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ORIGINAL ARTICLE

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Correlation of preoperative imaging characteristics with donor outcomes and operative difficulty in laparoscopic donor nephrectomy

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This study aimed to understand the relationship of preoperative measurements and risk factors on operative time and outcomes of laparoscopic donor nephrectomy. Two hundred forty-two kidney donors between 2010 and 2017 were identified. Patients' demographic, anthropomorphic, and operative characteristics were abstracted from the electronic medical record. Glomerular filtration rates (GFR) were documented before surgery, within 24 hours, 6, 12, and 24 months after surgery. Standard radiological measures and kidney volumes, and subcutaneous and perinephric fat thicknesses were assessed by three radiologists. Data were analyzed using standard statistical measures. There was significant correlation between cranio-caudal and latero-lateral diameters ($P < .0001$) and kidney volume. The left kidney was transplanted in 92.6% of cases and the larger kidney in 69.2%. Kidney choice (smaller vs. larger) had no statistically significant impact on the rate of change of donor kidney function over time adjusting for age, sex and race ($P = .61$). Perinephric fat thickness (+4.08 minutes) and surgery after 2011 were significantly correlated with operative time ($P \leq .01$). In conclusion, cranio-caudal diameters can be used as a surrogate measure for volume in the majority of donors. Size may not be a decisive factor for long-term donor kidney function. Perinephric fat around the donor kidney should be reported to facilitate operative planning.

KEYWORDS
clinical research / practice, diagnostic techniques and imaging: computed tomography, donor nephrectomy, donors and donation: donor evaluation, glomerular filtration rate (GFR), health services and outcomes research, kidney transplantation / nephrology, kidney transplantation: living donor, organ transplantation in general

1 | INTRODUCTION

First described over 20 years ago[1] laparoscopic donor nephrectomy is the standard operation for retrieval of kidneys for living donor donation. Given the ubiquity of the procedure and the need for favorable outcomes, as it is an elective operation on otherwise healthy patients, it is imperative to ensure appropriate preoperative risk stratification and anticipate intraoperative challenges.[2] One of

Abbreviations: Ap, anteroposterior; BMI, Body Mass Index; cc, cranio-caudal; CI, confidence interval; cm, centimeters; CT, Computed Tomography; GFR, Glomerular filtration rate; IQR, Interquartile Range; kg, kilograms; ll, latero-lateral; SD, standard deviation.

the advantages that all patients undergoing donor nephrectomy have is that they have completed a preoperative computed tomography (CT) scan to define their vascular anatomy in order to ensure that it is amenable for transplantation.[3] At the moment practice at our institution automatically disqualifies potential donors with either kidney having a cc-diameter of <8 cm. When both the kidneys are >8 cm long but there is a length discrepancy of 20 mm or more, a split renal function study is performed to decide on laterality. If the difference in GFR is higher than 10 mL/min, the candidate is excluded, as well. This scan additionally provides crucial information to the transplant surgeon for the appropriate donor selection and preoperative planning.[4]

Two areas where a preoperative CT scan may be helpful are in determining operative difficulty and predicting donor outcome. In regards to operative difficulty, one area of investigation is focused on higher Body Mass Index (BMI) patients.[5] As obesity becomes increasingly common in the United States, more potential kidney donors are likely to be obese as defined by BMI, with 63.6% of donors classified as overweight or obese in a review from 2015.[6,7]

Though BMI is correlated with both operative difficulty and postoperative donor and recipient outcomes, it is a frequently criticized measure and inconsistent results have been reported.[8-10] It may be incorrectly elevated or depressed in certain populations and may not adequately account for specific anatomy.[11] For example, perinephric fat has been shown to be thicker in males than in females regardless of BMI.[12,13] Additionally, it is increasingly understood that measures of visceral fat are superior to BMI for delineating those patients with more severe metabolic syndromes.[14]

A recent paper by Segev et al found no association of surgical mortality and obesity in kidney donors, but Holscher et al reported donor BMI was associated with death-censored graft failure in recipients, and Ahmandi et al recommended not basing donor eligibility solely on BMI values.[15-17] Our center currently excludes patients with a BMI of 35 kg/cm^2 or higher.

The number of arteries in the donated kidney is another variable which has been found to be an important factor, with Kok et al showing increased operating times of more than 20 minutes and increased recipient ureteral complications up to 47%, if lower pole arteries were present. A recent meta-analysis showed a 13.8% complication rate in recipients of kidneys with multiple arteries, delayed graft function in 10.3% and graft survival of 93.2% compared to recipients of single-artery kidneys with 94.5% (P = .034).[18,19]

Given these challenges, we sought to understand donor variables, specifically radiographic variables that were correlated with both operative difficulty and postoperative outcomes. One area of literature, more prevalent in urology, centers on the quantity and quality of perinephric fat.[20,21] We aimed to assess the relationship of preoperative risk factors, including BMI, perinephric, and subcutaneous fat, on the operative time and outcomes of laparoscopic donor nephrectomy.

2 | MATERIALS AND METHODS

2.1 | Patient identification and data collection

This retrospective study was Health Insurance Portability and Accountability Act (HIPPA) compliant and received Institutional Review Board approval (Pro00086638). All patients who underwent elective laparoscopic donor nephrectomy between 2010 and 2017 at our large academic center, performing an average of 150 kidney transplants per year,[22] were identified using an existing patient registry. Patients' demographic, anthropomorphic, and operative characteristics, such as operative technique, operating surgeon, and operating time, were abstracted from the electronic medical record. With regards to operative technique, all nephrectomies were performed by a total of four surgeons in either a totally laparoscopic fashion, with extraction through a low Pfannenstiel incision, or in a hand-assisted technique with a supraumbilical handport[23] through an approximately 7-cm incision, depending on the operating surgeon's preference.

Glomerular filtration rates (GFR) were documented before surgery, within 24 hours of surgery, 6, 12, and 24 months after surgery as well as for the most distant time point available. The GFRs were estimated using the MDRD equation (175 × [creatinine value at timepoint]$^{-1.154}$ × [age at timepoint]$^{-0.203}$ × [0.742 if female] × [1.212 if African American]).[24] History and type of previous abdominal surgery was noted (Table S1).

2.2 | Radiologic variables

Patients' preoperative CT studies were acquired on six different CT scanners including two dual-source scanners (Siemens SOMATOM Force and Flash with 256 and 192 slices, Siemens Healthineers, Forchheim, Germany), one 128 slice single-source spectral CT (GE Discovery CT 750HD, GE Healthcare, Chicago, IL), two 64-slice single-source CTs (Siemens SOMATOM Sensation 64 and GE Lightspeed VCT) and one single-source 16 slice CT (GE Lightspeed 16), reflecting advances in CT scanning technology between 2010 and 2017. This did not influence diameter or volume measurement because all scans were acquired with a minimum slice thickness of 1 mm. CT provides better spatial resolution and faster scan times than MRI, resulting in less movement artifacts. Measurements made on CT images are less operator dependent than those made on ultrasound images.

Standard measures including renal arterial and venous number, volumes and diameters (cranio-caudal [cc], anteroposterior [ap], latero-lateral [ll]) were assessed on thin slices of 0.6 to 1 mm thickness by three independent radiologists (FS: PGY 5, FG: 2 years of experience, FR: PGY 4) using a commercially available off-Picture Archiving and Communication System (PACS) software (TeraRecon, Foster City, CA).

Kidney volumes were measured using gradient auto-detection between hand-drawn contours excluding the kidney hilum (Figure 1).

The conventional kidney diameters were assessed on both sides after adjusting the CT planes to a coronal oblique image resulting in the longest cc-diameter of each kidney.

Subcutaneous fat thickness was measured on axial slices in the ventral abdominal wall at the level of the kidney hilum. Taking into account that the reported measurements by Anderson et al correlated both anterior and posterior perinephric fat thicknesses with OR times (r = .28 and .2) our measurements were taken on axial slices at the level of the kidney hilum parallel to the kidney vasculature towards the posterior abdominal wall, as this measurement was considered more robust than the anterior one (eg, bowel loops might be in different configurations, while posterior abdominal wall should not change; Figure 2). If the hila were not in the same plane, subcutaneous fat thickness was measured at the level of the right kidney hilum.

2.3 | Statistical analysis

Demographic, baseline, and procedure characteristics were summarized using mean with standard deviation (SD), median with interquartile range (IQR), and ranges (minimum and maximum), or frequency with percentage (where appropriate). Spearman Correlation Hypothesis tests were considered (with the application of a Bonferroni correction) to determine whether a correlation between each kidney's volume and its three respective unidimensional measures of length existed. The same tests were used to determine whether there was a correlation between perinephric fat of the transplanted kidney, subcutaneous fat, and BMI. A linear mixed effects model was postulated to evaluate the effect of kidney choice (larger vs. smaller) on posttransplant kidney function (GFR values) as a function of time since surgery. Subjects were taken as a random effect to account for the repeated measures on the same subject. A linear mixed effects model was postulated to evaluate the effect of the percentage difference in kidney volume on posttransplant kidney function. An adjusted multiple linear regression model was postulated to examine the relationship between perinephric fat and operative time, after adjusting for relevant confounders (demographic variables, BMI, thickness of subcutaneous fat, history of abdominal surgery, and operating surgeon). The threshold for assessing statistical significance was set at $\alpha = 0.05$. Analyses were conducted using R version 3.4.3 (Vienna, Austria).

3 | RESULTS

3.1 | Demographics

Data on a total of 242 individuals that underwent living donor nephrectomy for transplantation were collected; two patients were excluded from the radiological analysis due to a missing arterial phase and motion artifacts (Figure 3). Demographic data are summarized in Table 1. Overall, the cohort was mostly white (72.6%) and female (66%) with a median age of 42 years. The median BMI for this cohort was in the "overweight" category (26.8 kg/cm^2; normal range: 18.5-24.9 kg/cm^2), though the interquartile range (IQR: 23.5, 29.2) shows that the majority of donations was made by individuals not considered obese (BMI ≥ 30 kg/ cm^2). Approximately 20% of the

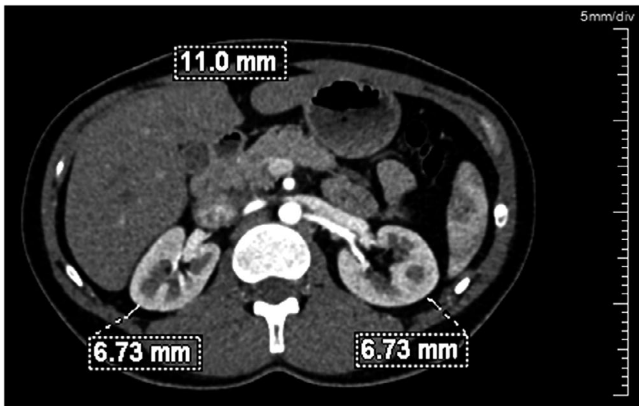

FIGURE 2 Axial, contrast enhanced CT image, demonstrating the simple measurement of perinephric and subcutaneous fat in a 21-year-old female kidney donor (software: TeraRecon, Foster City, CA)

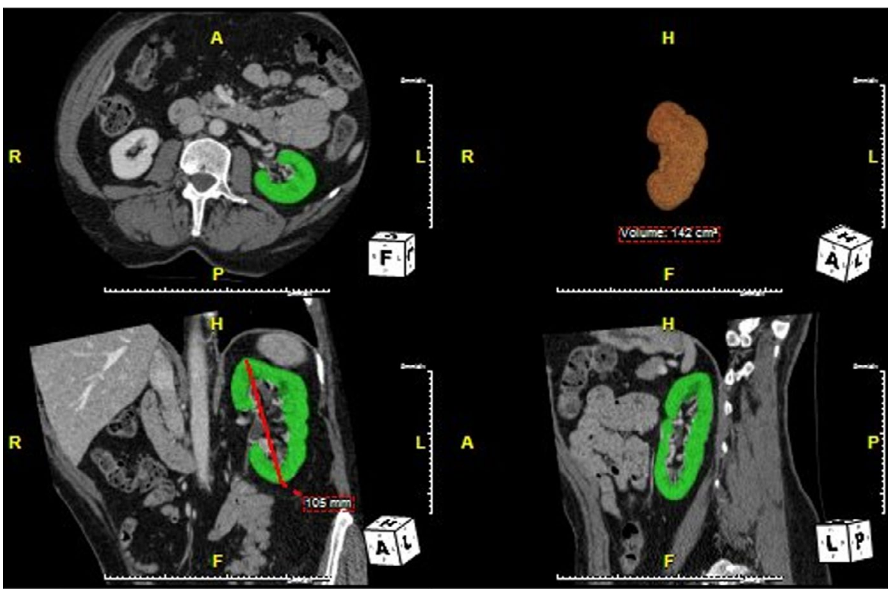

FIGURE 1 Demonstrates the technique used for measurement of kidney diameters (cranio-caudal diameter shown on bottom left) and kidney volume. The area in green denotes kidney parenchyma in all three image planes, with the software producing a 3D rendering with volume measurement (top right) [Color figure can be viewed at wileyonlinelibrary.com]

donors had multiple arteries in the donor kidney and over 40% had undergone previous abdominal surgery (Table 2).

3.2 | Correlation of kidney volumes and diameters

Average kidney lengths and volumes are summarized in Table 2. There was a good correlation of cc- (correlation coefficient of 0.62 left and 0.61 right kidney; $P < .0001$; Table 3) and ll-diameters with kidney volume (correlation coefficient of 0.56 and 0.67, respectively; $P < .0001$). Weaker correlations were shown between ap-diameters and volume (correlation coefficients of 0.14 and 0.19, respectively) Figure 4.

3.3 | Choice of kidney for nephrectomy and donor outcome

The left kidney was transplanted in 92.6% of cases and the larger of the two kidneys, as determined by volume, was transplanted in 69.2% of cases. For the 135 subjects with relevant data, average GFR recovered from 58.2 ± 16.7 mL/min/1.73 m^2 within 24 hours after surgery to 60.9 ± 13.2 mL/min/1.73 m^2 24 months after surgery. Choice of kidney (ie, explanting the smaller or the larger kidney) had no statistically significant effect on posttransplant donor GFR and the rate of change of donor GFR over time, after adjusting for age, sex, and race (baseline estimate: 1.45, 95% CI: −1.88, 4.77, $P = .40$; interaction with time: −0.05, 95% CI: −0.25, 0.15, $P = .61$; Table 4 and Figure 5). In an additional model, the percentage difference in kidney volume had no statistically significant effect on posttransplant donor GFR and the rate of change of donor GFR over time, after adjusting for the same covariates as above (Table S2).

3.4 | Correlation of subcutaneous/perinephric fat with BMI

Whereas subcutaneous fat was well correlated with BMI in both men and women ($\rho = 0.56$, $P < .001$ and $\rho = 0.71$, $P < .001$, respectively, Figure 6), perinephric fat had a weaker correlation with BMI ($\rho = 0.40$, $P < .001$ and $\rho = 0.30$, $P < .001$, respectively, Figure 7).

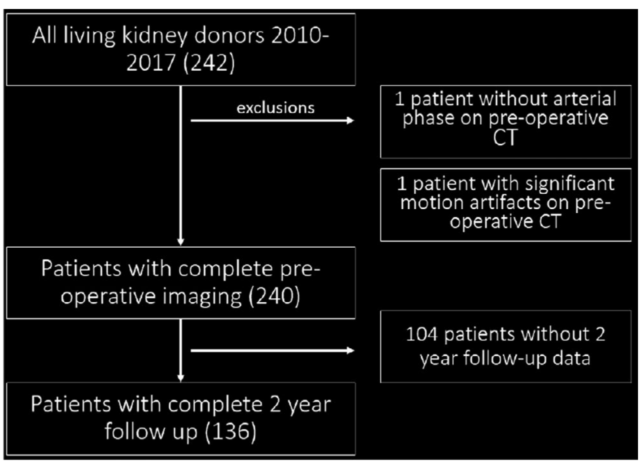

FIGURE 3 Flow chart, showing patient selection and exclusion criteria

3.5 | Multivariable linear regression for operative times

Correlates of operative difficulty, including perinephric and subcutaneous fat thicknesses and number of renal arteries are part of the CT-based measurements in Table 2.

TABLE 1 Demographic data and clinical history

	Total (N = 242)
Sex (male), n (%)	83 (34.3)
Age at transplantation (in years), med (IQR)	43.0 (34.0, 51.0)
Height (in cm), med (IQR)	168.0 (161.0, 177.8)
Weight (in kg), med (IQR)	76.3 (65.4, 87.6)
BMI, Med (IQR)	26.8 (23.5, 29.2)
Race, n (%)	6 (2.5)
Asian	44 (18.6)
Black	7 (3)
Latino	5 (2.1)
Native American	3 (1.3)
Other	172 (72.6)
White	
History of abdominal surgery, n (%)	106 (43.8)

BMI, body mass index; IQR, interquartile range.

TABLE 2 Kidney volumes and diameters, number of arteries and thickness of perinephric and subcutaneous fat

	Total (N = 240)
Volume of left kidney, mean ± SD (range)	162.9 ± 33.1 (99.0-263.0)
Volume of right kidney, mean ± SD (range)	155.2 ± 31.2 (86.7-257.0)
Left cc kidney diameter (in cm), ± SD (range)	11.1 ± 0.9 (7.9-13.7)
Right cc kidney diameter (in cm), ± SD (range)	10.9 ± 1.1 (1.1-14.4)
Left ap kidney diameter (in cm), ± SD (range)	4.1 ± 5.6 (1.5-26.9)
Right ap kidney diameter (in cm), ± SD (range)	2.5 ± 0.5 (1.6-4.8)
Left ll kidney diameter (in cm), ± SD (range)	8.3 ± 11.8 (1.9-55.9)
Right ll kidney diameter (in cm), ± SD (range)	4.5 ±2.0 (2.1-34.8)
Multiple arteries, n (%)	49 (20.2)
Thickness of perinephric fat (left), med (IQR)	5.0 (3.3, 7.4)
Thickness of perinephric fat (right), med (IQR)	4.8 (3.1, 7.4)
Thickness of subcutaneous fat, med (IQR)	20.4 (14.6, 27.6)

ap, anteroposterior; cc, cranio-caudal; cm, centimeters; ll-latero-lateral; SD, standard deviation.

TABLE 3 Spearman's rank correlations comparing kidney volume and relevant kidney diameters (N = 240)

Correlation test	Correlation coefficient	Adjusted *P*-value
Left kidney volume vs. left cc kidney diameter	0.62	<.0001
Right kidney volume vs. right cc kidney diameter	0.61	<.0001
Left kidney volume vs. left ap kidney diameter	0.14	.09
Right kidney volume vs. right ap kidney diameter	0.19	.01
Left kidney volume vs. left ll kidney diameter	0.56	<.0001
Right kidney volume vs. right ll kidney diameter	0.67	<.0001

ap, anteroposterior; cc, cranio-caudal; ll, latero-lateral.

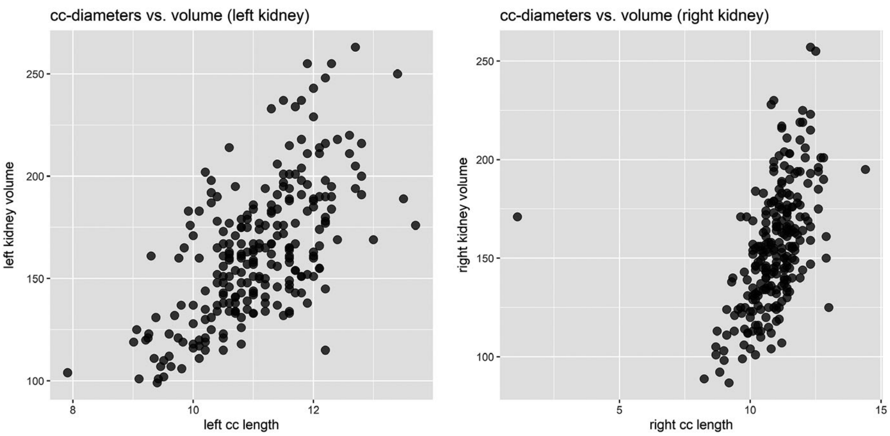

FIGURE 4 Correlation of kidney volumes and kidney cc-diameters

TABLE 4 Linear estimates and 95% confidence intervals for fixed effects when modeling age, race, sex, and "smaller kidney transplanted" on renal function (N = 709, 228 subjects)

	Estimate (95% CI)	*P*-value
Intercept	70.25 (64.80, 75.71)	<.0001
Time since transplantation	0.18 (0.08, 0.28)	<.0001
Smaller kidney chosen for transplantation	1.45 (−1.88, 4.77)	.40
(smaller kidney chosen for transplantation) × (time)	−0.05 (−0.25, 0.15)	.61
Age	−0.31 (−0.42, −0.19)	<.0001
Race (black) (reference = not black)	7.69 (4.24, 11.13)	<.0001
Sex (male) (reference = female)	−3.04 (−5.77, −0.30)	.03

The results of the multivariable linear regression model assessing the relationship between multiple preoperative variables and operative time are summarized in Table 5. One variable that correlated significantly with operative time was thickness of perinephric fat. Our model showed that for each additional millimeter of perinephric fat, there was a 4.08-minute increase in operative time (95% CI: 1.71-6.46, $P < .001$). We also calculated the average operative times based on quintile of perinephric fat, which shows an increase for each quintile, with the average time in the lowest quintile (260 min) approximately 70 minutes less than the average time in the highest quintile (329 min) (Table 6). There was no statistically significant relationship between surgical technique and operative time, BMI, and operative time, or the interaction of BMI and gender and operative time after adjusting for relevant confounders.

The only other variable that significantly correlated with operating time was performance of surgery after the year 2011. After 2011, we had a change in staffing at our center and donor nephrectomies, which were previously staffed by a single attending only, became teaching cases.

4 | DISCUSSION

Our study adds to the literature of living donor kidney transplantation in multiple ways. First, we show that cc and ll kidney diameters are highly correlated with kidney volumes as measured by CT. Next, we demonstrate that kidney choice (smaller or larger kidney explanted) has no statistically significant effect on donor GFR in a contemporary cohort, suggesting that volumetric measurements are likely superfluous in most patients. Finally, we demonstrate that perinephric fat is strongly correlated with operative times and perinephric fat is not as well correlated with BMI. Taken together, these findings should help inform the most important variables (cc-diameter, number of renal arteries, thickness of perinephric fat) to be reported by radiologists to transplant surgeons.

The necessity for radiologic measurements of kidney volumes has been discussed as possibly superior to simple kidney diameters.[25]

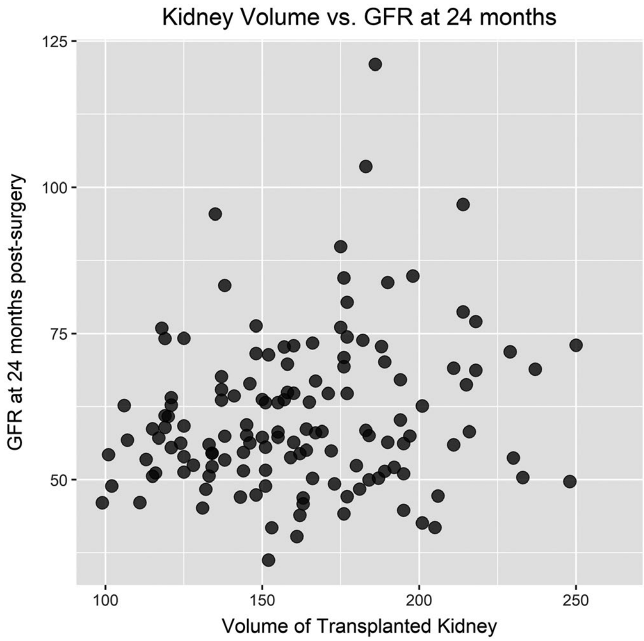

FIGURE 5 Correlation of volume of explanted kidney and GFR at 24 months (N = 141)

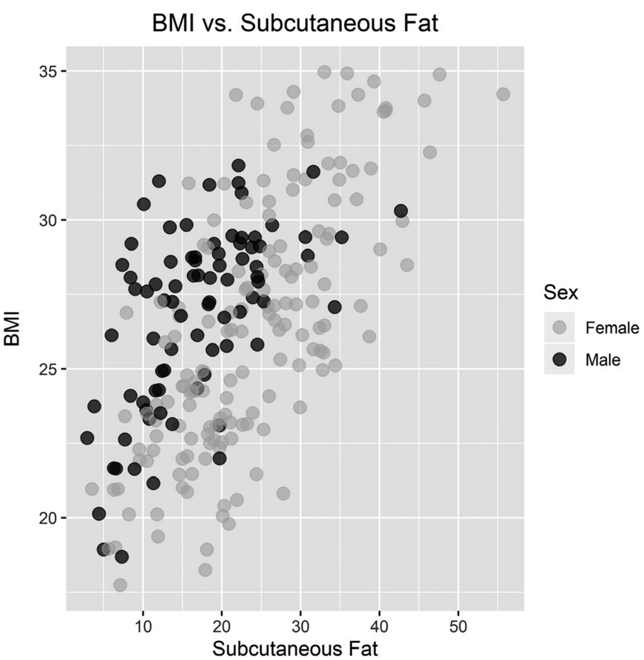

FIGURE 6 Correlation between subcutaneous fat and BMI by gender for men (ρ = 0.56, P < .001) and women (ρ = 0.71, P < .001)

This study shows that the cc- and ll-diameter correlate well with kidney volume. A recent study has also shown that kidney volume measurement on CT is not superior to clinical diethylenetriamine penta-acetic acid (DTPA) measurements.[26]

Even though the larger donor kidney was explanted in 69.2% of cases, this choice showed no statistically significant difference in the rate of improvement of donor GFR over time. Therefore, kidney size might only be a minor factor in choosing the correct kidney to explant from a donor perspective.

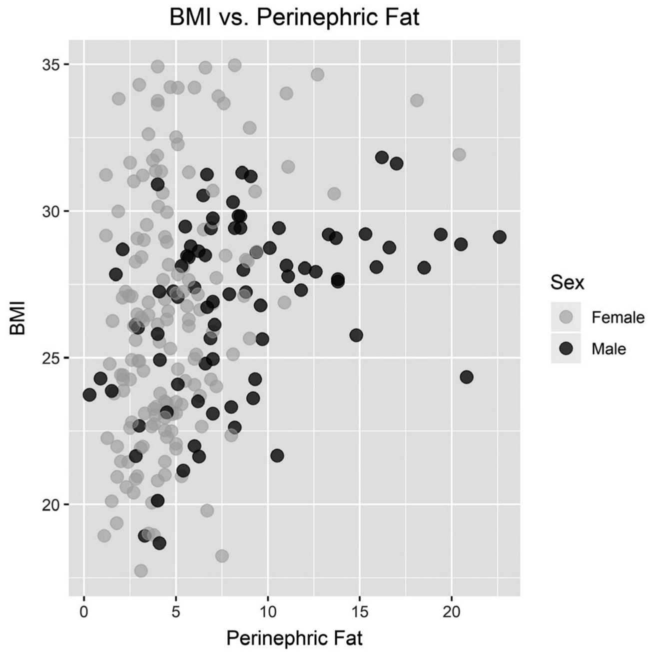

FIGURE 7 Correlation between perinephric fat and BMI by gender for men (ρ = 0.40, P < .001) and women (ρ = 0.30, P < .001)

TABLE 5 Linear estimates and 95% confidence intervals when modeling thickness of perinephric fat in transplanted kidney on operative time (adjusted for confounders) (N = 232)

	Estimate (95% CI)	*P*-value
Intercept	169.56 (19.30, 319.83)	.03
Thickness of perinephric fat in transplanted kidney	4.08 (1.71, 6.46)	.001
Age at transplantation	0.40 (−0.35, 1.16)	.29
Race (black) (reference = not black)	16.06 (−5.21, 37.32)	.14
Sex (male) (reference = female)	−27.94 (−173.34, 117.45)	.70
BMI	0.95 (−4.87, 6.77)	.75
Thickness of subcutaneous fat	2.82 (−3.10, 8.74)	.35
BMI × thickness of subcutaneous fat	−0.08 (−0.30, 0.12)	.43
BMI × sex (male) (reference = female)	1.89 (−3.61, 7.39)	.50
Kidney transplanted (right) (reference = left)	−13.56 (−44.33, 17.20)	.39
Multiple renal arteries in transplanted kidney	11.75 (−8.09, 31.58)	.24
History of abdominal surgery	5.78 (−11.84, 23.40)	.52
Operative surgeon (reference = median surgeon)	1.56 (−18.01, 21.13)	.88
Surgery after 2011	35.23 (7.87, 62.59)	.01
Surgical technique: lap only or open (reference = hand assist)	−5.30 (−25.27, 14.66)	.60

BMI, body mass index; CI, confidence interval.

TABLE 6 Operative time stratified by perinephric fat quintile

	Surgery time (by Transplanted Perinephric Fat Quintile)					
	Quintile 1 (N = 50)	Quintile 2 (N = 52)	Quintile 3 (N = 42)	Quintile 4 (N = 48)	Quintile 5 (N = 48)	Total (N = 240)
Thickness of perinephric fat, mean (SD)	2.2 (0.7)	3.8 (0.4)	5.1 (0.4)	7.0 (0.7)	12.5 (4.0)	6.1 (4.0)
Range	(0.3-3.0)	(3.1-4.4)	(4.5-5.8)	(6.0-8.4)	(8.5-22.6)	(0.3-22.6)
Surgery time (in minutes), mean (SD)	260.3 (60.4)	283.5 (60.2)	292.5 (70.1)	296.9 (59.8)	329.3 (57.5)	292.2 (65.0)
Missing	1	0	1	1	0	3
Range	(160.0-392.0)	(132.0-449.0)	(160.0-478.0)	(167.0-392.0)	(243.0-512.0)	(132.0-512.0)

SD, standard deviation.

Perinephric fat is an important correlate of operative time and operative difficulty in laparoscopic donor nephrectomy for kidney transplant. We show that this measure is both easily obtainable and relevant for surgical planning. Other traditional measures of surgical difficulty did not have a statistically significant impact on the operating times in this study. Though previous studies have shown both BMI and number of arteries to correlate with operative time, this was not replicated in this study, possibly due to the relatively low number of patients with multiple arteries in the explanted kidney and poor correlation of BMI with perinephric fat.[8,27] Knowing the number of arteries in the transplanted kidney in advance is important to surgeons during planning though and should always be included in reports. This analysis did however, corroborate earlier reports that perinephric fat was a predictor of operative time[13] and that the distribution of perinephric and subcutaneous fat was different between men and women.[28]

Each additional millimeter of perinephric fat contributed more than 4 minutes of surgery time and the average operative time in the highest quintile of perinephric fat was nearly 70 minutes longer than the average time in the lowest quintile. More accurate predictions of surgical time can lead to exponential efficiencies as this is one of the few situations in which the initiation one surgery is dictated by the efficiency of the other. Additionally, operating room time is exceedingly expensive, though the cost is highly variable depending on the complexity of the procedure. One 2018 study calculated that each additional minute of operating time costs approximately $35.[29] More practically, a higher perinephric fat thickness may inform operative technique, with patients with higher perinephric fat perhaps more amenable to a hand-assisted approach. Finally, the thickness of perinephric fat may also inform whether or how much of a case is a teaching case. As all medical specialties, including surgery, moves towards frameworks of entrustable professional activities and more concrete measures of trainee autonomy,[30] objective measures of operative difficulty will become increasingly important.

The effect modification of BMI and gender was modeled to control for differential distributions of perinephric and subcutaneous fat; however, this variable was not significant. This confirms the importance of perinephric fat over BMI when planning donor nephrectomies.[15,17] As the BMI of the general population increases[31,32] it may be important to find more specific measures of operative difficulty when considering a weight or BMI cutoff.

There are several limitations to our study. First, it is a single center study with a relatively small number of patients and therefore we may have been unable to detect differences due to lower power. However, these findings are generally in line with other findings in the literature and our in-depth analysis of donor preoperative imaging adds to the richness of the study. Second, due to the small number of patients with complications that were trackable at our center, we did not achieve adequate statistical power for an analysis of this outcome parameter. Future studies should aim to acquire more data on long-term surgical complications as our cohort accrues or by seeking out information on postsurgical complications, as patients may receive care at other institutions than our own. Another line of future inquiry could be whether a decrease can be seen in recipient's GFR, if the operative time was increased.

5 | CONCLUSION

Simple cranio-caudal and latero-lateral kidney diameters correlate well with overall kidney volumes and can be used as a surrogate measure in the majority of donors. Choice of donor kidney (smaller or larger) had no statistically significant effect on the rate of change of donor GFR over time in this study. Perinephric fat thickness should be reported to surgeons for optimal operative planning. Additionally, further study of anthropomorphic variables besides BMI as a cutoff for kidney donation is warranted, especially given rising BMIs in the general population.

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DISCLOSURE

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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