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ORIGINAL PAPER

Time-Zero Biopsies in Deceased-Donor Kidney Transplantation: Predictive Value of Histological Findings on Long-Term Graft Function

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ABSTRACT

Background: Time-zero biopsies (TzB) provide insights into donor-derived lesions, but their predictive value for long-term outcomes remains uncertain. We aimed to identify clinical and histological factors from TzB of deceased donors influencing glomerular filtration rate (GFR) at 3- and 5-year post-transplantation. **Methods:** We retrospectively analyzed TzB performed from January 2015 to August 2019. Nineteen biopsies were excluded due to recipient death before 3 years. We examined donor and recipient-related characteristics and histological findings categorized using the Banff scoring system. **Results:** Among 147 biopsies, 61.9% of donors were male, with a mean age of 51.8 ± 13.5 years, and 27.2% met expanded criteria. Histologic analysis revealed 44.2% had alterations in the Banff chronic scoring system: 29.1% in vascular fibrous intimal thickening (Cv), 26.6% in arteriolar hyalinosis (Ah), and 8.3% in interstitial fibrosis (Ci)/tubular atrophy (Ct). Mean GFR was 54.8 ± 21.2 and 52.3 ± 23.0 mL/min/1.73 m^2 at 3 and 5 years, respectively. At 3 years, Ah > 0, Ci/Ct > 0, Cv > 0, Banff chronic sum score > 0, glomerulosclerosis (GE), donor age > 50 years, expanded criteria donors, and rejection episodes were significantly associated with lower GFR. With the exception of Ci/Ct, all other parameters were also significantly associated with lower GFR at 5 years. Linear regression indicated donor age [β (95%CI) = -0.257 (-0.783, -0.021); p = 0.039] and arteriolar hyalinosis [β (95%CI) = -0.207 (-16.767, -0.448); p = 0.039]; p = 0.039) as predictors of GFR at 3 years, with donor age maintaining predictive value at 5 years [β (95%CI) = -0.276 (-0.776, -0.137); p = 0.006]. A tendency towards predictive value for GFR at 5 years was noted for GE [β (95%CI) = -0.198 (120.0, 1.038); p = 0.054]. **Conclusion:** TzB provide valuable prognostic information for long-term graft function with histological findings (particularly arteriolar hyalinosis and GE) and donor age serving as significant predictors of GFR at 3 and 5 years post-transplantation. These findings suggest TzB can be useful for risk stratification and personalized management of KT recipients.

Descriptors: Kidney Transplantation; Biopsy; Histology; Allografts.

Biópsias de Tempo Zero no Transplante Renal de Doador Falecido: Valor Preditivo dos Achados Histológicos na Função do Enxerto a Longo Prazo

RESUMO

Introdução: As biópsias de tempo zero [*time-zero biopsies* (TzB)] fornecem informações sobre lesões provenientes do doador, mas seu valor preditivo para os resultados a longo prazo permanece incerto. O objetivo deste trabalho foi identificar fatores clínicos e histológicos das TzB de doadores falecidos que influenciam a taxa de filtração glomerular (TFG) aos 3 e 5 anos pós-transplante renal. **Métodos:** Analisámos retrospectivamente TzB realizadas de janeiro de 2015 a agosto de 2019. Foram excluídas 19 biópsias por óbito do receptor antes de 3 anos de seguimento. Avaliamos características relacionadas

ao doador e receptor, além dos achados histológicos categorizados usando o sistema de escore de Banff. **Resultados:** Dentre 147 biópsias, 61,9% dos dadores eram do sexo masculino, com idade média de 51,8 ± 13,5 anos, e 27,2% eram doadores de critérios expandidos. A análise histológica revelou que 44,2% apresentavam alterações no escore de Banff crónico: 29,1% com alterações em Cv (*vascular fibrous intimal thickening*), 26,6% em Ah (*arteriolar hyalinosis*) e 8,3% em Ci (*interstitial fibrosis*)/Ct (*tubular atrophy*). A TFG média foi de 54,8 ± 21,2 e 52,3 ± 23,0 mL/min/1,73 m^2 aos 3 e 5 anos, respectivamente. Aos 3 anos, Ah > 0, Ci/Ct > 0, Cv > 0, escore de Banff crônico > 0, glomeruloesclerose, idade do doador > 50 anos, doador de critérios expandidos e episódios de rejeição associaram-se significativamente a uma TFG mais baixa. Com exceção de Ci/Ct, todos os outros parâmetros também apresentaram associação significativa com TFG reduzida aos 5 anos. A regressão linear indicou que a idade do doador [β (IC95%) = -0,257 (-0,783, -0,021); p = 0,039] e hialinose arteriolar [β (IC95%) = -0,207 (-16,767, -0,448); p = 0,039] foram preditores de TFG aos 3 anos, sendo que a idade do doador manteve valor preditivo aos 5 anos [β (IC95%) = -0,276 (-0,776, -0,137); p = 0,006]. Observou-se uma tendência de valor preditivo para TFG aos 5 anos para glomeruloesclerose [β (IC95%) = -0,198 (-120,0, 1,038); p = 0,054]. **Conclusão:** As TzB fornecem informações prognósticas valiosas sobre a função do enxerto a longo prazo, sendo os achados histológicos (particularmente hialinose arteriolar e glomeruloesclerose) e a idade do doador preditores significativos da TFG aos 3 e 5 anos pós-transplante. Esses achados sugerem que as TzB podem ser úteis na estratificação de risco e na gestão personalizada de receptores de transplante renal.

Descritores: Transplante de Rim; Biópsia; Histologia; Aloenxertos.

INTRODUCTION

Kidney transplantation (KT) remains the preferred treatment for end-stage renal disease (ESRD) due to its benefits on patient survival and quality of life compared to dialysis.[1,2] However, optimizing long-term transplant outcomes remains a challenge, especially given the multifactorial causes of graft failure.

Under the current Portuguese allocation system, deceased donor kidneys are primarily allocated via ABO-identical, and a point system based on a combination of time on dialysis and HLA mismatching. Additional points account for sensitized candidates, patients' ages, and prior transplants. This system prioritizes time on dialysis, often at the expense of achieving optimal HLA matching.[3] A procurement kidney biopsy is performed during the organ retrieval process to evaluate whether a deceased donor kidney is suitable for transplantation, particularly in specific circumstances, such as extended criteria donors (ECD) and donors with specific risk factors such as proteinuria or hematuria on pre-donation tests or history of systemic diseases that may affect the kidneys (e.g., vasculitis, lupus). These kidneys are typically discarded when they exhibit severe glomerulosclerosis [> 20-30% in a procurement biopsy (PB)] and/or extensive interstitial fibrosis or tubular atrophy (> 30-40%).

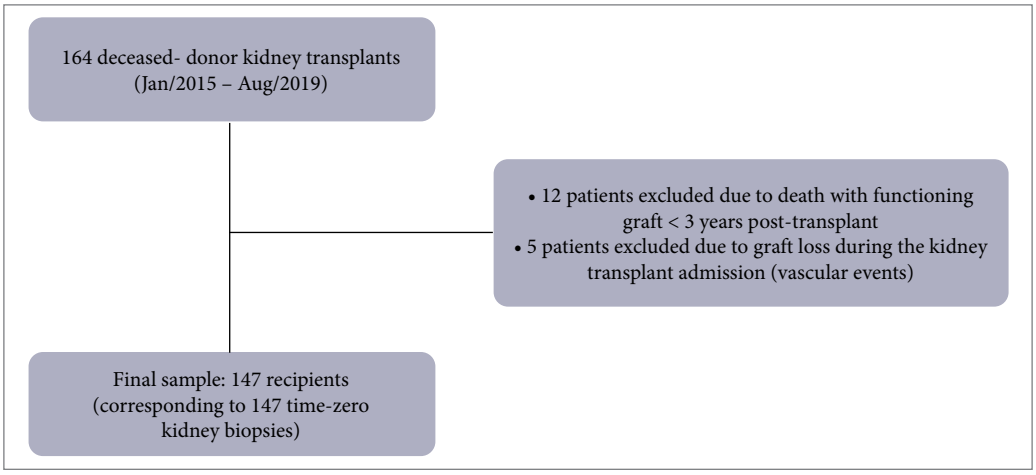
Time-zero biopsies (TzB), routinely performed at the time of transplantation in many centers, present a promising tool for assessing preexisting donor kidney lesions. These biopsies have the potential to reveal histological indicators that might predict long-term graft function. Yet, their predictive value for long-term outcomes remains uncertain.[4,5]

With the growing scarcity of available organs, understanding the true predictive value of TzB findings is crucial.[4] If TzB can reliably identify high-risk kidneys, they could play a key role in optimizing organ utilization by highlighting critical histological factors that predict long-term graft function. This understanding could not only help prevent the unnecessary discard of viable kidneys but also guide clinicians in selecting tailored management strategies, ultimately enhancing allograft longevity.[4] However, current evidence regarding the predictive value of TzB is inconsistent. For instance, a recent systematic review found no consistent association between TzB findings and post-transplant outcomes, highlighting methodological variability among studies.[5] Differences in biopsy technique (frozen vs. paraffin sections, wedge vs. needle biopsy), histological assessment, and variability in follow-up periods contribute to these discrepancies, complicating the generalization of TzB findings to clinical practice.

This study aims to determine the impact of histological factors observed in zero-time biopsies of deceased donors on 3- and 5-year post-transplant kidney allograft function.

METHODS

We conducted a single-center retrospective study of consecutive deceased-donor kidney transplant recipients with TzB performed at our center from January 2015 to August 2019. We identified TzB by reviewing the renal pathology database of all kidney transplant biopsies performed during the study period. Recipients who died before 3 years post-transplant were excluded (Fig. 1).



Source: Elaborated by the authors.

Figure 1. Flow diagram illustrating the patient selection process for the study cohort.

In our institution, TzB are routinely performed in all deceased-donor kidney transplants, following a standardized protocol, where a sample of kidney tissue is obtained during back-table preparation, immediately before organ implantation. All biopsies are analyzed by two nephrologists specialized in renal pathology.

Chronic changes in vessels, tubules, and interstitium [arteriolar hyalinosis (Ah), vascular fibrous intimal thickening (Cv), tubular atrophy (Ct), interstitial fibrosis (Ci)] were semi-quantitatively scored (0-3) using the Banff Working Classification. By adding these individual chronic changes, a Banff chronic sum score was generated. We did not include the glomerular basement membrane double contours score since these lesions were not found in our cohort. GE and GE/total glomerulus were registered.

The primary endpoint was allograft function at 3- and 5-year post-transplant, assessed using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation to calculate the estimated glomerular filtration rate (eGFR).

In addition to the histological data, general information about the recipient and the donor, such as sex, age, and presence of comorbidities, was collected. Episodes of biopsy-proven acute rejection (BPAR) occurring during follow-up (cellular, antibody-mediated, or mixed) were also recorded. Induction immunosuppression was either rabbit anti-thymocyte globulin (4.5 mg/kg total dose) or basiliximab in all participants. Maintenance immunosuppression included tacrolimus, mycophenolate mofetil, and prednisone. The choice of induction agent was determined by the treating physicians.

Statistical analysis

Statistical analyses were performed using IBM SPSS version 28 (SPSS, Chicago, IL, USA). Categorical variables are expressed as numbers and percentages, and continuous variables are expressed as mean ± standard deviation (SD). The Pearson χ^2 test or Fisher's exact test was used to analyze categorical variables. For continuous variables, the means were compared using the Student's *t*-test.

In analyses requiring a dichotomous categorical exposure variable, the combined chronic Banff score was modeled as a categorical variable (ci + ct + cv + ah > 0 vs. = 0).

A linear regression model was constructed to predict renal function at 3- and 5-year post-transplantation, considering the characteristics of TzB and the clinical characteristics of the donor and the recipient.

Graft survival was analyzed using the Kaplan-Meier method, and a multivariate Cox proportional hazards model was used to identify factors that were independently associated with graft survival.

All statistical tests were two-tailed, with statistical significance defined as $p < 0.05$.

RESULTS

After the exclusion of deaths, the final sample was composed of 147 patients. The mean follow-up time after transplantation was 7.6 ± 5.3 years, and all recipients were followed for at least 3 years. Ninety-one (61.9%) donors were male, with a mean age of 51.8 ± 13.5 years, and 40 (27.2%) were ECD. The clinical characteristics of the population are shown in Table 1. The mean recipient age was 51 ± 12.4 years, and 67.3% were male.

Table 1. Baseline demographic and clinical characteristics of the population.

Baseline characteristics	
Donor age (years), mean ± SD	51.8 ± 13.5
Donor's sex (male), n (%)	91 (61.9)
Recipients age (years), mean ± SD	51.0 ± 12.4
Recipient's sex (male), n (%)	99 (67.3)
Cold ischemia time (hours), mean ± SD	12.9 ± 3.5
HLA mismatch (A, B, DR), mean ± SD	3.8 ± 1.3
DR HLA mismatch, mean ± SD	1.32 ± 1.0
PRA, mean ± SD	10.0 ± 20.4
PRA < 25%, n (%)	108 (88.5)
PRA 25-75%, n (%)	11 (9.0)
PRA > 75%, n (%)	3 (2.5)

Source: Elaborated by the authors.

Histological data

Histologic analysis revealed that 44.2% of the TzB had alterations in the Banff chronic score (n = 65). Ah, Cv, Ct, and Ci were present in 25.9, 27.9, 8.2, and 8.2% of the biopsy samples, respectively. Most histological findings were of mild degree according to the Banff criteria (Table 2). Global GE was found in 30.6%. GE/total glomerulus was on average 0.05 ± 0.12. None of the TzB showed other specific diagnostic findings, such as glomerulonephritis.

Table 2. Histological findings of the time-zero kidney biopsies semi-quantitatively scored (0-3) using the Banff Working Classification.

Histological findings	
Banff chronic score sum, mean ± SD	1.02 ± 1.67
Arteriolar hyalinosis (Ah score), n (%)	
0	109 (74.1)
1	29 (19.7)
2	6 (4.1)
3	3 (2.1)
Vascular fibrous intimal thickening (Cv score), n (%)	
0	106 (72.1)
1	25 (17.0)
2	11 (7.5)
3	5 (3.4)
Tubular atrophy/interstitial fibrosis (Ct and Ci scores), n (%)	
0	135 (91.8)
1	6 (4.1)
2	5 (3.4)
3	1 (0.7)

Source: Elaborated by the authors.

The histological findings in TzB were associated with donors' clinical features, namely age and ECD. Donor age was significantly increased in the TzB that presented Ah > 0 (54.6 vs. 49.8 years old; $p = 0.016$), Ci/Ct > 0 (59.8 vs. 50.7 years; $p = 0.026$), and Cv > 0 (58.3 vs. 48.2 years; $p < 0.001$). Similarly, expanded criteria donors were more likely to have altered Ci/Ct and Cv scores ($p = 0.02$ and $p = 0.006$, respectively), with no difference in the Ah score ($p = 0.21$).

Allograft outcomes

Twenty of the 147 recipients (13.6%) had at least one episode of acute rejection during follow-up: T-cell mediated in nine patients, antibody-mediated in six, and mixed in five. The mean eGFR at 3 years and 5 years after transplantation was 54.8 ± 21.2 and 52.3 ± 23.0 mL/min/1.73 m^2, respectively.

In the univariate analysis, Banff chronic score sum > 0 and individual histological parameters Ah > 0, Ci/Ct > 0 and Cv > 0, presence of GE, donor age > 50 years, ECD, and rejection episodes were significantly associated with lower eGFR at 3 years post-transplant (Table 3). All these parameters, with the exception of the Ci/Ct score, showed a significant association with inferior eGFR at 5 years.

Table 3. Effects of clinical and histological features on 3- and 5-year post-transplant renal function (univariate analysis).

Clinical and histological features	n (%)	eGFR at 3 years		eGFR at 5 years	
		Mean ± SD	*p*-value	Mean ± SD	*p*-value
Banff chronic score sum					
> 0	65 (44.2)	47.3 ± 17.5	< 0.001	43.7 ± 17.3	< 0.001
= 0	82 (55.8)	60.4 ± 21.9		57.5 ± 24.6	
Arteriolar hyalinosis					
Present	38 (25.9)	44.6 ± 17.8	< 0.001	43.2 ± 18.2	0.005
Absent	109 (74.1)	58.7 ± 21.3		55.8 ± 24	
Vascular fibrous intimal thickening					
Present	41 (27.9)	36.7 ± 15.2	0.04	43.0 ± 16.2	0.008
Absent	106 (27.9)	56.1 ± 21.1		55.6 ± 24.1	
Tubular atrophy/interstitial fibrosis					
Present	12 (8.2)	47.8 ± 18.8	0.006	41.9 ± 13.6	0.100
Absent	135 (91.8)	58.2 ± 21.5		53.4 ± 23.3	
Global GE (%)					
0	45 (30.6)	58.9 ± 20.7	< 0.001	56.4 ± 23.7	0.001
> 0	102 (69.4)	44.8 ± 19.2		42.6 ± 18.6	
Donor age (years)					
> 50	73 (49.7)	47.1 ± 15.3	< 0.001	45.2 ± 18.9	< 0.001
≤ 50	74 (50.3)	64.5 ± 23.1		60.0 ± 24.7	
Expanded criteria donors					
Yes	40 (27.2)	44.8 ± 18.8	< 0.001	40.6 ± 19.8	0.001
No	107 (72.8)	58.3 ± 20.8		55.6 ± 22.9	
Acute rejection episodes					
Yes	20 (13.6)	43.8 ± 24.1	0.016	39.9 ± 15.8	0.031
No	127 (86.4)	56.1 ± 20.4		53.5 ± 23.3	

Source: Elaborated by the authors.

In the multivariate logistic regression analysis (Table 4), donor age [β (95%CI) = -0.349 (-0.786, -0.266); $p < 0.001$] and arteriolar hyalinosis [β (95%CI) = -0.224 (-13.46, -1.95); $p = 0.009$] were independent predictors of lower eGFR at 3 years. At 5 years post-transplant, only donor age remained an independent predictor for lower eGFR [β (95%CI) = -0.276 (-0.776, -0.137); $p = 0.006$]. A trend towards statistical significance was noted for GE as a predictor of lower eGFR at 5 years [β (95%CI) = -0.198 (-1.200, 1.038); $p = 0.054$].

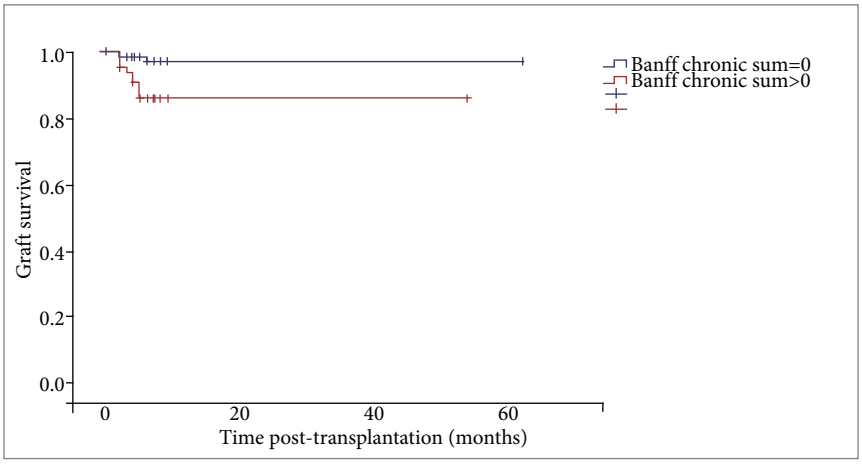
Table 4. Effects of clinical and histological parameters on 3- and 5-year post-transplant renal function in multivariate analysis.

Clinical and histological features	eGFR at 3 years		eGFR at 5 years	
	β (95%CI)	*p*-value	β (95%CI)	*p*-value
Ah score	-0.224 (-13.46, -1.95)	0.009	-0.067 (-10.55, 5.07)	0.488
Cv score	-0.076 (-7.25, 2.93)	0.402	-0.153 (-10.55, -5.07)	0.115
Ct/Ci score	-0.101 (-15.33, 4.03)	0.250	0.050 (-8.83, 15.14)	0.603
Global GE	0.008 (-29.04, 31.92)	0.926	-0.198 (-11.57, 1.27)	0.054
Acute rejection episodes	-0.114 (-19.68, 3.52)	0.170	-0.160 (-29.42, 1.77)	0.082
Donor age	-0.349 (-0.79, -0.27)	< 0.001	-0.276 (-0.78, -0.14)	0.006
Cold ischemia time	0.079 (-0.490, 1.413)	0.339	-0.078 (-1.63, 0.65)	0.394

Source: Elaborated by the authors.

Survival analysis

Graft failure occurred in 11 (7.5%) patients during the follow-up period. Graft survival rates at 3, 5, and 7 years were 97.3, 95.2, and 92%, respectively. Graft survival time was significantly lower in the group with abnormal time-zero histology (Banff chronic score sum > 0) (Fig. 2). In the multivariable Cox regression model (Table 5), the presence of an altered Cv score in TzB was independently associated with a 5.2-fold greater hazard for graft loss.



Source: Elaborated by the authors.

Figure 2. Kaplan-Meier plot comparing time to graft loss between the abnormal time-zero histology group (Banff chronic score sum > 0) and the Banff chronic score sum = 0 group using the log-rank test.

Table 5. Multivariable Cox modeling of predictive factors for graft survival.

Variable	Multivariable Hazard ratio	95%CI	*p*-value
Expanded criteria donor	3.04	0.687-13.474	0.143
HLA mismatch	1.21	0.660-2.213	0.539
Ct score > 0	2.59	0.538-12.465	0.236
Ah score > 0	3.07	0.693-13.577	0.140
Cv score > 0	5.21	1.009-26.934	0.049

Source: Elaborated by the authors.

DISCUSSION

In the present study, we assessed the role of TzB findings in predicting long-term outcomes in kidney transplant recipients, focusing on the relationship between donor-derived histological lesions at the time of transplant and subsequent graft function. Post-transplant renal function at 3 years was found to be independently associated with donor age and Ah score. At 5 years post-transplant, only donor age was a significant predictor of graft function.

Our results indicate that chronic histological changes, such as arteriolar hyalinosis, vascular intimal thickening, and tubular atrophy, were present in nearly half of the TzB samples and were significantly associated with donor characteristics, particularly age and expanded criteria donor status. Donor age is a well-established predictor of graft outcomes.[6-9] Similarly, our findings show a strong correlation between donor age and renal function at 3 and 5 years post-transplant, with this association remaining significant in the multivariate analysis.

Previous studies have linked time-zero histology to poor post-transplant outcomes, especially short-term outcomes such as delayed graft function (DGF) and lower eGFR at 6 months and 1-year post-transplant.[10-17] At 3-year post-transplant, Ah > 0, Ci/Ct > 0 and Cv > 0, as well as the presence of GE were significantly associated with lower eGFR in our study. However, in the multivariate analysis, only the Ah score and donor age were independent predictors of poorer graft function. These findings align with the results from Taub et al.,[18] which found that Ah scores were associated with DGF, lower 6-month eGFR, and allograft failure. In that study, the Cv score was also associated with worse kidney transplant outcomes, an association we did not find in the multivariate analysis. In the study by Lee et al.,[14] post-transplant renal function at 1 year was found to be significantly associated with donor age, Ah, and Ci in the multivariate analysis. Similarly, one large TzB study by Cockfield et al.[19] showed that Ah scores were associated with allograft failure, and Cv scores wereassociated with lower 6-month eGFR. Another recent study also found that chronic vascular injury scores (Cv and Ah) were associated with lower 12-month eGFR.[16]

Some studies have reported an association between tubulointerstitial lesions and renal graft function at 1 year post-transplant.[12,14,16,20] In the present study, these changes (Ci/Ct) were not independently associated with long term graft function, with their effect being attenuated by other histological and clinical parameters in the multivariate analysis.

The presence and degree of GE have been inconsistently associated with poorer graft outcomes.[5] Gaber et al.[10] evaluated the impact of time-zero histology on graft outcomes in kidney transplants from older donors, suggesting that GE > 20% in the TzB was associated with worse graft survival. In one report by Randhawa et al.,[20] the percentage of GS and Ci scores independently predicted graft renal function at 1 year. On the other hand, Lee et al.[14] did not find deceased donor graft function to be associated with GS. In our study, the effect of GS on graft function at 3 and 5 years post-transplant was mitigated by donor age in the multivariate analysis, as GS is as a reliable histological marker of age-related changes.

Although several studies have reported associations between histological findings of TzB and poorer graft outcomes, consistent links between donor biopsy results and post-transplant outcomes remain inconsistent.[4,5] In the study by Reese et al.,[4] time-zero histology was not significantly associated with allograft failure.

The independent effect of arteriolar hyalinosis in predicting allograft function 3 years post-transplantation in our study, even when adjusting for donor age, ECD status, and episodes of BPAR, suggests that Ah might have a lasting impact on graft function. The renal vasculature is susceptible to several transplant-specific injuries, such as ischemia-reperfusion injury, calcineurin inhibitor toxicity, and antibody-mediated rejection. Therefore, preexisting donor vascular damage, namely arteriolar hyalinosis, might be a significant predictor of graft outcomes.[5] However, these structural changes were not independently associated with graft function at 5 years, likely due to the more substantial long-term influence of factors such as donor age and potentially unmeasured post-transplant variables, including medication adherence, development of de novo donor-specific alloantibodies, and alterations in treatment based on subsequent biopsy results or major intercurrent events.

Several factors may explain the differences between our study and previous research regarding the effects of Ci/Ct, Cv, and GS on graft renal function. First, other studies typically had shorter follow-up periods, assessing graft function at 6 months or 1 year, whereas we examined outcomes at 3 and 5 years post-transplant. To our knowledge, no other studies have evaluated the impact of TzB histology on long-term kidney transplant outcomes, making direct comparison and generalization of results challenging. Other possible explanations include variations in donor characteristics and the fact that we used multivariate analysis to assess the impact of clinical and histological findings on graft outcomes, an approach not consistently applied in previous studies.

Furthermore, caution is needed when comparing results due to regional differences in biopsy practices, definitions of biopsy abnormalities, scoring systems, and outcome measurements. In our study, back-table TzB were routinely performed for all deceased-donor kidney transplants, meaning donor selection was unaffected by pre-implantation biopsy results, eliminating potential selection bias and focusing solely on post-transplant outcomes.

We used the Banff scoring criteria to grade histological lesions, as it is the most widely used system in TzB studies due to its familiarity, accessibility, and relative reproducibility, despite being originally designed for post-transplant kidney allograft assessments.[21] The scores were based on original biopsy readings, not a centralized review with the latest Banff updates. This raises concerns about the reproducibility of time-zero histology scores, but it likely did not affect the outcomes, as the Banff criteria for Ci, Ct, Cv, and Ah scores have remained consistent across recent updates.

TzB and PB play distinct roles in KT. PBs, performed during organ retrieval, are used to assess donor kidney quality and guide acceptance decisions, especially for marginal or extended-criteria donors. TzB are performed immediately before organ implantation, and their results do not affect donor selection. TzB provide a baseline histological assessment, identifying both chronic and acute injuries, and offering prognostic value for post-transplant management. While PBs are valuable for pre-transplant candidate selection, TzB play an important role in post-transplant prognostication. Together, these tools can be used to optimize organ allocation and possibly improve patient outcomes.

While our findings provide valuable insights into the role of TzB in predicting kidney transplant outcomes, several limitations must be acknowledged. Firstly, the retrospective and single-center design may restrict the generalizability of the results. Secondly, the exclusion of recipients who died within the first 3 years post-transplant, although applied to ensure a minimum follow-up period, may introduce "survivorship bias" by omitting higher-risk patients with poorer early outcomes. Thus, our study sample may represent a relatively healthier cohort, possibly skewing the findings toward more favorable outcomes and underestimating the true impact of TzB findings on graft function. Finally, unmeasured or unaccounted-for confounding variables may influence both histological findings at TzB and long-term graft outcomes; while we controlled for several known risk factors, factors such as environmental exposures, recipient adherence to immunosuppression, and post-transplant intercurrent events were not analyzed, potentially affecting the observed associations and making it difficult to draw definitive conclusions. Overall, these limitations emphasize the need for multi-center, prospective studies with larger and more diverse patient populations to validate our findings and clarify the clinical value of TzB.

CONCLUSION

In conclusion, TzB provide valuable prognostic information for long-term graft function, with histological findings, particularly arteriolar hyalinosis, and donor age serving as significant predictors of GFR at 3 and 5 years post-transplantation. Additionally, the presence of vascular fibrous intimal thickening was independently associated with a greater risk of graft loss. The findings of our study reinforce the prognostic relevance of chronic vascular changes, which may assist clinicians in determining the optimal level of intervention or investment for a given kidney transplant.

CONFLICT OF INTEREST

Nothing to declare.

AUTHOR'S CONTRIBUTION

Substantive scientific and intellectual contributions to the study: Beirão B, Borges H, Medeiros JT, Rodrigues FF, Pena A, Góis M, Viana H, Jorge C.; **Conception and design:** Beirão B, Borges H, Medeiros JT, Rodrigues FF, Góis M, Viana H.; **Data analysis and interpretation:** Beirão B, Borges H, Medeiros JT, Rodrigues FF, Viana H; **Article writing:** Beirão B; **Critical revision:** Pena A, Góis M, Viana H, Jorge C; **Final approval:** Beirão B.

DATA AVAILABILITY STATEMENT

All data were generated and/or analyzed in this study.

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