

**HUE UNIVERSITY
UNIVERSITY OF MEDICINE AND PHARMACY**

DUONG PHUOC HUNG

**VALUE OF MULTISLICE COMPUTED
TOMOGRAPHY IN ASSESSING KIDNEY
MORPHOLOGY AND FUNCTION
AMONG LIVING KIDNEY DONORS**

**SUMMARY OF MEDICAL DOCTORAL
DISSERTATION**

HUE, 2024

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**Major: Radiology and Nuclear Medicine
Code: 9 72 01 11**

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Academic advisors:

**ASSOC. PROF. LE TRONG KHOAN
ASSOC. PROF. NGUYEN KHOA HUNG**

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INTRODUCTION

1. RATIONALE FOR THE STUDY

Preoperative evaluation aims to confirm the retention of a normal, functional kidney in a living donor, ensuring that the transplanted kidney shows no significant abnormalities, and determining key features of the patient's renal vascular anatomy. Various effective diagnostic imaging and nuclear medicine techniques are available for assessing kidney selection in living kidney donors (LKD), including ultrasound, digital angiography, magnetic resonance imaging, kidney scintigraphy, Single Photon Emission Computed Tomography (SPECT), and Positron Emission Tomography (PET). However, each technique has its own set of limitations.

Multislice computed tomography (MSCT) is a comprehensive technique that aids in evaluating kidney morphology in LKD before surgery with a high accuracy ranging from 95% to 100%, and it can effectively assesses normal or pathological kidney parenchyma, kidney vascular anatomy, ureter anatomy, urinary tract epithelium, the glomerular filtration rate (GFR) of each individual kidney. However, in Vietnam, previous studies limited investigations simultaneously evaluating both morphology and function, particularly the assessment of GFR via MSCT scan. Therefore, we initiated the project titled "Value of MSCT in assessing kidney morphology and function among LKD," with 3 main objectives:

1. *To evaluate kidney morphology in LKD using MSCT.*
2. *To assess kidney function in LKD using MSCT.*
3. *To determine the utility of MSCT in evaluating both the morphology and function of selected kidneys for transplant in LKD.*

2. SCIENTIFIC AND PRACTICAL SIGNIFICANCE

The study holds scientific significance in determining the accuracy of assessing kidney size, volume, blood vessels, and abnormalities on MSCT compared to measurements taken during kidney transplant surgery. Furthermore, the study provides valuable results for scientists in kidney transplantation field, through publication in domestic and international journals, as well as presentations at international conferences.

In terms of practical significance, MSCT can evaluate the GFR of each individual kidney, in addition to assessing kidney morphology. This is a crucial criterion for determining kidney function when selecting a kidney for transplant. Until the time of this study, there had been no research or data in Vietnam evaluating both kidney morphology and function in LKD using MSCT

simultaneously. Therefore, the research results hold practical significance in providing clinicians with more evidence to guide their decision-making regarding kidney assessment methods before kidney transplant surgery.

3. CONTRIBUTION OF THE THESIS

This study represents the first comprehensive investigation in Vietnam with a relatively large sample size, focusing on the utilization of MSCT to assess preoperative kidney morphology and function in LKD. Notably, MSCT has demonstrated the capability to evaluate the GFR of each kidney individually. These values are instrumental in optimizing kidney selection for transplant and ensuring surgical safety during kidney transplant procedures. Furthermore, data analysis from the study reveals similarities in glomerular filtration function between MSCT and functional kidney scintigraphy SPECT. These findings aid clinicians in selecting the most appropriate method for evaluating glomerular filtration function.

4. STRUCTURE OF THE THESIS

The thesis spans 136 pages, comprising a 2-page introduction, a 34-page literature review, a 23-page segment on study objects and methodology, a 43-page results section, a 32-page discussion, and a 3-page conclusion, limitations, and recommendations segment. The thesis integrates 66 tables, 12 charts, 22 figures, 1 diagrams, and 2 graphs. It includes 153 references, 29 in Vietnamese, 122 in English, and 2 in French with 55 references from the past 5 years, representing 35.95% of the total.

Chapter 1 LITERATURE REVIEW

1.1. FUNCTION AND MORPHOLOGY OF THE KIDNEYS

1.1.1. Morphology of the kidney

1.1.1.1. Appearance, location and size

The kidneys are bean-shaped, reddish-brown in color, and possess a smooth surface, encapsulated by fibrous tissue. Positioned behind the peritoneum, between the XI rib and the lumbar spine, they lie anterior to the psoas muscle. Each kidney measures approximately 12cm in length, 6cm in width, and 3cm in thickness. The left kidney is typically slightly longer and narrower than the right. On average, the weight of each kidney is around 150g.

1.1.1.2. Nearby structures

The right and left kidneys are anatomically related to distinct structures anteriorly, posteriorly, medially, and externally.

1.1.1.3. Internal shape and general structure

The kidney is encased in a thin fibrous capsule composed of collagen-rich connective tissue. Within this capsule lies the renal sinus, which is surrounded by renal parenchyma consisting of the renal medulla and renal cortex, each containing smooth and elastic muscle fibers.

1.1.1.4. Renal artery

The renal artery (RA) is usually large in size to meet the functional needs of the kidney. The typical main RA is about 40 - 60mm in length and about 5 - 6mm in diameter.

1.1.1.5. Renal vein

The right renal vein (RV) is shorter than left RV, with an average length of about 2 - 4cm, and it flows into the right border of the inferior vena cava, usually slightly lower than the left RV. The left RV is usually longer, averaging about 6 - 10cm, and passes in front of the aorta just below the superior mesenteric artery, draining into the inferior vena cava.

Identifying veins draining into the RV before surgery is important in LKD because these veins are difficult to see during surgery. The left kidney is often chosen in LKD because the RV is longer and easier to surgically remove.

1.1.1.6. Lymph vessels

The lymphatic vessels in the kidney mainly drain into the lymph nodes around the renal pedicle.

1.1.1.7. Nerves

The kidneys are innervated by branches of the renal plexus, part of the autonomic nervous system, along the RA. Most of these nerves are vasomotor. The pain-sensing nerves are mainly located in the renal pelvis, entering the spinal cord through the splanchnic nerves.

1.1.2. Functional characteristics of the kidney

The kidneys are responsible for regulating water and electrolytes, excreting waste products, secreting renin and erythropoietin, and aiding in the conversion of inactive Vitamin D into its active form. The GFR per unit time in healthy adults varies greatly with body size and is often normalized to account for this.

1.2. ASSESSMENT OF MORPHOLOGICAL AND FUNCTIONAL OF THE KIDNEY AMONG LKD BY MSCT

1.2.1. Multislice computed tomography

MSCT of renal vessels with three-dimensional image reconstruction processing programs according to MPR, MIP, VRT, and Curved MPR techniques can accurately identify anatomical variations of vessels. From

simple to complex anatomical variations, kidney blood contributes significantly to the field of kidney transplantation. Currently, MSCT scans have become the first choice for imaging diagnostic methods to evaluate morphological lesions and kidney function. MSCT has proven to be highly effective in detecting variations in renal vascular anatomy, with a sensitivity and specificity of over 90% according to many reported studies.

1.2.2. Assessment of kidney function on MSCT

1.2.2.1. History

Dawson and Peter (1993) described a method for measuring the relative glomerular filtration function per milliliter of renal parenchyma by dynamic CT scanning at a transrenal resection site during contrast injection. Patlak et al. (1983) used a similar approach (Patlak plot) to measure the transport constants of the cerebrovascular barrier using dynamic CT imaging at a single location for investigation.

1.2.2.2. Principles

The Patlak-Rutland equation is the basis for calculating glomerular filtration function. However, we found that the density of the aortic artery measured in the unmedicated phase differs depending on the type of CT machine used from different manufacturers.

1.2.2.3. Measurement of the entire kidney density

The average density and area of the right and left kidneys were measured using ROI (Region of interest) drawn on all slices according to the density measurement program of the CT scanner. The measurement ROI area needs to be as close to the outer surface of the kidney as possible. Only the renal parenchymal area was measured in the ROI region.

1.2.2.4. Measurement of the aortic artery density

The aortic density measurement ROI is circular and carefully placed in the center of the aortic lumen, excluding the aortic wall to avoid atherosclerosis in some cases. The integral of the aortic density curve needs to be determined to calculate the glomerular filtration function. The area under the curve is determined to calculate the integral from $t = 0$ to t_1 and from $t = 0$ to t_2 , with t_1 and t_2 defined as the midpoint of the renal resection time in the arterial and parenchymal phases.

1.3. SINGLE-PHOTON EMISSION COMPUTED TOMOGRAPHY

Labeled Radioactive isotopes or radiopharmaceuticals are injected into the patient, mainly eliminated through kidney excretion. Dynamic images and graphs track radioactivity over time for each kidney, evaluating its glomerular filtration function qualitatively and quantitatively.

1.4. KIDNEY DONOR SELECTION PROCEDURE AND KIDNEY TRANSPLANT SELECTION

Based on Decision No. 43/2006/QĐ-BYT of the Ministry of Health on the technical procedure of kidney and liver transplantation from living donors.

1.5. RELEVANT RESEARCH IN VIETNAM AND ABROAD

1.5.1. International studies

1.5.1.1. Studies related to kidney morphology

Various studies by Kawamoto et al (2004), Steven et al (2006), Petridis et al (2008), Silverman et al (2009), Su et al (2010), Bouali et al (2012), Su et al (2013), Asghari et al (2013), Çınar et al (2016), Al-Oraifi et al (2017), Hostiuc et al (2019), Garcia et al (2021), Nerli et al (2023) have evaluated the values of CT in developing show blood vessels, number of arteries, early branches, number of veins, late confluence and upper urinary tract.

1.5.1.2. Studies related to kidney function

Authors' studies related to assessment of kidney function by CT include O'Reilly et al (1986), Dawson and Peter (1993), Tsushima et al (1999), Tsushima et al (2001), Hackstein et al (2002-2004), Kim et al (2010), Su et al (2010), Helck et al (2014), Kwon et al (2015), Zhang et al (2017), Jiang et al (2019).

1.5.2. Domestic studies

1.5.2.1. Studies related to kidney morphology

Authors' studies used CT to determine the number of RA and RV, early branching, and short RV include Trinh Xuan Dan (1999), Chau Quy Thuan (2012), Hoang Minh Thang (2014), Nguyen Van Quoc Anh (2021), Do Thanh Nam (2022), Quach Do La (2023), Ninh Viet Khai et al. (2023)

1.5.2.2. Studies related to kidney function

Currently, there have been no studies reporting on the assessment of GFR on MSCT in evaluating the kidneys among LKD.

Chapter 2 STUDY SUBJECTS AND METHODOLOGY

2.1. STUDY SUBJECTS, TIME AND SAMPLE SIZE

2.1.1. Study Subjects: 338 kidney donors underwent MSCT scans and nephrectomies for kidney transplant purposes. One kidney was taken for transplant purposes, and the remaining kidney was retained at Hue Central Hospital.

Inclusion criteria: LKD volunteered for donation and submitted a voluntary kidney donation application. They were selected according to

the Ministry of Health's organ transplant process, possessed complete legal documents, and were approved by the Kidney Transplant Council of Hue Central Hospital for kidney donation.

Exclusion criteria: LKD with acute kidney dysfunction, contraindications to CT scans with intravenous contrast, or contraindications to nephrectomy after having had a MSCT scan.

2.1.2. Research Period: January 2017 to December 2019.

2.1.3. Sample Size: The sample size calculation formula was based on Sensitivity (Se) and Specificity (Sp). According to Sahani et al. (2005), Sp was all 100%, so we used the highest Se of 75%. The required sample size was 313 patients, and the actual sample size was 338 patients.

2.2. RESEARCH METHODOLOGY

2.2.1. Study design: this is a cross-sectional study.

2.2.2. Study equipments

MSCT machine with Brilliance brand from Philips - USA. SPECT machine with Brightview XCT brand from Philips - USA. Ultrasound machine ACUSON Antares and ALOCA from Hitachi - Japan. CR digital X-ray machine. Blood testing machine Sysmex XS - 1000i and ADVIA 2120i brands from Siemens - Germany.

2.2.3. Steps to conduct research

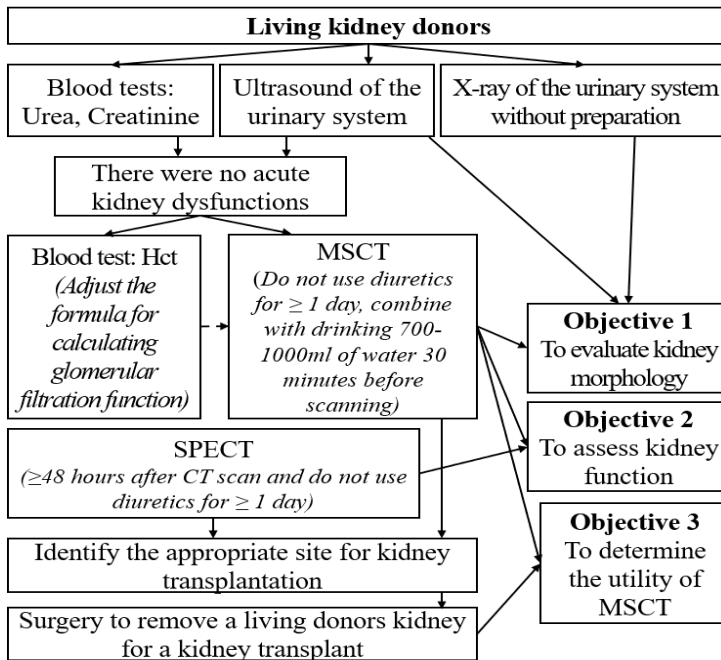


Figure 2.1. Study framework

2.2.4. Study procedures

Blood tests: Blood count tests: Hct. Kidney function: Urea, Creatinine.

Ultrasound examination of the urinary system: assesses kidney size, condition of the renal pelvis, ureters, and detects abnormalities such as stones, cysts, and tumors...

X-ray imaging of the urinary system, conducted without preparation: evaluates the positioning of the kidney shadow and identifies abnormal contrast images in the kidney area and urinary tract.

The MSCT scan: evaluates kidney morphology, including kidney parenchyma, vascular anatomy, and urinary tract, while also assessing the glomerular filtration function of each kidney separately. Total radiation dose: limiting radiation exposure is a matter of medical ethics, so CT scanning techniques must comply with ALARA principles. After CT scan: It is necessary to keep an intravenous line and monitor the patient for at least 30 minutes to promptly address any complications that may arise.

Kidney surgery for transplant: the location of the transplanted kidney is determined based on the excretion value of both kidneys as assessed by

the results of SPECT (selecting the kidney with better or worse function), and renal vascular characteristics evaluated through MSCT (choosing kidneys with one renal artery or arterial abnormalities). Additionally, priority is given to selecting kidneys with other abnormalities such as kidney stones, kidney cysts, or a double renal pelvis.

Kidney characteristics during surgery include: abnormalities such as protruding cysts on the kidney surface, the renal pelvis located outside the renal sinus, and a complete or incomplete double kidney.

Measure preoperative dimensions: including kidney size (length, thickness, width) using ultrasound, and assess kidney volume using ultrasound and CT. Additionally, measure blood vessel size (diameter, length) using CT scan.

Measurement tools during surgery: a standard ruler in millimeter units, divided into segments for measuring blood vessel diameter after sterilization with specialized instruments.

2.2.5. Research variables

Characteristics of LKD: age, gender.

Morphology of the kidneys

+ Evaluation includes kidney size, volume, structure, and renal pelvis condition. Assessment of drug absorption, excretion function, and drug passage in the urinary system, identifying abnormalities such as kidney stones, cysts, tumors, double renal pelvis, ureteral stones, urinary tract obstruction, and contrast agent levels. Detection of additional abnormalities beyond the urinary tract. Evaluation of RA and veins, including number, diameter, and characteristics, with consideration of vascular diseases.

+ Identification of variations in RA, including one artery, two main arteries, one main artery with an accessory artery, early branching arteries to the upper pole, renal hilum, or lower pole. This also encompasses variations like upper pole accessory arteries, branches from the inferior adrenal artery, inferior phrenic artery, or ureteral pelvis.

+ Assessment of the number, diameter, and characteristics of bilateral RV.

+ Assessment of RV includes variations like one vein, two veins, or multiple veins. Variants may involve confluent branches such as adrenal vein, genital vein, lumbar vein, late confluence, short common trunks, veins running behind or hugging the aorta, or division into two branches before the renal hilum.

Glomerular filtration function

Treatment method: calculating the glomerular filtration function must be based on a linear interpolation algorithm of the missing parts of the aortic

density curve. Therefore, we designed a software in C++ language to calculate this indicator to reduce data processing and calculation time.

SPECT: determines the excretion value and GFR of each kidney, evaluating the 3-phase nephrogram images. Function comparison between the kidneys: they are considered equivalent when the difference is less than 5%. If the right kidney's excretory function is greater than 52.5% and the left kidney's is less than 47.5%, the right kidney is deemed superior; if both kidneys' function falls between 47.5% and 52.5%, they are considered equivalent; and if the left kidney's function exceeds 52.5% while the right kidney's is below 47.5%, the left kidney is considered superior.

2.3. DATA COLLECTION AND ANALYSIS

2.3.1. Data collection and analysis softwares

Information was gathered through research forms based on a specified sample size and inputted into the computer utilizing Epidata 3.1. Data analysis and processing were conducted using SPSS version 20.0 for Windows, Chicago, IL. Graphs were generated using Microsoft Excel 365.

2.3.2. Data analysis

Descriptive statistics: presenting quantitative variables as the mean value \pm standard deviation, along with the minimum and maximum values. For qualitative variables, frequencies (n) and percentages (%) were provided.

Statistical analysis: comparing two mean values using t-tests or Mann-Whitney tests. Comparing mean differences before and during surgery using paired t-tests or Wilcoxon sign and rank tests. Correlation analysis employed Pearson or Spearman's rho. The similarity of measurement indexes was evaluated using the Bland-Altman method. Additionally, CT values in diagnosing and detecting graft renal vessels were compared with kidney transplant surgery results using sensitivity (Se), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV), and accuracy (Ac).

2.4. RESEARCH ETHICS

The study was approved by the Ethics Council of the University of Medicine and Pharmacy - Hue University, Board of Directors of Hue Central Hospital, and leaders of relevant Departments. LKD were completely voluntary and approved by the Kidney Transplant Council of Hue Central Hospital. Information about LKD was encrypted and confidential. The implementation process must reduce the maximum effective dose according to the ALARA principle.

Chapter 3

RESULTS

3.1. ASSESSMENT OF KIDNEY MORPHOLOGY IN LKD BY MSCT

3.1.1. General characteristics

Age and gender: average age was 30.73 ± 8.03 , youngest 20, oldest 60, age group 20 - 29 accounts for 58.9%. There were 268 males, accounting for 79.3% and 70 females, accounting for 20.7% (Table 3.1).

3.1.2. Morphological characteristics of the kidneys before surgery

Kidney size on ultrasound and CT scan: Right and left kidney sizes on ultrasound were different ($p < 0.001$), except for width. Right and left kidney sizes on CT scan were different ($p < 0.001$) (Table 3.2).

Kidney selected for transplant size on ultrasound and CT scan: Right and left kidney selected for transplant sizes on ultrasound was different ($p < 0.05$). Right and left kidney selected for transplant sizes on CT scan is different ($p < 0.01$) except for the width (Table 3.3).

Kidney volume on ultrasound and CT scan: There was a difference between left kidney volume on ultrasound and CT scan ($p < 0.05$) (Table 3.4).

Kidney selected for transplant volume on ultrasound and CT scan: The volume of the left kidney selected for transplantation were different between two methods ($p < 0.05$) (Table 3.5).

Renal parenchymal lesions

Kidney cyst: 81 cases of kidney cysts were detected on CT scan, average diameter was 1.37 ± 0.90 mm. There were only 4 cases detected on ultrasound of urinary system, average diameter was 4.50 ± 0.50 mm (Tables 3.6, 3.7).

Kidney tumor: both ultrasound and CT detected one case of lipomuscular angioma with 5 mm diameter in the right kidney (Tables 3.8, 3.9).

3.1.3. Renal artery characteristics

Main RA size: The mean length of the right RA was 26.46 ± 11.54 and the left RA was 21.77 ± 8.93 . There was a difference in the length of the right and left RA on CT scan ($p < 0.01$). The mean diameter of the right RA was 6.00 ± 0.65 and the left RA was 6.12 ± 0.63 . There was a difference in right and left RA diameter on CT scan ($p < 0.05$) (Table 3.10).

Number of RA: Accessory RA in the right kidney: 17.2%, left kidney: 23.6% (Table 3.11). Single artery in right kidney: 79.6%, left kidney: 68.6% (Table 3.12).

RA abnormalities

Early RA branching: Right RA: 26.9%, left RA: 33.7% (Table 3.13). Predominance of upper pole early branching: Right RA: 17.1%, left RA: 19.2% (Table 3.14).

Accessory RA: Upper pole artery common, right kidney: 8.3%, left kidney: 13.0%. Capsular artery type rare, mainly superior cortical accessory artery (Figure 3.1).

RA branches to nearby organs: Adrenal arteries in right kidney: 46.7%, left kidney: 26.6%. Phrenic artery in right kidney: 16.9%, left kidney: 1.2%. Both adrenal and phrenic artery branches in right kidney: 8%, left kidney: 0.6% (Table 3.15).

3.1.4. Renal vein characteristics

RV size: Right RV length: 17.73±5.95mm, left RV: 49.93±12.62mm. Significant difference in right and left RV length on CT scan ($p<0.01$). Right RV diameter: 11.16±0.87mm, left RV: 12.06±0.87mm. Significant difference in right and left RV diameter on CT scan ($p<0.01$) (Table 3.16).

Number of RV: Accessory RV common in right kidney (21.7%), left kidney only 1.5% (Table 3.17). Majority of kidneys have one vein: Right kidney 68.6%, left kidney 98.5% (Table 3.18).

RV abnormalities: Short veins predominantly in right kidney, 32.5%. Late confluent veins and abnormal RV reflux rare. Common hilar accessory renal vein type: Right kidney 24.3%, left kidney 0.9% (Table 3.19-3.21, Figure 3.2). Renal vein has other vein branches mainly confluent with adrenal vein (100%) and left gonadal vein branch, with 50.6% confluent with left lumbar vein (Table 3.22).

3.1.5. Characteristics of the upper urinary tract among LKD

Upper urinary tract lesions: 27 cases of kidney stones detected on CT scan, average diameter 1.15 ± 0.36 mm, accounting for 8.0%. No stones detected through ultrasound or X-ray urinary system (Tables 3.23, 3.24).

Contrast agent: No radiographic interference in renal parenchyma due to contrast agent in all cases. In 70.4% of cases, contrast agent filled entire upper urinary tract, and in all cases, it filled half of upper urinary tract simultaneously in both kidneys with one X-ray emission (Table 3.25).

Upper urinary tract abnormalities: Single upper urinary tract system predominant, right kidney 98.8%, left kidney 99.7% (Table 3.26).

3.2. ASSESSMENT OF KIDNEY FUNCTION IN MSCT

3.2.1. Kidney function in MSCT

Kidney excretory function: 100% Contrast agent was excreted into the renal pelvis and ureters in both kidneys (Table 3.27).

The glomerular filtration function of each kidney

Table 3.28. Distribution of blood Hct concentration and GFR-CT (n=338)

Index	Kidney	Mean ± SD
Blood Hct concentration	2 kidneys	37.31 ± 3.49
GFR-CT (ml/min)	Right kidney	53.74 ± 6.62
	Left kidney	57.36 ± 7.05

Kidney excretory function on SPECT

Table 3.29. Excretory function of each kidney (n=338)

Excretory function (%)	Right kidney	Left kidney	P-value
Mean ± SD	47.98 ± 2.65	52.02 ± 2.65	<0.001
Lowest – Highest	40.02 – 56.69	43.31 – 59.98	

Table 3.30. Comparing excretory function between two kidneys in SPECT

Excretory function	n	%
Left kidney function was better than right kidney	145	42.9
The functions of the two kidneys were equivalent	178	52.7
Right kidney function was better than left kidney	15	4.4
Total	338	100.0

Comparing GFR of each kidney in CT and SPECT: there was no difference between GFR on CT and SPECT. On average, GFR at left kidney was higher than right kidney in CT and SPECT ($p < 0.01$) (Table 3.31).

Correlation and similarity between GFR in CT and SPECT: Strong positive correlation observed for right and left kidney GFR ($r = 0.765$ and 0.763 , $p < 0.001$) (Table 3.32). Bland-Altman method showed mean difference in GFR between CT and SPECT: -0.20 ± 4.77 for right kidney, 0.58 ± 4.61 for left kidney. Percentage error (PE) for both kidneys was below 30% (right kidney: 22.15%, left kidney: 23.11%), indicating method similarity (Table 3.33).

Correlation between age and kidney morphology/function: Weak, positive correlation found between left RA/RV length and age ($r = 0.117$ and 0.133 , $p < 0.05$). Weak, negative correlation observed between right RA diameter and age ($r = -0.123$, $p < 0.05$). GFR-CT value negatively correlated with age, with weak correlation coefficient ($r = -0.128$, $p < 0.05$) (Table 3.34, 3.35).

3.3. MSCT'S ROLE IN ASSESSING KIDNEY TRANSPLANT SELECTION FOR MORPHOLOGY AND FUNCTION IN LKD

3.3.1. Number of kidneys selected for transplant

Table 3.36. Distribution of number of kidneys selected for transplant

Selected kidneys	n	%
Right kidney	176	52.1
Left kidney	162	47.9
Total	338	100.0

Surgical methods: there were 25 laparoscopic retroperitoneal surgeries (7.4%), and 313 open surgeries (92.6%) (Chart 3.7).

3.3.2. Kidney size selected for transplant

Table 3.37 showed the average dimensions of 176 right kidneys and 162 left kidneys chosen for transplant via ultrasound and CT. Table 3.38 presented the average dimensions of 338 kidneys selected for transplant during surgery.

3.3.3. Comparison of right kidney volume before and during surgery

No difference in volume between right and left kidneys chosen for transplant on preoperative and intraoperative CT ($p > 0.05$). Similarly, no difference in volume between right and left kidneys selected for transplantation before surgery on ultrasound and CT ($p > 0.05$) (Table 3.39).

3.3.4. Renal artery characteristics in selected kidneys for transplant

RA diameter before and during surgery: No difference in main RA diameter between right and left kidneys selected for transplant on CT before and during surgery ($p < 0.05$). Similarly, no difference in accessory artery diameter between right and left kidneys selected for transplant on CT before and during surgery ($p > 0.05$) (Table 3.40).

Table 3.41. The similarity between preoperative RA diameter in CT scan and during surgery (n=338)

RA diameter (mm)		n	Mean of both method	Mean difference	Limit of agreement	PE (%)
Main	Right	176	6.01 ± 0.62	0.01 ± 0.14	-0.27 – 0.29	20.24
	Left	162	6.06 ± 0.56	-0.15 ± 0.73	-1.58 – 1.28	18.08
Accessory	Right	21	2.70 ± 0.79	-0.02 ± 0.12	-0.26 – 0.22	57.16
	Left	30	2.54 ± 0.63	0.01 ± 0.11	-0.21 – 0.23	48.69

Number of RA: Before surgery, majority opted for a single-artery kidney, 86.9% on the right and 79.6% on the left (Table 3.42). During surgery, selection favored single-artery kidneys, with 87.5% for the

right and 79.0% for the left (Table 3.43).

Early RA branching: Selected for transplantation before and during surgery, accounting for 23.3% in the right kidney and 25.3% in the left kidney (Table 3.44). Upper pole early branching: Accounted for 17.0% in the right kidney and 13.6% in the left kidney (Table 3.45).

Accessory RA: The upper pole accessory artery in the selected kidney for transplant before and during surgery accounted for 6.3% in the right kidney and 8.6% in the left kidney (Figure 3.10).

CT values for RA before and during surgery: CT's Se, Sp, PPV, NPV, and Ac all 100% compared to surgery results (Table 3.46). CT accurately determines upper pole, hilum, lower pole, and capsule of accessory kidney, all reaching 100.0% agreement with surgery. For right RA, Se and PPV values not calculable, both registered as 0 (Table 3.47).

3.3.5. Renal vein characteristics in selected kidney for transplant

RV diameter before and during surgery: Significant difference observed in right and left main RV diameters ($p < 0.001$). Right accessory RV diameter appeared larger than left, but insufficient data to confirm this difference (Table 3.48).

Table 3.49. The similarity between preoperative RV diameter in CT and during surgery (n=338)

RV diameter (mm)	n	Mean of both method	Mean difference	Limit of agreement	PE (%)	
Main	Right	176	11.09 ± 1.02	-0.03 ± 0.21	-0.44 – 0.38	18.05
	Left	162	11.81 ± 1.00	0.07 ± 0.20	-0.33 – 0.48	16.61
Accessory	Right	44	4.64 ± 1.69	0.05 ± 0.09	-0.12 – 0.22	71.37

Number of RV: Before surgery, most kidneys had one RV, 72.2% on the right and 99.4% on the left (Table 3.50). During surgery, the right kidney had a vein in 71.6% of cases, while the left kidney had a vein in 99.4% of cases (Table 3.51).

Short RV: accounted for 31.8% in the right kidney vein before and during surgery while in the left kidney vein was 0% (Table 3.52).

RV abnormalities: Late confluence during surgery in the right kidney: 0.6%, left kidney: 1.9%. Abnormal reflux includes vein embracing abdominal aortic ring: 2.5% left kidney, vein bifurcating before renal hilum: 1.1% right kidney. Preoperative renal hilum veins: 22.2%, during surgery: 22.7%. Confluent right adrenal arteries branch before surgery: 1.7% right kidney, 100% left kidney. Confluent right

gonadal vein branch before surgery: 21% right kidney, 100% left kidney. Lumbar vein branches confluence: Left kidney 48.8% before surgery, 49.4% during surgery. Single confluent venous branches drain: Left kidney 8.0% before and during surgery (Table 3.53 - 3.59).

Values of CT in the RV before and during surgery: CT values show Se, Sp, PPV, NPV, and Ac at 100% compared to nephrectomy surgery results, except in rare cases. In some instances, values couldn't be calculated due to a frequency of 0. For determining lumbar vein branch confluent into the left kidney, CT demonstrates Se and Sp at 98.8% and 100.0% respectively, with PPV, NPV, and Ac at 100.0%, 98.0%, and 99.4% (Table 3.60). Regarding hilar accessory RV in the right kidney, CT shows Se at 97.5% and Sp at 100.0%, with PPV, NPV, and Ac at 100.0%, 83.3%, and 97.8% respectively. For upper and lower pole RV in both kidneys and renal hilum in the left kidney, CT yields either 100% accuracy or insufficient data for evaluation (Table 3.61).

3.3.6. Characteristics of the upper urinary tract in the selected kidney for transplant before and during surgery

Upper urinary tract abnormalities: Before surgery, single system predominant, 98.8% right kidney, 99.4% left kidney; rare double system found in 1.2% right kidney, 0.6% left kidney. During surgery, single system persists, accounting for 98.8% right kidney and 99.4% left kidney (Table 3.63).

Ureter length in kidneys selected for transplant during surgery showed no significant difference between right and left kidneys (Table 3.64).

3.3.7. Evaluation of radiation dose on MSCT

The average radiation dose was 14.04 ± 0.52 mSV, the highest was 15.95 mSV and the lowest was 12.21 mSV (Table 3.65).

Chapter 4

DISCUSSION

4.1. ASSESSMENT OF KIDNEY MORPHOLOGY IN LKD BY MSCT

4.1.1. General characteristics of LKD

Age: There were no cases under 18 years old for kidney donation, consistent with the Law on donation, removal, transplantation of human tissues and organs, and donation and removal of corpses of the National Assembly in 2006. Elderly individuals should refrain from kidney donation due to the increased risk of kidney fibrosis with age, posing potential hazards for both the donor and recipient, as elderly donors may experience reduced kidney function.

Gender: Males constitute the majority, accounting for 79.3%. This finding aligns with the research of Le Thi Huong Lan et al. (2022), where the male rate was 62.5%, and Dang Thai Tra (2021), where this rate was 71.4%.

4.1.2. Renal morphological characteristics before surgery

Kidney size: Ultrasound revealed a difference in size between the right and left kidneys, with the left kidney exhibiting greater length and thickness. While most ultrasound studies show no variation, CT scans also indicated size discrepancies, with the left kidney consistently larger.

Kidney volume on ultrasound and CT: there was a difference between the left kidney volume on ultrasound and CT ($p < 0.05$).

Renal parenchymal lesions: Ultrasound may overlook small or peripherally located cysts, particularly solid ones in the upper pole of the left kidney. As a result, MSCT detected kidney cysts significantly more often than ultrasound in this study. Regarding benign tumors, both ultrasound and CT identified a case of liposarcoma. Since lipomuscular angioma is benign, kidney resection posed no contraindication.

4.1.3. Renal artery characteristics

Main RA size: The length of the right and left RA on CT scan aligns with anatomical findings reported by Trinh Xuan Dan, Nguyen Quang Quyen, and Nguyen Minh Tuan. Furthermore, the diameter of the right and left RA on CT corresponds to previous research, ranging from 4 to 7mm.

Number of RA: The main RA comprises 82.8% of the right kidney and 76.4% of the left kidney, consistent with findings from prior studies by Do Thanh Nam (2022) and Vu Ngoc Thang et al. (2022).

RA abnormalities

Early RA branching: Right RA: 26.9%, left RA: 33.7%, predominantly upper pole. Compared to various studies, this rate exceeds the typical range of 1.7% to 21.8%.

Accessory RA: Superior pole accounted for 8.3% (right kidney) and 13.0% (left kidney). Renal hilum followed with 6.5% (right kidney) and 7.1% (left kidney), aligning with findings by Trinh Xuan Dan (1999).

RA branches to nearby organs: Adrenal arteries: 46.7% (right kidney) and 26.6% (left kidney). Phrenic artery branch: 16.9% (right kidney) and 1.2% (left kidney). Adrenal and phrenic artery branches: 8.0% (right kidney) and 0.6% (left kidney).

4.1.4. Renal vein characteristics

RV size: There was a difference in the length of the right and left RV on CT scan, consistent with the anatomical findings of Trinh Xuan Dan and

Nguyen Quang Quyen. Similarly, there was a discrepancy in the right and left RV diameter in CT scan, aligning with previous studies in the country.

Number of kidney veins: The majority comprised only one main vein, consistent with findings from previous studies in the country and globally.

Short vein: Short veins were predominantly found in the right kidney, accounting for 32.5%, in line with previous research by various authors.

RV abnormalities: Late confluent RV was rare, constituting only 0.3% in the right kidney and 0.9% in the left kidney, consistent with previous studies. Abnormal RV reflux was also infrequent. Hilar accessory RV was common, with a prevalence of 24.3% in the right kidney and 0.9% in the left kidney. Additionally, CT determined that the RV had other vein branches that converge, including the adrenal vein, genital vein, lumbar vein, and single vein.

Comparing the results of morphology and abnormalities in the RA and RV on CT with other imaging techniques and the consistency with previous studies, it is evident that CT offers numerous advantages.

4.1.5. Characteristics of the upper urinary tract in LKD

Upper urinary tract lesions: Among 27 cases of kidney stones detected in MSCT, none were identified on ultrasound or X-ray of the urinary system. This underscores the crucial role of CT in detecting upper urinary tract stones, aiding in the decision-making process for kidney transplant patients.

Characteristics of contrast agents in the upper urinary tract: Regarding image interference due to contrast agents, 100% of cases showed no radiographic interference in the kidney parenchyma, consistent with studies by Claebots C. et al. and Stuart G. Silverman et al. In terms of contrast medium filling level in the upper urinary tract, 70.4% of cases exhibited complete filling, while 100% filled at least half of the upper urinary tract simultaneously in both kidneys. This facilitates a more thorough examination of the integrity of the renal pelvis-ureter segment removed before transplantation.

Upper urinary tract abnormalities: The majority of kidneys presented a single upper urinary tract system, comprising 98.8% of the right kidney and 99.7% of the left kidney. Kidneys with a double system accounted for only 1.2% of the right kidney and 0.3% of the left kidney. MSCT had demonstrated high efficacy in evaluating upper urinary tract features such as stones and detecting renal anatomical variations, including complete or incomplete dual urinary tract system abnormalities.

4.2. ASSESSMENT OF KIDNEY FUNCTION IN MSCT

4.2.1. Excretory function of the kidneys

CT can effectively assess kidney function. We captured the images of the excretion phase 5 minutes after the rapid injection of contrast agent and 0.9% NaCl, observing contrast excretion into the upper urinary tract in all cases in both kidneys. This enabled us to determine that all LKD in the study exhibited good bilateral kidney function and facilitated reduced testing time.

4.2.2. Glomerular filtration function of each kidney in MSCT

Average Hct concentration was $37.31 \pm 3.49\%$. GFR calculated on CT was 53.74 ± 6.62 ml/min in the right kidney and 57.36 ± 7.05 ml/min in the left kidney, showing a significant difference ($p < 0.01$). This finding aligns with Tran Hoang Hiep et al.'s study (2022) but differs from that of Chau Quy Thuan (2012).

4.2.3. Excretory function of each kidney on SPECT

Kidneys function optimally when contributing over 52.5% to the total function of both kidneys. They are considered to have equivalent function when each kidney contributes 47.5% to 52.5% of the total excretion value. The right kidney's excretory function ($47.98 \pm 2.65\%$) is significantly lower than that of the left kidney ($52.02 \pm 2.65\%$) ($p < 0.01$) on SPECT. This finding is consistent with Nguyen Minh Tuan's research (2020) but differs from Chau Quy Thuan's study (2012).

4.2.4. Comparing the glomerular filtration function of each kidney between MSCT and SPECT

There was no difference in glomerular filtration function between the two measurement methods on MSCT and SPECT, with $p > 0.05$. However, when comparing these data between the left and right kidneys, significant differences in glomerular filtration function were observed ($p < 0.01$)

4.2.5. The correlation and similarity between glomerular filtration function calculated in MSCT and SPECT

There was a strong positive correlation between the glomerular filtration function of the right and left kidneys on CT and SPECT. The Bland-Altman method was used to evaluate the similarity between the glomerular filtration function of the right and left kidneys calculated on CT and SPECT. The PE between the two methods was 22.15% in the right kidney and 23.11% in the left kidney, both lower than 30%, indicating the similarity between these two methods when measuring GFR.

MSCT demonstrated the ability to effectively evaluate the glomerular filtration function of each individual kidney, contributing to the assessment of kidney selection in LKD. Our research results on assessing kidney function via CT scan were consistent with studies conducted by authors worldwide, such as Kwon et al., Zhang et al., Jiang K. et al., Kim H. et al., and Kim H. et al.

4.2.6. Correlation between age and kidney morphology/function

There were positive and weak correlations between left RA, RV length and age. Additionally, negative correlations and weak associations exist between right RA diameter and age. GFR-CT value showed a weak negative correlation with age, while there was no correlation between excretory function and age in LKD. Thus, most kidney morphological parameters exhibit weak or no correlation with the age of LKD.

4.3. MSCT'S ROLE IN ASSESSING KIDNEY TRANSPLANT SELECTION FOR MORPHOLOGY AND FUNCTION IN LKD

4.3.1. Number of kidneys selected for transplant

We relied on kidney morphology and function criteria for transplant selection. Following selection, 52.1% of the kidneys chosen for transplant were right kidneys, while 47.9% were left kidneys. In terms of surgical methods, laparoscopic surgery accounts for 7.4%, while open surgery accounts for 92.6%. This outcome mirrors Nguyen Minh Tuan's (2020) study, where the right kidney was favored for transplantation, contrasting with Chau Quy Thuan's (2012) research, where the left kidney was preferred.

4.3.2. Kidney size selected for transplant

The size of the selected kidney for transplant is measured using ultrasound and CT in terms of length, width, and thickness. During surgery, these dimensions are re-measured and found to be similar to those obtained from the CT scan conducted before surgery

4.3.3. Comparison of right kidney volume before and during surgery

There was no difference in the volume of the right and left kidneys selected for transplantation on CT scan and during surgery ($p>0.05$). Similarly, there was no disparity in the volume of the right kidney compared to the left kidney selected for transplantation before surgery, assessed using ultrasound and CT ($p>0.05$). Kidney volume serves as a criterion for evaluating post-transplant kidney recovery, with larger volumes indicating better recovery potential.

4.3.4. Renal artery characteristics in selected kidneys for transplant

Main RA diameter

Visually, the left RA had a larger diameter than the right RA, aligning with the left kidney's greater functional demands. Our study indicated larger RA diameters compared to Bui Trung Nghia et al.'s (2023).

Regarding the similarity between RA diameter on CT and during surgery according to Bland-Altman, PE in the main RA was under 30% for both the right (20.24%) and left (18.08%) kidneys, indicating concordance between pre-surgical CT and intraoperative measurements. However, for accessory RA, the PE exceeded 30% in both the right (57.16%) and left (48.69%) kidneys, likely due to the small sample size in this group.

In terms of the number of RA, the agreement between CT scan and surgery was complete, with 100% Se, Sp, PPV, NPV, and Ac. This consistency was reflected in previous studies utilizing CT for RA determination.

Early branching of RA showed consistent results before and during surgery, with rates higher than Aremu et al. (2021). Early branching forms, including upper pole and hilum, exhibited complete similarity between pre-surgery CT and intraoperative evaluation, achieving 100% Se, Sp, PPV, NPV, and Ac, as observed in studies by Steven SR et al. and Asghari et al.

Accessory RA: particularly upper pole and lower pole arteries, demonstrated consistent rates between CT scans and post-transplantation, achieving 100% Se, Sp, PPV, NPV, and Ac, corroborating previous CT studies on RA determination.

4.3.5. Renal vein characteristics in selected kidneys for transplant

RV diameter: Significant differences were observed in the main RV diameter between the right and left kidneys before and during surgery ($p < 0.001$). While the right accessory RV tended to be larger, this difference was not statistically significant.

Comparison of preoperative RA diameter on CT and intraoperative measurements using the Bland-Altman method revealed a PE below 30% for the main RVs, indicating agreement between CT and surgical findings. However, the PE for the accessory RV exceeded 30%, possibly due to the limited sample size.

Number of RV: Consistency was observed in the total number of major RVs before and during surgery, resulting in 100% agreement between CT and surgical assessments.

Short veins: were present in 31.8% of right kidneys before and during surgery, with no instances in the left kidney, achieving 100% agreement between CT and surgical results.

RV abnormalities: Consistency was noted in RV confluence selected for transplant before and during surgery, with 100% agreement in assessment.

Abnormal RV reflux: Abnormal reflux cases were minimal, with incidences of 2.5% and 1.1% in the left and right kidneys, respectively.

Accessory RV: Rates of accessory RV at the hilum remained consistent before and during surgery. CT showed high sensitivity (Se) at 97.5% and specificity (Sp) at 100.0% in determining the hilar accessory RV in the right kidney. Moreover, the evaluation indices for other RV branches consistently yielded 100% agreement.

The RV has other vein branches that flow into it

Renal vein branching: Adrenal vein branches confluent anteriorly during right kidney surgery occurred in 1.7% of cases, with 100% of left renal veins consistently draining via left adrenal veins before and during surgery, demonstrating 100% agreement across sensitivity (Se), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV), and accuracy (Ac) indicators.

Similarly, the presence of a confluent right gonadal vein branch in the right renal vein during surgery was observed in 21% of cases, with 100% consistency in left renal veins draining via left genital veins. As a result, all evaluation indices, including Se, Sp, PPV, NPV, and Ac, reached 100%.

The right renal vein also featured a confluent branch of the right lumbar vein, observed in 0% of cases during surgery. For the left kidney, CT scan detected 48.8% of cases with confluent lumbar vein branches before surgery, rising to 49.4% during surgery. CT's ability to determine the confluence of the lumbar vein branch to the left kidney showed high Se and Sp of 98.8% and 100.0%, respectively, with PPV, NPV, and Ac reaching or exceeding 98.0% and 99.4%.

Furthermore, a confluent right single venous branch was observed before surgery in 0% of right kidneys and 8.0% of left kidneys, which remained consistent during surgery. Hence, all evaluation indices, including Se, Sp, PPV, NPV, and Ac, achieved 100% consistency.

4.3.6. Characteristics of the upper urinary tract in selected kidneys for transplant before and during surgery

Upper urinary tract abnormalities: Before surgery, the single system predominated, comprising 98.8% of the right kidney and

99.4% of the left kidney, while the rare double system was found in 1.2% of the right kidney and 0.6% of the left kidney. During surgery, the single system remained prevalent, accounting for 98.8% of the right kidney and 99.4% of the left kidney. Consistency between normal and abnormal single urinary tract systems was 100% before and during surgery.

Ureter length in kidneys selected for transplant during surgery:

There was no significant difference in ureter length between the right and left kidneys selected for transplant during surgery ($p > 0.05$). The average length of the right ureter was 98.49 ± 12.71 mm, and the left ureter was 98.41 ± 11.64 mm.

4.3.7. Evaluation of radiation dose on MSCT

The average radiation dose on CT was 14.04 ± 0.52 mSV, with the highest being 15.95 mSV and the lowest 12.21 mSV. MSCT for kidney morphology and function evaluation met requirements for reducing radiation dose in LKD by limiting the field, adjusting kV, and optimizing mAs. The average effective dose in our study was lower than the estimated radiation dose of 16.9 mSv for the 120kVp technique in CT vascular assessment in LKD. Therefore, it's essential to prioritize good image quality while minimizing radiation dose, following the ALARA principle.

CONCLUSION

1. Kidney morphology in MSCT among LKD

Average transplant kidney size: The right kidney measured 97.41 mm in length, 55.74 mm in width, and 41.10 mm in thickness, while the left kidney measured 100.29 mm, 56.96 mm, and 44.64 mm, respectively.

Transplanted kidney volume: The average volume of the right kidney was 117.28 cm^3 , with the largest at 174.87 cm^3 and the smallest at 61.19 cm^3 . For the left kidney, the average volume was 134.59 cm^3 , ranging from 74.67 cm^3 to 274.11 cm^3 .

Diameter of RA for transplant: The average diameter of the right kidney's main RA was 6.00 ± 0.65 mm, with the largest at 7 mm and the smallest at 4 mm. Conversely, the average diameter of the left kidney's main RA was 6.13 ± 0.64 mm, also ranging from 4 mm to 7 mm.

Diameter of RV for transplant: The average diameter of the right kidney's RV was 11.07 ± 1.09 mm, with the largest at 12 mm and the smallest at 9 mm. Similarly, the average diameter of the left RV was

11.78 ± 1.05 mm, with the largest at 13 mm and the smallest at 9 mm.

Transplanted kidneys have a dominant main RA, with the right kidney selected for transplant in 269 cases out of 338 (79.6%) and the left kidney in 232 cases out of 338 (68.6%).

Transplanted kidneys have a dominant main RV, with the right kidney selected for transplant in 232 cases out of 338 (68.6%) and the left kidney in 333 cases out of 338 (98.5%).

2. Kidney function in MSCT among LKD

The left kidney exhibits a 42.9% better excretory function compared to the right kidney, while the right kidney shows a 4.4% better function than the left kidney, resulting in a 52.7% equivalent function between the two.

In MSCT and SPECT, the average of GFR were higher in the left kidney than the right ($p < 0.01$).

MSCT scans enable the evaluation of GFR for each kidney individually, aiding in kidney selection for transplant based on morphology and function before surgery:

- 104 out of 176 right kidneys (59.1%) were selected when the right kidney exhibited worse function than the left.
- Only 3 out of 162 left kidneys (1.9%) were chosen when the left kidney showed worse function than the right.
- 20 out of 176 right kidneys (11.4%) were selected when the right kidney displayed abnormalities despite equivalent function between both kidneys.
- Similarly, 19 out of 162 left kidneys (11.7%) were chosen when abnormalities were present in the left kidney despite equivalent function between both.

3. The value of MSCT scan in assessing morphology and function of selected kidneys for transplant among LKD

Kidney volume: There was no significant difference in the volume of the right and left kidneys selected for transplantation before surgery, as determined by ultrasound and CT ($p > 0.05$).

RA morphology:

- CT scan values for RA morphology exhibited Se, Sp, PPV, NPV, Ac of 100% compared to kidney transplant surgery results.
- CT accurately identified upper pole accessory RA, renal hilum, lower pole, and capsule with 100.0% accuracy compared to surgery.

- For the right RA, Se and PPV could not be calculated due to a value of 0.

RV morphology:

- CT scan values for RV morphology showed Se, Sp, PPV, NPV, Ac of 100% compared to kidney transplant surgery, except in cases where some values could not be calculated due to a frequency of 0.

- The accuracy of CT in determining the hilar accessory RV in the right kidney was Se 97.5% and Sp 100.0%.

- CT accurately identified upper and lower pole accessory RV in both kidneys, as well as the renal hilum in the left kidney, with 100% accuracy or insufficient data for evaluation.

- The accuracy of CT in identifying the confluent lumbar vein branch draining into the left kidney was Se 98.8% and Sp 100.0%.

Kidney function: A correlation was observed between the GFR of the left ($r=0.763$, $p<0.001$) and right ($r=0.765$, $p<0.001$) kidneys on both MSCT and SPECT scans. The similarity in GFR between CT and SPECT was confirmed with a PE of 22.15% in the right kidney and 23.11%, according to Bland Altman analysis.

STUDY LIMITATION

Despite the study's relatively large sample size, its conduct in a hospital with kidney transplant services rendered the sample unrepresentative of the total number of LKD in Vietnam.

RECOMMENDATION

1. Applying multislice computed tomography technique to provide parameters for selecting kidney transplants in LKD aims to improve the accuracy of assessing kidney morphology and function before surgery.

2. The study was conducted solely at one hospital performing organ transplants in the Central region. Studies at licensed organ transplant units nationwide are necessary to provide more comprehensive evidence on this topic.

LISTED OF RELATED SCIENTIFIC WORKS THAT HAD BEEN PUBLISHED

1. Duong Phuoc Hung, Le Trong Khoan, Nguyen Khoa Hung (2018). Computed tomography images of the upper urinary tract in living kidney donors. *Journal of Medicine and Pharmacy, University of Medicine and Pharmacy, Hue University*, No. 6, November 2018, Pp 89-98.
2. Duong Phuoc Hung, Le Trong Khoan and Nguyen Khoa Hung (2019). Multi-detector row CT in the preoperative evaluation of the vascular and upper urinary tract anatomy of living renal donors. The first national and international conference of Kalasin University 2019 Proceedings-Health Sciences, Science and Technology, Pp 38-51. Thailand.
3. Duong Phuoc Hung, Le Trong Khoan and Nguyen Khoa Hung (2020). Preoperative evaluation of vascular morphology and function of living renal donors on multi-detector row CT. *Journal of Clinical Medicine*, No.62, Pp. 65-75.