

Applying Artificial Intelligence to Quantify Body Composition on Abdominal CTs and Better Predict Kidney Transplantation Wait-List Mortality

CME

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Abstract

Background: Prekidney transplant evaluation routinely includes abdominal CT for presurgical vascular assessment. A wealth of body composition data are available from these CT examinations, but they remain an underused source of data, often missing from prognostication models, as these measurements require organ segmentation not routinely performed clinically by radiologists. We hypothesize that artificial intelligence facilitates accurate extraction of abdominal CT body composition data, allowing better prediction of outcomes.

Methods: We conducted a retrospective, single-center observational study of kidney transplant candidates wait-listed between January 1, 2007, and December 31, 2017, with available CT data. Validated deep learning models quantified body composition including fat, aortic calcification, bone density, and muscle mass. Logistic regression was used to compare body composition data to Expected Post-Transplant Survival Score (EPTS) as a predictor of 5-year wait-list mortality.

Results: In all, 899 patients were followed for a median 943 days (interquartile range 320-1,697). Of 899, 589 (65.5%) were men and 680 of 899 (75.6%) were White, non-Hispanic. Of 899, 167 patients (18.6%) died while on the waiting list. Myosteatosis (defined as the lowest tertile of muscle attenuation) and increased total aortic and abdominal calcification were associated with increased 5-year wait-list mortality. Logistic regression showed that imaging parameters performed similarly to EPTS at predicting 5-year wait-list mortality (area under receiver operating characteristic curve 0.70 [0.64-0.75] versus 0.67 [0.62-0.72], respectively), and combining body composition parameters with EPTS led to a slight improved survival prediction (area under receiver operating characteristic curve = 0.72, 95% confidence interval 0.66-0.76).

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Conclusions: Fully automated quantification of body composition in kidney transplant candidates is feasible. Myosteatosis and atherosclerosis are associated with 5-year wait-list mortality.

Key Words: Artificial intelligence, body composition, kidney, mortality, transplantation

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INTRODUCTION

Kidney transplantation remains the treatment of choice among patients with end-stage renal disease, offering lower mortality and improved quality of life, when compared with dialysis [1]. Deceased donor kidney transplants (DDKT) accounted for 78% of all renal allografts in the United States in 2022 [2]. Over the past decade, the median waiting time for a DDKT decreased to 4.05 years [3]; however, the 5-year survival after starting dialysis remains approximately 60% [4]. Identifying risk factors for wait-list mortality can inform transplant centers' decisions regarding donor-recipient matching and lead to better utilization of "marginal" kidneys, from older or higher-risk donors [5-8].

Most wait-listed patients undergo cross-sectional abdominal imaging early during the transplant evaluation process to assess the degree vascular calcification in the iliacs to determine surgical eligibility. A subset of patients also undergo abdominal imaging to decide on native kidney nephrectomy in polycystic kidney disease or assess for the presence of kidney malignancy [9]. In addition, CT scans may be obtained during health system encounters, such as emergency room visits, occurring while on the waiting list. These radiologic examinations represent an untapped resource measuring vascular calcifications, muscle size and attenuation, bone mineral density (BMD), and adipose tissue area and distribution pattern that are not routinely measured, due to time and the complexity of extracting these features through organ segmentation and financial limitations. Radiologic assessment of aortic calcification, myosteatosis, myopenia, and sarcopenia objectively measure biological phenomena such as atherosclerosis, frailty, and metabolic syndrome, which are associated with graft failure, as well as wait-list and posttransplant mortality [10-17].

Opportunistic screening [18], using automated algorithms to extract body composition data from examinations performed for any indication, has been successfully used to study cardiovascular disease [19], osteoporosis [20], and sarcopenia [21]. This fully automated approach is cost-effective [22] and does not represent an extra burden for radiologists. Furthermore, body composition biomarkers could be incorporated into machine-learning training datasets to optimize donor-recipient matching [23]. Semi-automated abdominal CT body composition measurements can predict kidney and liver transplant wait-list mortality [12,24].

However, this process is time intensive and requires the input of radiologists. In our study, we evaluate whether fully automated body composition measurements, using artificial intelligence, can predict kidney transplant 5-year wait-list mortality.

METHODS

Study Design

We conducted a single-center, retrospective, observational study of kidney transplant candidates added to the organ waiting list at a medical center from January 1st, 2007, through December 31st, 2017. We only included wait-listed individuals who had cross-sectional abdominal imaging performed for any indication, including but not limited to pretransplant evaluation. Patients were followed until they were removed from the waiting list, or until December 1st, 2023, whichever occurred earlier. We excluded transplant candidates removed from the waiting list for undocumented reasons, labeled as "other," or events that precluded further follow-up, such as "transferred to another center," "candidate removed in error," "refused transplant," or "unable to contact candidate." Patients with no confirmed status of death in the United Network for Organ Sharing database, including those with missing wait-list status, were considered living in our analyses due to the lack of verified mortality data, as reported in the Social Security Death Index. A detailed flowchart of selection criteria is depicted in Supplementary Figure 1.

Body Composition Measurements

One abdominal CT scan was chosen per patient. For patients that had multiple CT scans performed, we selected the imaging study that was performed at the earliest time point, in relation to the date of wait-listing. We used previously validated [25], fully automated artificial intelligence body composition tools (the tool is available for research upon reasonable request). The models measured muscle area and attenuation (mean Hounsfield Unit [HU]) at the L3 vertebral levels [21]; abdominal vascular and total aortic calcification (Agatston score) [19,26]; total, visceral, and subcutaneous adipose tissue area at the L1 vertebral level [27] and visceral-to-subcutaneous fat ratio; and BMD at the L1 vertebral body using standard and high-sensitivity attenuation (HU) [28]. We also measured the spleen attenuation to ascertain the absence of intravenous iodinated

 Table 1. Baseline characteristics of study participants

Characteristic	Cohort (n $=$ 899)	Dead (n = 167)	Alive $(n = 732)$	<i>P</i> Value
Age at transplantation, median (IQR)	58.0 (49.0-65.0)	63.0 (57.0-68.0)	56.5 (48.0-64.0)	<.005 [§]
Birth sex, n (%) Male Female	589 (65.5) 310 (34.5)	114 (68.3) 53 (31.7)	475 (64.9) 257 (35.1)	.408 .408 .408
Ethnicity, n (%) White Black Hispanic or Latino Asian American Indian or Alaska Native Multiracial	680 (75.6) 93 (10.3) 82 (9.1) 42 (4.7) 1 (0.1) 1 (0.1)	130 (77.8) 13 (7.8) 17 (10.2) 6 (3.6) 1 (0.6) 0 (0)	550 (75.1) 80 (10.9) 65 (8.9) 36 (4.9) 0 (0) 1 (0.1)	.149 [¶] .462 [¶] .229 [¶] .599 [¶] .548 [¶] .186 [¶] >.999 [¶]
Blood type, n (%) O A AB B B	400 (44.5) 342 (38.0) 37 (4.1) 120 (13.3)	76 (45.5) 66 (39.5) 4 (2.4) 21 (12.6)	324 (44.3) 276 (37.7) 33 (4.5) 99 (13.5)	.267 [¶] .770 [§] .663 [§] .281 [¶] .745 [§] .146 [§]
BMI at listing, median (IQR) Calculated PRA at listing, median (IQR)*	28.0 (24.3-32.5) 0 (0-0)	27.8 (25.0-33.0) 0 (0-0)	28.0 (24.1-32.2) 0 (0-0)	.631 [§]
Calculated EPTS at listing, median (IQR)	0.4 (0.2-0.6)	0.6 (0.4-0.7)	0.3 (0.2-0.6)	<.005
On dialysis at listing, n (%) Yes No	707 (78.6) 192 (21.4)	144 (86.2) 23 (13.8)	563 (76.9) 169 (23.1)	800. 800. 800.
Diabetes at listing, n (%) Yes No	707 (78.6) 192 (21.4)	144 (86.2) 23 (13.8)	563 (76.9) 169 (23.1)	<.001 <.001 <.001 <.001 <.001 <
PVD at listing, n (%) [†] No Yes Unknown	765 (85.2) 103 (11.5) 30 (3.3)	141 (84.4) 16 (9.6) 10 (6.0)	624 (85.4) 87 (11.9) 20 (2.7)	.036 [¶] .790 [∥] .399 [∥] .052 [¶]
Previous transplants, n (%) 0 1 2 3 4	784 (87.2) 97 (10.8) 16 (1.8) 1 (0.1) 1 (0.1)	142 (85.0) 23 (13.8) 2 (1.2) 0 (0) 0 (0)	642 (87.7) 74 (10.1) 14 (1.9) 1 (0.1) 1 (0.1)	.213 [¶] .350 .169 .750 [¶] >.999 [¶] >.999 [¶]

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Primary diagnosis at listing, n (%)	()	/>		.002¶
Diabetes	268 (29.8)	69 (41.3)	199 (27.2)	<.005 [∥]
Glomerular disease	128 (14.2)	15 (9.0)	113 (15.4)	.031
Hypertensive nephrosclerosis	106 (11.8)	22 (13.2)	84 (11.5)	.539
Hepatorenal syndrome	27 (3.0)	7 (4.2)	20 (2.7)	.317 [¶]
Polycystic kidneys	87 (9.7)	11 (6.6)	76 (10.4)	.134
Obstruction	19 (2.1)	0 (0)	19 (2.6)	.034 [¶]
Retransplant or graft failure	26 (2.9)	4 (2.4)	22 (3.0)	.803 [¶]
Other	238 (26.5)	39 (23.4)	199 (27.2)	.311
Days on waiting list, including inactive time, median (IQR)	943.0 (320.0-1697.0)	1147.0 (612.5-1752.0)	860.0 (295.8-1678.8)	.012 [§]
Reason for removal from the waiting list [‡] , n (%)				<.001
Death	167 (19.2)	167 (100.0)	0 (0)	<.001
Also waiting for isolated organ; received kidney	3 (0.3)	0 (0)	3 (0.4)	>.999 [¶]
Candidate condition deteriorated, too sick for transplant	111 (12.8)	0 (0)	111 (15.8)	<.001
Candidate condition improved; transplant not needed	5 (0.6)	0 (0)	5 (0.7)	.591 [¶]
Deceased donor kidney transplant	359 (41.4)	0 (0)	359 (51.2)	<.001
Liver donor kidney transplant	194 (22.4)	0 (0)	194 (27.7)	<.001
Transplant at another center (multilisted)	22 (2.5)	0 (0)	22 (3.1)	.022 [¶]
Transplanted in another country	1 (0.1)	0 (0)	1 (0.1)	>.999 [¶]
Changed to kidney pancreas transplant	6 (0.7)	0 (0)	6 (0.9)	.600 [¶]

BMI = body mass index; EPTS = estimated posttransplant survival; IQR = interquartile range; PRA = panel-reactive antibodies; PVD = peripheral vascular disease. *Eighteen missing values, total n = 881. † One missing value, total n = 898. ‡ Thirty-one missing values, total n = 868. ‡ Mann-Whitney U test. $^{\parallel}\chi^2$ test. ‡ Fisher's exact test.

Table 2. Summary data of automated body composition measurements among kidney transplantation candidates on the waiting list

Characteristic	Cohort (n = 899)	Dead (n = 167)	Alive (n = 732)	Missing Values	Adjusted <i>P</i> value	T3 versus T1 Odds Ratio (95% CI)	Adjusted <i>P</i> Value
L3 muscle attenuation (HU)	26.3 (16.2)	20.7 (15.5)	27.5 (16.1)	2	<.001	0.33 (0.21-0.53)	<.001
L3 muscle area (cm²)	154.6 (41.7)	156.4 (42.9)	154.1 (41.5)	2	>.999	0.96 (0.67-1.45)	>.999
Abdominal Agatston score	2718.9 (4621.9)	4016.2 (5889.1)	2422.9 (4230.1)	0	<.001	2.47 (1.58-3.88)	<.001
Total aortic Agatston score	4227.4 (6618.5)	6145.1 (8203.1)	3791.3 (6125.4)	m	<.001	2.36 (1.50-3.73)	.003
L1 BMD, standard attenuation (HU)	168.4 (61.2)	157.9 (53.0)	170.8 (62.8)	2	.120	0.61 (0.40- 0.93)	.261
L1 BMD, high-sensitivity attenuation (HU)	148.3 (52.0)	139.8 (45.2)	150.3 (53.3)	7	.380	0.60 (0.39- 0.91)	.195
L1 TAT (cm ²)	257.8 (162.9)	280.6 (180.6)	252.5 (158.3)	15	>.999	1.16 (0.77-1.74)	>.999
L1 VAT (cm ²)	125.9 (100.4)	142.4 (109.8)	122.2 (97.9)	15	096	1.47 (0.98-2.22)	.742
L1 SAT (cm ²)	131.8 (86.2)	138.2 (92.4)	130.4 (84.8)	15	>.999	1.18 (0.80-1.76)	>.999
L1 VATSAT ratio	1.0 (0.7)	1.1 (0.7)	1.0 (0.7)	17	>.999	1.24 (0.82-1.87)	>.999

Missing values represent instances in which the model failed to measure body composition. Missing values were excluded from analysis. Statistics by Mann-Whitney U test. Bonferroni adjustment applied to P values. BMD = bone mineral density; CI = confidence interval; HU = Hounsfield units; L1 SAT = subcutaneous adipose tissue area at the L1 vertebral level; L1 TAT = total adipose tissue Single variable logistic regression was used to obtain odds ratio of death comparing upper tertile (T3) versus lower tertile (T1) for each body composition parameter. All values represented as mean (5D), = visceral-to-subcutaneous fat ratio at the L1 vertebral level at the L1 vertebral level; L1 VATSAT ratio = visceral adipose tissue area area at the L1 vertebral level; L1

contrast administration, defined as spleen median HU < 60 [29]. We only analyzed noncontrasted CT scan series with slice thickness ≤ 5 mm. Body composition measurements outside the previously published reference ranges were attributed to model failure and were excluded [25] (Supplementary Table 1)

Statistical Analysis

Differences between continuous variables in the two groups were assessed using a Mann-Whitney test. Differences between categorical variables were assessed using a χ^2 test or Fisher's exact test, as appropriate. Univariable logistic regression was performed to obtain odds ratios (ORs) and 95% confidence intervals of death according to the upper tertile, as compared with lowest tertile, of body composition parameter. To study the association between 5-year wait-list mortality and body composition parameters, a single multivariable logistic regression was used to calculate the area under the receiver operating characteristic curves, with 95% confidence intervals computed via bootstrap resampling. In this analysis, the area under the receiver operating characteristic curve was computed for body composition parameters alone, body composition parameters in addition to estimated posttransplant survival (EPTS), and EPTS alone. Kaplan-Meier survival plots were generated, using the lifelines package, to study the association of 5-year survival probability on the transplant waiting list and body composition parameters (divided into tertiles). Pairwise log-rank test was used to compare tertiles. Missing values were dropped for individual body composition parameter analysis and only complete-case analyses were performed for logistic regression and timeto-event analyses. All P values were two-sided, with Bonferroni adjustment applied for multiple hypothesis testing. P values less than .05 were considered statistically significant. All graphs and statistics were generated using Python (version 3.9.13).

RESULTS

Patient Characteristics

The baseline characteristics of the study cohort are summarized in Table 1. In all, 899 patients met the inclusion criteria. Follow-up duration was the total number of days on the waiting list, including inactive time (median 943 days; interquartile range [IQR] 320-1697). Of 899 (65.5%) patients, 589 were men and 680 (75.6%) were White, non-Hispanic; the median age at listing was 58 years (IQR 49-65). The most common primary diagnosis at listing was diabetes (n = 268 of 899; 29.8%), and 707 of 899 (78.6%) transplant candidates were on dialysis, for a median duration of 0.9 years (IQR 0.37-1.83), before

wait-listing. Most candidates (n = 784 of 899; 87.2%) had never received a prior transplant. At the time of listing, median calculated EPTS and panel reactive antibodies scores were 40% (IQR 20.5-64.0) and 0 (IQR 0-0; range 0-81), respectively. Blood type O was the most frequent (n = 400 of 899; 44.5%). Among 868 patients with available United Network for Organ Sharing data on wait-list outcomes, death occurred in 167 of 868 patients (19.2%). In the surviving candidates, the most common reasons for removal from the waiting list included a deceased donor or a living donor kidney transplant at our center (n = 359 of 868, 41.4%; n = 194 of 868, 22.4%, respectively).

Body Composition Measurements and 5-Year Wait-List Mortality

Kidney transplant candidates who died while on the waiting list, compared with those alive at the end of follow-up, had a lower mean muscle attenuation at L3 (20.7 versus 27.5 HU; P < .001); increased mean abdominal and total aortic Agatston scores (4,016 versus 2,422, P < .001 and 6,145.1 versus 3,791.3, P < .001, respectively). There was no

statistically significant change in BMD at L1 (157.9 versus 170.8 HU, P = .120), visceral adipose tissue area at the L1 vertebral level area (142.4 versus 122.2 cm², P = .960), total adipose tissue area at the L1 vertebral level, or subcutaneous adipose tissue area at the L1 vertebral level (280.6 versus 252.5 cm², P > .999 and 138.2 versus 130.4 cm², P> .999, respectively; Table 2 and Fig. 1). The mean muscle area was similar between groups (156.4 versus 154.1 cm², P > .999). In patients with total aortic and abdominal Agatston score in the upper tertile, compared with those with values in the lowest tertile, the OR of 5-year mortality was higher for total aortic Agatston (OR 2.36 [1.50-3.73], P < .001 and abdominal Agatston score 2.47 [1.58-3.88], P < .001). Similarly, patients with higher muscle attenuation (less myosteatosis) at L3 had lower odds of 5-year mortality, compared with those with lower muscle attenuation (more myosteatosis; OR 0.33 (0.21-0.53), P < .001)

We sought to further study the association between 5-year wait-list mortality and body composition by dividing into tertiles the parameters that varied significantly among the study groups. We defined myosteatosis

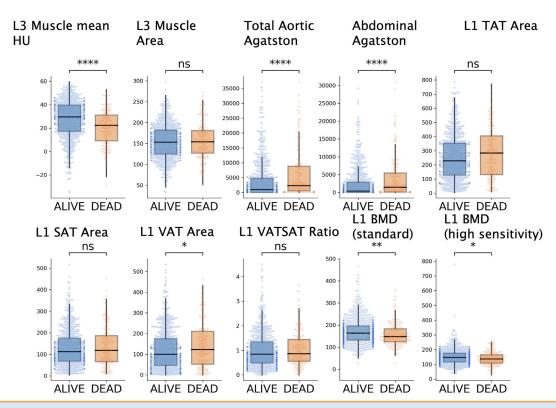


Fig. 1. Box-and-dot plots of body composition parameters stratified by outcome on kidney transplant waiting list. Box plots showing median and interquartile range. Dots represent individual measurements. Statistics using Mann Whitney. P * P < .05, **P = 0.01-0.001, ****P < .0001. n = 167 dead, n = 732 alive. BMD = bone mineral density; HU = Hounsfield units; L1 SAT = subcutaneous adipose tissue area at the L1 vertebral level; L1 TAT = total adipose tissue area at the L1 vertebral level; L1 VATSAT ratio = visceral-to-subcutaneous fat ratio at the L1 vertebral level; ns = not significant.

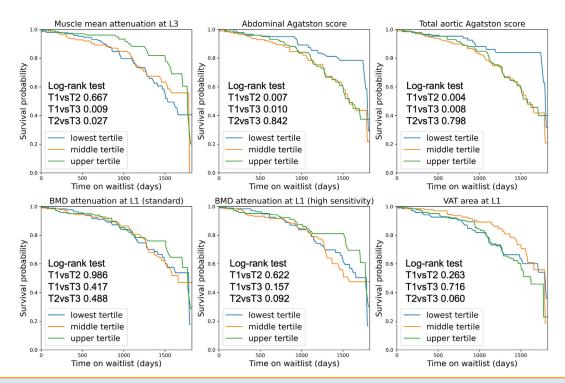


Fig. 2. Kaplan-Meier curves of 5-year survival on the kidney transplant waiting list according to body composition measurements by tertile. Statistics using pairwise log-rank test. BMD = bone mineral density; T1: lower tertile, T2: middle tertile, T3: upper tertile; VAT = visceral adipose tissue.

as the lowest tertile of muscle attenuation. Previous studies have defined ranges for myosteatosis in the general population [13] and patients with nondialysis chronic kidney disease [17], but not in dialysis-dependent

individuals, who represent most of our cohort. Similarly, we studied the effect of increased atherosclerosis (highest tertile of Agatston score), visceral adiposity (highest tertile of visceral adipose tissue area), and osteopenia (lowest

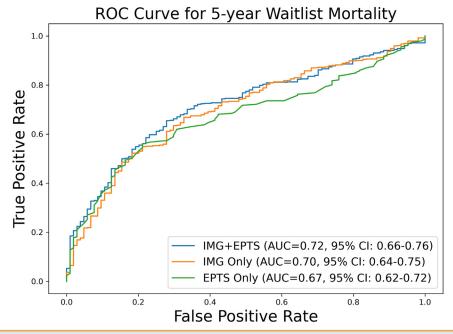


Fig. 3. Receiver operating characteristic (ROC) curve of the performance of imaging biomarkers (IMG) and EPTS as predictors of 5-year kidney transplant wait-list mortality. AUC = area under the ROC curve; CI = confidence interval; EPTS = expected posttransplant survival.

tertile of BMD). Myosteatosis and increased atherosclerosis were associated with increased 5-year wait-list mortality (Fig. 2).

Finally, we tested (1) whether the summation of body composition parameters can predict 5-year wait-list mortality and (2) how their performance compares with established clinical risk scores, such as EPTS. Combining EPTS and imaging biomarkers did not outperform either parameter in predicting 5-year mortality (area under receiver operating characteristic curve = 0.72 [95% confidence interval 0.66-0.76] for imaging + EPTS versus 0.70 [0.64-0.75] for imaging alone versus 0.67 [0.62-0.72] for EPTS alone) (Fig. 3).

DISCUSSION

To the best of our knowledge, our study is the first establishing the feasibility of fully automated quantification of body composition in kidney transplant wait-list candidates. In addition, we found that increased atherosclerosis and myosteatosis are associated with increased 5-year wait-list mortality. Quint et al [12] used manual segmentation, performed by a trained radiologist, of skeletal muscle area and muscle attenuation to study the relation between myopenia, myopenic obesity, sarcopenia, and myopenic obesity and mortality on the waiting list. Using a similar manual approach in liver transplant candidates, Ha et al showed that sarcopenic visceral obesity, defined as the presence of sarcopenia in the setting of elevated visceral to subcutaneous adipose tissue ratio, identified patients with a higher risk of wait-list mortality [24]. Our fully automated approach to capture body composition will result in a more expeditious approach and is less prone to interobserver variability. Future studies should test our approach in the posttransplant setting, since it has been shown that myosteatosis [30,31], and aorto-iliac calcification [32] are predictors of posttransplantation mortality.

The EPTS predicts the risk of posttransplant mortality based on recipient parameters and in external validation cohorts achieved a C-statistic of 0.68 [33,34]. The Organ Procurement and Transplantation Network kidney allocation system prioritizes matching deceased donor kidneys with "high-quality" kidneys with prolonged graft survival (Kidney Donor Performance Index [KDPI] < 20) with recipients having the lowest expected posttransplant mortality (EPTS < 20). However, the decision to match "marginal" kidneys, with higher KDPI or kidneys from older donors, to recipients, regardless of their EPTS, remains solely at the transplant provider's discretion. The complexity of donor-recipient matching, coupled with heterogenous

practices across US transplant centers, has resulted in a 25% discard rate of deceased donor kidneys (mean KDPI 51%) [35], whereas 4,900 patients died on the waiting list in 2023 (OPTN data), with DDKT recipients having a median of 17 organ offers [36]. There is an unmet need to improve our current organ allocation policies as the data show a survival benefit of receiving "marginal" kidneys over remaining on the waiting list [5,7,37]. Bae at al [6] developed a prediction tool for matching kidney transplant recipients and donors, based on EPTS and KDPI, respectively. If implemented, such prediction tools can decrease the organ shortage and wait-list mortality. In our cohort, imaging features performed similarly to EPTS, and there was a trend toward improved prediction of 5-year wait-list mortality when combining body composition parameters with EPTS. Our findings suggest a role for radiologic biomarkers as a complement and not a replacement to existing clinical scores.

Frailty, a clinical syndrome of age-related decline in physiological reserve and ability to overcome environmental stressors [38,39] is present in one in six kidney transplant candidates [15]. Frailty has been associated with worse pre- and posttransplantation outcomes including shorter time to death or permanent wait-list withdrawal [40], as well as prolonged duration of delayed graft function [15], respectively. However, there is no consensus on an ideal frailty metric [41], due to the multiple frailty assessment scores that have fair to moderate intertest agreement [40]. Radiologic assessment of sarcopenia, osteoporosis, myosteatosis, and adipose tissue distribution may provide an objective, multifaceted frailty metric [14,42]. Body composition measurements of abdominal CT of kidney transplant candidates revealed that myosteatosis and sarcopenia were associated with increased mortality [12]. Our study revealed the same association between increased mortality and myosteatosis. There was a nonstatistically significant trend toward increased mortality in patients with lower muscle mass, potentially due to a smaller effect size that was not detected in the small number of kidney transplant candidates in our study. Because of the absence of a frailty assessment at the time of listing, we were unable to test the correlation between radiologic and clinical measures of frailty [12]. Future studies evaluating the effects of prehabilitation before kidney transplantation should consider incorporating opportunistic radiologic frailty screening to identify responders [43,44].

Our study has multiple limitations. First, because of the retrospective observational design, we are unable to establish a causal link between body composition parameters and mortality. Second, because of missing imaging data, model failure, and excluding CT series with contrast and slice thickness >5 mm, our final cohort may not be fully representative of all wait-listed candidates. Finally, our fully automated model has been validated largely in asymptomatic adults. Because this is the first implementation in a cohort with renal disease awaiting transplant, future studies are needed to externally validate our findings.

TAKE-HOME POINTS

- We successfully applied a set of validated, fully automated body composition tools to a cohort of kidney transplant candidates on the waiting list.
- Myosteatosis and increased aortic calcifications were associated with increased 5-year wait-list mortality.
- Differences in BMD did not predict 5-year wait-list mortality.

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ADDITIONAL RESOURCES

Additional resources can be found online at: https://doi.org/10.1016/j.jacr.2025.01.004.

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