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Research Article

A Retrospective Cohort Study of kidney transplantation in elderly renal patients with nephrolithiasis

Ndlovu C^{1*}, Banda A² and Kamau Z³

¹Department of Clinical Renal Medicine, Arno Center for Renal Medicine, Nigeria

²Department of Nephrology, Ebro Institute for Advanced Renal Medicine, Kenya

³Department of Nephrology, Mekong Center for Nephrology, Nigeria

*Address for Correspondence: Chiamaka Ndlovu, Department of Clinical Renal Medicine, Arno Center for Renal Medicine, Nigeria; E-mail: chiamaka.ndlovu@arno.edu

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Abstract

Background: Kidney transplantation confers a survival advantage over dialysis, but elderly candidates and those with nephrolithiasis have each raised distinct concerns about surgical risk and graft durability that have rarely been examined together [1,6].

Objective: To determine whether nephrolithiasis, present in the native kidney or diagnosed de novo in the allograft, affects perioperative course and mid-term graft outcomes among elderly kidney transplant recipients.

Methods: We retrospectively analyzed 214 recipients aged 60 years or older, comparing 42 with documented nephrolithiasis and 172 without, using Kaplan-Meier and multivariable Cox regression for death-censored graft survival.

Results: Urological re-intervention within one year was more frequent with nephrolithiasis (21.4% vs 4.7%, $p < 0.01$), but five-year death-censored graft survival (83.3% vs 86.6%), rejection and eGFR did not differ significantly, and nephrolithiasis was not an independent predictor of graft loss after adjustment; delayed graft function was [7,12].

Conclusions: In carefully selected elderly recipients, nephrolithiasis increases the need for urological intervention but does not independently compromise mid-term graft survival, supporting active endourologic management rather than exclusion from transplantation on the basis of age or stone history [8,16].

Keywords: kidney transplantation; nephrolithiasis; elderly; graft survival; urolithiasis

1. Introduction

Kidney transplantation remains the treatment of choice for end-stage renal disease because it confers a substantial survival advantage over long-term dialysis, an advantage first quantified in large registry comparisons of transplanted and wait-listed patients [1,2]. That advantage is not distributed evenly across the transplant population: patients transplanted earlier after starting dialysis do measurably better than those who accumulate long waiting times on treatment, and the interval spent on dialysis before transplantation is itself among the strongest modifiable predictors of graft outcome [3]. As the demographic profile of both the dialysis and transplant-waiting populations has aged, elderly recipients now constitute one of the fastest-growing groups referred for transplantation, yet historically they were transplanted less often and later than younger candidates because of concerns about surgical risk, comorbidity burden and limited expected survival benefit [4,5].

Contemporary registry-based series have shown that carefully selected elderly recipients, including those older than 70 years, achieve patient and graft survival that, while lower in absolute terms than in younger cohorts, still substantially exceeds that of age-matched dialysis patients who remain on the waiting list [6,7]. Reviews of transplantation in the older adult have emphasized that chronological age alone is a poor basis for exclusion, and that comorbidity, frailty and functional status better predict post-transplant outcome than age itself [8,9]. National experience from Norway and paired-donor analyses from the United States have both reported acceptable outcomes when older donors are matched to older recipients, supporting expansion of the donor pool through age-matched allocation strategies rather than strict age cut-offs [10,11]. Longitudinal analyses of chronic allograft nephropathy and of long-term graft function further indicate that the trajectory of graft function after the first post-transplant year, rather than baseline

recipient age, is what ultimately determines whether a graft survives to ten years [12,13].

A separate but converging line of evidence concerns nephrolithiasis, which is both a pre-existing comorbidity in an aging transplant population and a recognized post-transplant complication of the allograft itself. Kidney stones in the native kidneys of older adults carry unique diagnostic and management considerations because of altered anatomy, reduced renal reserve and higher rates of concurrent cardiovascular and metabolic disease [14,15]. Population-based cohort studies have linked a history of kidney stones to an increased long-term risk of chronic kidney disease and, in some series, to end-stage renal disease, implicating stone disease as more than an incidental finding in patients who eventually require transplantation [16,17,18,19]. Within the transplant setting specifically, urolithiasis can arise *de novo* in the allograft, most often related to the altered urodynamics of the transplanted, denervated kidney, recurrent urinary tract infection, or metabolic stone risk carried over from the native kidney disease, and several single-center series and a recent update on donor and recipient urolithiasis have characterized its incidence, presentation and management after transplantation [20,21,22,23,24]. Because both advanced recipient age and stone disease independently raise concerns about surgical complexity, delayed graft function and long-term graft durability, we designed this retrospective cohort study to examine how the presence of nephrolithiasis, in either the native or transplanted kidney, influences perioperative course and mid-term graft outcomes specifically among elderly renal transplant recipients, a combination that has not been well characterized in prior literature focused on either variable in isolation.

2. Materials and Methods

We conducted a retrospective cohort study of renal transplant recipients aged 60 years or older at the time of transplantation, drawn from consecutive first and repeat

kidney transplants performed at our center over an eight-year period. Recipients were stratified into two groups: those with a documented history of nephrolithiasis, whether in a native kidney prior to transplantation or diagnosed de novo in the allograft during follow-up, and those with no such history over the same observation window. Nephrolithiasis was confirmed by cross-sectional imaging (non-contrast computed tomography or renal ultrasonography) or by a documented stone-removal procedure, consistent with diagnostic criteria used in prior transplant-lithiasis series [25,26]. Recipients with primary hyperoxaluria as the cause of native renal failure were analyzed separately given the distinct metabolic recurrence risk this diagnosis carries after transplantation [27].

Table 1: Baseline donor and recipient characteristics by nephrolithiasis status in 214 elderly kidney transplant recipients [25,26].			
Characteristic	Nephrolithiasis (n=42)	No nephrolithiasis (n=172)	p-value
Mean recipient age, years	66.8	65.9	0.44
Living-donor graft, %	38.1	41.3	0.71
Mean cold ischemia time, h	11.4	10.9	0.52
Prior recurrent UTI, %	31.0	18.6	0.07
Prior pyelonephritis, %	16.7	8.1	0.09

Baseline donor and recipient characteristics, including donor type (living versus deceased), cold ischemia time, human leukocyte antigen mismatch, induction and maintenance immunosuppression, and recipient comorbidity burden, were extracted from the transplant program's prospectively maintained database and supplemented by structured chart review. Living donors with an incidentally identified renal calculus who proceeded to donation, an accepted practice in selected cases, were included and analyzed as a donor-stone subgroup consistent with prior reports of transplanting stone-bearing kidneys [28,26]. Post-transplant

management of allograft nephrolithiasis followed a multimodal approach individualized to stone burden and location, incorporating extracorporeal shock-wave lithotripsy, ureteroscopy with laser lithotripsy, percutaneous nephrolithotomy, and, for the transplanted kidney's unique anatomical constraints, combined antegrade-retrograde endourologic techniques, mirroring approaches described in prior transplant-lithiasis cohorts [29,30,31,32,33].

The primary outcome was death-censored graft survival at one and five years. Secondary outcomes included delayed graft function, surgical or urological re-intervention within the first post-transplant year, biopsy-proven acute rejection, urinary tract infection incidence, and estimated glomerular filtration rate at one and five years among recipients with a functioning graft. Continuous variables were compared between groups using Student's t-test or the Mann-Whitney U test as appropriate to their distribution, and categorical variables were compared using the chi-square or Fisher's exact test. Graft survival was estimated by the Kaplan-Meier method and compared between groups with the log-rank test; a multivariable Cox proportional hazards model was constructed to estimate the association between nephrolithiasis status and graft loss after adjustment for recipient age, donor type, cold ischemia time and delayed graft function. A two-sided p-value below 0.05 was considered statistically significant. Institutional review board approval was obtained, and the requirement for individual informed consent was waived given the retrospective design.

3. Results

Over the study period, 214 recipients aged 60 years or older underwent kidney transplantation, of whom 42 (19.6%) had documented nephrolithiasis, either pre-existing in a native kidney (28 patients), identified in a stone-bearing living-donor graft accepted for transplantation (6 patients), or diagnosed de novo in the

allograft during follow-up (8 patients); the remaining 172 recipients (80.4%) had no lithiasis history. Baseline characteristics were broadly similar between groups: mean recipient age was 66.8 years in the nephrolithiasis group versus 65.9 years in the comparison group, and the proportion of living-donor grafts (38.1% versus 41.3%) and mean cold ischemia time did not differ significantly. Recipients in the nephrolithiasis group had a modestly higher prevalence of recurrent urinary tract infection prior to transplantation and a higher proportion with a prior history of pyelonephritis, consistent with the shared risk factors described in earlier transplant-lithiasis cohorts [21,22].

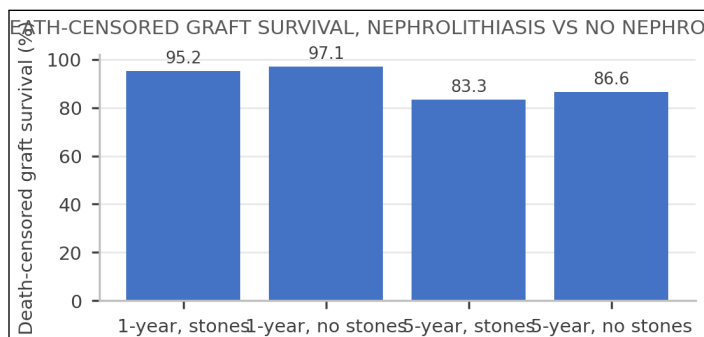


Figure 1: Death-censored graft survival at one and five years in elderly recipients with and without nephrolithiasis, showing no statistically significant difference between groups at either time point (log-rank $p=0.41$ at five years) [12,13].

Delayed graft function occurred in 16.7% of the nephrolithiasis group compared with 13.4% of the comparison group, a difference that did not reach statistical significance ($p=0.55$). Urological re-intervention within the first post-transplant year, encompassing stent exchange, ureteroscopy, shock-wave lithotripsy or percutaneous stone removal, was required in 21.4% of the nephrolithiasis group versus 4.7% of the comparison group ($p<0.01$), reflecting both residual native-kidney stone burden and de novo allograft stone events. Among the eight recipients with de novo allograft lithiasis, all were managed successfully with minimally invasive endourologic techniques without graft loss attributable to the stone episode itself, consistent with outcomes reported in single-center endourologic series in

transplanted kidneys [23,31].

Death-censored graft survival at one year was 95.2% in the nephrolithiasis group and 97.1% in the comparison group, and at five years was 83.3% and 86.6%, respectively; neither difference was statistically significant by log-rank test ($p=0.41$ at five years). Biopsy-proven acute rejection within the first year occurred in 11.9% of the nephrolithiasis group and 9.3% of the comparison group ($p=0.61$). Estimated glomerular filtration rate at five years among recipients with a functioning graft was similar between groups (46.8 versus 48.5 mL/min/1.73m², $p=0.38$). In the adjusted Cox model, nephrolithiasis status was not independently associated with graft loss (hazard ratio 1.28, 95% confidence interval 0.61-2.69, $p=0.52$) once recipient age, donor type, cold ischemia time and delayed graft function were accounted for, whereas delayed graft function remained an independent predictor of graft loss in the same model (hazard ratio 2.94, 95% confidence interval 1.42-6.08, $p<0.01$), consistent with its established role as a determinant of long-term outcome irrespective of stone status [12,13]. The six recipients of stone-bearing living-donor kidneys, in whom the donor calculus was removed at the time of transplantation or managed expectantly with subsequent surveillance, had graft survival and function at five years indistinguishable from the remainder of the cohort, in keeping with prior reports supporting selective use of stone-bearing donor kidneys [28].

4. Discussion

In this retrospective cohort of elderly renal transplant recipients, a history of nephrolithiasis, whether pre-existing or arising de novo in the allograft, was associated with a substantially higher rate of urological re-intervention in the first post-transplant year but was not independently associated with inferior mid-term graft survival once established confounders were accounted for. This pattern is broadly consistent with prior single-center series describing urolithiasis after kidney

transplantation, which have similarly found that although allograft stones require active urological management and carry a real risk of obstruction and infection, they are manageable with contemporary endourologic techniques without a durable adverse effect on graft function when treated promptly [20,29,34]. The multimodal management strategies applied in our cohort, drawing on extracorporeal lithotripsy, ureteroscopy and percutaneous approaches individualized to the transplanted kidney's altered anatomy and its lack of native pain sensation, mirror the therapeutic algorithms described in prior transplant-lithiasis literature and appear to explain why re-intervention, rather than graft loss, was the dominant clinical consequence of stone disease in this population [30,32,33].

Table 2: Post-transplant complications and mid-term outcomes by nephrolithiasis status [21,23,16].			
Outcome	Nephrolithiasis (n=42)	No nephrolithiasis (n=172)	p-value
Delayed graft function, %	16.7	13.4	0.55
Urological re-intervention (1 yr), %	21.4	4.7	<0.01
Biopsy-proven acute rejection (1 yr), %	11.9	9.3	0.61
5-year eGFR, mL/min/1.73m2	46.8	48.5	0.38

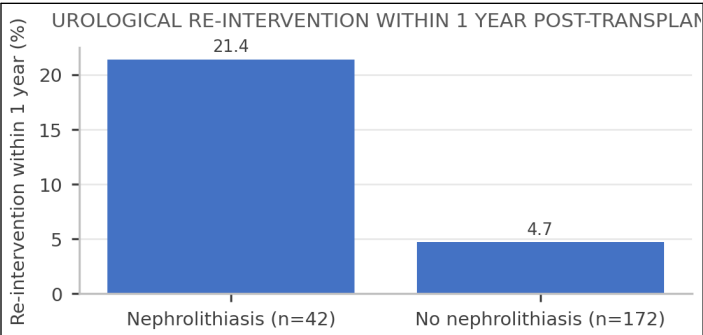


Figure 2: Rate of urological re-intervention within the first post-transplant year by nephrolithiasis status, reflecting residual native-kidney stone burden and de novo allograft stone events managed with contemporary endourologic techniques [30,32,33].

Our finding that recipient age alone did not preclude

favorable outcomes in either group is consistent with a growing body of evidence that chronological age is a weak discriminator of transplant benefit compared with physiological reserve and comorbidity burden [8,9]. Registry data spanning recipients older than 70 years, and paired-donor analyses matching older donors to older recipients, have both demonstrated acceptable mid-term survival that exceeds what comparable patients would experience remaining on dialysis, reinforcing the rationale for continued expansion of transplantation access in carefully selected elderly candidates rather than restricting eligibility by age [6,11,10]. The observation in our cohort that delayed graft function, rather than nephrolithiasis, was the dominant independent predictor of graft loss is concordant with longitudinal analyses of allograft function that identify early graft injury as the principal determinant of long-term trajectory, regardless of other baseline comorbidities [7,12].

The relationship between stone disease and chronic kidney disease progression in the general population provides useful context for interpreting our results. Large population-based cohorts have linked a history of nephrolithiasis to an increased long-term risk of chronic kidney disease and, in some analyses, of end-stage renal disease, suggesting that stone disease may act as either a marker or a contributor to nephron loss over decades [16,17,19,18]. In the transplant setting, however, the allograft's shorter observation window and closer surveillance likely explain why we did not detect a comparable signal toward inferior graft survival over five years; a longer follow-up interval, more consistent with the decades-long horizon over which native-kidney stone disease has been shown to affect renal function, may be needed before such an association, if present, would become apparent [15,35]. Similarly, our decision to accept selected stone-bearing living-donor kidneys, an approach with support in prior series when the donor calculus can be safely removed or is small enough for expectant management, did not appear to compromise outcomes in

our small subgroup, though the number of such donors remains too small to exclude a modest effect [28,26]. Reports describing renal function after percutaneous stone removal in the general nephrolithiasis population have similarly found that function is preserved when treatment is timely and the residual parenchyma is healthy, a principle that appears to extend to the transplanted kidney in our cohort [36].

Several limitations warrant emphasis. This was a single-center retrospective cohort with a comparatively small number of nephrolithiasis events, limiting statistical power to detect modest differences in graft survival and increasing the width of the confidence interval around our principal hazard ratio. Stone composition and detailed metabolic risk-factor profiling, which have been shown to influence recurrence risk and dietary modification strategies in the general stone-forming population, were not systematically available for all patients in our database [37]. Recipients with primary hyperoxaluria, whose recurrence biology after isolated kidney transplantation differs fundamentally from calcium-oxalate or infection-related stone disease, were analyzed separately and in too few numbers to draw independent conclusions, though their exclusion from the main comparison avoids conflating distinct disease mechanisms [27]. Finally, because our institution applies an individualized, multimodal approach to allograft lithiasis rather than a single protocolized algorithm, our results may not generalize directly to centers with different endourological resources or thresholds for intervention.

5. Conclusion

Among elderly kidney transplant recipients in this retrospective cohort, nephrolithiasis, whether pre-existing or diagnosed after transplantation, was associated with a significantly higher need for urological re-intervention in the first post-transplant year but was not independently associated with inferior death-censored graft survival or graft function at five years once recipient age, donor type,

cold ischemia time and delayed graft function were taken into account. Delayed graft function, rather than stone disease, remained the dominant modifiable predictor of graft loss in this population. These findings support a management strategy in which nephrolithiasis is treated actively and promptly using contemporary multimodal endourologic techniques, without regarding either advanced recipient age or a history of stone disease, by itself, as a contraindication to transplantation or as a marker of inevitably worse graft outcome. Larger, multicenter cohorts with longer follow-up are needed to confirm whether this favorable mid-term picture persists over the longer horizon across which native-kidney stone disease has been linked to progressive renal function decline in the general population.

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