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Original Article

ORIGINAL ARTICLE

T1 mapping magnetic resonance imaging predicts decline of kidney function

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ABSTRACT

Background. Renal cortical interstitial fibrosis, typically assessed by biopsy, is crucial for kidney function prognosis. Magnetic resonance imaging (MRI) is a promising method to assess fibrosis non-invasively. Diffusion-weighted (DW) MRI correlates with renal fibrosis and predicts kidney function decline in chronic kidney disease (CKD) and kidney allograft patients. This study evaluates whether T1 and T2 mapping predict kidney function decline and if their simultaneous use enhances the predictive power of a DW-MRI-based model.

Methods. We prospectively included 197 patients (42 CKD, 155 allograft kidneys). Each underwent a biopsy followed by multiparametric MRI without contrast within 1 week. Over a median follow-up of 2.2 years, laboratory parameters were recorded. The primary endpoint was a rapid decline in kidney function [glomerular filtration rate (GFR) reduction >30%] or replacement therapy initiation. The ability of T1 and T2 mapping sequences to predict poor renal outcome was examined using multivariable Cox regression models, incorporating MRI-derived parameters, estimated GFR (eGFR) and proteinuria.

Results. Renal outcome occurred in 54 patients after a median of 1.1 years (interquartile range 0.9–2.1). Univariable survival analysis showed cortical T1 was associated with poor renal outcome {hazard ratio [HR] 3.02 [95% confidence interval (CI) 1.44–6.33]}, while T2 sequences had no significant predictive value. Adding cortical T1 to the established model (ΔADC, eGFR, proteinuria) did not improve the HR [from 4.62 (95% CI 1.56–13.67) to 4.36 (95% CI 1.46–13.02)] and marginally increased Harrell's C-index (0.77 to 0.79). Adjusting the regression model for ΔT2 yielded no enhancement in predictive power.

Conclusions. Cortical T1 is strongly associated with poor renal outcome but did not enhance prognostic power of the DW-MRI-based model.

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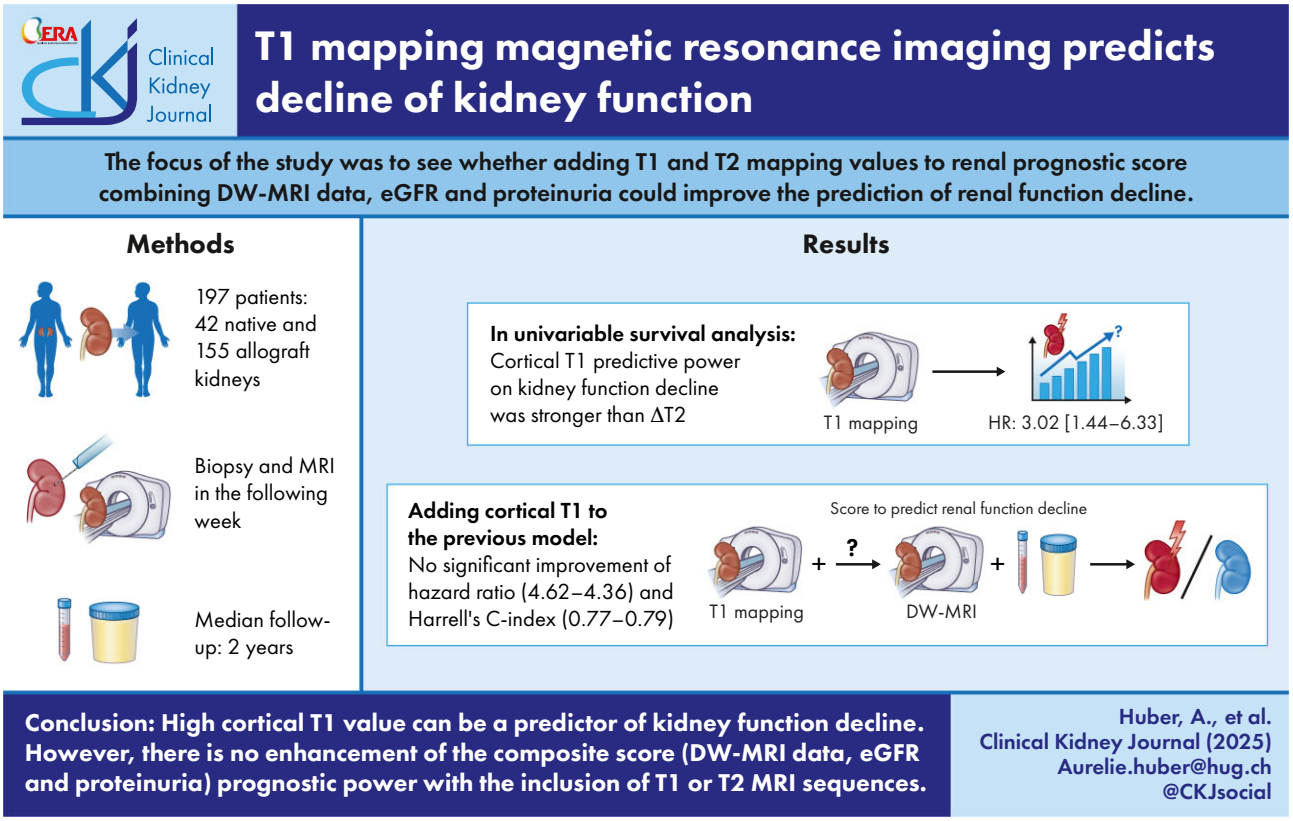
GRAPHICAL ABSTRACT



Keywords: chronic kidney disease, magnetic resonance imaging, prediction, renal fibrosis, renal function decline

KEY LEARNING POINTS

What was known:

- Renal cortical fibrosis, traditionally evaluated via biopsy, is a predictor of renal function decline.
- Magnetic resonance imaging (MRI) offers a promising non-invasive alternative for assessing fibrosis.
- Diffusion-weighted MRI (DW-MRI) has demonstrated correlations with renal fibrosis and can predict kidney function decline in patients with chronic kidney disease (CKD) and kidney allografts.

This study adds:

- In this cohort of 197 patients, comprising individuals with CKD and kidney allografts, our findings indicate that T1 mapping is predictive of renal function decline, whereas T2 mapping is not.
- However, the addition of T1 sequence values to the DW-MRI-based predictive model does not enhance its predictive capability.

Potential impact:

- This study emphasizes that MRI could become a valuable non-invasive tool for assessing renal function.
- T1 MRI may improve the assessment of individual renal prognosis, particularly in patients for whom biopsy is challenging or not clearly indicated and could help identify patients who require closer follow-up to prevent disease progression.

INTRODUCTION

Chronic kidney disease (CKD) is characterized by abnormal kidney structure and/or function lasting >3 months. It affects ≈13% of the global population [1]. End-stage kidney disease (ESKD) is less frequent, with a prevalence estimated at 1 in 1000 CKD patients, but significantly impacts morbidity, mortality and healthcare costs [1]. Early identification, prevention and management can reduce CKD progression to ESKD in high-risk patients.

Classic biomarkers, such as serum creatinine and albuminuria, have limitations in identifying CKD and predicting progression to ESKD [2]. Creatinine levels are influenced by muscle mass, age, sex, medication and diet, while albuminuria is absent in up to 30% of patients progressing to ESKD. More than

50% of nephrons can be lost before creatinine-based glomerular filtration rate (GFR) estimates decrease, when significant kidney injury, inflammation and fibrosis have already occurred. This is due to compensatory hyperfiltration and glomerular hypertrophy in the remaining nephrons [3, 4], potentially delaying CKD diagnosis. Thus GFR could be considered more reactive than prognostic. Albuminuria indicates glomerular injury, which manifests after prolonged inflammation, cellular injury, fibrosis and glomerular hyperfiltration [5]. These markers identify disease progression after it has occurred, missing opportunities for early intervention and prevention [6].

The common histological feature of CKD is cortical interstitial fibrosis (IF), which correlates with and predicts renal function loss better than other histological lesions or biomarkers [7, 8]. Current methods for assessing renal fibrosis are mainly limited to kidney biopsies. While informative, biopsies provide random, focal assessments of the kidney [9] and are associated with risks such as haemorrhage and pain, limiting their use for serial disease monitoring [10]. Currently, no recognized non-invasive method is generalized to assess global, diffuse renal fibrosis.

Advancements in magnetic resonance imaging (MRI) have prompted its consideration as a non-invasive tool for assessing renal structure and function [11]. Diffusion-weighted MRI (DW-MRI) measures the Brownian motion of water molecules in tissues, providing insights into tissue microstructure. DW-MRI has shown promising results in assessing renal fibrosis [12]. The apparent diffusion coefficient (ADC) measured by DW-MRI strongly correlates with estimated GFR (eGFR) and renal fibrosis in murine models and CKD patients [13–16]. Improved DWI-MRI resolution, achieved with the RESOLVE sequence [17], has identified a strong correlation between interstitial fibrosis and the corticomedullary difference in ADC (ΔADC) [16, 18]. This DW-MRI parameter is also a strong and independent predictor of renal function decline [19].

T1 mapping quantifies longitudinal (spin–lattice) relaxation time of proton spins, influenced by tissue composition such as fat, water, iron and proteins [20]. This technique, used to assess cardiac fibrosis [21], holds potential for non-invasive evaluation of renal diseases. Previously, we reported an association between the corticomedullary difference in T1 (ΔT1) and renal fibrosis in both native and transplanted kidneys [22]. Shi *et al.* [23] demonstrated that higher cortical T1 values in native CKD patients correlate with worse prognosis and higher risk of adverse renal events in an Asian population.

T2 mapping measures the transverse (spin–spin) relaxation time of proton spins and is sensitive to water content, with prolonged values indicating oedema caused by inflammation or reperfusion. T2 mapping is a potential quantitative parameter for assessing pathophysiological changes in the kidney's structural and functional organization. Although limited studies exist, T2 mapping has shown promise in detecting fluid accumulation, such as oedema or inflammation, and tracking the progression of autosomal dominant polycystic kidney disease (ADPKD) [24].

Multiparametric MRI integrates multiple parametric or quantitative imaging techniques. In this study, we combined DW-MRI, T1 mapping and T2 mapping.

Recently, we developed a model to calculate a risk score for future renal function decline based on changes in ADC, eGFR and proteinuria [19]. In this study, we investigate whether T1 and T2 mapping sequences can independently predict poor renal outcomes. T1 and T2 mapping sequences offer detailed tissue characteristics, potentially reflecting changes in kidney structure and function not captured by ΔADC, eGFR and proteinuria alone. We hypothesized that adding T1 and T2 mapping sequences to the existing model could improve its prognostic accuracy.

MATERIALS AND METHODS

Study design and population

This study was performed in a single-centre prospective cohort, including individuals ≥18 years of age who received a kidney transplant or have CKD [15]. Participants were recruited based on their clinical need for a kidney biopsy from August 2013 to October 2018, with clinical follow-up until 2023. Exclusion criteria included MRI contraindications such as implanted pacemakers, current pregnancy, known claustrophobia or declined participation. Eligible patients provided written informed consent, authored by the research team. The biopsy was conducted by the attending nephrologist, unaffiliated with the research team. Participants underwent a multiparametric MRI, preferably on the same day as the biopsy or within 1 week. Concurrently, blood and urine were collected and cryopreserved at −80°C. Annual follow-ups entailed clinical assessments and periodic blood and urine evaluations by the nephrology department for up to 5 years. The local ethics committee approved the study protocol (CCER 11-160) and the study adhered to the principles of the Declaration of Helsinki.

Data collection

Data acquisition included demographic information, comorbidities, medical history, medication regimens and laboratory results from samples taken on the biopsy day, as recorded in the electronic health records. Biopsy and MRI results were documented according to the protocol.

During standard clinical follow-up, laboratory results were collected. Creatinine and albumin levels, along with other standard tests, were conducted on blood and urine specimens. The eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) 2021 formula, with creatinine measurements adhering to the Jaffe kinetic method calibrated against isotopic dilution mass spectrometry. In the absence of 24-h urine protein data, proteinuria was estimated using the urine protein:creatinine ratio in a single urine sample.

Renal fibrosis quantification

Renal fibrosis was determined by an expert pathologist employing a semi-quantitative method on Masson's trichrome–stained sections [9], the standard in most centres [25, 26].

MRI

The multiparametric MRI protocol was executed on the Magnetom Prisma 3-Tesla MR system (Siemens Healthineers, Erlagen, Germany), leveraging a 32-element spine coil for enhanced signal:noise ratio in spine-adjacent structures such as the kidney, combined with an 18-element phased-array abdominal coil for homogeneous signal in the abdomen. Regions of interest were identified on the T1 map by a specialized MR physicist, blind to additional data, covering approximately 1 cm^2 for the cortex and 20 mm^2 across three medullary zones (avoiding cysts, haematomas or scars) [17]. These areas were analysed across sequences, as previously validated [18]. The imaging protocol included T1 and T2 mapping, as previously published [22], along

with DW-MRI employing the readout segmented RESOLVE sequence that enables measurement of the corticomedullary differences in the apparent diffusion coefficient (ΔADC) [18]. The T1 mapping used the MOLLI sequence, in agreement with the international recommendations for renal imaging [27].

The reproducibility of MR-derived variables was verified by two independent readers on a sample of the scans, achieving intraclass correlation coefficients >0.91 [95% confidence interval (CI) 0.92–0.99] [16].

Outcomes

The primary outcome was defined as either a reduction in eGFR >30% during the follow-up period (termed rapid renal function decline) or the initiation of renal replacement therapy (RRT) [28]. For participants who passed away, the most recent eGFR measurement was utilized for outcome assessment.

Statistical analysis

In our study, continuous variables were presented as means with 95% CIs or medians with interquartile ranges (IQRs), based on their distribution. Frequencies and percentages were used for categorical variables.

A post hoc power analysis based on the observed results indicated a power of 82%, which is generally considered adequate for detecting significant associations in clinical studies.

To investigate the advantage of adding other MRI information to the previously validated prognostic score for renal function decline (including eGFR, proteinuria and ΔADC), we first tested different MRI sequences (diffusion, T1 mapping and T2 mapping) and found no collinearity using the variance inflation factor (VIF) and correlation calculations. Specifically, for cortical T1 and ΔADC, the VIF was 1.45 and the correlation coefficient (R) was −0.17, confirming the absence of significant collinearity.

To ascertain if T1 or T2 values can predict renal function deterioration, we employed Kaplan–Meier survival analysis and univariable Cox regression to calculate HRs for the cortex, medulla and corticomedullary differential using T1 and T2 mapping MRI sequences. Each variable was categorized into tertiles. The logrank test was used for survival curve comparisons. HRs, 95% CIs and *P*-values were derived from Cox models.

We further analysed the data using multivariable Cox proportional hazards modelling, initially including ΔADC, eGFR and proteinuria (model 1), followed by the addition of cortical T1 (model 2). Harrell's C-index was employed to evaluate model performance. The inclusion of eGFR and proteinuria as covariates was based on established scientific literature. Additionally, we compared the discriminative performances of two predictive models using receiver operating characteristics (ROC) curves and their area under the curve (AUC). A calibration plot was used to assess the agreement between predicted and observed probabilities, ensuring that the models provide reliable predictions across the spectrum of risk levels. Logistic regression was performed separately for each model (ΔADC, eGFR and proteinuria for model 1 and with the addition of cortical T1 for model 2) and the chi-squared test was used to evaluate differences between the two corresponding ROC curves. Statistical significance for all analyses was set at a two-tailed α of 0.05.

Statistical analyses were performed using Stata 18 (StataCorp, College Station, TX, USA).

RESULTS

Population description

The study cohort included 197 patients who underwent biopsies from August 2013 to October 2018. Among them, 78.2% (154 patients) had kidney transplantation and 21.8% (43 patients) were evaluated for native kidney issues. The majority were male (68.0%), with an average age of 54 years [standard deviation (SD) 14.0] and a normal body mass index [BMI; 24.5 kg/m^2 (SD 5.7)]. At baseline, the mean eGFR was 54.4 ml/min/1.73 m^2 (SD 23.6) using the CKD-EPI 2021 equation and mean proteinuria was 0.9 g/24 h (IQR 0.06–0.47). Detailed characteristics of the patients are displayed in Table 1.

Biopsies on native kidneys were predominantly performed for acute kidney injury (19.5%) or chronic renal dysfunction with proteinuria or haematuria (80.5%) Allograft biopsies were conducted according to protocol at 1-year post-transplant (52.3%) or in response to allograft dysfunction indicators, such as increased creatinine (18.1%), new-onset proteinuria (7.8%) or the emergence of *de novo* donor-specific antibodies (9%). Other indications for transplant biopsies included post-rejection treatment, BK virus evaluation and pre-immunosuppression change (12.8%).

All patients in the cohort underwent an MRI. T1 mapping sequence data were available for 194 patients, T2 data for 156 patients and ADC sequences for 188 patients. Missing MRI data were due to image acquisition artifacts or incomplete exams caused by technical reasons or patient refusal during the MRI.

Outcome description

During the follow-up period, which had a median duration of 2.2 years (IQR 1.1–3.7) post-biopsy, rapid renal function decline or RRT initiation was diagnosed in 54 patients, within a median time frame of 1.1 years (IQR 0.9–2.1). The outcome is illustrated by a Kaplan–Meier survival curve (Supplementary Fig. 1). Of the 11 patients who passed away during follow-up, 5 had met the criteria for rapid renal function decline or RRT initiation prior to their death. For the remaining six, categorized as non-rapid decliners, their last recorded eGFR was incorporated into the analysis.

When comparing patients based on renal outcomes, demographic characteristics were similar, as shown in Table 1. However, participants who experienced adverse renal outcomes had significantly lower baseline mean eGFR and higher proteinuria and fibrosis levels. Regarding MRI-derived parameters, significant differences were observed in ΔADC, cortical T1 and ΔT1 measurements.

To further investigate the relationship between baseline eGFR and T1 values, we calculated the Pearson correlation, which was low (for cortical T1: $R = -0.1$, $P = .197$; for medullary T1: $R = 0.2$, $P = .017$; for ΔT1: $R = -0.3$, $P < .001$), as shown in Supplementary Fig. 5.

Univariable analysis

Univariable survival analyses for rapid renal function decline or RRT initiation were conducted for each independent T1 and T2 mapping MRI sequence (cortical T1, medullary T1, ΔT1, cortical T2, medullary T2 and ΔT2); results are in Table 2.

Cortical T1 demonstrated the strongest predictive value, with an HR of 2.20 (95% CI 1.02–4.70, $P = .044$) for T1 values of 1500–1617 $\times 10^{-6}$ mm^2/s and 3.02 (95% CI 1.44–6.33, $P = .003$) for

Table 1: Baseline demographic, clinical and radiologic characteristics of study participants, categorized by the presence or absence of the renal outcome.

Characteristics	Missing values, *n*	Total (*N* = 197)	Renal outcome		*P*-value[c]
			Absent [*n* = 143 (72.6%)]	Present [*n* = 54 (27.4%)]	
Demographic characteristics					
Male, *n* (%)	0	134 (68.0)	102 (71.3)	32 (59.3)	.105
Age (years), mean (SD)	0	54.1 (14.0)	53.9 (14.0)	54.6 (14.0)	.750
BMI (kg/m^2), mean (SD)	0	24.9 (5.7)	24.8 (5.4)	25.2 (6.5)	.675
Native kidneys, *n* (%)	0	43 (21.8)	29 (20.3)	14 (25.9)	.392
Allograft kidneys, *n* (%)	0	154 (78.2)	114 (79.7)	40 (74.1)	.392
Laboratory findings					
eGFR[a] (ml/min/1.73 m^2), mean (SD)	0	54.4 (23.6)	57.2 (20.8)	46.9 (28.6)	.006
≥60	0	71 (36.0)	55 (38.5)	16 (29.6)	<.001
<60–≥30	0	102 (51.8)	80 (55.9)	22 (40.7)	
<30	0	24 (12.2)	8 (5.6)	16 (29.6)	
Proteinuria[b] (g/24 h), mean (IQR)	20	0.9 (0.06–0.47)	0.6 (1.9)	1.8 (3.5)	.004
<0.3	20	119 (67.2)	98 (74.8)	21 (45.7)	
≥0.3–<3.0	20	45 (25.4)	28 (21.4)	17 (37.0)	
≥3.0	20	13 (7.3)	5 (3.8)	8 (17.4)	
Histologic findings	1	28 (19)	24 (15)	39 (25)	<.001
Fibrosis level (%), mean (SD)					
MRI parameters (×10^{-6} mm^2/s), mean (SD)					
ADC cortex	9	1811.0 (232.6)	1808.3 (228.7)	1817.6 (243.9)	.807
ADC medulla	9	1838.4 (248.7)	1849.3 (237.5)	1811.5 (275.0)	.347
ΔADC	9	28.0 (110.3)	41.8 (111.9)	−6.2 (98.9)	.007
T1 cortex	3	1541.4 (171.6)	1520.0 (163.2)	1598.3 (181.8)	.004
T1 medulla	3	1853.5 (215.3)	1861.5 (215.736)	1832.3 (214.8)	.401
ΔT1	1	−310.5 (154.7)	−339.1 (144.7)	−234.1 (155.8)	<.001
T2 cortex	41	78.2 (17.5)	77.4 (17.2)	80.3 (18.3)	.354
T2 medulla	41	72.7 (17.3)	71.7 (17.1)	75.5 (17.8)	.236
ΔT2	41	5.4 (6.5)	5.6 (6.7)	4.9 (6.0)	.510
Follow-up duration (years)	0	2.5	2.9	1.6	<.001

[a]eGFR was calculated with the CKD-EPI 2021 equation.
[b]Proteinuria in 24 h. In the absence of 24-h urine protein data, proteinuria was estimated using the protein:creatinine ratio.
[c]Statistical differences between the outcome groups were assessed using Pearson chi-squared test for categorial variables and Student's *t*-test for continuous variable, with assessment of *P*-value.

cortical T1 values exceeding 1617 × 10^{-6} mm^2/s. This is illustrated in the Kaplan–Meier survival curve in Fig. 1, with distinct curves across the three cortical T1 categories (logrank test). Medullary T1 values were not significant, while the T1 corticomedullary difference was statistically significant in the third tertile [HR 2.20 (95% CI 1.08–4.52), *P* = .031] (Table 2). Subgroup analysis for natives and allograft kidneys showed similar results, but the sample size was limited (Supplementary Figs. 2 and 3). In eGFR-stratified subgroups, high cortical T1 shows a stronger predictive value for eGFR ≥60 ml/min/1.73 m^2, suggesting its potential as an early prognostic tool, particularly before detectable changes in eGFR. However, the small subgroup sample size limits its statistical power and interpretation (Supplementary Table 3).

Change in T2 relaxation time was not predictive of renal function decline. The HR for corticomedullary difference measurements (ΔT2) was significant only for the second category (3–7 × 10^{-6} mm^2/s), with an HR of 1.56 (95% CI 1.14–5.76, *P* = .023). The overall logrank test for ΔT2 was not significant, as depicted in the Kaplan–Meier graph with crossing curves in the last two categories (Fig. 2). Medullary and cortical T2 values had non-significant HRs (Table 2).

Moreover, subgroup analysis of 88 per-protocol biopsies and 112 acute-settings biopsies showed no significant differences in survival curves or HRs for the T1 and T2 mapping sequences (*P* > .05).

Multivariable analysis

Multivariate analyses were conducted to evaluate the association between cortical T1, which showed the best predictive value in univariable analysis, and renal function deterioration. These analyses also included other components of the previously published composite score, such as ΔADC, eGFR and proteinuria. Proportional multivariable Cox regression models identified negative ΔADC, decreased eGFR, elevated proteinuria and increased cortical T1 as independent predictors of renal function decline. However, the HR for cortical T1 did not reach statistical significance. Table 3 sums up the component of this regression model. The overall prognostic accuracy, assessed by Harrell's C-index, was 0.79 for the model incorporating all the aforementioned variables, which was marginally greater than the 0.77 achieved by the model including only ΔADC, eGFR and proteinuria. This marginal increase was not deemed clinically significant. As univariable analysis showed no predictive value in T2 mapping sequences, we had no argument to add them to the prognostic score. The HRs from different multivariable models, adjusted to eGFR alone, and for both eGFR and proteinuria, did not reach statistical significance but showed a trend toward predicting renal function decline (Supplementary Table 4).

Table 2: Univariable Cox regression for renal outcome according to the cortical, medullary and corticomedullary difference measurement in T1 and T2 MRI sequences.

		Univariate	
MRI sequence	($\times 10^{-6}$ mm^2/s)	HR (95% CI)	P-value
T1 cortex	<−1500	Reference	
	≥−1500 and <1617	2.19 (1.02–4.70)	.044[a]
	≥1617	3.02 (1.44–6.33)	.003[a]
T1 medulla	<1820	Reference	
	≥1820 and <1970	1.5 (0.70–2.87)	.212
	≥1970	0.8 [0.43–1.83]	.743
ΔT1	<−396	Reference	
	≥−396 and <−224	1.6 (0.75–3.47)	.225
	≥−224	2.2 (1.08–4.52)	.031[a]
T2 cortex	<88.5	Reference	
	≥88.5 and <74.5	1.1 (0.51–2.15)	.893
	≥74.5	1.4 (0.65–3.02)	.397
T2 medulla	<82.6	Reference	
	≥82.6 and <71.5	0.9 (0.42–1.80)	.687
	≥71.5	1.2 (0.57–2.60)	.609
ΔT2	>7	Reference	
	≤7 and >3.2	2.56 (1.14–5.76)	.023[a]
	≤3.2	1.94 (0.86–4.39)	.113

[a]Statistical significance at $P < .05$.

ROC curves were used to further compare the prognostic models. The AUC for predicting renal adverse outcomes for cortical T1, ΔADC, eGFR and proteinuria were 0.61, 0.63, 0.66 and 0.71, respectively (Supplementary Fig. 4). A prognostic score combining ΔADC, eGFR and proteinuria had an AUC of 0.69, which improved to 0.73 after incorporating cortical T1 into the model (Fig. 3).

DISCUSSION

Predicting CKD progression remains challenging, and non-invasive MRI-derived parameters may offer valuable insights. In a cohort of 197 patients who underwent kidney biopsies for medical reasons—comprising 154 allografts and 43 native kidneys—we found that high cortical T1 values predict rapid renal function decline and RRT initiation.

Participants having experienced rapid renal function decline had significantly lower baseline mean eGFR, higher proteinuria levels and greater fibrosis ($P < .05$). Significant differences in MRI parameter measurements between these two groups were observed for ΔADC, cortical T1 and ΔT1 ($P < .05$), but not for other MRI-derived parameters.

Univariable analysis for T1 mapping indicated that cortical values had the strongest association with renal function decline and RRT initiation, outperforming medullary and corticomedullary difference values. This may be due to the location of glomeruli in the renal cortex compared with the medulla, making it more susceptible to CKD progression. Higher cortical T1 values correlated positively with an increased risk of renal function decline and RRT initiation. Kaplan–Meier analysis revealed significant differences in renal outcomes among low, moderate and high cortical T1 values, suggesting that cortical T1 could potentially become a useful non-invasive predictive tool for CKD progression. Stratification by eGFR demonstrated greater predictive power for baseline eGFR ≥60 ml/min/1.73 m^2, highlighting its potential as an early indicator of renal function decline, especially before measurable changes in eGFR occur.

High cortical T1 values have been measured in immunoglobulin A nephropathy [20] and CKD patients [29, 30], supporting our results. Moreover, an association between cortical T1 values and renal fibrosis has been confirmed in several studies [31–34], reinforcing the potential of T1 mapping sequences as a prognostic tool for renal function decline, as cortical fibrosis is an early histological change preceding GFR decline. This association with interstitial fibrosis was also confirmed in allograft biopsies [22, 34, 35], suggesting its potential for the evaluation of chronic allograft damage.

Prior investigations of this cohort revealed that baseline eGFR, proteinuria and a negative ΔADC correlated with accelerated renal function deterioration through univariate analysis. Consequently, a composite score comprising these variables was established to forecast renal function decline [19]. When adding cortical T1 to this risk score model for renal function decline, we did not observe a significant improvement in the predictive power of the model, as confirmed by a similar Harrell's C-index.

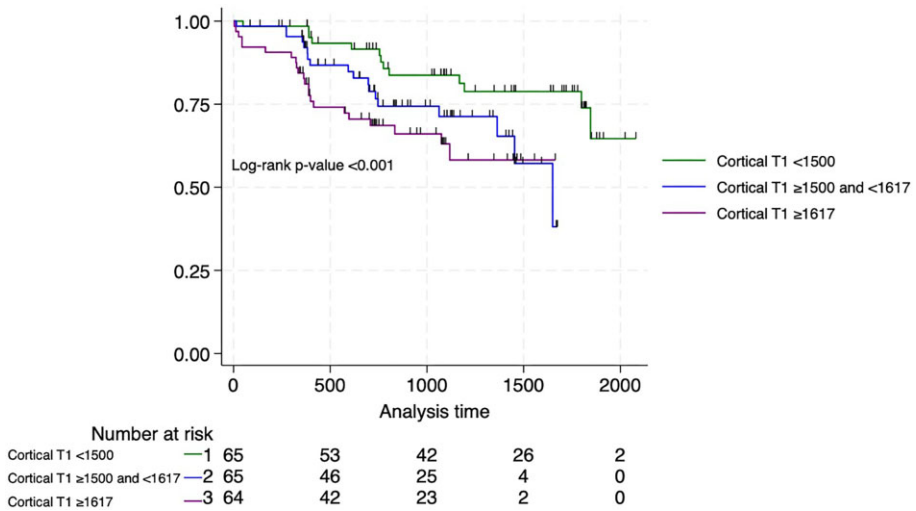


Figure 1: Kaplan–Meier survival curve for renal outcome, stratified according to cortical T1 categories (tertile).

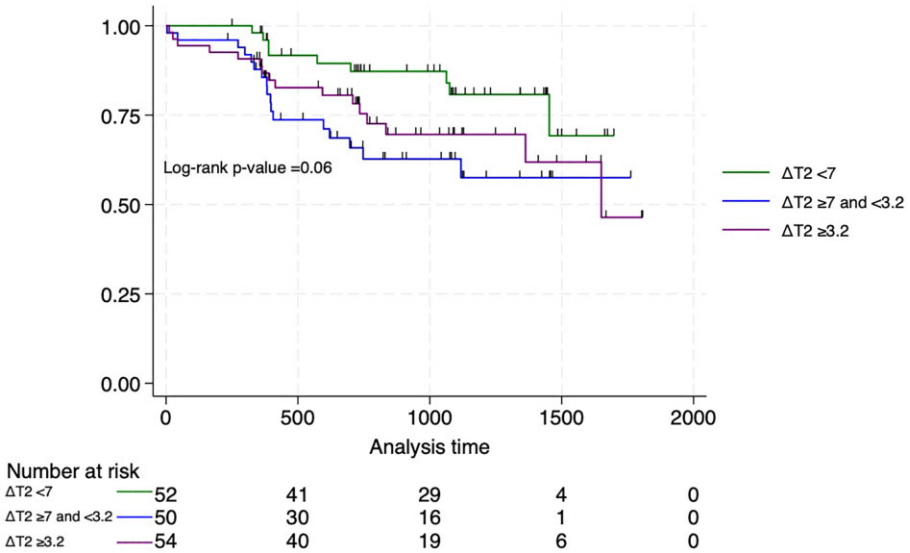


Figure 2: Kaplan–Meier survival curve for renal outcome, stratified according to corticomedullary difference T2 categories (tertile).

Table 3: Composite score including ΔADC, eGFR and proteinuria and cortical T1 to predict the renal function decline.

Multivariable model	Coefficient beta	HR (95% CI)	*P*-value
ΔADC ≥0 and ≤100 × 10^{-6} mm^2/s	0.67	1.96 (0.69–5.57)	.208
ΔADC <0 × 10^{-6} mm^2/s	1.47	4.35 (1.45–13.09)	.009[a]
Cortical T1 ≥−1500 and <1617 × 10^{-6} mm^2/s	0.70	2.00 (0.90–4.48)	.091
Cortical T1 ≥1617 × 10^{-6} mm^2/s	0.54	1.72 (0.76–3.93)	.196
eGFR ≥30 and <60 ml/min/1.73 m^2	0.14	1.15 (0.54–2.46)	.721
eGFR <30 ml/min/1.73 m^2	1.04	2.65 (1.10–7.24)	.031[a]
Proteinuria ≥0.3 and <3.0 g/24 h	1.10	3.00 (1.43–6.31)	.004[a]
Proteinuria ≥3.0 g/24 h	0.98	2.65 (1.05–6.71)	.039[a]

[a]Statistical significance at $P < .05$.

Although the absence of collinearity between ADC and T1 sequences confirms that they measure different aspects of renal physiology, there may be an overlap in the information provided by ΔADC and cortical T1 values, as both are strongly correlated with fibrosis [16]. Moreover, T1 values are not specific to interstitial fibrosis and also increase with other histological lesions such as tubular atrophy and interstitial inflammatory cell infiltration [7, 32], which can be reversible and hence impact the association with renal function decline [34]. To complete the evaluation of our model, we used ROC curves that showed a small improvement in the AUC after adding cortical T1 (from 0.69 to 0.73). This suggests a potential predictive benefit in adding cortical T1, even though we could not establish statistical significance.

To the best of our knowledge, only one other study has investigated the predictive power of T1 mapping in renal decline [23]. Shi *et al.* [23] demonstrated an association between cortical T1 values and CKD as well as a poorer renal prognosis in a cohort of 119 CKD patients with the same renal endpoints and follow-up period as ours. Their ROC curves analysis showed that combining cortical T1 values with cystatin C and haemoglobin levels enhanced the predictive power for renal function decline. Their findings are consistent with our univariable analysis, where patients with high cortical T1 values had poorer survival. In our study, adding T1 mapping sequences to the existing risk model resulted in a higher AUC value, indicating improved predictive accuracy for renal outcomes. However, the increase was not statistically significant. This discrepancy may be due to differences in the components of the risk models (haemoglobin and cystatin C versus eGFR, proteinuria and ΔADC in our study) or the different thresholds used in T1 mapping. Specifically, we divided T1 measurements into tertiles to ensure a balanced distribution of data points and facilitate a more detailed analysis, as suggested in previous studies. In contrast, Shi *et al.* [23] defined low/high T1 values as ≤/>90% of the highest T1 value, which corresponded to <5% of our cohort. Additionally, their study was performed in an Asian population, did not include allograft patients and only a minority had undergone a simultaneous kidney biopsy. Hence the clinical settings were different, limiting the comparison of the studies. Also, by using survival analysis that considers time-to-event data, we could evaluate changes in risk over time, include covariates and understand their effects on survival time. Thus, while cortical T1 shows promise, further validation is needed to establish its added predictive value over existing biomarkers.

T2 mapping sequences did not show a significant association with renal function decline. One previous study found a significant increase in T2 values in allograft patients compared with healthy subjects, but no association with allograft function was observed [36]. Additionally, two other studies did not find any correlation between T2 results and renal fibrosis [22, 35], which

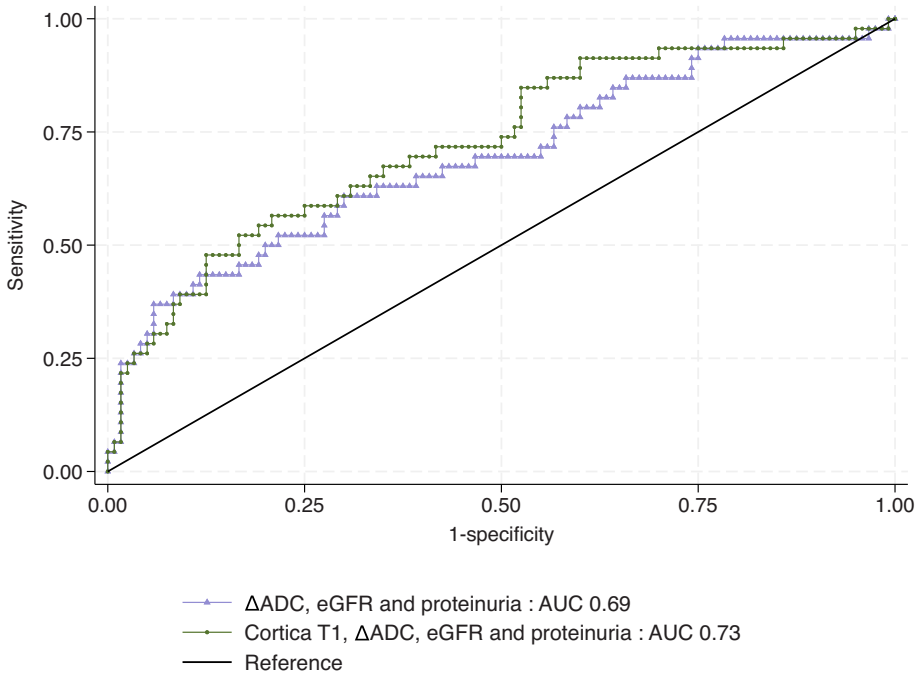


Figure 3: ROC curve for renal adverse endpoint using prognostic composite scores.

is consistent with our findings. T2 values capture different information than T1 values. Specifically, T2 values are more sensitive to interstitial oedema, a parameter that is present in acute situations, although its role in long-term outcomes is uncertain. We did not find a significant difference between per-protocol biopsies and those performed in acute settings, which could be attributed to the small sample size or the lack of influence of this parameter on T2 values. Given the limited clinical studies on T2 mapping for renal function assessment, further research is necessary to evaluate its potential in this area. Animal model results suggest a role for T2 mapping in the early evaluation of ADPKD [37]. Additionally, secondary analysis of Beck-Tölly *et al.*'s study [35] indicates potential for investigating glomerulitis associated with antibody-mediated rejection.

The strengths of our study include the demographic characteristics of the patients who are typically seen in clinical practice. Moreover, with a median follow-up of 2.2 years, this study represents the largest investigation to date into the use of T1 and T2 mapping sequences for renal function prediction. However, we acknowledge that the relatively short follow-up is a limitation to the study. As a result, it is possible that some patients with high T1 values may develop renal dysfunction later, which was not captured within the current follow-up duration.

The monocentric nature of our study limits the generalizability of the results. However, our relatively large cohort, which includes both native and allograft patients, is a strength compared with other studies on the same topic. Our cohort encompasses all patients who underwent biopsy for medical reasons or as part of a transplantation follow-up protocol. The heterogeneity of biopsy indications, ranging from acute to chronic clinical settings, may obscure specific effects or weaken existing associations. Nonetheless, this diversity makes our findings more representative of the broader nephrology patient population. We encountered some technical limitations, including missing T2 mapping sequence data due to imaging artifacts, which reduced the statistical power to detect associations. While the prospective cohort design has many strengths, it does not guarantee adjustment for all potential confounding variables. Future studies could focus on the association between renal T1 mapping and pathophysiological processes to better elucidate its clinical utility, particularly in patients with normal eGFR who could develop CKD.

While MRI offers valuable non-invasive insights into renal structure and function, its accessibility is limited in certain clinical settings due to cost, availability and the need for specialized equipment. This may restrict its widespread use.

In conclusion, our data indicate that high cortical T1 values are predictive of rapid renal function decline and RRT initiation. T1 is therefore a promising non-invasive tool to assess renal outcome. However, incorporating this parameter into the existing predictive model, which includes eGFR, proteinuria and ΔADC, did not enhance its predictive accuracy. Therefore, the addition of multiparametric MRI-derived parameters did not improve renal outcome prediction.

SUPPLEMENTARY DATA

Supplementary data are available at *Clinical Kidney Journal* online.

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AUTHORS' CONTRIBUTIONS

A.H. and L.B. contributed to the study design, statistical analysis and manuscript writing. I.A. and L.C. contributed to MRI acquisition, analysis and manuscript revision. J.P.V. contributed to the study design, MRI supervision and manuscript revision. S.d.S., M.P. and T.d.P. contributed to the study design and manuscript revision. All authors read and approved the published version of the manuscript. JPV is supported by a grant from the Swiss National Science Foundation (320038_159714, IZCOZO_177140). This work was supported in part by the Centre for Biomedical Imaging (CIBM) of EPFL, University of Geneva and the University Hospitals of Geneva and Lausanne and the Swiss National Foundation for its financial support for the PRISMA MRI (R'Equip grants: SNF No. 326030_150816).

DATA AVAILABILITY STATEMENT

The data underlying this article will be shared upon reasonable request to the corresponding author.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest.

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