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Mayo Imaging Classification May Be Useful in Determining the Need for Nephrectomy in ADPKD

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Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is the most common cause of inherited kidney disease, comprising about 7%–10% of the prevalent ESKD population. Kidney transplantation is the best choice of RRT in patients with ADPKD (1,2).

Kidney cysts grow exponentially, increasing total kidney volume (TKV), which is predictive of disease progression and loss of renal function (3). In addition, patients with ADPKD may have hypertension, abdominal fullness, episodes of cyst rupture or hemorrhage, nephrolithiasis, cyst infection, and reduced quality of life (4). Recurrent infection, or hemorrhage, may lead to the decision to perform a nephrectomy, either pretransplant or concurrent with kidney transplant; but the decision is more often made on the basis of space concerns relating to the placement of the donor kidney in the pelvis.

There is no formal consensus in identifying candidates for nephrectomy, and the matter of timing and indication remains debatable (5). We hypothesized that height-adjusted TKV (ht-TKV), assessed using the Mayo imaging classification tool, could be used as part of an objective measurement to evaluate pretransplant

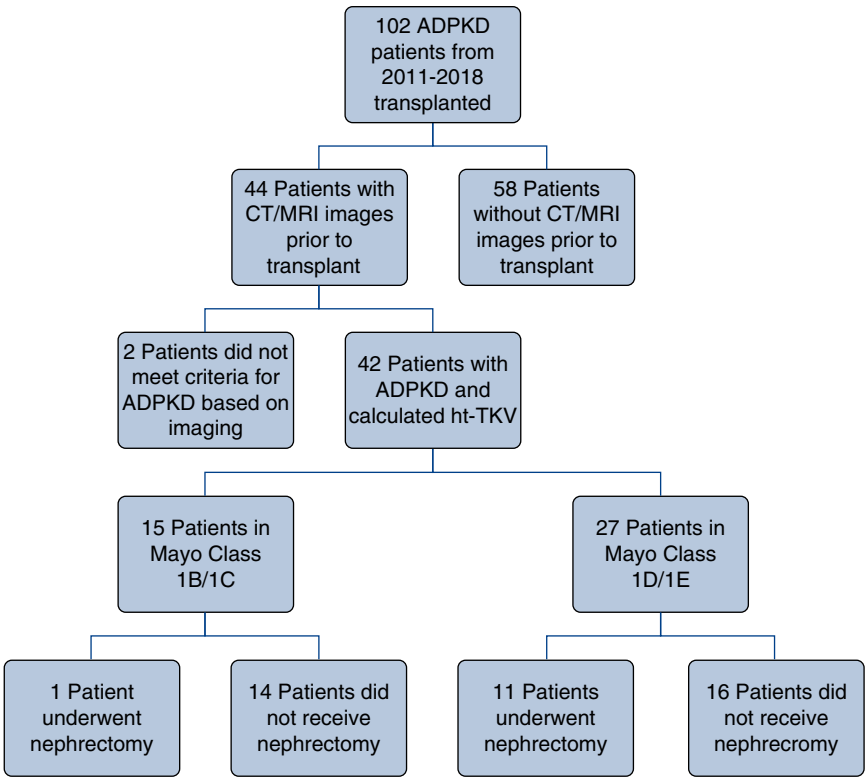

Figure 1. | **Initial screening of 102 transplant patients with ADPKD at Yale New Haven Hospital from 2011 to 2018.** CT/MRI were available for 44 patients before transplant, of which 42 met the imaging criteria for ADPKD and were included in the analysis. These 42 patients were further categorized by Mayo classification (1B/1C/1D/1E) and nephrectomy status. ADPKD, autosomal dominant polycystic kidney disease; CT, computed tomography; ht-TKV, height-adjusted total kidney volume; MRI, magnetic resonance imaging.

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Table 1. Summary of clinical variables by Mayo classification

Variables	Mayo Class 1B/1C (*N*=15)	Mayo Class 1D/1E (*N*=27)	Total (*N*=42)	*P* Value
Age (yr) at time of transplant	59.87 (11.53)	52.93 (8.01)	55.40 (9.87)	0.03
Weight (kg) at transplant	72.16 (13.06)	86.21 (24.00)	81.27 (21.70)	0.03
Height (cm) at listing	169.16 (5.75)	173.14 (10.45)	171.72 (9.18)	0.12
Creatinine (mg/dL) at discharge	1.1 (1.0–1.4)	1.5 (0.9–2.1)	1.2 (0.9–2.1)	0.37
Average ht-TKV (ml/m)	1254.6 (955.9–1835.9)	3262.7 (2384.1–4196.9)	2555.6 (1511.9–3362.8)	<0.001
Nephrectomy, *n* (%)				0.03
No	14 (93)	16 (59)	30 (71)	
Yes	1 (7)	11 (41)	12 (29)	
Sex, *n* (%)				0.004
Female	12 (80)	9 (33)	21 (50)	
Male	3 (20)	18 (67)	21 (50)	
Donor type, *n* (%)				0.70
Deceased	4 (27)	5 (19)	9 (21)	
Living	11 (73)	22 (81)	33 (79)	
Blood type, *n* (%)				0.92
A	7 (47)	10 (37)	17 (40)	
AB	1 (7)	1 (4)	2 (5)	
B	2 (13)	5 (19)	7 (17)	
O	5 (33)	11 (41)	16 (38)	
Diabetes at listing, *n* (%)				0.16
No	11 (73)	25 (93)	36 (86)	
Type 2	4 (27)	2 (7)	6 (14)	
Coronary artery disease, *n* (%)				0.33
No	12 (80)	25 (93)	37 (88)	
Yes	3 (20)	2 (7)	5 (12)	
Atrial fibrillation, *n* (%)				>0.99
No	13 (87)	24 (89)	37 (88)	
Yes	2 (13)	3 (11)	5 (12)	
Pulmonary hypertension, *n* (%)				>0.99
No	15 (100)	27 (100)	42 (100)	
Yes	0 (0)	0 (0)	0 (0)	
Hypertension, *n* (%)				>0.99
No	0 (0)	1 (4)	1 (2)	
Yes	15 (100)	26 (96)	41 (98)	

Data were presented as mean (SD), median (interquartile range), or frequency (%). ht-TKV, height-adjusted total kidney volume.

status and the clinical decision of nephrectomy in patients with ADPKD.

The Mayo imaging classification tool is a prognostic model used to predict loss of renal function on the basis of TKV-based orthogonal dimensions of the kidneys, age, height, sex, race, and serum creatinine (6). Measurement of sagittal length, coronal length, width, and depth of the right and left kidneys allows for determination of TKV. TKV can be adjusted for height (ht-TKV). ht-TKV is stratified into classes (1A–1E, in increasing order) on the basis of kidney size and age. We evaluated whether the Mayo imaging classification and/or clinical indicators such as age, weight, body mass index, diabetes, and hypertension correlate with undergoing nephrectomy in ADPKD.

Materials and Methods

The study was approved by the Yale Institutional Review Board under Human Investigations Committee number 2000024129.

Using the Organ Transplantation and Procurement database, we conducted a retrospective chart review of 102 patients with ADPKD who underwent a kidney transplant at Yale New Haven Hospital from January 1, 2011 to December 31, 2018. Clinical and demographic information—including age at time of transplant, weight at listing and at time of transplant, sex, reason and timing of nephrectomy, and presence of other comorbidities (including diabetes, hypertension, coronary artery disease, atrial fibrillation, and pulmonary hypertension)—was collected from the electronic medical record. The decision to perform a nephrectomy was made on the basis of routine clinical assessment of the patients independently by one of the four abdominal transplant surgeons at our center.

Computed tomography (CT) or magnetic resonance imaging (MRI) of the abdomen performed closest to the time of transplant were available for 44 patients and reviewed by three independent investigators to determine average ht-TKV. The remaining 58 patients were excluded from the study because there was no abdominal imaging available in the electronic medical record. Two patients were excluded from the final analysis for not meeting the criteria for ADPKD on the basis of radiologic imaging. The ht-TKV was determined using the Mayo imaging classification tool, using the inputs of patient age and height, and then sagittal length, coronal length, width, and depth of the right and left kidneys. On the basis of ht-TKV, patients were stratified into Mayo classes (1B–1E). We then compared clinical and biochemical data collected between groups 1B/1C (15 patients) versus 1D/1E (27 patients). We then used coronal-length measurements of the right and left kidney to determine the larger kidney length. This number was adjusted for patient

Table 2. Summary of clinical variables by nephrectomy status

Variables	Nephrectomy		Total (N=42)	P Value
	Yes (N=12)	No (N=30)		
Age (yr) at time of transplant	53.92 (7.97)	56.00 (10.60)	55.40 (9.87)	0.54
Weight (kg) at transplant	87.08 (14.83)	84.22 (23.04)	85.03 (20.88)	0.69
Height (cm) at listing	172.88 (9.61)	171.26 (9.14)	171.72 (9.18)	0.61
BMI (kg/m^2)	29.09 (5.87)	28.52 (6.45)	28.69 (5.87)	0.78
Creatinine (mg/dL) at discharge	2.1 (2.0–2.6)	1.0 (0.9–1.4)	1.2 (0.9–2.1)	<0.001
Average ht-TKV (ml/m)	3875.2 (3278.8–5596.1)	1960.0 (1254.6–2742.3)	2555.6 (1511.9–3362.8)	<0.001
Sex, *n* (%)				0.04
Female	3 (25)	18 (60)	21 (50)	
Male	9 (75)	12 (40)	21 (50)	
Donor type, *n* (%)				0.009
Deceased	6 (50)	3 (10)	9 (21)	
Living	6 (50)	27 (90)	33 (79)	
Blood type, *n* (%)				0.75
A	5 (42)	12 (40)	17 (40)	
AB	1 (8)	1 (3)	2 (5)	
B	1 (8)	6 (20)	7 (17)	
O	5 (42)	11 (37)	16 (38)	
Diabetes at listing, *n* (%)				0.16
No	12 (100)	24 (80)	36 (86)	
Type 2	0 (0)	6 (20)	6 (14)	
Coronary artery disease, *n* (%)				0.61
No	10 (83)	27 (90)	37 (88)	
Yes	2 (17)	3 (10)	5 (12)	
Atrial fibrillation, *n* (%)				>0.99
No	11 (92)	26 (87)	37 (88)	
Yes	1 (8)	4 (13)	5 (12)	
Pulmonary hypertension, *n* (%)				>0.99
No	12 (100)	30 (100)	42 (100)	
Yes	0 (0)	0 (0)	0 (0)	
Hypertension, *n* (%)				>0.99
No	0 (0)	1 (3)	1 (2)	
Yes	12 (100)	29 (97)	41 (98)	
Mayo class, *n* (%)				0.03
Very large kidney 1D and 1E	11 (92)	16 (53)	27 (64)	
Other sizes	1 (8)	14 (47)	15 (36)	
Height-adjusted kidney length (cm/m)	14.6 (2.3)	11.2 (1.9)	12.2 (2.5)	0.0002

Data were presented as mean (SD), median (interquartile range), or frequency (%). BMI, body mass index; ht-TKV, height-adjusted total kidney volume.

height and is presented as height-adjusted kidney length (hKL) in centimeters per meter.

For descriptive statistics, we calculated the mean (SD) or median (interquartile range) for continuous variables, and frequency (%) for categoric variables. For between-group comparisons, the Welch t test or Mann–Whitney U test was used for continuous variables, and the chi-squared test or Fisher exact test was used for categoric variables. All the statistical analyses were performed using the statistical software SAS version 9.4 (SAS, Cary, NC). A P value of <0.05 was considered statistically significant.

Results

Patients were screened from the Yale New Haven Hospital database, as outlined in Figure 1. Of the 44 patients with CT/MRI images before transplant, 42 met the criteria for having ADPKD with bilaterally enlarged kidneys and were included in the analysis. The median time between imaging and transplant was 154 days, with a minimum of 18 days and a maximum of 951 days.

Of the 42 total patients, 27 were classified as having Mayo class 1D/1E kidneys, and 15 were classified as Mayo class 1B/1C. None of the patients met class 1A criteria. Patients within the 1D/1E group were found to be younger males (average age of 52.9 years) and have a higher weight (86.21 kg) at the time of transplant (P=0.03; Table 1). Other clinical information collected on comorbidities at listing, including diabetes, coronary artery disease, atrial fibrillation, pulmonary hypertension, and hypertension, were not significantly different between the two groups (Table 2).

A total of 12 of 42 patients underwent nephrectomy, and 11 of the 12 (92%) were in the 1D/1E group, which is statistically higher than that in the patients not having nephrectomy (16/30 or 55%; P=0.03; Table 2). Of 30 patients, 22 (73%) underwent a pre-emptive kidney transplant without native nephrectomy.

No statistically significant differences were found for age (P=0.54), weight (P=0.69), body mass index (P=0.78), diabetes (P=0.16), and hypertension ($P\geq$0.99) between patients who had a nephrectomy versus those who did not (Table 2).

We then looked at hKL as a surrogate marker for need for nephrectomy, and found that the nephrectomy group had a significantly larger hKL (ranging from 11.8 to 17.6 cm/m).

Table 3. Comparison of calculated prenephrectomy TKV and actual nephrectomy weight

Age (yr) and Sex	Mayo Class	Days between Imaging and Nephrectomy	Calculated Prenephrectomy TKV (Mayo Tool), ml	Total Weight (bilateral nephrectomies), g	Nephrectomy Specimens (L×W×D), cm		Reason for Nephrectomy
					Right	Left	
68, F	1C	281	5200	4076	28×13×12	25×15×8	Frequent UTI, cyst rupture
64, M	1D	733	5487	5485	25×18×11	30×16×11	Space
54, M	1D	769	4298	3199	21×13×9	22×12×9	Pain, cyst hemorrhage, post-transplant
57, M	1D	27	7190	5820	32×15×13	29×16×13	Space
59, M	1D	91	7033	6110	27×20×13	27×18×12	Space
48, M	1E	43	14,752	11,270	41×28×11	39×24×14	Space
47, M	1E	126	5777	4770	26×14×13	16×16×12	Space
45, M	1E	586	6132	7510	28×17×12	31×18×13	Space
54, M	1E	79	7460	6230	30×14×10	27×19×10	Space
59, F	1E	94	10,869	4880	24×17×7	29×19×10	Space
41, M	1E	670	16,329	13,040	36×24×13	32×33×13	Space
51, M	1E	126	5856	4480	27×14×12	33×19×10	Space

TKV, total kidney volume; L, length; W, width; D, depth; F, female; UTI, urinary tract infection; M, male.

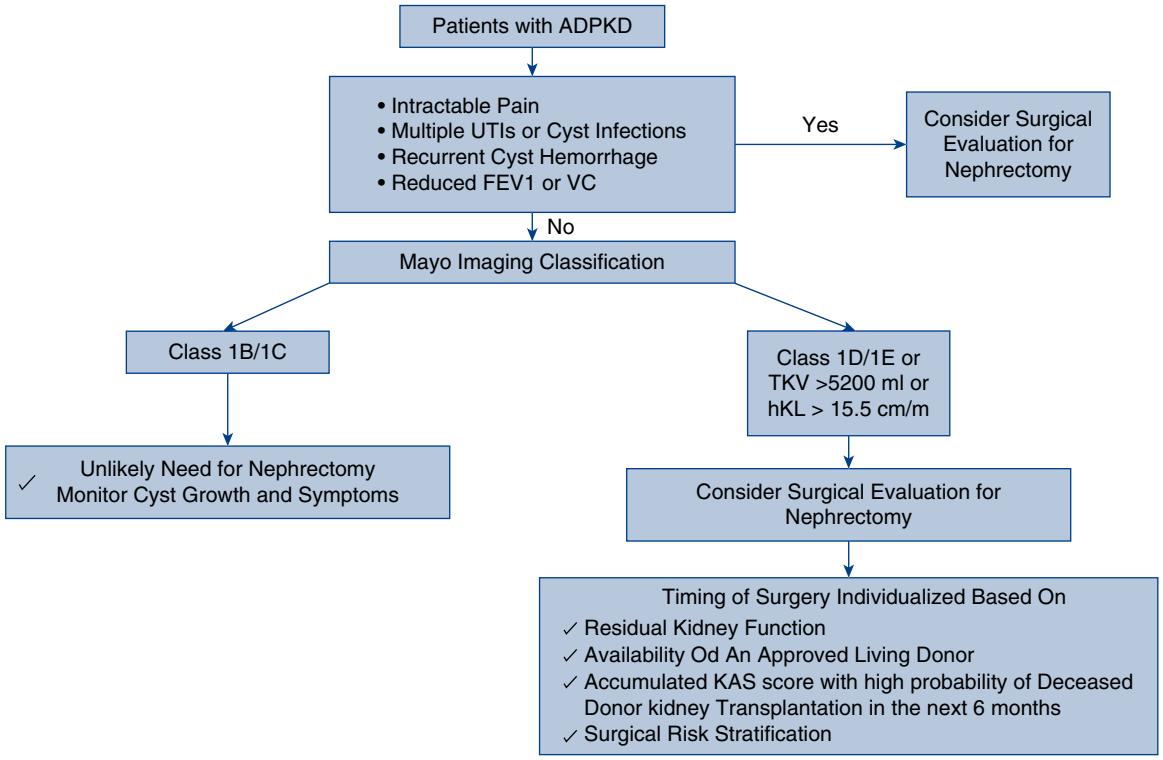

Figure 2. | **Asymptomatic ADPKD patients may be candidates for nephrectomy if they are Mayo class 1D/1E or have a TKV >5200 ml, or have a hKL >15.5 cm/m.** FEV1, forced expiratory volume in 1 second; hKL, height-adjusted kidney length; KAS, kidney allocation system; TKV, total kidney volume; UTI, urinary tract infection; VC, vital capacity.

In comparison, the no-nephrectomy group had an hKL ranging from 7.9 to 15.3 cm/m (Table 2). Thus, an hKL >15.5 cm/m may also help to identify a patient who is likely to undergo nephrectomy.

There was no difference in the 1-year graft survival rates between the patients in the 1D/1E group who underwent a nephrectomy and those who did not (data not shown).

Table 3 shows the difference between the calculated TKV and the actual weight of the nephrectomy specimens, along with the nephrectomy dimensions. In ten of the 12 patients, the primary reason for nephrectomy was to make space for the transplant. Of the remaining two patients, one patient in class 1D/1E underwent nephrectomy for management of pain and hemorrhagic cysts post-transplant, whereas the sole nephrectomy in class 1B/C was performed for recurrent urinary tract infections (Table 3). The variability between the calculated prenephrectomy TKV and actual nephrectomy weight may be related to length of ESKD before transplant, or the length of time between imaging and transplant, or the difference in kidney volume in perfused organs.

Five patients (three women, two men, aged 37–52) with class 1E kidneys did not undergo nephrectomy. All had calculated TKVs <3500 ml and met 1E criteria because of their younger age. In contrast, the smallest calculated TKV for the pretransplant nephrectomy group was 5200 ml for the 1C patient (Table 3). Thus, a patient with a TKV >5200 ml, regardless of Mayo imaging classification, may be more likely to undergo pretransplant nephrectomy.

Discussion

Most patients with ADPKD undergo early assessment and activation on the kidney transplantation wait list, however, no guidelines regarding evaluation for pretransplant nephrectomy exist (5). Most (91%) of our patients with ADPKD that underwent nephrectomy were classified as Mayo class 1D/E. These patients were younger males, with a heavier weight at the time of transplant.

Although we were limited by a small number of patients as a single center, our data suggest that patients with ADPKD who undergo nephrectomy are more likely to be younger males with Mayo 1D or 1E kidneys. In a former single-center, retrospective study, maximal kidney length alone was used to evaluate the need for nephrectomy in patients with ADPKD (7). This study showed that maximal kidney length was a strong predictor of nephrectomy status, but pointed out that a more accurate measure of kidney size, such as ht-TKV, could improve the selectivity of nephrectomy and could be useful in the clinical setting (7). Others have previously suggested the use of radiologic imaging and volumetry to guide decisions around nephrectomy (8).

We suggest the pretransplant evaluation for patients with ADPKD include either MRI or CT imaging of the abdomen, determination of TKV and hKL, and Mayo imaging classification at the time of listing. Patients with 1D or 1E kidneys should be further evaluated for perioperative nephrectomy. In addition, patients with an hKL >15.5 cm/m or a TKV >5200 ml may be candidates for nephrectomy. Patients with 1B or 1C kidneys may only need nephrectomy if there are

other clinical concerns, such as recurrent infection or hemorrhage (Figure 2).

Disclosures

N.K. Dahl is a principal investigator for ongoing trials with Kadmon, Sanofi, Reata, and Regulus, and is a consultant for Otsuka, and Natera. All remaining authors have nothing to disclose.

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Author Contributions

N.K. Dahl conceptualized the study and provided supervision; F. Dai and S. Klarman were responsible for methodology; F. Dai, S. Klarman, S. Rosenberg, S. Santovasi, and S. Virmani were responsible for data curation; F. Dai and S. Santovasi were responsible for formal analysis; S. Rosenberg wrote the original draft; S. Rosenberg, S. Santovasi, and S. Virmani were responsible for investigation; and all authors reviewed and edited the manuscript.

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