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Quantitative Abdominal Arterial Calcification Correlates with Kidney Transplant Waitlist Mortality

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Keywords
Abdominal arterial calcification · Kidney transplant · Waitlist · Mortality · End-stage kidney disease

Abstract

Introduction: The scarcity of available organs for kidney transplantation has resulted in a substantial waiting time for patients with end-stage kidney disease. This prolonged wait contributes to an increased risk of cardiovascular mortality. Calcification of large arteries is a high-risk factor in the development of cardiovascular diseases, and it is common among candidates for kidney transplant. The aim of this study was to correlate abdominal arterial calcification (AAC) score value with mortality on the waitlist. ***Methods:*** We modified the coronary calcium score and used it to quantitate the AAC. We conducted a retrospective clinical study of all adult patients who were listed for kidney transplant, between 2005 and 2015, and had abdominal computed tomography scan. Patients were divided into two groups: those who died on the waiting list group and those who survived on the waiting list group. ***Results:*** Each 1,000 increase in the AAC score value of the sum score of the abdominal aorta, bilateral common iliac, bilateral external iliac, and bilateral internal iliac was associated with increased risk of death (HR 1.034, 95% CI: 1.013, 1.055) ($p = 0.001$). This association remained significant even after adjusting for various patient characteristics, including age, tobacco use, diabetes, coronary artery disease, and dialysis status. ***Conclusion:*** The study highlights the potential value of the AAC score as a noninvasive imaging biomarker for kidney transplant waitlist patients. Incorporating the AAC scoring system into routine imaging reports could facilitate improved risk assessment and personalized care for kidney transplant candidates.

Introduction

More patients with end-stage kidney disease (ESKD) are waiting for a transplant than available organs [1]. This fact contributes to the significant waiting time before receiving

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a kidney transplant and the associated increased risk of cardiovascular mortality caused by ESKD [2, 3]. Transplant professionals are thus faced with the difficult task of timely and judiciously allocating limited organs to a vulnerable patients' population with a substantially increased risk of morbidity and mortality [4, 5]. The selection of appropriate recipients for kidney transplantation is a complex multidisciplinary process exacerbated by limited healthcare resources [6–8]. Furthermore, once patients are approved as kidney transplant candidates, they are often placed on the waitlist due to the lack of available living donors [9]. These waitlist patients must be continually re-evaluated to ensure they remain appropriate candidates, especially since many die on the waitlist and never have received an organ [10]. New cost-effective and readily available biomarkers are needed to assist transplant professionals in the evaluation and risk stratification of kidney transplant candidates to allocate organs wisely.

Cardiovascular pathology remains the most common cause of death among ESKD patients, both pre- and post-transplant [11–13]. Coronary artery calcification scoring has been utilized for the noninvasive evaluation of vascular calcification and atherosclerosis. It has been validated to provide prognostic risk for cardiovascular disease and all-cause mortality [14–16]. There has been similar interest in the use of abdominal artery vascular calcification as a prognostic factor for survival [17], and studies have shown an associated higher risk for cardiovascular events and all-cause mortality with abdominal aortic calcification, especially in patients with chronic kidney disease [18]. Abdominal imaging is a common component of the pre-transplant evaluation to assess a patient's surgical anatomy for organ vascular anastomosis. Our transplant center performs a non-contrast abdominal and pelvic CT as part of the transplant evaluation protocol. We hypothesized that applying a standardized abdominal arterial calcification (AAC) scoring for abdominal vasculature using available pre-transplant CT scans would serve as a novel imaging biomarker to assist transplant centers in the evaluation and recurring triage of kidney transplant candidates and waitlist patients. This study investigated the association between the arterial calcification score value of abdominal vessels and mortality in kidney waitlist patients.

Material and Methods

Study Population and Design

Our internal Institutional Review Board approved a retrospective study of patients from 2005 to 2015. Data were collected using the electronic medical record system by study investigators. Inclusion criteria consisted of the following: (1) all adults (greater than 18 years old) approved for a kidney transplant and placed on the transplant waiting list, (2) had a non-contrast abdominal and pelvic CT done within 2 years of listing. Exclusion criteria consisted of patients who were actively listed for combined organ transplants and/or listed for a second kidney transplant. Patients were divided into 2 groups: (i) group 1 – died on the waiting list (DWL), and (ii) group 2 – survived on the waiting list (SWL). The SWL group study-end-date was the date they received a transplant, and the DWL group study-end-date was their date of death.

AAC Score System

At our transplant center, the evaluation protocol includes a non-contrast abdominal and pelvic CT for every patient with either diabetes (regardless of age) or those older than 50 years of age. The most recent non-contrast abdominopelvic CT performed within 2 years before the listing date was selected for analysis. Images were obtained from Visage's picture archiving and communication system (version 7.1.14, Visage Imaging, Inc., San Diego, CA, USA). A modified Agatston method to measure coronary calcifications was applied to generate a scoring system based on the abdominal arteries (aorta, common iliac, external iliac, and internal iliac) [19, 20]. This was completed by marking arterial calcification with a semiautomated software package (syngo.via Client 5.1, Siemens Healthcare, Erlangen, Germany, or TeraRecon Aquarius iNtuition ver 4.4.13.P6, Durham, NC, USA) designed for quantifying coronary artery calcium by the Agatston method. In brief, the software automatically identifies calcium using a density threshold of 130 Hounsfield units or higher and measures the area of each calcification. The software calculated the score by multiplying each area of calcification by an established weighted value determined from the maximum Hounsfield unit in that calcification. Since the software identifies the calcium but cannot determine its anatomic location, a study researcher assigns the scored calcification to the appropriate anatomic labeling, with two study radiologists' subsequent review of labeling. The total calcium score was calculated as the sum of the calcium scores measured in the abdominal aorta (from beneath the celiac artery origin to the iliac bifurcation), the bilateral common iliac arteries, the bilateral internal iliac arteries (from iliac bifurcation to the first branch), and the external iliac arteries (from the iliac bifurcation to the inferior epigastric artery).

Variables

The outcomes of interest consisted of overall patient survival and mortality on the transplant waiting list. Follow-up time started at the time of listing and ended with death for the DWL group or transplantation for the SWL group.

Predictor variables included patient characteristics, which consisted of the following: age, sex, race, ethnicity, body weight at listing, body height at listing, BMI, cholesterol levels, albumin, troponin, hemoglobin, left ventricular ejection fraction percent, tobacco history, hypertension, diabetes mellitus, coronary artery disease (CAD), history of neurologic event, and dialysis status and time from dialysis to listing. Online supplementary Table 1 (see https://doi.org/10.1159/000539012) shows the causes of death among DWL patients with their respective frequencies.

Table 1. Baseline patient characteristics

	N	DWL (*N* = 151)	Received transplant (SWL) (*N* = 334)	HR (95% CI)	*p* value
Age at listing, years	485	60 (52, 67)	55 (45, 64)	1.026 (1.010, 1.042)	0.002
Sex	485				
Male		102 (67.5)	198 (59.3)	Reference	
Female		49 (32.5)	136 (40.7)	0.778 (0.552, 1.095)	0.15
Race	485				
White		79 (52.3)	195 (58.4)	Reference	
Black		60 (39.7)	111 (33.2)	0.790 (0.563, 1.107)	0.17
Asian		6 (4.0)	14 (4.2)	0.933 (0.406, 2.145)	0.87
Unknown		6 (4.0)	14 (4.2)	0.921 (0.401, 2.116)	0.85
BMI	483	28.0 (25.0, 32.7)	29.7 (25.8, 34.1)	0.974 (0.944, 1.005)	0.095
LDL	440	84.0 (63.5, 109.5)	89.0 (67.0, 116.0)	0.996 (0.991, 1.001)	0.097
HDL	456	48.0 (39.0, 59.0)	47.0 (38.0, 61.0)	1.003 (0.994, 1.012)	0.46
Triglyceride	455	124.0 (87.5, 180.5)	131.0 (90.0, 197.0)	1.000 (0.999, 1.002)	0.64
Albumin	443	4.1 (3.8, 4.4)	4.2 (3.8, 4.4)	0.761 (0.547, 1.059)	0.11
Troponin	319	0.0 (0.0, 0.1)	0.0 (0.0, 0.1)	3.078 (0.472, 20.086)	0.24
Hemoglobin	468	11.3 (10.1, 12.1)	11.2 (10.1, 12.3)	0.986 (0.898, 1.084)	0.78
LVEF	475	63.0 (59.0, 67.0)	63.0 (59.0, 67.0)	0.988 (0.968, 1.009)	0.26
Time from echo to listing, days	467	79.0 (41.5, 170.5)	62.5 (29.0, 114.0)	1.001 (1.000, 1.002)	0.15
Tobacco use at time of listing	485				
Never smoker		87 (57.6)	207 (62.0)	Reference	
Current or former smoker		64 (42.3)	127 (38.0)	1.631 (1.163, 2.289)	0.005
Hypertension	485	134 (88.7)	295 (88.3)	1.158 (0.696, 1.924)	0.57
Diabetes	484	72 (47.7)	76 (22.8)	1.830 (1.329, 2.520)	<0.001
CAD	485	35 (23.2)	43 (12.9)	1.507 (1.031, 2.203)	0.034
Dialysis at the time of listing	485	119 (78.8)	200 (59.9)	2.198 (1.486, 3.250)	<0.001

This table presents a comprehensive analysis of 485 patients who were on the waiting list for kidney transplantation during the follow-up period. They were divided to DWL and SWL groups and were compared based on demographic and clinical factors, including sex, race, body mass index (BMI), lipid profile, albumin levels, hemoglobin levels, LVEF, hypertension, and history of CAD at the time of listing. No significant association with increased risk of death was observed for any of these factors. However, it was noted that the DWL patients had a higher median age at the time of listing compared to the SWL patients. Additionally, smoking ($p = 0.005$), diabetes ($p < 0.001$), and being on dialysis at the time of listing ($p < 0.001$) were all found to be associated with a higher risk of death. HR, hazard ratio; BMI, basic metabolic index; LDL, low-density lipoprotein; HDL, high-density lipoprotein; LVEF, left-ventricle ejection fraction.

Statistical Analysis

Continuous variables were summarized as median (Q1, Q3), while categorical variables were reported as frequency (percentage). Survival after listing was estimated using the Kaplan-Meier (KM) method where censoring occurred on the date of transplant. KM estimates and 95% confidence intervals (CIs) were calculated at 1-year, 3-year, and 5-year survival. Median survival times and 95% CIs were estimated, and survival differences were assessed using log-rank tests. Associations of baseline characteristics with occurrence of death after listing were evaluated using unadjusted Cox proportional hazard regression models. Hazard ratios (HRs) and 95% CIs were estimated. Additionally, associations of AAC scores with mortality were evaluated using multivariate Cox proportional hazard regression models that were adjusted for age at listing, tobacco use, diabetes, CAD, and dialysis status at the time of listing. Optimal cut-points for each of the AAC scores were determined by using maximally selected rank statistics. These cutoff values correspond to the most significant difference in survival. All tests were two-sided with *p* value <0.05 considered statistically significant. Statistical analyses were performed using R Statistical Software (version 4.1.2; R Foundation for Statistical Computing, Vienna, Austria).

Table 2. Multivariable models were adjusted for age at listing, tobacco use, diabetes, CAD, and dialysis status at the time of listing

Calcification score	Multivariable analysis		
	patients, *n*	HR (95% CI)	*p* value
Aorta (1,000-point increase)	484	1.065 (1.025, 1.106)	0.001
Common iliac bilal (1,000-point increase)	467	1.085 (1.027, 1.145)	0.003
External iliac bilal (1,000-point increase)	455	1.189 (1.034, 1.367)	0.015
Internal iliac bilal (1,000-point increase)	457	1.132 (0.980, 1.307)	0.092
Total (1,000-point increase)	484	1.034 (1.013, 1.055)	0.001

This table presents the results of a multivariable Cox regression model assessing the association between calcification scores of selected abdominal large vessels and the risk of death in patients on the kidney transplantation waiting list. The total calcification score of selected abdominal large vessels demonstrated a significantly increased risk of death with each 1,000-unit increase in the AAC score value ($p = 0.001$). Similarly, individual large blood vessels showed a comparable association of increased risk of death with every 1,000-unit increase in their respective calcification score values. Specifically, the abdominal aorta exhibited a higher risk of death with each 1,000-unit increase in the calcification score value ($p = 0.001$). The bilateral internal iliac; an increased risk of death was observed with each 1,000-unit increase in the calcification score value; however, this association did not reach statistical significance ($p = 0.092$).

Table 3. Median and survival estimated cutoff AAC values of patients from DWL, SWL, and all patients

	Patients, *n*	DWL patients (*N* = 151)	SWL patients (*N* = 334)	All patients (*N* = 485)	Cutoff calcification value
		median AAC (Q1, Q3)			
Aorta	485	2,452.2 (757.0, 6,747.9)	247.6 (0.0, 1,974.5)	702.8 (9.2, 3,282.1)	2,185.1
Common iliac bilal	468	1,614.7 (438.3, 4,244.5)	89.7 (0.0, 1,005.0)	316.0 (0.0, 2,229.2)	2,129.0
External iliac bilal	456	47.7 (0.0, 287.4)	0.0 (0.0, 0.8)	0.0 (0.0, 76.7)	144.4
Internal iliac bilal	458	742.4 (221.2, 1,566.1)	62.4 (0.0, 494.2)	200.3 (0.0, 973.2)	186.0
Total Ca score	485	5,832.0 (1,658.8, 12,687.8)	639.9 (6.2, 4,064.7)	1,525.4 (124.4, 7,255.9)	4,807.4

This table shows the median values and interquartile ranges (Q1, Q3) of the total and individual blood vessel AAC scores for patients in the DWL group, SWL group, and the combined all-patient group. The results demonstrate that both the total AAC scores and individual blood vessel AAC scores were consistently higher among patients from the DWL group compared to patients from the SWL group. Furthermore, the total and individual AAC scores showed variations across all-patient groups, indicating potential differences in calcification patterns and severity among the studied cohorts. Cutoff calcification values were determined by using maximally selected rank statistics. These cutoff values correspond to the most significant difference in survival.

Results

Baseline Characteristics and Comorbidities

A total of 485 patients on the kidney transplant waitlist from 2005 to 2015 met the study criteria in this single-center study. Table 1 shows 151 DWL group patients, and 334 SWL group patients received kidney transplantation during the follow-up period. DWL and SWL patients were similar based on sex, race, BMI, lipid profile, albumin, hemoglobin, left ventricular EF, hypertension, and history of CAD at the time of listing, with no significant association with increased risk of death. However, DWL patients had a higher median age at the time of listing: 60 (IQR: 52, 67) versus 55 (IQR: 45, 64) with a significantly higher risk of death (HR 1.026, 95% CI: 1.010, 1.042) ($p = 0.002$) (Table 1). Smoking (current or former) was associated with a higher risk of death (HR 1.63, 95% CI: 1.16, 2.28) ($p = 0.005$), and 42.3% of patients from the DWL group were smokers versus 38.0% from the SWL group (Table 1). Diabetes showed a significantly

Table 4. KM survival based on the proposed cutoff AAC score value

	Total	Total events	1-year freedom from death	3-year freedom from death	5-year freedom from death	Median survival in years (95% CI)	*p* value
All	485	151	95% (93, 97)	73% (68, 79)	47% (41, 55)	4.81 (4.44, 5.32)	
Total calcium							<0.001
High	158	84	90.3% (85.6, 95.3)	59.3% (50.8, 69.2)	25.6% (17.2, 37.9)	3.33 (3.01, 4.41)	
Low	327	67	97.6% (95.8, 99.4)	81.9% (76.2, 88.0)	61.5% (53.2, 71.2)	5.86 (5.04, NA)	
Aorta							<0.001
High	155	80	90.0% (85.1, 95.1)	58.9% (50.2, 69.0)	25.3% (16.7, 38.4)	3.37 (3.01, 4.46)	
Low	330	71	97.7% (96.0, 99.4)	81.8% (76.2, 87.9)	60.4% (52.2, 69.9)	5.86 (5.04, 6.43)	
Common iliac bilal							<0.001
High	122	68	89.0% (83.4, 95.1)	56.3% (46.8, 67.8)	28.5% (19.3, 42.1)	3.19 (2.68, 4.26)	
Low	346	77	97.4% (95.6, 99.2)	81.2% (75.6, 87.1)	56.6% (48.2, 66.4)	5.48 (4.81, 6.43)	
External iliac bilal							<0.001
High	97	58	90.2% (84.3, 96.5)	53.4% (42.8, 66.6)	18.1% (10.1, 32.5)	3.08 (2.53, 3.48)	
Low	359	83	96.3% (94.2, 98.5)	80.4% (74.9, 86.3)	58.6% (50.5, 68.0)	5.73 (5.03, 6.64)	
Internal iliac bilal							<0.001
High	233	112	92.3% (88.7, 96.0)	63.7% (56.7, 71.7)	32.4% (24.7, 42.4)	4.05 (3.19, 4.68)	
Low	225	31	98.0% (96.1, 100.0)	87.7% (81.5, 94.3)	73.4% (63.8, 84.4)	6.64 (6.02, NA)	

This table presents the overall survival data for all patients based on AAC scores, demonstrating a median survival of 4.81 years. The 1-year, 3-year, and 5-year survival rates were found to be 95%, 73%, and 47%, respectively. The 1-year, 3-year, and 5-year survival rates were also significantly better for patients with individual blood vessel AAC scores lower than the respective cutoff points. Patients were further subgrouped based on their cutoff survival AAC score value, dividing them into two categories: those with AAC scores greater than the cutoff value versus those with AAC scores less than or equal to the cutoff value. The KM analysis revealed significantly longer patient survival for those with lower total AA.

increased risk of death among DWL patients (HR 1.83, 95% CI: 1.32, 2.52) ($p < 0.001$), and 47.7% from DWL were diabetics versus 22.8% of patients from SWL group (Table 1). Dialysis, in comparison with pre-emptive transplantation, at the time of listing was significantly associated with increased risk of death (HR 2.19, 95% CI: 1.48, 3.25) ($p < 0.001$). A total of 78% of patients from the DWL group were on dialysis at the time of listing versus 59.9% of SWL patients (Table 1).

AAC Score and Mortality Risk

In Table 2, the multivariable Cox regression model, adjusting for age at listing, tobacco use, diabetes, CAD, and dialysis status at the time of listing, showed the total calcification score of selected abdominal large vessels (the sum score of the abdominal aorta, bilateral common iliac, bilateral external iliac, and bilateral internal iliac) to have a significantly increased risk of death with each 1,000 increase in the AAC score value (HR 1.034, 95% CI: 1.013, 1.055) ($p = 0.001$) (Table 2). Individual large blood vessels showed the same association of increased risk of death with every 1,000 value increase in the calcification score value: the abdominal aorta (HR 1.065, 95% CI: 1.025, 1.106) ($p = 0.001$), the bilateral common iliac (HR 1.085, 95% CI: 1.027, 1.145) ($p = 0.003$), and bilateral external iliac (HR 1.189, 95% CI: 1.034, 1.367) ($p = 0.015$) (Table 2). The bilateral internal iliac showed the same association of increased, but not significant, risk of death with every 1,000 increase in calcification score value (HR 1.132, 95% CI: 0.98, 1.307) ($p = 0.092$) (Table 2).

The KM Survival Analysis

Table 3 shows the median value and interquartile range (Q1, Q3) of the total and individual blood vessel AAC score value of DWL, SWL, and all-patient groups. All individual blood vessel score values and total score values were higher among patients from the DWL group when compared to patients from the SWL group. The optimal cut-points correspond to the most significant difference in survival, for the calcification scores were determined using

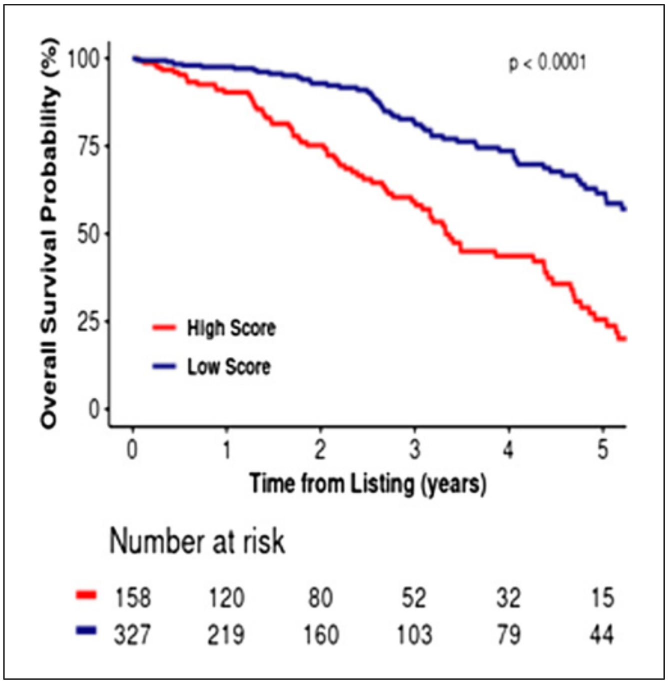

Fig. 1. Overall survival KM curve for total calcium score: the KM survival curves for patients based on their total AAC scores. The graph illustrates the survival probabilities over time for patients with lower AAC scores (below the cutoff value) and those with higher AAC scores (above the cutoff value). The analysis demonstrates that patients with lower total AAC scores experienced significantly longer median survival (5.86 years) compared to patients with higher AAC scores (3.33 years) ($p < 0.001$).

maximally selected rank statistics. The KM overall median survival was 4.81 years for all patients (Table 4). The 1-year, 3-year, and 5-year survival were 95%, 73%, and 47%, respectively. Patients were then subgrouped based on their cutoff survival AAC score value: greater than the cutoff versus less than or equal to the cutoff value (Table 4). Patient survival via KM analysis shown in Figure 1 was significantly longer for patients with a lower total AAC score value (5.86 years vs. 3.33 years, respectively) ($p < 0.001$) (Table 4). The 1-year, 3-year, and 5-year survival were also significantly better when the individual blood vessel AAC score was lower than the cutoff point value of individual blood vessels. When evaluating the abdominal aorta, the median survival in years was 5.86 for patients with a low AAC score versus 3.37 years for patients with a higher score ($p < 0.001$) (Table 4). When evaluating the bilateral common iliac artery AAC score, the median survival in years was 5.48 for patients with a low AAC score versus 3.19 years for patients with a higher score ($p < 0.001$) (Table 4). When evaluating the bilateral external iliac artery AAC score, the median survival in years was 5.73 for patients with a low AAC score versus 3.08 years for patients with a higher score ($p < 0.001$) (Table 4). When evaluating the bilateral internal iliac artery AAC score, the median survival in years was 6.64 for patients with a low AAC score versus 4.05 years for patients with a higher score ($p < 0.001$) (Table 4).

Discussion

We applied a modified coronary artery calcium score method to quantify the AAC. We showed a significant association between the value of large vessel calcification score and survival among patients listed for kidney transplantation. This finding is an added step toward developing a comprehensive survival biomarker profile to help identify patients with the greatest survival benefit once receiving a kidney transplant.

Medical providers have previously established the association between vascular calcification and atherosclerotic disease [21], and medical knowledge and technology have now reached a crossroads where the pathophysiologic disease processes can be detected by routine, reproducible, and cost-effective testing that is widely available. The novel application of a radiographic calcification score system to quantify the degree of AAC found on computed tomography in transplant patients may fulfill this pressing need. We and others have shown the AAC score to be associated with patients' survival and kidney allograft function after kidney transplant [20, 22–24]. However, the methods to evaluate arterial calcification used in prior studies were not universal and did not use a unified score system to correlate with patients' survival. By modifying the Agatston method, we developed a reproducible imaging biomarker that can be used to evaluate kidney transplant candidate survival risk before receiving the transplant.

The application of AAC scoring to the transplant population may carry far-reaching impacts on both the field of transplant and nephrology by individualizing care. With increasing advances in CT imaging technology and the application of artificial intelligence to augment diagnostic imaging, the AAC score can be readily calculated and incorporated as part of the standard radiology assessment report without increased demand on the existing healthcare workforce shortage [25].

The primary aim of our study was thus to investigate the ability of AAC score to predict mortality in eligible pre-transplant, ESKD candidates placed on the waiting list. Our study demonstrated that the AAC scoring is prognostic for mortality in eligible kidney transplant candidates on the waiting list. The AAC provides an additional imaging biomarker to help transplant center triage patients at high risk for deleterious outcomes in the setting of life-changing but limited organ availability.

There are several limitations to our study. First, it is noticeable that patients who received a kidney transplant were significantly younger than those who died on the transplant list. Patients who received a kidney transplant also were less likely to have been former or current smokers and have less comorbid diabetes mellitus, CAD. Further, they were more likely to be on dialysis at the time of listing. Aging and these comorbidities are associated with increased vascular calcification [26, 27]. However, all of these factors were adjusted for in the Cox models. As this was a retrospective study and due to the referral patterns to a transplant center, there may have been unaccounted factors or missing data that preceded kidney transplant evaluation that may have affected the association between AAC and mortality. For instance, physicians can order a CT at any time of transplant evaluation based on concerns of perioperative risks. This for-indication rather than protocol CT may have inadvertently introduced bias. These limitations argue for the need for the AAC score to be validated by future studies.

In summary, this study demonstrates the probable use of a widely available, noninvasive, and reproducible, imaging biomarker through the AAC score that can serve as a prognostic tool for improved management of waitlist kidney transplant candidates. As this biomarker can be applied retrospectively, future studies are needed to validate its more widespread application in other clinical scenarios.

Conclusion

This study sheds light on the potential significance of the AAC score as a valuable noninvasive imaging biomarker for kidney transplant waitlist patients. The findings provide evidence that a higher AAC score, indicative of increased AAC, is associated with a higher risk of mortality among individuals awaiting kidney transplantation. Importantly, this association remains robust even after adjusting for various patient characteristics, including age, tobacco use, diabetes, CAD, and dialysis status. Moreover, the study highlights the feasibility of incorporating the AAC scoring system into routine imaging reports, making it accessible and practical for healthcare professionals. This step toward personalized risk assessment has the potential to enhance the management of kidney transplant candidates, optimize resource allocation, and ultimately improve patient outcomes.

Statement of Ethics

I confirm that the research described in this manuscript has been conducted in accordance with ethical principles outlined in the Declaration of Helsinki and has received approval from the Institutional Review Board at our institution. The Mayo Clinic Institutional Review Board waived the requirement for informed consent. This study protocol was reviewed and approved by the Mayo Clinic Internal Review Board, Approval No. [21-005015].

Conflict of Interest Statement

The authors have no conflicts of interest to report.

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Author Contributions

Tambi Jarmi, MD, designed and formulated the hypothesis; provided overall supervision and guidance throughout the research project; played a key role in the conceptualization and design of the study, ensuring its scientific rigor and relevance; also contributed significantly to the interpretation of the results; and provided critical feedback during the manuscript drafting and revision process. Tareq Hanouneh, MD, played a pivotal role in conceptualizing and designing the research project; conducted extensive data collection; and performed the calcification scoring, contributing significantly to the interpretation of the findings and writing the manuscript. Michael Mao, MD, made significant contributions to various aspects of the research project; played a pivotal role in the design and execution of the study; and was responsible for coordinating the data collection process, ensuring adherence to the established protocols. Shennen Mao, MD, made significant contributions to various aspects of the research project; played a pivotal role in the design and execution of the study; and was responsible for coordinating the data collection process, ensuring adherence to the established protocols. Aaron C. Spaulding, PhD, and Hojjat Salehinejad, PhD: responsible for the statistical design and analyses, data collection and integrity, and ensuring accurate and meaningful interpretation of the results. Maia C. Youn, BA: in the pursuit of this research, gathering relevant and high-quality data was of utmost importance; demonstrated exceptional skills in designing data collection methods and implementing data acquisition processes; her attention to detail and meticulousness

ensured that the data collected were accurate and reliable, forming the foundation of our analysis. David M. Sella, MD, and Lauren Alexander, MD: responsible for the modification of the coronary calcium score and development of the applied abdominal vascular calcification score system. Houssam Farres, MD, designed and formulated the hypothesis; provided overall supervision and guidance throughout the research project; contributed significantly to the interpretation of the results; and provided critical feedback during the manuscript drafting and revision process. Emily C. Craver, Ms., played a pivotal role in addressing queries raised by the reviewers, providing insightful responses that enhanced the clarity and rigor of the manuscript, and furthermore, created the cause of death table.

Data Availability Statement

The data that support the findings of this study are not publicly available due to HIPAA guidelines, but are available from Tambi Jarmi, MD, upon reasonable request.

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