Self-limited, sodium-dependent osmotic diuresis causes polyuria after living donor kidney transplantation

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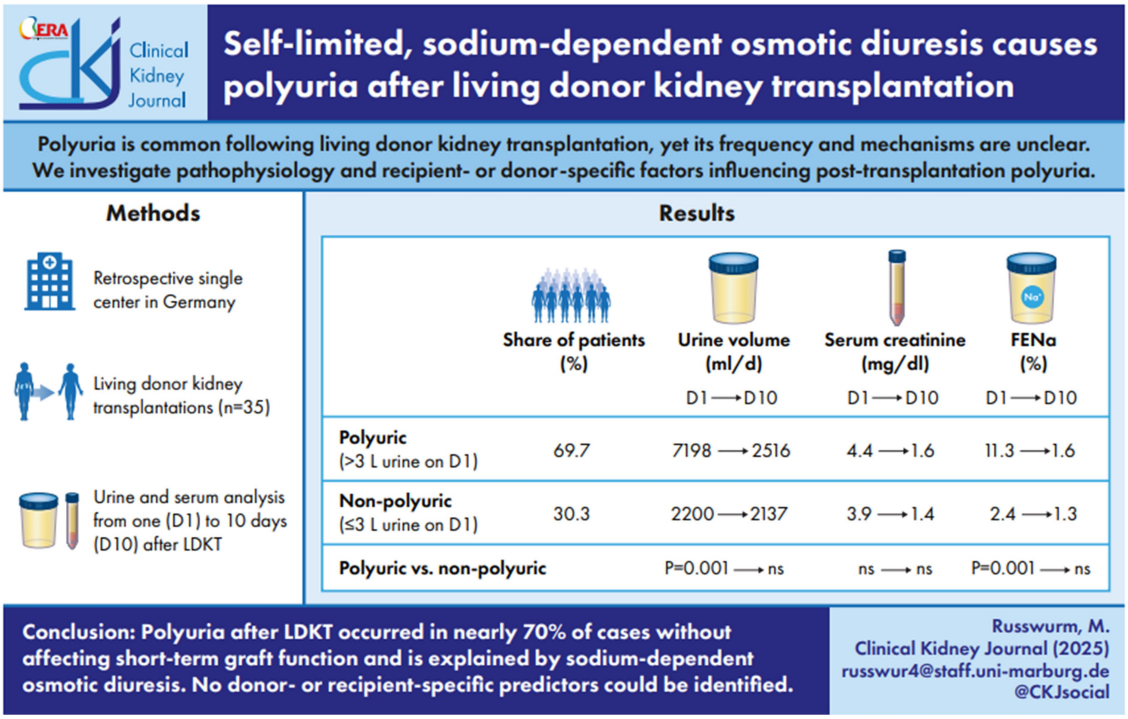
Running head: Polyuria after living donor kidney transplant

GRAPHICAL ABSTRACT



ABSTRACT

Background and hypothesis. Polyuria, defined as urine output exceeding 3 liters per day, is common following living donor kidney transplantation, yet its frequency and mechanisms are unclear. This study investigates the pathophysiology and potential recipient- or donor-specific factors influencing post-transplantation polyuria.

Methods. We retrospectively evaluated 35 consecutive living donor kidney transplantations performed at the University Medical Center Marburg between 2018 and 2024. Clinical and laboratory characteristics of recipients and donors as well as the daily routine blood tests and 24-hour urine collections of the first ten days post-transplantation were analyzed.

Results. Polyuria occurred in 69.7% of recipients on the first day post-transplantation, independent of residual diuresis, ischemia time, or donor pre-transplantation urine volume. Urine output decreased to normal within ten days, with no differences in serum creatinine or urinary kidney injury markers between polyuric and non-polyuric patients. Mechanistically, polyuria was driven by sodium-dependent

osmotic diuresis, with sodium excretion being the sole decisive driver of early post-transplantation urine volume.

Conclusions. Polyuria after living donor kidney transplantation occurred in nearly 70% of cases without affecting short-term graft function and is explained by sodium-dependent osmotic diuresis. No donor- or recipient-specific predictors could be identified. Careful volume management is crucial in managing this condition.

KEY LEARNING POINTS

What was known:

- Polyuria is common after living donor kidney transplantation, but its prevalence and underlying mechanisms were poorly understood.
- The roles of recipient and donor-specific factors in post-transplantation polyuria were unclear.
- There was a need to determine whether polyuria impacts short-term graft function or requires specific management strategies.

This study adds:

- Polyuria occurs in 69.7% of living donor kidney transplant recipients on the first day post-transplantation and resolves within ten days without affecting short-term graft function.
- Sodium-dependent osmotic diuresis is the primary mechanism driving early post-transplantation polyuria, rather than donor- or recipient-specific factors.
- Careful volume management is essential in addressing early post-transplantation polyuria.

Potential impact:

- This study provides reassurance that early post-transplantation polyuria does not harm short-term graft function.
- By identifying sodium excretion as the primary mechanism, clinicians can focus on tailored interventions to manage fluid balance effectively.
- These findings may influence perioperative fluid management protocols, potentially improving patient outcomes and resource allocation.

Keywords: living donor kidney transplantation, osmotic diuresis, polyuria

Introduction

In clinical practice, polyuria offers the opportunity to delve deep into renal physiology. Polyuria in adult patients is defined as daily urine excretion of more than 3 liters[1]. It can be further classified into water diuresis and solute (osmotic) diuresis. In water diuresis, high volumes of diluted and therefore low-osmolar urine (below 100 mosm/l) are excreted. In solute (osmotic) diuresis, the kidneys fail to reabsorb a significant proportion of the filtered osmolytes resulting in higher urine osmolality (above 300 mosm/l) as well as a total daily osmolar output above 1000 mosmol/day[2].

Polyuria is a common phenomenon in the early phase following living donor kidney transplantation (LDKT). Just over a decade after the first successful living donor kidney transplantation in 1954, Ogden et al. delineated characteristics of urine output in six patients in the immediate postoperative period[3]. Of those patients five out of six showed polyuria on the first day after allografting. The authors hypothesized that unclassified osmotic diuresis was the reason for high urine volumes observed in those patients. Noteworthily, patients in that study had been undergoing bilateral native nephrectomy simultaneously to renal allografting. At approximately the same time, Henderson et al. suggested defects in the proximal tubular transport systems for sodium and glucose as a mechanism for polyuria after LDKT[4] – notably after analyzing only four patients. Although polyuria appears to be common in clinical practice after LDKT, no empirically sound statement concerning true incidence can be made, as all available data only amount to case series at best[3,5].

Furthermore, no longitudinal study has either systematically collected and analyzed blood and urine parameters, or thoroughly analyzed recipient- and donor characteristics. Although there are various hypotheses as to why polyuria occurs after LDKT (increased fluid administration during and after surgery, direct or remote effects of diuretics, or transient nephrogenic diabetes insipidus), consequently, there is no generally accepted theory in the field regarding the etiology, pathophysiology and ramifications of polyuria after LDKT. Additionally, it is not known whether specific clinical signatures can be identified predicting the occurrence or resolution of polyuria after transplantation.

In our retrospective single-center analysis, we aimed to investigate if recipient- or donor-specific factors influence the development of polyuria after transplantation and how polyuria can be further characterized and understood.

Materials and Methods

We retrospectively evaluated 35 consecutive cases of living donor kidney transplantations between 2018 and 2024 in the University Medical Center Marburg, Germany. The study was approved by the institutional ethics review board (24-139 RS, Ethics Committee Philipps University Marburg) and conducted in accordance with the declaration of Helsinki. Given its retrospective nature, informed consent was not required.

Patients received at least one blood analysis before LDKT and consecutive daily blood analyses as well as 24h urine collections during the first ten days after transplantation as part of the clinical routine defined by standard operating procedures of the transplantation center. Standard immunosuppression in the initial phase after transplantation consisted of Tacrolimus, Mycophenolate mofetil, steroids and basiliximab. All kidney donors underwent a 24h urine collection examination before and after donation. All urine and serum parameters were measured in a certified clinical laboratory as part of the daily diagnostic routine.

Fractional excretion of sodium (FENa), urea (FEUrea), glucose (FEGlucose) and potassium (FEK) were calculated from blood and 24 h urine values using the following standard formula[6]: $FE(X) = 100\times ([X]_{Urine} \times [Creatinine]_{Plasma}) \div ([X]_{Plasma} \times [Creatinine]_{Urine})$. Endogenous creatinine clearance was calculated using the following standard formula[7,8]: Creatinine Clearance (ml/min) = (24h Urine Volume × $[Creatinine]_{Urine}$) ÷ ($[Creatinine]_{Serum}$ x 1440). Free Water Clearance was calculated as follows: $C_{water} = 24h\ Volume_{Urine} \times (1 - Osm_u/Osm_p)$ [9]. Plasma osmolality was calculated using the Worthley equation [10]: $P_{osm}=2x\ [Na]_{Plasma} + [Glucose]_{Plasma}/18 + [Urea]_{Plasma}/2.8$.

Statistical analysis was conducted using the GraphPad Prism software (version 10; GraphPad Software Inc., San Diego, CA, USA). Data are displayed as individual values or mean ± standard error of the mean (S.E.M). The data were subjected to a D'Agostino and Pearson test to ascertain whether they exhibited a normal distribution. Descriptive statistics for relevant patient-characteristics comparisons of living donor kidney transplantation patients with and without polyuria

on day one after transplantation are presented as the median and standard deviation (SD) or absolute numbers and corresponding percentages. We tested these comparisons of the continuous variables using the Mann-Whitney-U test or t-Test and the comparisons of categorical variables with the Fisher's exact as appropriate. We used 2way ANOVA with Sidak's multiple comparison test and simple linear regression where appropriate. A multiple linear regression was performed for urine volume on day one after transplantation as dependent variable including UVNa, UVUrea, UVK and UVGlucose. p values of < 0.05 were considered significant and marked by asterisks (*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$).

Results

Polyuria is common and is not contingent on pre-transplantation variables

After excluding two of the 35 consecutively studied cases due to missing 24-hour urine data from the first two days post-transplantation, 23 of the remaining 33 patients (69.70%) met the criteria for polyuria on day 1, defined as a urine volume exceeding 3000 ml. For subsequent analyses, patients were categorized into two groups based on their urine output on day one post-transplantation: polyuric (urine output > 3000 ml/24 hours) and non-polyuric (urine output ≤ 3000 ml/24 hours). Importantly, none of the patients received any diuretic medication, neither intraoperatively nor at any point during the first ten days following LDKT.

The first objective was to investigate whether any baseline characteristics of the recipient or donor correlated with post-transplantation polyuria. Regarding recipient baseline characteristics, no significant differences were observed between polyuric versus non-polyuric patients in terms of age (44.13 ± 12.67 vs. 51.30 ± 12.88 years, p=0.16), sex (27.3% females in the polyuric vs. 12.1% in the non-polyuric group, p=0.61), body mass index (25.41 ± 4.69 vs. 27.69 ± 5.10, p=0.23), or underlying kidney disease (**Table 1**). Neither the duration of dialysis treatment (18.52 ± 23.94 months vs. 9.8 ± 11.03 months, p=0.29) nor the volume of residual diuresis (1404 ± 825.53 ml vs. 1760 ± 1139.47 ml, p=0.33) differed significantly between the two groups. Lastly, total ischemia time was basically identical between polyuric versus non-polyuric patients (236.0 ± 37.8 min vs. 240.1 ± 28.9 min, p=0.77).

Next, we analyzed donor baseline characteristics to determine their impact on post-transplantation polyuria (**Table 2**). There were no significant differences in donor age (53.00 ± 9.73 vs. 55.60 ± 12.70 years, p=0.52), sex (65% female donors in the polyuric vs. 80% female donors in the non-polyuric group, p=0.39), or body weight (76.67 ± 15.59 vs. 74.29 ± 11.73 kg, p=0.67) between the two groups. Additionally, pre-transplantation donor renal function parameters showed no relevant differences: Donor diuresis (1869 ± 698 ml vs. 2160 ± 782 ml, p=0.30), serum creatinine (0.77 ± 0.13 mg/dl vs. 0.79 ± 0.09 mg/dl, p=0.62), and endogenous creatinine clearance (111.1 ± 51.52 ml/min vs. 115.7 ± 28.73 ml/min, p=0.79) were similar between polyuric versus non-polyuric recipients. Intraoperative fluid balance also did not differ between the two groups (**Figure S1**).

Simple linear regression analyses of urine volume on the first day after LDKT and pre-transplantation donor characteristics revealed no significant correlations. Donor age (R^2=0.018, p=0.45), body weight (R^2=0.001, p=0.89), pre-transplantation donor urine volume (R^2=0.019, p=0.45), serum creatinine (R^2=0.027, p=0.35), and pre-transplantation donor creatinine clearance (R^2=0.016, p=0.49) did not correlate with post-transplantation urine volume in recipients (**Table 3**).

Polyuria does not correlate with allograft markers

We analyzed blood and 24-hour urine parameters in detail for all 33 included patients. In the overall cohort, daily urine output decreased from 5684 ± 3767 ml on day one to 2412 ± 752.3 ml on day ten post-transplantation (**Figure 1A**). The mean volume of urine excreted by patients with polyuria on the first day of the study was 7198.39 ± 3547.83 ml, while the mean volume excreted by the non-polyuric group was 2200 ± 574 ml. Urine excretion differed significantly between the two groups for the first three days (**Figure 1B**). By day four, the difference in urine output was no longer significant (3721 ± 1490 ml/d vs. 1920 ± 561 ml/d, p=0.053). In contrast to diuresis, serum creatinine levels (**Figure 1C**) and endogenous creatinine clearance (**Figure 1D**) did not differ between polyuric and non-polyuric patients at any point. Additionally, we found no differences in urinary protein markers of glomerular or tubular injury. Total protein, albumin, and α1-microglobulin excretion, normalized by

urinary creatinine, were similar in polyuric versus non-polyuric patients during the early phase post-transplantation (**Figure S2**).

To address polyuria and prevent life-threatening dehydration, intravenous volume administration represents a crucial aspect of clinical care. In accordance with the high urine output observed during the first three days, there were notable differences in intravenous volume (Ringer's lactate) administration (**Figure 1E**). Interestingly, in our cohort of LDKT recipients, the resulting stable volume balance between fluid intake and urine output did not differ between the two groups (**Figure 1F**), resulting in a neutral balance by the second day post-transplantation. Furthermore, changes in body weight did not differ between the two groups (**Figure S3**). Thus, it can be stated with confidence that volume status was effectively maintained in our patients and did not affect renal water and solute balance.

Solute diuresis drives the polyuria

To characterize the observed polyuria and to evaluate the underlying (patho-)physiological processes, we analyzed urine osmolality and osmolyte excretion rates during the first ten days following LDKT. Significant differences in urine osmolality were found between polyuric and non-polyuric patients on the first two days post-transplantation (Day 1: 455 ± 123 mosmol/l vs. 677 ± 87 mosmol/l, p=0.019; Day 2: 452 ± 114 mosmol/l vs. 628 ± 143 mosmol/l, p=0.03) (**Figure 2A**). The urine osmolality of polyuric patients remained significantly above the 300 mosmol/l threshold and their osmolyte excretion rate exceeded 1 mosmol/l per minute (**Figure 2B**), indicating osmotic diuresis. Pronounced negative free water clearance in both groups indicated sufficient antidiuretic response to antidiuretic hormone (ADH), thus excluding water diuresis (**Figure 2C**).

Simple linear correlation analyses between urine volume and urine osmolyte excretion (UV 2Na2KUreaGlucose) on day one (**Figure 2D**) and day ten (**Figure 2E**) post-transplantation illustrated a highly significant direct linear correlation between urine volume and osmolyte excretion in polyuric patients on day one. However, this correlation was no longer present by day ten, indicating that osmotic diuresis had been resolved by then.

Osmotic polyuria is exclusively sodium-dependent

We continued our analysis by examining the urinary excretion of all osmolytes using a multiple linear regression model to explore the relationship between urine volume on day one post-transplantation and urinary sodium excretion (UVNa), potassium excretion (UVK), glucose excretion (UVGlucose), and urea excretion (UVUrea) (**Table 4**). Our results indicate that urinary sodium excretion is the sole significant predictor of solute-dependent urine volume on day one after living-donor kidney transplantation ($p \leq 0.0001$). Consistent with this finding, a highly significant linear correlation was observed between urinary sodium excretion and urine volume ($R^2 = 0.88$, $p \leq 0.0001$) in polyuric patients on day one (**Figure 3A**), while urinary urea excretion did not correlate with urine volume ($R^2 = 0.01$, $p = 0.59$) (**Figure 3B**). Analyses of urine solute composition revealed that in polyuric patients, sodium was the predominant osmolyte on the first day after transplantation, while urea was the main osmolyte in non-polyuric patients (**Figure 3C**). By day ten, only a weak correlation remained between urine volume and sodium excretion (**Figure 3D**), and urinary urea excretion still did not correlate with urine volume (**Figure 3E**). Additionally, urine osmolyte composition on day ten showed no differences between patients who were polyuric or non-polyuric after transplantation, with urea being the leading urinary solute in both groups (**Figure 3F**).

The critical role of renal sodium handling was further confirmed by significant differences in fractional sodium excretion (FENa) between polyuric and non-polyuric patients during the first two days post-transplantation (**Figure 3G**), while fractional excretion of urea (FEUrea) remained unchanged between the groups (**Figure 3H**). Total and fractional excretion of glucose (FEGlucose) and of potassium (FEK) did not differ between polyuric and non-polyuric patients (**Figure S4**). We calculated the ratio of polyuric to non-polyuric patients for FENa and FEUrea over the first ten days post-transplantation, showing that FENa is 4.71 ± 2.94 times higher in polyuric patients on day one, whereas FEUrea is not altered (**Figure 3I**). Despite high urinary sodium excretion in polyuric patients, serum concentrations of sodium serum osmolality were not altered in the two groups (**Figure S5**).

Discussion

Our data indicate that polyuria is common among living donor kidney transplant recipients. We were able to demonstrate that on the first day following transplantation, 69.70 % of patients met the criteria for polyuria with a urine volume exceeding 3000 ml per day. Polyuria had no influence on serum creatinine values or endogenous creatinine clearance, both of which indicated excellent transplantation function in both groups. As is common in LDKT[11], we did not observe delayed graft function in any recipient. It has been clearly shown that optimal fluid therapy reduces delayed graft function after kidney transplantation[12]. Hourly measurement of diuresis with consecutive hourly adjustment of the intravenous volume administration to guarantee optimal stability of the volume balance is considered as crucial part of post-transplantation care in our department. This rigorous volume management is reflected by similar overall volume balances in polyuric versus non-polyuric patients. It must be clearly stated that in both groups the infusion volume of Ringer's lactate was adjusted to the previous hourly diuresis. The conclusion that a high intravenous volume results in a high diuresis and thus a simplified explanation of the pathogenesis of polyuria is therefore not tenable. We interpret our data—showing similar volume balances, comparable changes in body weight, and equivalent creatinine clearance between both groups—as support for the notion that meticulous volume management is a crucial component of early post-transplantation care.

We investigated whether differences in baseline characteristics could be detected between recipients who exhibited polyuria on the first day and those who did not. Our cohort of LDKT recipients was very consistent with previous publications in terms of baseline characteristics (age, sex distribution)[13,14]. Our data indicate that recipient age, sex, and underlying kidney disease do not correlate with post-transplantation polyuria. Interestingly, there was no correlation between residual urine output prior to transplantation and post-transplantation polyuria. Unfortunately, we are unable to provide numeric data on volume status, such as central venous pressure or body composition measurements, which could further elucidate the influence of pre- and peri-transplant volume status on the observed effects[15]. Nevertheless, the comparable changes in body weight relative to pre-transplant values provide at least indirect evidence that the patients in both groups presented in a similar pre-transplant volume status.

We found no correlation between ischemia time and urine output on the occurrence of polyuria. In a mixed cohort with a 32.1% proportion of living donor kidneys, a correlation was observed between recipient age and urine output, as well as between ischemia time and urine output following transplantation[16]. From these data, it can be inferred that the 152 patients in the cohort who received a living donor kidney had an average urine output of 2.6 ml/kg/h on day one, which is comparable to the volumes observed in our study. Nevertheless, additional analyses concerning urine output and associated factors were not differentiated between deceased and living donor kidneys. Given the substantial evidence that prolonged periods of ischemia have deleterious effects on urine output and overall outcomes in deceased donor transplants[17,18], a combined analysis of these groups is of limited informative value and cannot be compared to living donor transplants.

Kidneys from living donors perform significantly better than those from deceased donors with a 5-year graft survival rate of 80.8% (for recipients aged 65 and older) and 90.0% (for recipients aged 18 to 34)[19]. Among shorter cold ischemia times, the better outcomes of living donor kidney transplants over deceased donor kidneys are caused by the high quality of the transplanted kidneys which are thoroughly assessed pre-transplantation[20]. At our transplantation center, a thorough evaluation of donors is conducted prior to transplantation, which extends beyond immunological characteristics and includes a comprehensive assessment of donor kidney function. Our analysis indicates that our donor cohort aligns well with other reported cohorts [13,21]. We could not identify donor-related predictors for polyuria, as neither donor age, urine output, nor creatinine clearance before transplantation correlated with post-transplantation polyuria. Following the KDIGO guidelines, "KDIGO Clinical Practice Guideline on the Evaluation and Care of Living Kidney Donors"[22], our transplantation center adopts the criteria of a GFR ≥ 90 mL/min/1.73 m² as acceptable for donation (candidates with a GFR of 70-89 mL/min/1.73 m² are evaluated individually based on their demographic and health profile). This ensures that only donors with (objectively) healthy kidneys are selected. According to our data, the existing differences in donor GFR within the normal range do not impact the occurrence of post-transplantation polyuria.

The question remained as to the underlying pathophysiology. Following the canonical classification of polyuria[2], our results show a sodium-dependent osmotic diuresis with urine osmolality over 450 mosmol/l and corresponding osmolyte

excretion of 2800 mosmol/d. Our findings revealed striking parallels to previous publications from the early days of kidney transplantation[3,4]. Free water clearance is defined as the difference between the total volume of urine excreted and the volume of urine that would be required to excrete the same amount of solutes in a solution with the same osmolarity as plasma[9]. A negative free water clearance as seen in our study in both, polyuric and non-polyuric patients, occurs when the kidneys are conserving water, resulting in concentrated urine with a higher osmolarity than plasma[23]. As this process depends on ADH, we interpret negative free water clearance in our patients as surrogate for adequate antidiuretic response given that ADH levels were not routinely assessed in our patients.

High fractional sodium excretion in polyuric patients indicates that reduced sodium reabsorption in the transplanted kidney drives tubular sodium-osmolyte accumulation and induces osmotic diuresis. These results once again challenge an oversimplified interpretation that infusion volume alone is the primary cause of polyuria. This explanation fails to account for the observed effects on fractional sodium excretion and cannot explain the discrepancy between fractional sodium excretion and fractional urea excretion. Consequently, large volumes of Ringer's lactate, with a sodium concentration of 131 mmol/L—lower than the serum sodium concentration—fail to induce sodium-dependent osmotic diuresis in the absence of pre-existing impairment in renal sodium handling. Identifying the exact transport process underlying reduced sodium reabsorption is challenging and requires a stepwise analysis of tubular sodium transport. Although our data does not permit a definitive identification of specific sodium transport defects, they allow narrowing down the possibilities. Approximately 66% of sodium reabsorption occurs in the proximal tubule, facilitated by key transporters such as Sodium-Glucose Transporters (SGLT1, SGLT2), the H^+ Exchanger 3 (NHE3) and the sodium-bicarbonate cotransporter[24]. We observed no differences in urinary fractional excretion of glucose between both groups, suggesting that SGLT function is likely unaffected. In the thick ascending limb of the loop of Henle, about 25% of filtered sodium is reabsorbed via the Na-K-2Cl symporter, the Na-H antiporter, and paracellular diffusion[25]. Given that fractional potassium excretion differed significantly only on the first day post-transplantation while polyuria persisted until day three, we consider a major defect in the Na-K-2Cl symporter unlikely. Sodium reabsorption in the distal convoluted tubules, mediated by Na-Cl cotransport and conductive sodium entry, accounts for

5%-10% of renal sodium reabsorption in healthy individuals. Finally, about 1% of filtered sodium is reabsorbed in the cortical and medullary collecting ducts[24]. The sodium excretion volume in our cohort of polyuric patients after living donor kidney transplantation suggests that isolated defects in collecting duct transport are improbable. The collective urine composition analyses presented here indicate that sodium loss is the decisive driver of post-LDKT polyuria. These findings suggest that the underlying mechanism may involve a defect in the proximal tubular transport machinery. This assumption is in line with a body of evidence indicating that the proximal tubule due to its near exclusive reliance on aerobic oxidative metabolism is prone to injury following states of impaired oxygen supply[26] as in ischemia reperfusion injury (IRI) during transplantation. In conjunction with the observed absence of urinary biomarkers of tubular injury in polyuric patients, we infer that on a cellular level there is a sub-lethal yet clinically significant tubular stress responsible for post-LDKT polyuria. It is well recognized that IRI-induced tubular stress can lead to profound alterations in the physiological transport capacity of the proximal tubule[27,28], e.g. resulting in failures of apico-basal polarization in proximal tubular epithelial cells or down-regulation of solute carriers[29]. These IRI-induced tubular stress responses might cause the salt loss nephropathy-like phenotype observed in post-LDKT polyuria. Under these premises post-LDKT polyuria, although transient, could arguably be interpreted as a sign of harm to the kidney rather than a desirable indicator of swift restauration of kidney function and volume homeostasis. In this sense, planned kidney biopsy and thorough investigations of the tubular transport machinery scientifically would be desirable. Nevertheless, the often-benign short-term clinical course of LDKT in our center does not trigger kidney biopsy during polyuric phases at our center.

The retrospective approach of our study and its single-center scope represent limitations to our findings. This holds especially true, as varying standard operation procedures of the transplant centers result in limited transferability. In particular, the rigid volume management in our cohort should be mentioned, which led to the finding that patients achieve a balanced fluid balance from the first day after transplantation, regardless of their urine volume. A multimodal assessment of volume status was not performed, limiting our ability to draw detailed conclusions in this regard. Finally, we cannot provide data for hormonal axes regulating renal water- and sodium-handling

as they were not part of the clinical routine, therefore only conclusions based on physiological assumptions are possible regarding the underlying processes.

In summary, our data support the conclusion that polyuria following renal transplantation is a common finding. To our knowledge, this is the first study to systematically investigate frequency, kinetics and mechanisms of post-LDKT polyuria in a robust number of patients. Mechanistically, post-LDKT polyuria is driven by sodium-dependent osmotic diuresis. In our patient cohort, we did not find any donor- or recipient-specific characteristics that could predict which living transplant recipients might experience post-LDKT polyuria. Further, our data highlights the importance of meticulous volume management in care of patients after LDKT. Finally, polyuria did not adversely affect short-term graft function by the means presented here, but we emphasize the possibility of delayed harm to the graft in polyuric patients.

Conflict of Interest Statement

The authors of this manuscript have no conflicts of interest to disclose.

Authors' Contributions

Research Desing, Conceptualization and Methodology: JW, JH, MR. Data acquisition: AF, LP and JW. Writing (original draft) MR, JW. Writing (review and editing): FCL, BKG, JH, JW.

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Data availability statement

All data are presented in the manuscript and its accompanying files.

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Table 1: Baseline characteristics of living donor kidney transplantation recipients stratified by polyuria (urine volume over 3000ml) on day one following transplantation. Chi-square test (female, cause of end-stage kidney disease (ESKD), Preemptive transplantation, residual diuresis yes, ABO incompatibility) or t-test (all remaining parameters).

	All	Polyuric	Non-polyuric	p-value
	n=33	n=23 (69.70)	n=10 (30.30)	
Age in years at transplant, median (SD)	46.30 (13.15)	44.13 (12.67)	51.30 (12.88)	0.16
Female (%)	13 (39.60)	9 (39.13)	4 (40.00)	0.61
Body Mass Index (SD)	26.10 (4.93)	25.41 (4.69)	27.69 (5.10)	0.23
Cause of ESKD				
Diabetes/Hypertension (%)	5 (15.15)	4 (17.40)	1 (10.00)	0.99
Cystic Disease (%)	3 (9.09)	0	3 (30.00)	0.02
Focal Segmental Glomerulosclerosis (%)	7 (21.21)	5 (21.73)	2 (20.00)	0.99
IgA Nephropathy (%)	6 (18.18)	5 (21.73)	1 (10.00)	0.64
Alport Syndrome (%)	4 (12.12)	4 (17.39)	0	0.29
Others (%)	8 (24.24)	5 (21.73)	3 (30.00)	0.67
Preemptive transplant (%)	11 (33.33)	7 (30.43)	4 (40.00)	0.70
Month on Dialysis before LDKT (SD)	15.88 (21.27)	18.52 (23.94)	9.8 (11.03)	0.29
Residual Diuresis yes (%)	30 (90.09)	21 (91.30)	9 (90.00)	0.99
Residual Diuresis in ml (SD)	1512 (946.12)	1404 (825.53)	1760 (1139.47)	0.33
ABO Incompatibility (%)	12 (36.36)	10 (43.47)	2 (20.00)	0.19
Mismatches (SD)	3.79 (1.32)	3.73 (1.22)	3.90 (1.22)	0.76
Ischemia Time in min (SD)	237.24 (35.42)	236.00 (37.80)	240.10 (28.99)	0.77

Table 2: Baseline characteristics of donors stratified by recipient polyuria (urine volume over 3000ml) on day one after transplant. Chi-square test (female) or t-test (all remaining parameters).

	All	Polyuric	Non-polyuric	p-value
	n=33	n=23 (69.70)	n=10 (30.30)	
Donor Age in years, median (SD)	53.78 (10.58)	53.00 (9.73)	55.60 (12.7)	0.52
Female (%)	23 (69.69)	15 (65.20)	8 (80.01)	0.39
Bodyweight in kg (SD)	75.95 (14.66)	76.67 (15.95)	74.29 (11.73)	0.67
Diuresis before donation in ml (SD)	1963 (726.9)	1869 (698)	2160 (782)	0.30
Serum Creatinine before donation in mg/dl (SD)	0.78 (0.12)	0.77 (0.13)	0.79 (0.09)	0.62
Creatinine Clearance before donation in ml/min (SD)	112.6 (44.97)	111.1 (51.52)	115.7 (28.73)	0.79

Table 3: Simple linear regression between urine volume on day one following living donor kidney transplant and pre-transplant characteristics of the donor.

	R^2	Equation	p-value
Age in years at donation	0.018	Y = -0.0003846*X + 55.97	0.45
Body Weight	0.001	Y = -9.582e-005*X + 76.50	0.89
Urine Output in ml before donation	0.019	Y = -0.02929*X + 2118	0.45
Serum Creatinine before donation	0.027	Y = 5.547e-006*X + 0.7491	0.35
Creatinine Clearance before donation	0.016	Y = -0.001673*X + 121.4	0.49

Table 4: Multiple linear regression model for the relationship of urine volume on day one following living donor kidney transplant and urinary Na (UVNa), K (UVK), Glucose (UVGlucose) and Urea excretion (UVUrea). Odds ratio (OR), 95% Confidence Interval (95%CI).

Variable	Estimate	Standard error	95% CI (asymptotic)	|t|	P value
Intercept	52.64	544.7	-1069 – 1175	0.09	0.92
UVNa	**7.12**	**0.49**	**6.11 – 8.14**	**14.50**	**≤0.0001**
UVK	7.35	7.35	-5.87 – 24.44	1.26	0.22
UVGlucose	30.87	17.20	-4.55 – 66.29	1.79	0.08
UVUrea	0.26	0.54	-0.86 – 1.39	0.47	0.64

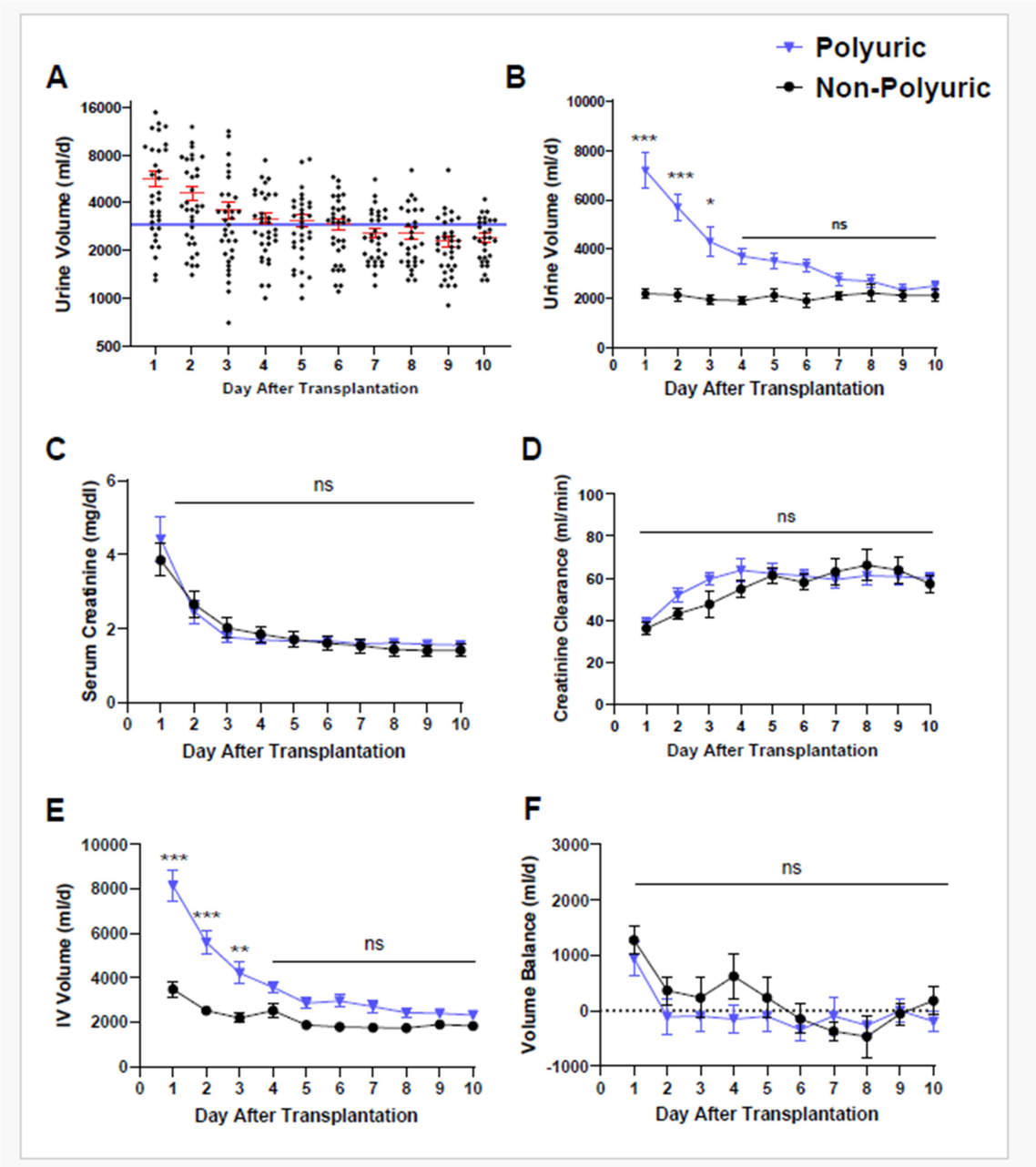

Figure 1: 24h urine volume, creatinine clearance and volume balance in living donor kidney transplant recipients during the first 10 days following transplantation

(A) Urine volume in the first ten days after living kidney transplant. N=33, single values. Blue line indicates the threshold of 3000ml per day. (B) 24h urine volume in polyuric vs. non-polyuric patients in the first ten days after living donor kidney transplant defined by urine output on day one. N=23 vs. 10, 2way ANOVA with Sidak's multiple comparison test. (C) Serum creatinine and (D) creatinine clearance in polyuric vs. non-polyuric patients in the first ten days after living donor kidney

transplantation defined by urine output on day one. N=23 vs. 10, 2way ANOVA with Sidak's multiple comparison test. (E) Intravenously administered fluid volume and (F) volume balance (iv volume per 24h – urine output per 24h) in polyuric vs. non-polyuric patients in the first ten days after living donor kidney transplantation defined by urine output on day one. N=23 vs. 10, 2way ANOVA with Sidak's multiple comparison test.

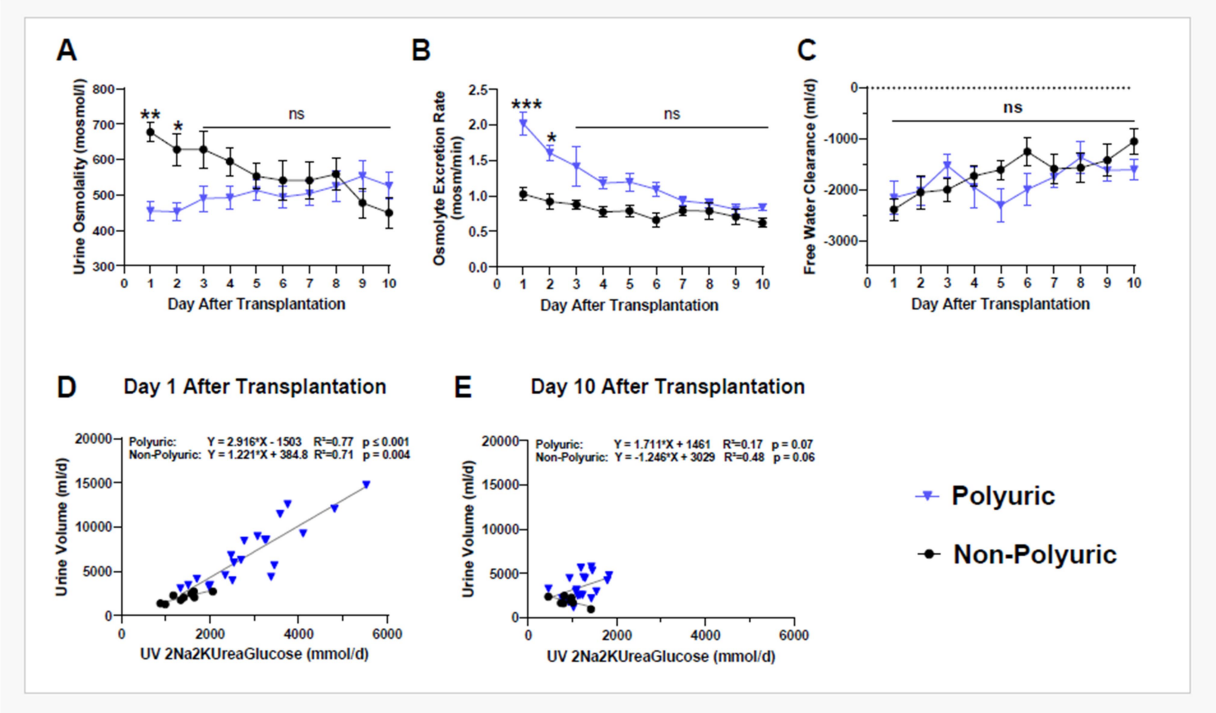

Figure 2: Urine osmolality, and renal overall osmolyte excretion and free water clearance following living donor kidney transplantation

(A) Urine osmolality, (B) urinary osmolyte excretion rate and (C) Free water clearance in polyuric vs. non-polyuric patients in the first ten days after living donor kidney transplantation defined by urine output on day one. N=23 vs. 10, 2way ANOVA with Sidak's multiple comparison test. Simple linear regression between urine volume and urine osmolyte excretion (UV 2Na2KUreaGlucose) on day 1 (D) and 10 (E) in polyuric vs. non-polyuric patients after living donor kidney transplantation (N=22 vs. 9).

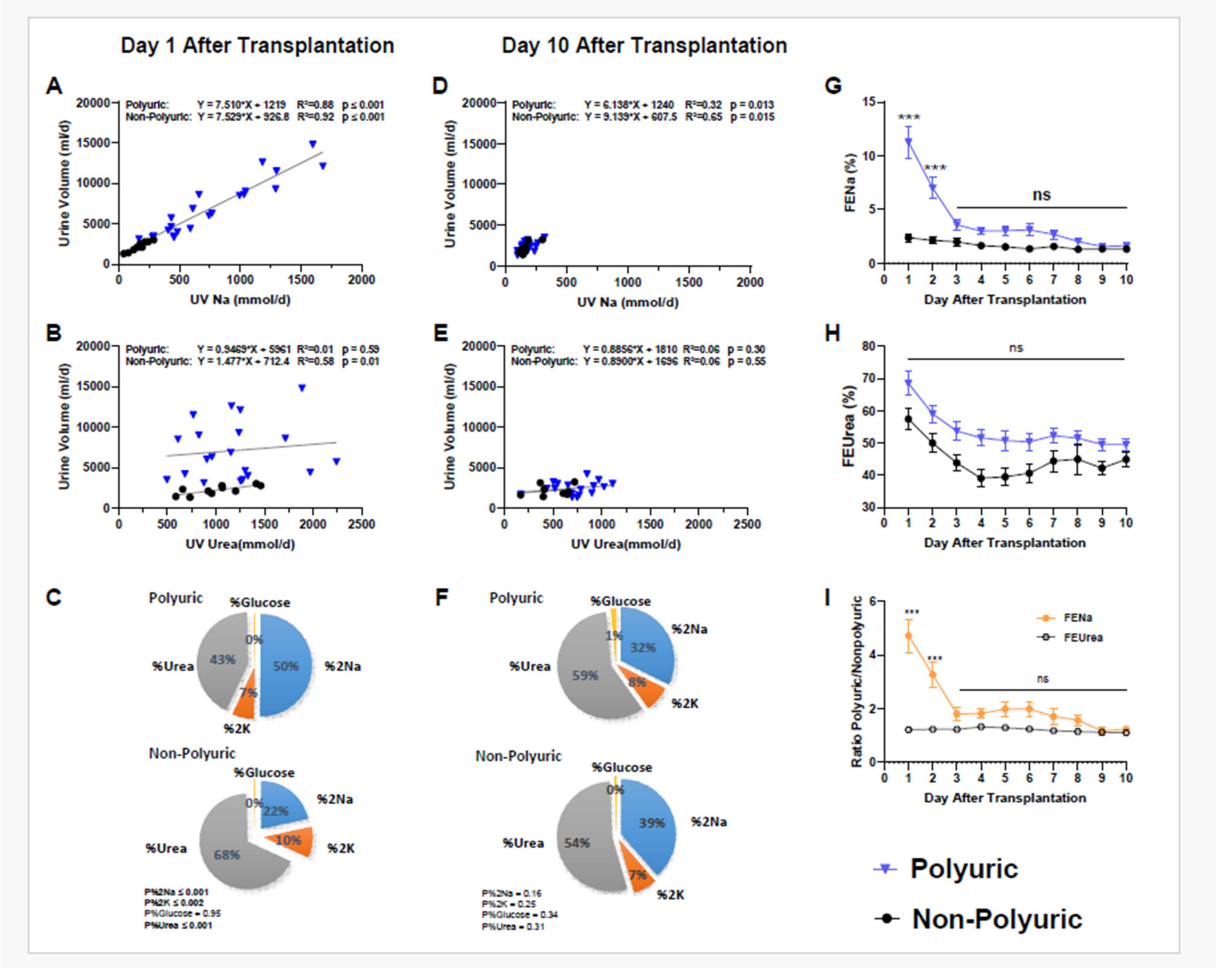

Figure 3: Urine osmolyte excretion and fractional sodium and urea excretion following living donor kidney transplantation

Simple linear regression between urine volume and urinary sodium (UV Na) (A) and urea excretion (UV Urea) (B) on day 1 after living donor kidney transplantation in polyuric vs. non-polyuric patients (N=22 vs. 10). (C) Urine osmolyte composition in polyuric and non-polyuric patients on day 1 after living donor kidney transplantation, N=22 vs. 10, Unpaired t-test. Simple linear regression between urine volume and urinary sodium (UV Na) (D) and urea excretion (UV Urea) (E) on day 10 after living donor kidney transplantation in polyuric vs. non-polyuric patients (N=20 vs. 8). (F) Urine osmolyte composition in polyuric and non-polyuric patients on day 10 after living donor kidney transplantation, N=20 vs. 8, Unpaired t-test. (G) Fractional sodium excretion (FENa) in % and (H) fractional excretion of urea (FEUrea) in polyuric vs. non-polyuric patients in the first ten days after living donor kidney transplantation

defined by urine output on day one. N=22 vs. 10, 2way ANOVA with Sidak's multiple comparison test. (I) FeNa and FEUrea ration of polyuric/non-polyuric patients during the first ten days after living donor kidney transplantation defined by urine output on day one. N=22 vs. 10, 2way ANOVA with Sidak's multiple comparison test.