Application of a Novel CT-Based Iliac Artery Calcification Scoring System for Predicting Renal Transplant Outcomes

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OBJECTIVE. The objective of our study was to assess whether the degree and distribution of iliac artery calcifications as determined by a CT-based calcium scoring system correlates with outcomes after renal transplant.

MATERIALS AND METHODS. A retrospective review of renal transplant recipients who underwent CT of the pelvis within 2 years before surgery yielded 131 patients: 75 men and 56 women with a mean age of 52 years. Three radiologists assigned a separate semiquantitative score for calcification length, circumferential involvement, and morphology for the common iliac arteries and for the external iliac arteries. The operative and clinical notes were reviewed to determine which iliac arterial segment was used for anastomosis, the complexity of the operation, and whether delayed graft function (DGF) occurred. Renal allograft survival and patient survival were calculated using the Kaplan-Meier technique.

RESULTS. Excellent interobserver agreement was noted for each calcification score category. The common iliac arteries showed significantly higher average calcification scores than the external iliac arteries for all categories. Advanced age and diabetes mellitus were independently predictive of higher scores in each category, whereas hypertension, cigarette smoking, hyperlipidemia, and sex were not. Based on multivariate analysis, only the calcification morphology score of the arterial segment used for anastomosis was independently predictive of a higher rate of surgical complexity and of DGF. None of the scores was predictive of graft or patient survival. However, patients with CT evidence of iliac arterial calcification had a lower 1-year survival after transplant than those who did not (92% vs 98%, respectively; $p = 0.05$).

CONCLUSION. Only the calcification morphology score of the arterial segment used for anastomosis was significantly predictive of surgical complexity and of DGF. Routine pretransplant CT for calcification scoring in patients of advanced age or those with diabetes mellitus may enable selection of the optimal artery for anastomosis to optimize outcomes.

Keywords: anastomosis, calcium scoring, renal transplant

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With more than 16,800 renal transplants performed in 2010 and more than 75,800 patients on the waiting list, a renal transplant is the most common solid organ transplant performed in the United States [1]. Given the large discrepancy between the number of recipients and the number of donors, all reasonable measures should be taken to optimize transplant outcomes.

Arterial calcifications are commonly encountered in patients with chronic kidney disease (CKD) [2, 3]. The pathogenesis is multifactorial and includes the sequelae of hyperparathyroidism, diabetes mellitus, cigarette smoking, hypercholesterolemia, and advanced age [3]. Higher degrees of arterial calcifications based on a subjective rating scale were shown to result in significantly higher rates of technical failure of arterial anastomosis creation in patients with end-stage renal disease undergoing arteriovenous thigh graft creation for hemodialysis access [4]. The degree of iliac arterial calcification assessed on conventional radiographs was also shown to be correlated with significantly shorter allograft survival, significantly more intraoperative vascular complications, and a significantly lower 5-year survival rate [5]. However, the sensitivity and specificity of pelvic radiography for the assessment of iliac arterial calcifications have been reported to be unreliable [6]. Although CT has been reported to be the most accurate test for the assessment of iliac arterial calcifications in renal transplant candidates [7], correlation of CT findings of iliac arterial calcifications correlation on renal transplant outcomes has not been performed to date.

Multiple society guidelines for the pretransplant evaluation of renal transplant candidates include a large assortment of screening measures involving nearly all organ systems and a variety of modalities; however, the recommendations for radiologic screening are vague and sparse [7, 8]. Although scattered reports suggest the possibility that arterial calcifications may affect renal transplant outcomes [5, 6], the scoring systems are vague and thus are difficult to implement. Therefore, the purpose of this study was to assess whether the degree and distribution of iliac artery calcifications determined by radiologists using a CT-based calcium scoring system correlate with outcomes after renal transplant.

Materials and Methods

Patient Population

This retrospective study was approved by our institutional review board. A waiver of informed consent was obtained. Review of the patient database at our institution revealed that 402 patients underwent renal transplant between February 2005 and September 2013. Of these patients, 131 patients (75 men and 56 women) underwent CT of the pelvis within 2 years before transplant, thus constituting our study population. The mean age of the patient population was 52 years (age range, 28–74 years). Clinical records were reviewed to assess demographic variables (age and sex), comorbidities (hypertension, diabetes mellitus, cigarette smoking, and hyperlipidemia), transplant outcomes (delayed graft function [DGF] and graft survival), and patient survival.

TABLE 1: Calcification Scoring System Detailing the Three Assessed Calcification Categories

Category and Score	Definition
Morphology	Greatest degree of calcification based on appearance and pattern
0	No calcifications
1	Thin linear calcifications ≤ 1 mm in maximal thickness (“eggshell” type)
2	Thick linear calcifications > 1 mm in maximal thickness but with convex margins throughout
3	Bulky calcifications > 2 mm in maximal thickness but with convex luminal margins
Circumference	Greatest percentage circumference involvement of arterial segment
0	No calcifications
1	1–25%
2	26–50%
3	51–75%
4	76–100%
Length	Percentage length involvement of arterial segment
0	No calcifications
1	1–25%
2	26–50%
3	51–75%
4	76–100%

Image Analysis

CT examinations were performed with (n = 53) or without (n = 78) contrast material using different techniques and for different indications. The CT images were independently analyzed by three radiologists who had 16, 8, and 4 years of experience interpreting cardiovascular imaging at the time of the study. A semiquantitative calcification scoring system was used to evaluate the degree and distribution patterns of iliac artery calcifications based on morphology, circumference, and length of involvement. The bilateral common iliac artery and external iliac artery were scored separately for each patient (Table 1 and Fig. 1). The calcification morphology was assigned a numeric score as follows on a scale of 0–3 (ranging from none to worst). For arterial segments with more than one classification of calcifications, the highest rating for a given arterial segment was assigned. The calcification circumference and length scores were assigned on the basis of the maximal cir-

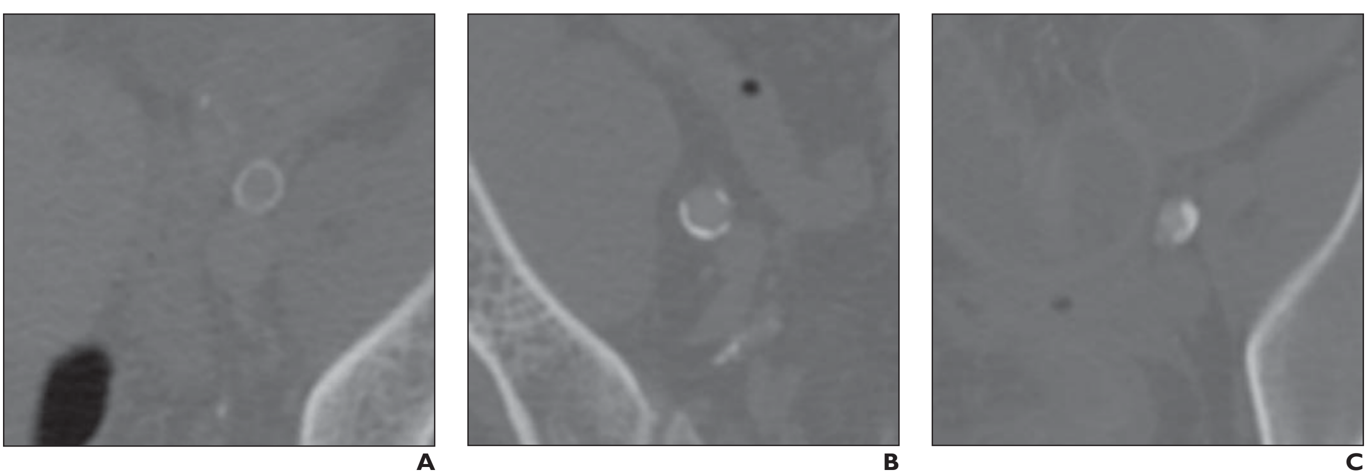

Fig. 1—CT scans show findings that are characteristic of different calcification morphology scores.
A, Thin linear calcifications are defined as score of 1. Patient is 63-year-old man.
B, Thick linear calcifications are defined as score of 2. Patient is 79-year-old man.
C, Bulky calcifications are defined as score of 3. Patient is 81-year-old man.

cumferential and length involvement, respectively, within an analyzed segment on a scale of 0–4 (ranging from none to worst). Only axial images obtained with a 5-mm slice thickness were reviewed. The reviewers used standard bone window settings (width, 3077 HU; level, 570 HU) on a clinical PACS system for evaluating the calcifications.

For the purposes of this study, the origin of the common iliac artery was defined as the inferior aspect of the aortic bifurcation. The margin of the common to external iliac artery was defined as the inferior aspect of the common iliac artery bifurcation. The inferior extent of the external iliac artery was defined as the level of the superior aspect of the femoral head.

Renal Transplant Technique

The kidney was routinely implanted in the iliac fossa with the vascular anastomosis performed to the external iliac vessels. However, if significant atherosclerosis of the external iliac vessels was present, the common iliac artery was used. Factors that determined the laterality of implantation (right or left) included the quality of the external iliac artery, the existence of a prior renal allograft, the presence of peripheral arterial disease in the lower extremity, and in rare instances the quality of the external iliac vein. Briefly, the technique is as follows: If the side of the implant had been predetermined with certainty, a standard retroperitoneal approach was used and the incision was placed in the iliac fossa. However, if there was significant atherosclerotic disease of the common and external iliac arteries based on any prior imaging or an abnormal finding at femoral pulse examination, a lower midline intraperitoneal approach was used. This approach allowed access to the common and external iliac arteries on both sides to determine the best site for implantation. The vascular anastomosis was created in a standard fashion using 5–0 and 6–0 polypropylene sutures for the venous and arterial anastomoses, respectively. The ureter was implanted into the urinary bladder using the modified Lich-Gregoir technique. The use of a drain and the use of a ureteric stent were determined by the surgeon.

Outcomes Analysis

The operative reports were reviewed for details pertaining to the choice of the artery for anastomosis, any difficulties related to the creation of the anastomosis, and the kidney donor source. The operation was categorized as high complexity when more than one arterial segment was inspected because of technical concerns for arterial adequacy, when intraoperative consultation with a vascular surgeon was obtained, or when any other adjunct arterial surgery was performed because of technical difficulty or arterial complications.

Posttransplant allograft function was assessed on the basis of the presence of DGF and allograft survival. DGF was defined as the need for dialysis within the first week after transplant. Graft failure was defined as a return to dialysis, death related to renal failure, or retransplant during the follow-up period. The electronic medical records at our institution—including inpatient and outpatient charts, imaging studies, and laboratory values—were retrospectively reviewed.

Statistical Analysis

All statistical analyses were performed using R statistical software, version 3.1 (The R Foundation). Interobserver agreement for calcification morphology, circumference, and length scores of the left and right common and external iliac arteries of each patient was measured using the Spearman correlation coefficient. Comparison of calcification scores among segments was performed using the Wilcoxon rank sum test. Multivariate linear regression analysis was used to determine whether demographic variables or comorbidities were independently associated with each of the three calcification scores. Logistic regression was used to test for an association between demographic variables and calcification scores and between comorbidities and calcification scores for the anastomosed artery and the binary outcomes of intraoperative complexity and DGF. To determine which calcification features were most important in predicting renal transplant outcomes, we performed multivariate logistic regression analysis including all three calcification features in the model and sex, age, and comorbidities. Graft survival and overall patient survival were analyzed using the Kaplan-Meier test. For estimation of graft survival, patients were censored if they died of reasons other than renal failure, were still alive at the time of data collection, or were lost to follow-up. For estimation of survival, patients were censored if they were still alive at the time of data collection or were lost to follow-up. Univariate analysis for survival was performed using the log-rank test. Tests for independent association between calcification scores and graft survival were performed using the Cox proportional hazards regression model. A p value ≤ 0.05 was considered to be statistically significant.

Results

Calcification Scoring System

Analysis of the bilateral common and external iliac arteries of 131 patients revealed that 90 patients (69%) had arterial calcification. Of the 524 arterial segments analyzed,

TABLE 2: Predictors of Higher Calcification Scores in Each Calcification Category

	Regression Coefficient Estimate		
Predictors	Reader 1	Reader 2	Reader 3
Length score			
Age	0.020 (0.02)	0.018 (0.05)	0.018 (0.046)
Male sex	0.051 (0.81)	−0.070 (0.74)	−0.16 (0.44)
Hypertension	0.33 (0.30)	0.31 (0.33)	−0.089 (0.78)
Diabetes mellitus	0.52 (0.013)	0.50 (0.018)	0.61 (0.003)
Cigarette smoking	0.15 (0.57)	0.32 (0.23)	0.32 (0.22)
Hyperlipidemia	−0.15 (0.47)	−0.089 (0.67)	0.011 (0.96)
Circumference score			
Age	0.021 (0.022)	0.019 (0.057)	0.015 (0.079)
Male sex	0.060 (0.78)	0.012 (0.96)	−0.089 (0.66)
Hypertension	0.28 (0.39)	0.35 (0.31)	−0.057 (0.85)
Diabetes mellitus	0.50 (0.019)	0.49 (0.030)	0.56 (0.006)
Cigarette smoking	0.23 (0.40)	0.35 (0.22)	0.032 (0.9)
Hyperlipidemia	−0.085 (0.69)	0.015 (0.95)	0.024 (0.91)
Morphology score			
Age	0.021 (0.004)	0.026 (0.001)	0.021 (< 0.001)
Male sex	0.12 (0.46)	0.029 (0.86)	0.047 (0.71)
Hypertension	0.27 (0.29)	0.25 (0.34)	0.088 (0.65)
Diabetes mellitus	0.35 (0.034)	0.33 (0.05)	0.28 (0.029)
Cigarette smoking	0.11 (0.58)	0.052 (0.81)	−0.026 (0.87)
Hyperlipidemia	−0.028 (0.86)	0.021 (0.90)	−0.17 (0.17)

Note—The values shown in parentheses are p values.

247 (47%) had calcifications: 82 (69%) right common, 82 (63%) left common, 43 (33%) right external, and 40 (31%) left external iliac arterial segments. There was excellent interobserver agreement among the three readers for the calcification morphology, calcification circumference, and calcification length scores assigned to each arterial segment; correlation coefficients ranged from 0.87 to 0.98. The average calcification scores for morphology, circumference, and length were significantly higher for the common iliac arteries (1.4, 1.3, and 1.4) than for the external iliac arteries (0.5, 0.6, and 0.6) ($p < 0.001$ for all three scores). The mean calcification scores were not significantly different when comparing the left and right sides for calcification morphology, circumference, and length scores ($p = 0.56$, 0.69, and 0.48, respectively).

Impact of Age, Sex, and Comorbidities

The comorbidities of the study population include hypertension (88%, $n = 115$), diabetes mellitus (52%, $n = 68$), cigarette smoking (21%, $n = 27$), and hyperlipidemia (51%, $n = 67$). An analysis of age, sex, hypertension, diabetes mellitus, cigarette smoking, and hyperlipidemia for each of the three calcification score categories revealed that advanced age and diabetes mellitus were independent predictors of higher scores in the calcification length, circumference, and morphology categories (Table 2). The other covariates were not significantly correlated with any of the calcification scores.

A multivariate analysis of the effect of age, sex, and comorbidities on surgical complexity, DGF, and allograft survival revealed that neither sex nor any of the comorbidities was an independent predictor of outcome. Although advanced age was an independent predictor of surgical complexity in this analysis, it was no longer a significant predictor when combined with calcification scores.

Surgical Complexity

The renal transplant surgery was rated as complex in 18% of the operations ($n = 23$). Based on univariate logistic regression models on the iliac arterial segment used for anastomosis, each of the three calcification scores was significantly predictive of surgical complexity for all three readers ($p < 0.001$ for all readers and all calcification scores) (Table 3). However, on multivariate analysis, only the calcification morphology score was found to be a significant independent predictor of surgical complexity (odds ratio range, 3.0–5.9; $p < 0.01$ for all three readers). Neither the calcification length score nor the calcification circumference score was independently predictive for any of the readers.

TABLE 3: Prediction of Operative Complexity Based on Univariate and Multivariate Logistic Regression Models Analyzing Calcification Morphology, Circumference, and Length Scores

	Odds Ratio for Surgical Complexity		
Score	Reader 1	Reader 2	Reader 3
Univariate analysis			
Morphology score	4.2 (< 0.001)	3.9 (< 0.001)	7.1 (< 0.001)
Circumference score	2.5 (< 0.001)	2.0 (< 0.001)	2.2 (< 0.001)
Length score	2.8 (< 0.001)	2.5 (< 0.001)	2.4 (< 0.001)
Multivariate analysis			
Morphology score	3.0 (0.007)	3.1 (0.002)	5.9 (< 0.001)
Circumference score	0.42 (0.30)	0.27 (0.12)	0.76 (0.59)
Length score	3.5 (0.12)	5.0 (0.067)	1.5 (0.39)

Note—The values shown in parentheses are *p* values.

TABLE 4: Prediction of Delayed Graft Function Based on Univariate and Multivariate Logistic Regression Models Analyzing Calcification Morphology, Circumference, and Length Scores

	Odds Ratio for Delayed Graft Function		
Score	Reader 1	Reader 2	Reader 3
Univariate analysis			
Morphology score	2.5 (0.00031)	1.9 (0.0084)	2.5 (0.0021)
Circumference score	1.8 (0.0021)	1.3 (0.098)	1.2 (0.42)
Length score	1.7 (0.0062)	1.4 (0.076)	1.3 (0.15)
Multivariate analysis			
Morphology score	2.6 (0.023)	2.1 (0.038)	4.8 (0.0036)
Circumference score	1.7 (0.34)	0.94 (0.91)	0.35 (0.16)
Length score	0.56 (0.32)	0.93 (0.90)	1.3 (0.62)

Note—The values shown in parentheses are *p* values.

Delayed Graft Function

DGF was identified in 13% of patients ($n = 17$) after renal transplant. When the iliac arterial segment used for anastomosis was analyzed in separate univariate logistic regression models, the circumferential extent and length of involvement were inconsistent predictors of DGF with variation among readers (Table 4), whereas the calcification morphology score was a significant predictor of DGF across all readers. On multivariate analysis, the morphology score was the only significant independent predictor of DGF.

Allograft Survival and Patient Survival

During the study period, 14 renal transplants failed and 21 patients died. None of the calcification scores of the iliac artery segment used for anastomosis was significantly correlated with graft survival on univariate analysis. The kidney graft was from a living related donor in 30 patients and a cadaveric donor in 131 patients. Univariate analysis showed no impact of graft type on graft survival.

Similarly, none of the calcification scores of the iliac arterial segment used for anastomosis correlated significantly with overall patient survival. However, when analyzing the entire bilateral common and external iliac arterial system, patients with no iliac arterial calcifications had a significantly longer survival than patients with any degree of iliac calcifications (3-year survival = 94% vs 87%, respectively; $p = 0.045$) (Fig. 2). The mean clinical follow-up interval after transplant was 34.1 months (interquartile range, 14.1–51.6 months).

Discussion

The presence of severe arterial calcifications is often assumed to be suboptimal for the creation of an arterial anastomosis, although there is a paucity of data in the literature confirming or characterizing this relationship. In the current study, we found that our proposed calcification scoring system was robust with high interobserver reliability. More important, when we analyzed the iliac arterial segments used for anastomosis creation, our data showed that there was a significant correlation between the presence of iliac arterial calcifications and surgical complexity and DGF and that the calcification morphology score was the only independent predictor of these negative outcomes.

Two prior studies have examined the impact of iliac arterial calcifications on renal transplant outcomes. Aitken et al. [5] retrospectively analyzed pelvic radiographs; in that study, reviewers graded the degree of calcification of the entire iliac arterial system as none, mild, moderate, or severe, but a description of the imaging criteria for each grade was not included in their study. They reported that patients with moderate or severe iliac calcifications had significantly higher rates of intraoperative vascular complications, graft loss, amputation, and death with a functioning transplant but that the presence of calcifications did not have any impact on DGF, renal function, or graft rejection. Aalten et al. [6] also retrospectively analyzed pelvic radiographs; for that study, reviewers graded the degree of calcification of the entire right iliac system and left iliac system as none, moderate, or severe and they excluded patients with patchy calcifications. Their results showed a significantly higher incidence of "problems with arterial anastomosis due to calcifications" in patients with any degree of calcifications versus those with no calcifications and showed no difference in graft or patient survival in patients with calcifications versus those without calcifications. Furthermore, these authors concluded that pelvic radiographs are unreliable for assessing the degree of calcification of the iliac system because of poor correlation of radiographic findings with intraoperative findings. Both of these studies are significantly limited by the analysis of the entire iliac system or entire ipsilateral iliac system for correlation with outcomes, whereas in our study we analyzed the specific iliac arterial segment used for anastomosis. Furthermore, their calcification scoring systems rely on radiographs and the criteria for the different scores of their calcification scoring systems are subjective and vague. Our study divided calcification characteristics into three distinct features—circumference, length, and morphology—and the scores for each feature were defined.

Lockhart et al. [4] described a pelvic arterial calcification grading system for correlation with arteriovenous thigh graft outcomes; they reported their grading system was correlated with a significantly higher rate of technical graft failure but not with a significant difference in 1-year graft patency rates. Their results are parallel to the results of the current study. However, although the pelvic arterial calcification grading system used in that study did include the degree of circumference involvement, it did not take into account the calcium morphology—which is the only factor to be independently associated with outcomes in our study. Furthermore, their calcification grading system was devised to apply a single grade to the entire bilateral iliac arterial system, whereas the one proposed in the current study was devised to apply a grade to individual arterial segments. By assessing individual arterial segments, one could theoretically compare arterial segments with one another, which may be useful for the selection of the artery that is best suited for the creation of an anastomosis.

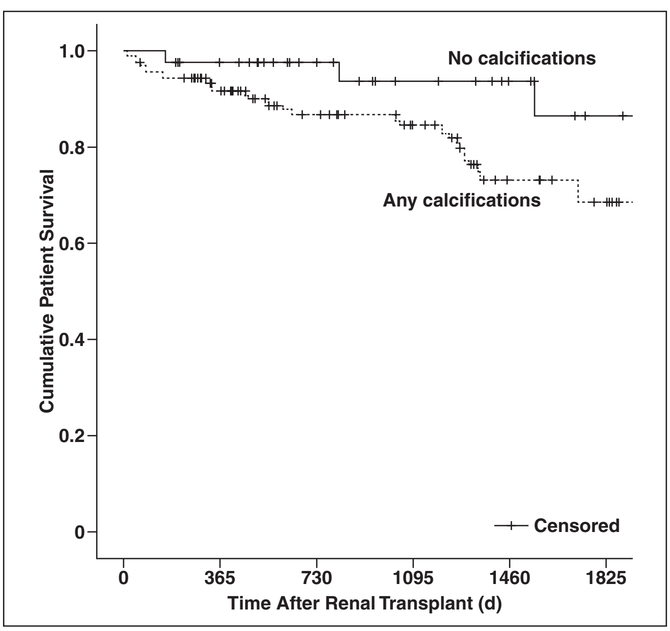

Fig. 2—Kaplan-Meier survival curve shows results for patients with calcifications of common or external iliac artery compared with those without calcifications ($p = 0.045$). For estimation of survival, patients were censored if they were still alive at data collection or were lost to follow-up.

The current guidelines for evaluation of renal transplant candidates recommend an extensive variety of tests and criteria based on the presence of malignancies, infectious processes, a history of substance abuse, cardiovascular status, and other comorbidities [8–11]. However, imaging screening is not considered a routine component of preprocedural evaluation, and the recommendations for imaging are vague as to which patients should undergo imaging before renal transplant, under what circumstances imaging should be performed, and which imaging modality should be used. Thus, it is not surprising that there is great variation among transplant centers in choosing which patients should be screened with imaging. Subesinghe et al. [12] evaluated 112 patients with imaging (MR angiography, $n = 101$ patients; contrast-enhanced angiography, $n = 11$ patients) and determined that the patients with abnormal imaging findings were significantly older than those with normal imaging findings (mean age, 60 vs 53 years, respectively) and that there was a higher prevalence of diabetes mellitus in the group of patients with abnormal imaging findings.

The finding that arterial calcification score is predictive of a higher risk of operative complexity is not surprising and is consistent with prior studies [5–7]. However, the finding that only a bulky morphology of calcifications is predictive of higher surgical complexity suggests that thin or thick linear calcifications throughout the arterial system may not be problematic. As described by Andres et al. [7], CT is an ideal modality for assessing the entire iliac arterial system to allow preoperative identification of the ideal target artery and the ideal site for the anastomosis.

DGF is a form of acute kidney injury in the immediate posttransplant period that results in oliguria, an increased risk of episodes of acute rejection, and decreased long-term patient survival [13]; the reported incidence of DGF is 27% [14]. Known risk factors for DGF include risk factors related to organ procurement, the donor, and the recipient [13, 15]. DGF also results in increased morbidity, increased cost, prolonged hospital stay, and the necessity for dialysis [16]. Therefore, the predictors of DGF and the measures to avoid it are important for optimizing renal transplant outcomes. The results of our study showed that a higher calcification morphology score of the recipient iliac artery was a significant independent predictor of DGF, whereas the overall score of the bilateral iliac arteries was not. Similarly, Aitken et al. [5] reported no correlation between overall iliac arterial calcification (based on common, internal, and external iliac arteries) as assessed on conventional radiography and DGF, although they did not specifically assess for any correlation between calcification of the recipient iliac artery and DGF. The explanation for our observation may be the overall significantly higher burden of calcification within the common iliac arteries as opposed to within the external iliac arteries, which are more commonly used. Furthermore, the artery selected for anastomosis may be more likely to be less calcified than the other arteries. Our findings suggest that CT evaluation of the external iliac arteries for calcification morphology in the pretransplant evaluation may be helpful for minimizing the risk of DGF.

Our analysis of the iliac arterial segment used for anastomosis creation showed that none of the calcification scores was independently predictive of graft survival or patient survival. Whereas Aalten et al. [6] also reported no correlation in either outcome, Aitken et al. [5] reported a higher incidence of graft loss and a higher risk of death in patients with moderate to severe calcifications of the entire iliac arterial system on radiographs. However, the fact that our analysis showed a small but statistically significantly lower survival in patients with any degree of iliac arterial calcification suggests that the reason for the differing results may be related to sample size or to calcification grading methods.

Our study is significantly limited by its retrospective nature. Because we analyzed only patients who underwent CT before renal transplant, there may be a selection bias in our study population. If patients with severe comorbidities are more likely to undergo CT, the prevalence of iliac arterial calcification may be overestimated. However, the association between calcification scores should not be skewed because of enrichment with a highly calcified population, particularly considering that approximately half of the study patients had no significant arterial calcifications. Although the proposed system characterizes each arterial segment as a whole, in reality, there may be a calcification-free segment that is amenable to the creation of an arterial anastomosis. The likelihood of this possibility may be implicit in segments with a low circumference score and low length score. Another limitation is the lack of CT protocol uniformity in the CT examinations used for the assessment of calcifications. Furthermore, the calcification criteria we used have not been previously validated or used in previously published studies. Finally, there are a variety of additional factors that may influence patient and graft outcomes, such as immunologic factors predisposing to rejection and donor graft factors that may lead to poorer graft quality, that we were unable to assess and include in our study population. However, our multivariate analysis that included both calcium scores and patient comorbidities helps to minimize confounders with the available data.

The proposed calcification scoring system was shown to be robust with a high interobserver correlation. The presence and features of calcifications of the iliac arterial segment used for anastomosis creation—specifically, the calcification morphology—were independently predictive of surgical complexity and DGF. Thus, pretransplant CT of the pelvic vasculature may be helpful for determining the optimal arterial segment for anastomosis. The nonpredictive results with calcification length and circumference scores suggest that widespread thin linear calcifications are inconsequential and do not need to be avoided, whereas segments containing bulky calcifications should be avoided or used with appropriate precautions. Because both advanced age and the presence of diabetes mellitus were shown to be independent predictors of higher calcification morphology scores, these two factors may be most appropriate in choosing the at-risk population in need of CT screening. Given the results of this study, a prospective evaluation of CT screening before renal transplant may be warranted to identify whether there are improvements in clinical outcome based on operating room time, surgical morbidity, and graft outcomes.

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