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The Relationship between Residual Kidney Function and Symptom Burden in Hemodialysis Patients

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Peter Mount – oversight, supervision of data collection, data analysis and interpretation, manuscript revision

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

INTRODUCTION

In hemodialysis (HD) patients, higher levels of residual kidney function (RKF) have been correlated with better outcomes including improved survival, nutrition (1), anaemia (2), and phosphate control (3). Despite this, in contrast to peritoneal dialysis, RKF is not routinely monitored in most HD patients, so the effects of RKF on the control of uremia in HD patients is frequently overlooked. In contrast to the intermittent nature of HD, RKF achieves continuous solute clearance and fluid removal, such that even low levels of RKF could have meaningful effects. HD dose is most commonly determined and monitored by the urea clearance of an individual treatment session, not taking into account RKF. Nonetheless, various methods such as standard Kt/V (stdKt/V) (4) and equivalent renal urea clearance (5)

have been developed, aiming to integrate the dialysis clearance with RKF. The US Kidney Disease Outcomes Quality Initiative (KDOQI) guideline suggests that for hemodialysis patients with RKF of ≥2 ml/min/1.73m^2 urea clearance (KRU), the dose of hemodialysis may be reduced provided RKF is measured periodically to avoid inadequate dialysis (6).

End stage kidney disease (ESKD) is associated with reduced quality of life and a large symptom burden (7). Whilst HD prolongs life in ESKD, the burden of uremic symptoms remains high in these patients (8). Disappointingly, more intensive HD regimens do not necessarily improve quality of life in HD patients (9). The high symptom burden in HD patients might be related to some extent to the poor removal of certain uremic solutes by HD (10). Whereas HD efficiently removes low molecular weight uremic toxins, RKF is comparatively more efficient for larger molecular weight and protein bound uremic solutes, which are poorly removed by HD (10). Recently, there has been renewed interest in the role of RKF in HD patients, and how RKF might be integrated into the care of HD patients. Little is known about the relationship between RKF and symptom burden in HD patients.

The aim of this study was to determine the prevalence of RKF in a cohort of HD patients, and to examine the associations of RKF with symptom burden and solute clearance, hypothesising that higher levels of RKF in HD patients will be associated with improvements of these parameters.

METHODS

This is a single centre, retrospective, observational study. Ethics approval was granted by The Austin Health Human Research Ethics Committee as a low risk study (LNR/17/Austin/414).

Patients

We extracted medical record data from all hemodialysis patients aged > 18 years treated under Austin Health from 1 October, 2017 through 1 May, 2018. All were clinically stable at the time of the study and were treated with high-flux membranes produced by Baxter (Revaclear and Polyflux).

Data Collection

RKF was assessed by a timed interdialytic urine collection between the first and second dialysis session of the week. Patients with self-reported urine output of less than 200ml over the interdialytic period were considered to have an RKF value of 0ml/min/1.73m^2. Patients who had a self-reported interdialytic urine output ≥ 200ml but were unwilling or unable to perform a timed urine collection were excluded from the study.

Symptom burden was measured using the palliative care outcome scale symptom questionnaire modified for use in patients with renal failure (POS renal). Functional status was assessed with the Karnofsky performance score. The POS renal questionnaire includes seventeen symptoms, each graded from 0-4 as absent (0), mild (1), moderate (2), severe (3) or overwhelming (4). A total symptom score was calculated by adding the graded score for each individual symptom (possible

range = 0-68). Data was collected retrospectively using the most recently available completed questionnaire.

Demographic, Clinical, and Laboratory Measures

Demographics and medication use were obtained from the electronic medical record. Comorbidities were assessed using the Charlson Comorbidity Index (CCI). Laboratory data were available from routine patient care. Dialysis information were obtained from the second dialysis session of the week of the RKF assessment. Blood pressure (BP) measurements were performed before and after each dialysis session in a seated position.

Total Solute Clearance and Dialysis Adequacy

Renal urea clearance (KRU) and creatinine clearances were calculated from timed urine collection and corrected for a body surface area of $1.73m^2$ (Mosteller equation). Urine collections began at the end of the first dialysis session of the week until the commencement of the next session (approximately 43.5 hours). Mean interdialytic urea and creatinine concentration were calculated using the mean of the pre- and post-dialytic plasma concentrations. Post –dialysis blood tests were performed using the slow pump method, in which the blood flow is reduced to 50-100 ml/min for two minutes whilst the dialysate flow is ceased, prior to taking the blood sample. Residual GFR as $ml/min/1.73m^2$ was defined as mean of urea and creatinine clearances, as per European Best Practice Guidelines (11).

Total weekly dialysis clearances were determined by urea clearance, using the standard Kt/V (StdKt/V) derived from Gotch and Leypoldt's fixed volume equation as adapted by Daugirdas (4), calculated by using an available online calculator (www.hdcn/calf/ley.htm). To allow summation of dialysis and native clearances the total weekly renal urea clearance was converted to a weekly renal stdKt/V. Total body water was determined by the Watson equation. The total (dialysis + renal) weekly stdKt/V was determined by adding the dialysis and renal stdKt/V values.

Statistical Methods

Categorical variables were summarised as percentages. Continuous variables were reported as means with standard deviations (SD). Means were compared using one sample t test. Baseline characteristics of participants were compared based on their KRU using Mann-Whitney test or Chi-square test, as appropriate. Fisher's exact test was used for categorical variables with $n<5$ for one or more comparator groups. Pearson correlation analysis was used to model the association between measures of RKF and continuous variables including β2M, potassium, hemoglobin, CRP, time on renal replacement therapy, and number of symptoms. Statistical analyses were performed using GraphPad InStat software, version 3.10. Graphs were generated using GraphPad Prism software, version 7.04 or Microsoft Excel 2016 MSO version (16.0.9330.2073). Statistical significance was defined as $p \leq 0.05$ using 2-tailed tests.

RESULTS

Participant Characteristics

101 maintenance HD patients were screened, and 90 were included in the study. 11 non-anuric patients in the cohort were excluded from the study due to lack of timed urine collection for analysis (8 patients refused, 3 were unable to perform).

Baseline characteristics of the participants were stratified by KRU level <1 and ≥1ml/min/1.73m2, as described in Table 1. Of the 90 patients, 61.1% of patients were anuric, defined as a measured or self-reported urine output of less than 200 ml over the interdialytic period. The mean KRU was 0.91 ± 1.37 ml/min/1.73m2. The mean GFR was 1.53 ± 2.16 ml/min/1.73m2. Patients with higher levels of RKF were younger (p=0.042) and more likely to be male (p=0.040) and Asian (p=0.038). They also had a shorter duration of renal replacement therapy (p<0.0001) and HD therapy (p<0.0001). A higher proportion of patients with greater RKF were on diuretic therapy, with 39.3% of patients with KRU ≥1ml/min/1.73m2 on diuretics compared to 9.7% in patients with KRU <1ml/min/1.73m2 (p=0.0024).

Prevalence and Trend of RKF

The prevalence of RKF, expressed in percentages, is shown in Figure 1. Of the 90 patients, 31.1% of patients have KRU ≥1ml/min/1.73m^2 and 17.8% of patients have KRU ≥2ml/min/1.73m^2. The mean time on HD for patients with KRU <1 and ≥1ml/min/1.73m^2 were 6.5 ± 7.8 and 1.6 ± 1.7 years respectively. Longer duration on HD therapy significantly correlated with lower KRU levels (p<0.0001) as shown in Figure 1B. All of the patients who had been on hemodialysis for 9 years or more (n=13) were anuric (Table 2).

Clinical and Biochemical Correlations with RKF

Table 2 compares dialysis parameters and biochemical data for participants, stratified according to degree of RKF. The pre-dialysis and post-dialysis diastolic BPs in patients with KRU ≥1ml/min/1.73m2 were significantly higher compared to patients with KRU <1ml/min/1.73m2, but there was no significant difference in systolic blood pressure or pulse pressures between the two groups.

Higher KRU ≥1ml/min/1.73m2 was significantly associated with lower serum β2M levels ($p<0.0001$) and lower serum potassium ($p = 0.027$). Hemoglobin, phosphate, albumin, PTH and C-reactive protein were not related to the KRU level. There was also no difference in erythropoietin requirements. By correlation analysis, higher KRU correlated with lower serum levels of β2M and potassium (Fig 3A, 3B). These differences existed despite the fact that patients with low KRU <1ml/min/1.73m2 were managed with longer hours of hemodialysis and had a higher proportion of patients treated with hemodiafiltration. Further analysis of potassium parameters between the two groups found similar rates of hyperkalaemia and use of low potassium dialysate.

The low KRU group were treated with slightly more intensive dialysis as indicated by longer treatment times ($p = 0.049$) and a higher dialysis weekly StdKt/V (2.46±0.21 vs 2.30±0.24 $p=0.0007$) (Table 2). This difference was despite the fact that no policy was in place in our hospital at the time of the study to adjust the dialysis prescription according to RKF. However, when the residual renal clearance was added to the dialysis clearance, the total urea clearance as measured by total StdKt/V was significantly higher in the high KRU group (2.97 ± 0.42 vs 2.51 ± 0.23) ($p<0.0001$). Figure 3C illustrates the contribution of the RKF (renal StdKt/V) to the total urea clearance in the study cohort, with the RKF contributing up to a maximum of 38% of the total StdKt/V.

Symptom Burden

The symptom burden of the patient cohort is summarised in Table 3. Self-reported symptom questionnaires were completed by 53 patients in the low RKF group and 26 patient in the high RKF group. Across the entire cohort the most common symptom was weakness/lack of energy (72.7%). However, pain was the symptom most commonly rated as severe or overwhelming (16.5%). Patients with KRU ≥1ml/min/1.73m^2 reported fewer symptoms than patients with KRU <1ml/min/1.73m^2 (5.3 ± 3.5 vs 7.7 ± 3.8, p=0.014). Non-severe symptoms (score 1 or 2) were more common than severe symptoms (score 3 or 4), and accounted for the differences between the two groups. With respect to specific symptoms, vomiting, shortness of breath, poor appetite and poor mobility were more common in patients with KRU <1ml/min/1.73m^2 (Table 4). Fifteen of the seventeen symptoms were numerically more common in the low RKF group. Karnofsky performance scores were similar in the two groups (78.8±14.5 vs. 74.8±13.3, p=0.17) (Table 3).

A negative correlation was noted between KRU and the number of patient-reported symptoms (Fig 2A) (r = -0.212, p=0.05). There was also a trend to fewer symptoms with higher weekly standard Kt/V (renal plus dialysis) (Fig 2C). However, interestingly there was no correlation between the number of symptoms and dialysis clearance of urea (spKt/V) (Fig 2B). Higher levels of β2M correlated with a greater number of symptoms (Fig 2D) (r = 0.234, p=0.033). There were no significant correlations observed between the number of symptoms and age or dialysis vintage (Fig 2E and 2F).

DISCUSSION

This analysis of RKF from a cohort study of maintenance HD patients demonstrates that there is a subgroup of HD patients with significant RKF, at a level that contributes meaningfully to their total solute clearance, including urea kinetics, middle molecule and potassium homeostasis. In addition, we observed that ESKD patients on hemodialysis patients with higher levels of RKF have fewer uremic symptoms.

Whilst RKF has been associated with a better quality of life in peritoneal dialysis and HD patients (12, 13), the relationship between RKF and symptom burden in hemodialysis patients has not previously been studied. In the present study we observed that HD patients with lower RKF had a higher number of self-reported symptoms. The relationship between RKF and symptoms varied substantially between symptoms, for example shortness of breath and vomiting were significantly more common among those with low RKF, while various other symptoms were not different between groups. Interestingly, whilst RFK negatively correlated with the number of symptoms, there was no relationship between symptoms and the clearance of urea by haemodialysis, measured by spKt/V. In addition, a relationship was noted between serum β2M and number of symptoms, whereas there was no relationship between number of symptoms and either age or the number of years of RRT. Whilst such observational data are hypothesis generating rather than conclusive, they suggests that the beneficial effect of RKF in relieving the burden of uremic symptoms extend beyond the clearance of low molecular weight solutes such as urea. A limitation of our study is that our observations regarding uraemic toxins were limited to urea, potassium and β2-microblobulin. Importantly, however, RKF contributes to the clearance of a broad range or uraemic toxins. For example, it was recently reported that even very low level RKF less than 1.5 ml/min, was associated with lower serum levels of a range of uraemic solutes including hippurate, trimethylamine-N-oxide and asymmetric dimethylarginine (14). In addition to the role of glomerular filtration, RKF is also reported to increase clearance of

secreted protein bound solutes such as indoxyl sulfate, p-cresol sulfate and homocysteine (15, 16). Enhanced clearance of these uremic solutes such as these by RKF may contribute clinical benefits in patients on dialysis. It is worth noting that while symptom burden was lower in the RKF group, on average these patients still reported the presence of more than 5 symptoms. Furthermore, on average patients reported 1 symptom as being severe or overwhelming with no significant difference between groups in the number of these severe symptoms. This high burden of symptoms in HD patients has been well documented by previous studies (7, 8)) and indicates an ongoing need for better symptom management in these patients.

While RKF has been reported to be preserved better with peritoneal dialysis compared with HD, there is emerging evidence that a substantial proportion of HD patients retain significant degrees of RKF, and use of high-flux biocompatible dialysers may contribute to better preservation of RKF in the modern era. (12, 17). Vilar *et al*. reported that 58.1% and 31% of 650 HD patients had a KRU $\geq$1ml/min/1.73m^2 at 2 years and 5 years after HD initiation respectively (2). Consistent with this, the present study also found a subgroup of HD patients with significant levels of RKF - 31.1% of patients had KRU $\geq$1ml/min/1.73m^2 and 17.8% of patients had KRU$\geq$2ml/min/1.73m^2. The prevalence of RKF in our patient cohort may be underestimated with exclusion of non-anuric subjects who were unwilling or unable to perform a timed urine collection, whereas the anuric patients remained included in our analysis. In accordance with previous studies, our study also shows that longer duration on HD therapy significantly correlates with lower RKF (2, 17).

Whilst our study was not powered to detect a difference in mortality, previous studies have found an association between RKF and improved survival in HD patients (13, 18, 19). For example, in the NECOSAD study of 740 incident HD patients, mortality was 56% lower with each 1.0 unit increase in renal urea StdKt/V per week over the median follow-up time of 1.7 years (12). The survival benefit conferred by RKF may be partly attributed to better clearance of solutes, including that of middle

molecular weight uremic toxins such as β2M, which are poorly cleared by HD (20). We confirmed that a higher level of RKF is significantly associated with lower serum β2M. In our cohort, this was despite the greater use of HDF in the low RKF group, which would may have diluted the effect of RKF on β2M that we observed. Our results are consistent with those reported in the study by Fry *et al*., where patients with KRU of 0.5-1ml/min had significantly lower β2M levels compared to those with KRU<0.5ml/min (20), suggesting that even low levels of RKF may contribute to substantial solute clearance.

An interesting finding in our study is that RKF was significantly associated with lower serum potassium, which was observed despite no difference in dialysate potassium concentration between the two groups. The observation that patients with KRU≥1 ml/min1.73m^2 had significantly lower serum potassium, suggests that even low levels of RKF may significantly contribute to overall potassium balance. The difference in serum potassium levels may also be partly attributed to the higher incidence of use of diuretic in patients with higher RKF levels, consistent with a study from the Dialysis Outcomes and Practice Patterns Study finding that HD patients on diuretics have a lower risk of hyperkalemia (21). One limitation of our analysis that should be addressed in future studies is that we did not directly measured urinary potassium excretion in the HD patients.

In contrast to previous studies, we did not observe any significant association between RKF and anaemia, inflammation, interdialytic weight gain or serum albumin (2, 13, 22, 23), suggesting that these factors do not explain the differences in symptoms we observed. The explanation for the present study not confirming some previously noted associations is unclear, but might reflect the overall good control of nutrition, inflammation, anaemia and mineral metabolism in our cohort. In addition, our study may have lacked sufficient power to detect some of these differences.

Despite recommendations from some guidelines, RKF is not routinely factored into HD prescription and measures of HD adequacy. This is likely due to concerns regarding the inconvenience of timed urine collections, further compounded by the complexity and lack of consensus regarding the methods for integrating the continuous clearance of RKF with the intermittent clearance of HD. In our study, we adopted Gotch and Leypoldt's fixed volume equation to convert intermittent dialyzer clearance into weekly equivalent continuous clearance – standard Kt/V (24). In the current study, the mean renal StdKt/V in patients with KRU $\geq$1ml/min/1.73m^2 was 0.67, contributing 33.5% of the recommended KDOQI weekly StdKt/V target of 2.0 (25), and renal StdKt/V contributed to up to 38% of the total StdKt/V in our patient cohort. Patients with higher RKF levels had higher total StdKt/V despite receiving a lower dialysis dose, highlighting the significant role of RKF in overall solute clearance.

Relevant limitations of this study relate to its observational and cross-sectional nature, the limited size of the study population, and the fact that it is limited to a single centre. Hence, our study was not designed to be able to confirm the effect of RKF on hard outcomes such as mortality, that have previously been identified by others (2, 13). Due to the observational nature of the study, it is not possible to demonstrate causality of RKF in affecting any of the observed different outcomes between groups. Another limitation in the study is the relatively high proportion of anuric patients in the cohort. Despite the limitations, the present study confirms the previously observed relationship between RKF and uremic solute clearance as measured by serum β2M and urea kinetics, and extends this with novel findings in relation to symptom burden and potassium homeostasis. Larger multicentre studies are recommended to further study these relationships.

CONCLUSION

This study provides a signal for beneficial effects of RKF in HD patients. We observed a relationship between RKF, as defined by KRU, with lower symptom burden, improved middle molecule clearance, greater total urea clearance, and lower serum potassium. These results raise the possibility that routine monitoring of RKF may be warranted and strategies to preserve RKF in HD patients may improve patient outcomes. Further studies are needed to validate and understand the benefits conferred by RKF in the HD patient population, and the role of RKF in the care of ESKD patients managed with HD.

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FIGURE LEGENDS

Figure 1. 1A. Histogram showing proportion of patients with RKF as defined by KRU (ml/min/1.73m2). [ ] denotes inclusive interval; ( ) denotes exclusive interval. 1B. Linear regression showing correlation between KRU and time on HD. All patients who were on HD for 9 years or more (n=13) were anuric and were not included in this figure and analysis.

Figure 2. Linear regression analyses correlating the number of symptoms on the POS-renal questionnaire with residual kidney function (KRU) (2A), dialysis clearance (Kt/V) (2B), total urea clearance (Std Kt/V) (2C), serum β2M (mg/L) (2D), years of RRT (2E) and age (2F).

Figure 3. Relationship between RKF, uraemic solutes and urea kinetics. Correlation between KRU and serum β2M level (3A) and serum potassium level (3B) by linear regression. 3C. Stacked columns showing renal and dialysis StdKt/V for each individual patient, ranked in order from highest to lowest renal Std Kt/V.

Table 1. Baseline characteristics of 90 maintenance HD Patients

	Total	KRU <1ml/min/1.73m^2	KRU ≥1ml/min/1.73m^2	P value
N	90	62	28	
Demographics				
Age (years)	69.3 ± 13.3	71.2 ± 12.8	65.2 ± 13.6	0.042*
Gender (%)				
Male	61.1	53	79	0.040*
Female	38.9	47	21	
Base weight (kg)	80.1 ± 17.7	78.9 ± 17.2	82.75 ± 18.7	0.36
Height (cm)	167.2 ± 9.8	166.1 ± 9.4	169.7 ± 10.2	0.14
BMI	28.7 ± 6.3	28.8 ± 6.9	28.5 ± 4.9	0.82
BSA (m^2)	1.92 ± 0.23	1.90 ± 0.22	1.97 ± 0.27	0.27
Ethnicity (%)				
Caucasian	86.7	91.9	75.0	0.038*
Asian	12.2	6.5	25.0	
Other	1.1	1.6	0	
Time on RRT (years)	5.7 ± 7.5	7.5 ± 8.4	1.6 ± 1.7	<0.0001*
Time on HD (years)	5.0 ± 6.9	6.5 ± 7.8	1.6 ± 1.7	<0.0001*
Primary renal disease (%)				
Diabetes	38.9	35.5	46.4	0.88
Glomerulonephritis	26.7	29.0	21.4	
Polycystic kidney disease	5.6	4.8	7.1	
Hypertension or renovascular	6.7	8.1	3.6	
Other	11.1	11.3	10.7	
Unknown	11.1	11.3	10.7	
Co-morbidity				
Charlson Co-morbidity Index	7 ± 2	7 ± 2	6 ± 3	0.54
Presence of diabetes (%)	57.8	58.1	57.1	0.93
Presence of atheromatous disease (%)	53.3	54.8	50.0	0.84
Presence of malignancy (%)	7.8	8.1	7.7	0.88
KRU (ml/min/1.73m^2)	0.91 ± 1.37	0.13 ± 0.26	2.66 ± 1.20	<0.0001*
Residual GFR (ml/min/1.73m^2)	1.53 ± 2.16	0.29 ± 0.68	4.27 ± 1.75	<0.0001*
Interdialytic urine volume (ml)	342 ± 574	48 ± 98	992 ± 654	<0.0001*
Anuric patients (%)	61.1	88.7	0	<0.0001*
Diuretic use (%)	18.9	9.7	39.3	0.0024*
ACEi/ARB use (%)	24.4	19.4	35.7	0.12
EPO dose (units per week)	6522 ± 7594	6468 ± 7208	6648 ± 8560	0.73

Values indicate means ± SD or percentage. BMI = Body mass index; BSA = body surface area; RRT = Renal replacement therapy; HD = haemodialysis; HDF = haemodiafiltration; KRU = residual urea clearance; GFR = glomerular filtration rate; EPO = erythropoietin, ACEi = inhibitor of angiotensin converting enzyme, ARB = angiotensin receptor blocker *p<0.05

Table 2. Laboratory and dialysis parameters of 90 maintenance HD patients.

	Total	KRU <1ml/min/1.73m^2	KRU ≥1ml/min/1.73m^2	P value
N	90	62	28	
Laboratory Parameters				
Serum albumin (g/L)	33 ± 3	33 ± 3	34 ± 3	0.33
Serum potassium (mM)	5.1 ± 0.7	5.2 ± 0.7	4.9 ± 0.7	0.027*
Serum potassium ≥ 6.0 mM	11.1%	12.9%	7.1%	0.72
Serum phosphate (mM)	1.55 ± 0.45	1.52 ± 0.47	1.61 ± 0.39	0.19
Hb (g/L)	110 ± 12	109 ± 11	111 ± 14	0.45
PTH (pmol/L)	31.2 ± 24.8	31.4 ± 25.5	30.7 ± 23.5	0.96
CRP (mg/L)	8.9 ± 10.8	9.5 ± 11.9	7.6 ± 7.9	0.52
β2M (mg/L)	24.8 ± 9.0	27.2 ± 9.5	19.9 ± 4.9	<0.0001*
Dialysis Parameters				
Type of dialysis				
HDF (%)	14.4	19.4	3.6	0.057
High flux HD (%)	85.6	80.6	96.4	
Vascular Access				0.065
CVC (%)	16.7	11.3	28.6	
AVF (%)	83.3	88.7	71.4	
Weekly HD duration (hours)	12.7 ± 2.3	13.0 ± 2.0	12.0 ± 2.8	0.049*
Diastolic BP mmHG	72±13	70±14	78±13	0.013
Dialysate potassium ≤ 1 mM	11.1%	14.5%	10.7%	0.74
Ultrafiltration volume (l)	2.6 ± 0.9	2.74 ± 0.85	2.42 ± 0.94	0.21
IDWG (kg)	1.9 ± 0.9	1.94 ± 0.85	1.65 ± 1.09	0.32
StdKt/V (renal)	0.23 ± 0.35	0.037 ± 0.080	0.67 ± 0.33	0.0005*
StdKt/V (dialyzer)	2.41 ± 0.23	2.46 ± 0.21	2.30 ± 0.24	0.0007*
Total StdKt/V (renal + dialyzer)	2.65 ± 0.37	2.51 ± 0.23	2.97 ± 0.42	<0.0001*

Values indicate means ± SD or percentage. HD = haemodialysis; HDF = hemodiafiltration; KRU = residual urea clearance; Hb = haemoglobin; CRP = C-reactive Protein; β2M = beta-2 microglobulin; IDWG = interdialytic weight gain; StdKt/V = standard Kt/V, CVC = central venous catheter, AVF = arteriovenous fistula, BP = blood pressure. *p<0.05

Table 3. Relationship between residual kidney function and burden of uremic symptoms

	KRU<1ml/min/1.73m2	**KRU≥1ml/min/1.73m2**	**P-value**
N	53	26	
No. of symptoms	7.7 ± 3.8	5.3 ± 3.5	0.014*
No. of non-severe symptoms (mild or moderate)	6.4 ± 3.2	4.3 ± 3.0	0.011*
No. of severe symptoms (severe or overwhelming)	1.3 ± 1.9	1.0 ± 1.5	0.67
Total symptom score	13.2 ± 8.7	9.2 ± 7.4	0.053
N	50	25	
Karnofsky score	74.8 ± 13.3	78.8 ± 14.5	0.17
Values expressed in mean ± SD. *p<0.05			

Table 4: Prevalence of individual symptoms according to level of residual kidney function.

	KRU<1ml/min/1.73m2	***KRU≥1ml/min/1.73m2***	***P-value****
Pain			
Y	43%	42%	1.0
N	57%	58%	
Shortness of breath			
Y	55%	15%	0.0013*
N	45%	85%	
Weakness/lack energy			
Y	80%	58%	0.057
N	20%	42%	
Nausea			
Y	34%	23%	0.44
N	66%	77%	
Vomiting			
Y	30%	0%	0.0016*
N	70%	100%	
Poor appetite			
Y	40%	15%	0.040*
N	60%	85%	
Constipation			
Y	36%	50%	0.33
N	64%	50%	
Mouth problems			
Y	11%	23%	1.0
N	89%	77%	
Drowsiness			
Y	50%	27%	0.058
N	50%	73%	
Poor mobility			
Y	77%	50%	0.021*
N	23%	50%	
Itching			
Y	54%	46%	0.63
N	46%	54%	
Difficulty sleeping			
Y	73%	58%	0.20
N	27%	42%	
Restless legs			
Y	41%	35%	0.63
N	59%	65%	
Feeling anxious			
Y	53%	35%	0.15
N	47%	65%	
Feeling depressed			
Y	36%	35%	1.0
N	64%	65%	
Changes in skin			
Y	40%	27%	0.32
N	60%	73%	

Diarrhoea			
Y	18%	15%	1.0
N	82%	85%	

*P values by Fisher's exact test.

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ABSTRACT

Background: Residual kidney function (RKF) has been associated with improved solute clearance and survival in hemodialysis (HD) patients. However, whether RKF impacts symptom burden in HD patients is unknown.

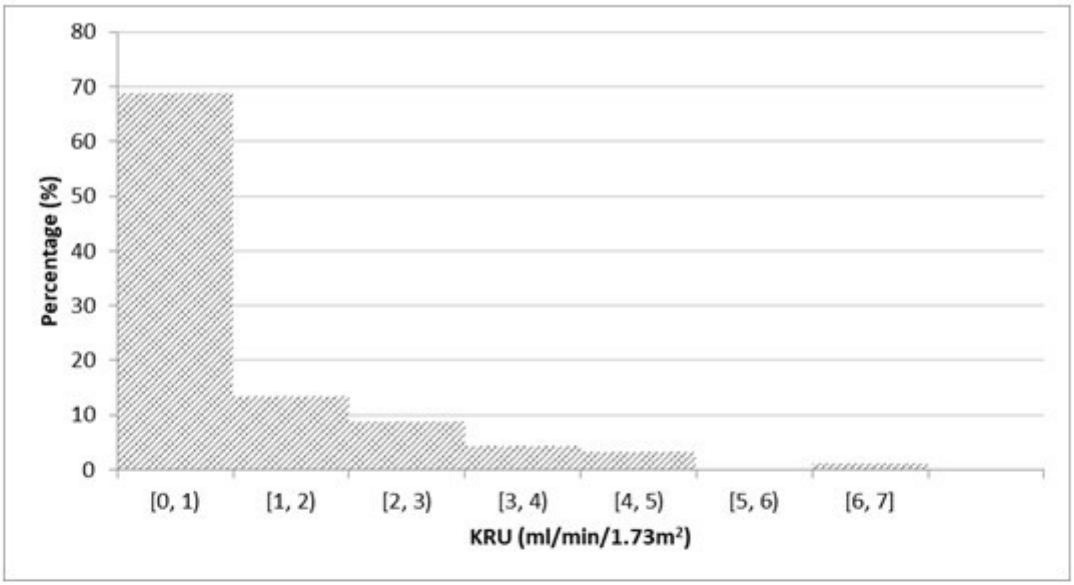
Aims: To determine the prevalence of RKF in HD patients and to explore associations between higher levels of RKF with symptom burden, as well as clinical and biochemical parameters.

Methods: This is a single centre, retrospective, observational study. RKF was assessed as urea clearance (KRU) by interdialytic urine collection. Symptom burden was measured using the palliative care outcome scale renal questionnaire.

Results: 90 maintenance HD patients were recruited. 31.9% had KRU ≥1ml/min/1.73m2. Patients with KRU ≥1ml/min/1.73m2 reported fewer symptoms (5.3 ± 3.5 vs 7.7 ± 3.8) (p=0.011), including less shortness of breath (15% vs 55%) (p=0.0013) and vomiting (0% vs 30%) (p=0.0016). Higher RKF was associated with lower β2-microglobilin (p<0.0001), and lower serum potassium (p=0.02), but no difference in phosphate, hemoglobin, C-reactive protein or serum albumin.

Conclusion: Higher RKF was significantly associated with fewer symptoms, and lower serum β2-microglobilin and potassium, suggesting that strategies to preserve RKF may be beneficial.

1A



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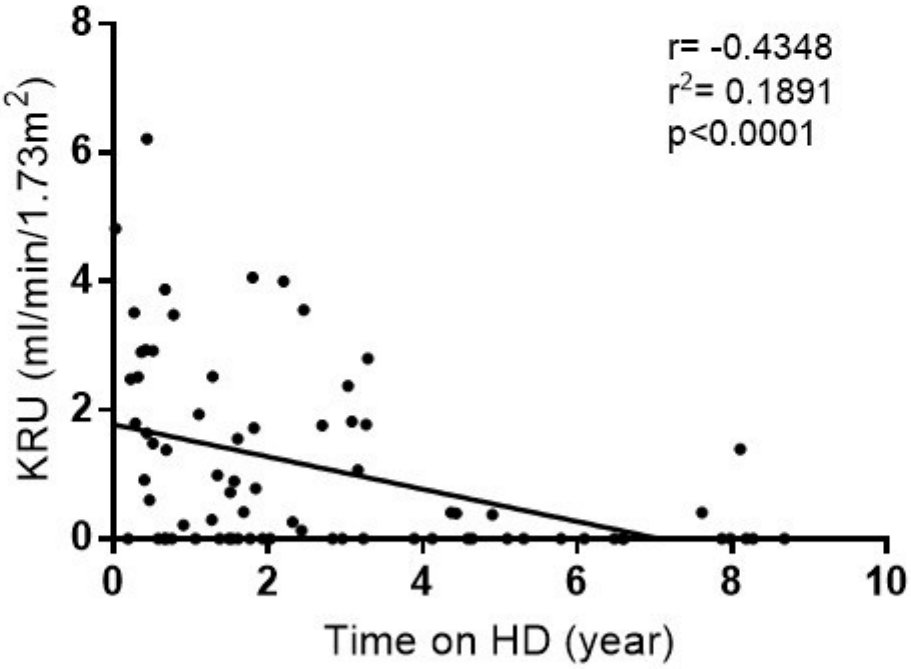

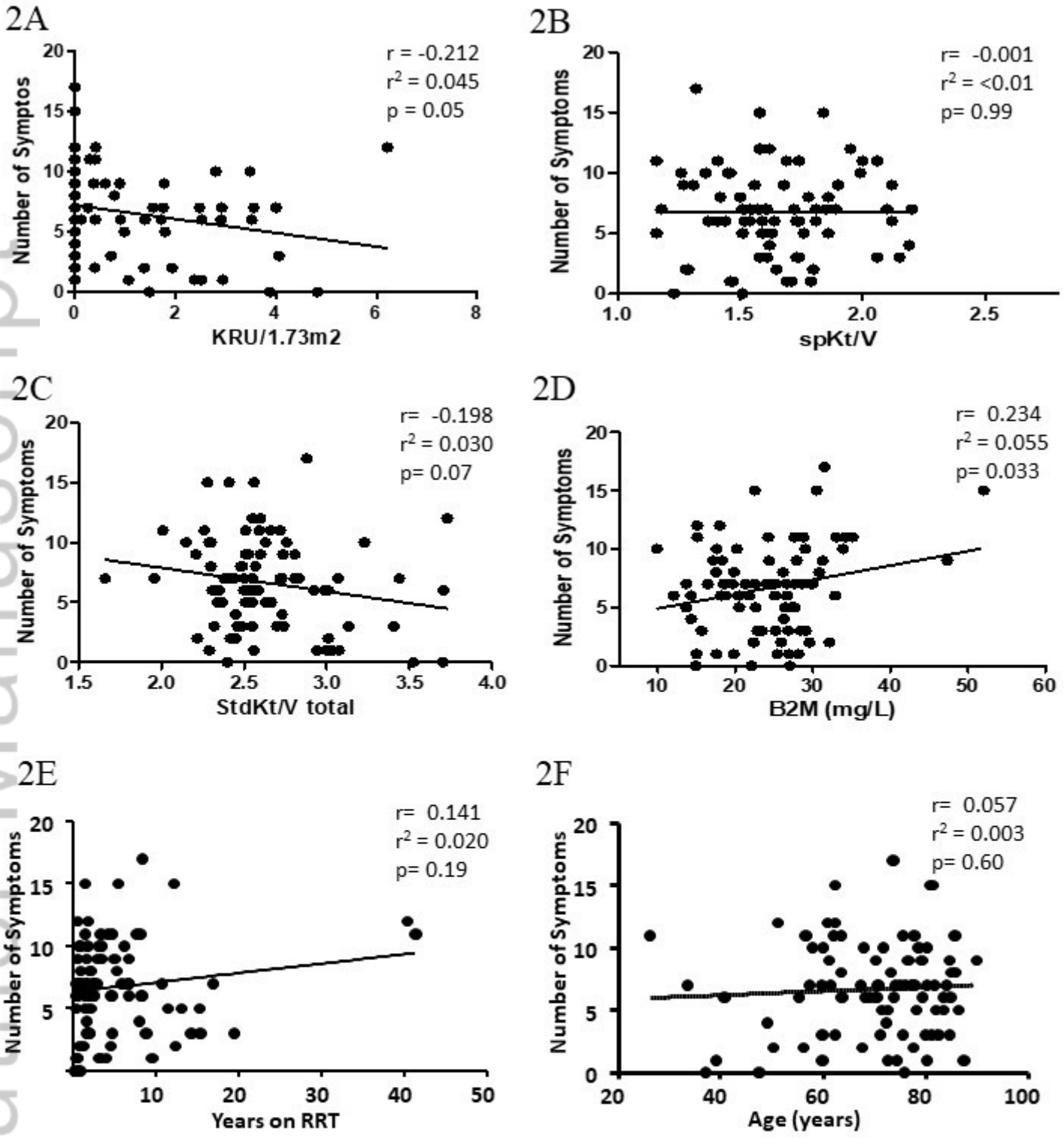

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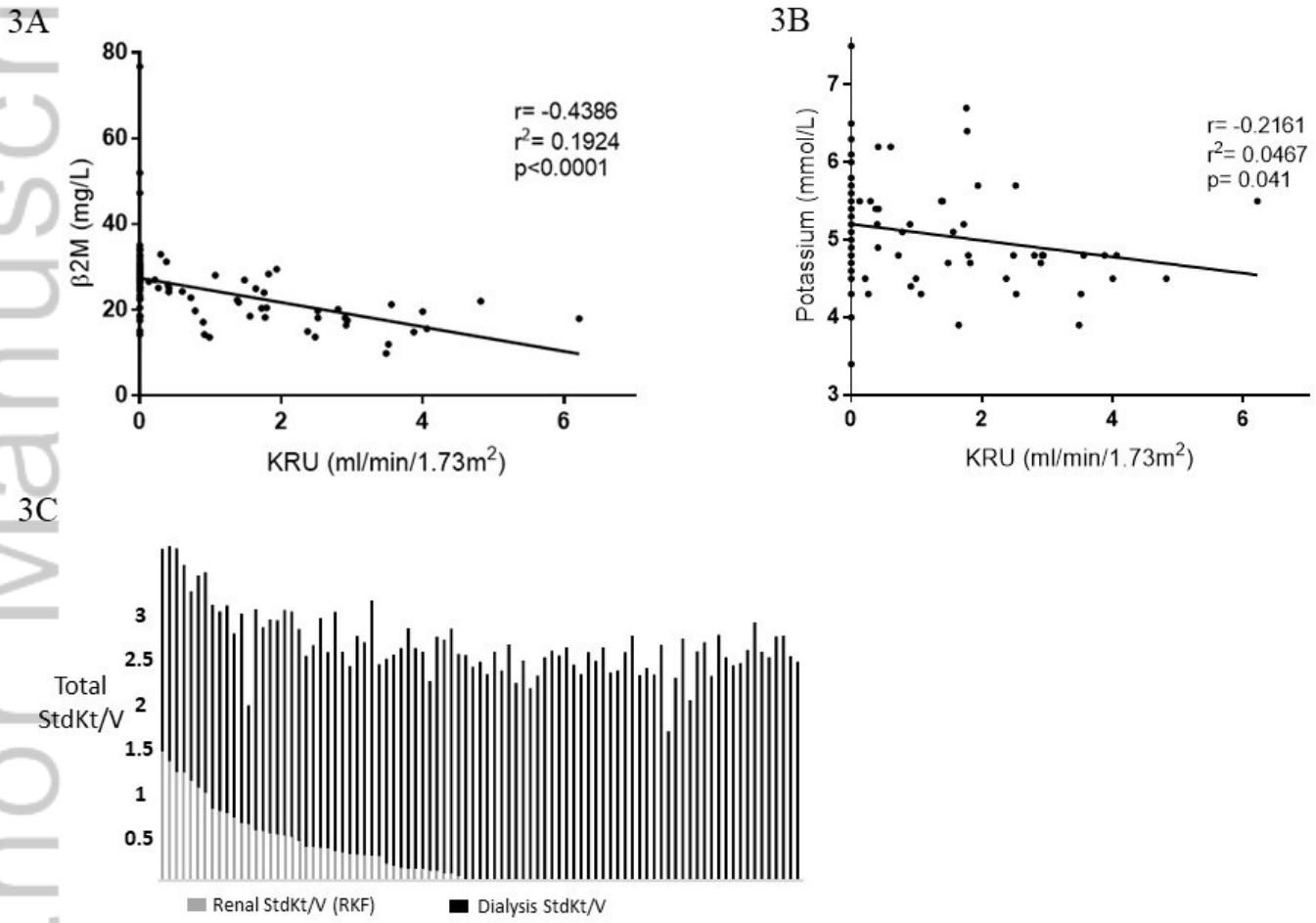

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The Relationship between Residual Kidney Function and Symptom Burden in Hemodialysis Patients

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Matthew Davies – data analysis and interpretation, manuscript revision

Peter Mount – oversight, supervision of data collection, data analysis and interpretation, manuscript revision

KEY WORDS: residual kidney function, hemodialysis, uremic symptoms, β2-microglobulin, potassium

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.