using TPV. For example, Valero et al⁵ have shown that sarcopenia assessed by TPV is an independent factor predictive of post-operative complications following surgical intervention for primary hepatic malignancies. Amini et al¹⁰ have also shown that sarcopenia assessed by TPV is strongly associated with short- and long-term outcomes after pancreatic resection. However, there is no article which shows TPV to be more useful than TPA in relation to evaluating the post-operative risks of LDLT patients. We tested the predictive power for post-operative respiratory complications of LDLT patients with TPA and TPV using the OR. Although the OR of TPV was higher than that of TPA in males, the OR of TPV was the same as that of TPA in females. This discrepancy may be explained by the fact that the correlation between TPA and TPV in females was stronger than in males. This means that TPV may have a stronger predictive power for post-operative respiratory complications than TPA.

This study has some unique characteristics, different from other studies. First, subjects of this research were all Japanese. To reduce the effect caused by the difference of skeletal muscle mass based on race, we set no absolute threshold of sarcopenia such as that of previous studies.^{5,10,14} Instead, we used the median as a relative threshold of sarcopenia. Second, subjects of this research were not deceased-donor liver transplantation but LDLT.

Several limitations must be kept in mind when considering the present study. First, the number of cases is small. This means that selection bias for patients may have been large. Actually, CIs of the OR were considerably wide. However, because the aim of this study was to demonstrate the feasibility of TPV comparing TPA, the small number of cases may not be a fatal problem. To confirm the conclusions of this study, more cases must be accumulated. Second, this study has no gold standard for TPA/TPV, although every study dealing with sarcopenia suffers from the lack of true muscle volume data. If psoas major muscles were not correctly contoured by software, we

Table 3. Odds ratio of post-operative respiratory complications

Sex	Measurement	Odds ratio	95% CI	p-value
Males	nTPA	3.33	0.36–30.70	0.28
Males	nTPV	15.00	1.03–218.31	0.031
Females	nTPA	4.00	0.56–28.40	0.16
Females	nTPV	4.00	0.56–28.40	0.16

CI, confidence interval; nTPA, normalized total psoas area; nTPV, normalized total psoas volume.

modified manually under the leadership of an experienced radiologist. Third, because there were variations in CT models involved in this study, the Hounsfield unit values of these models may be different. However, it is thought that the impact of this is negligibly small.

CONCLUSION

Pre-operative volume of skeletal muscles might be a better predictor for post-operative risks in LDLT recipients rather than area. Further studies with larger numbers of cases are required to confirm this.

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