

# Benefits of Preserving Residual Urine Output in Patients Undergoing Maintenance Haemodialysis

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**Introduction:** Chronic kidney disease is a widespread medical problem that leads to higher morbidity, mortality, and a decrease in the overall well-being of the general population. This is especially expressed in patients with end-stage renal disease (ESRD) undergoing maintenance haemodialysis. Several variables could be used to evaluate those patients' well-being and mortality risk. One of them is the presence of residual urine output.

**Materials and Methods:** The study was conducted on 485 patients treated with maintenance haemodialysis. After enrollment in the study, which consisted of medical history, physical examination, hydration assessment, and blood sampling, each patient was followed up for 24 months. We used residual urine output (RUO) as a measure of residual renal function (RRF). The entire cohort was divided into 4 subgroups based on the daily urinary output ( $\leq 100$  mL per day,  $>100$  mL to  $\leq 500$  mL,  $>500$  mL to  $\leq 1000$  mL and  $>1000$  mL).

**Results:** The data show that the mortality rate was significantly higher in groups with lower RUO, which was caused mainly by cardiovascular events. Also, patients with higher RUO achieved better sodium, potassium, calcium, and phosphate balance. They were also less prone to overhydration and had a better nutritional status. Preserved RRF also had a positive impact on markers of cardiovascular damage, such as NT-proBNP as well as TnT.

**Conclusion:** In conclusion, preserving residual urine output in ESRD patients undergoing maintenance haemodialysis is invaluable in reducing their morbidity and mortality rates and enhancing other favourable parameters of those patients.

**Keywords:** end stage renal disease, haemodialysis, residual urine output, cardiovascular risk, mortality

## Introduction

Chronic kidney disease is a widespread medical problem that leads to higher morbidity, mortality, and a decrease in the overall well-being of the general population. This is especially evident in patients with end-stage renal disease (ESRD) undergoing maintenance haemodialysis (HD). The main cause of death in this population are cardiovascular (CV) events.<sup>1-4</sup> As for the year 2022, chronic kidney disease affects more than 10% of the population across the world, which amounts to over 800 million individuals. It has emerged as one of the leading causes of mortality worldwide, and it is one of a small number of non-communicable diseases that have shown an increase in associated deaths over the past 2 decades. Chronic kidney disease poses a significant challenge, particularly in low- and middle-income countries, where resources and infrastructure to address its impact are limited. These countries face a disproportionate burden due to their relatively fewer capabilities in managing the consequences of this disease.<sup>5</sup> Nearly 4 million people in the world are living on renal replacement therapy (RRT), and haemodialysis (HD) remains the most typical form of RRT, accounting for approximately 69% of all RRT and 89% of all dialysis.<sup>6</sup> In Poland, at the end of the year 2022, there were 20,198 patients undergoing dialysis, 19,389 on haemodialysis and 809 on peritoneal dialysis.<sup>7</sup> Several variables help evaluate the general condition and prognosis in haemodialysis patients, including nutritional status, fluid balance, the presence of chronic low-grade inflammation, kidney-related anaemia, oxidative stress, soft tissue calcifications and residual renal function (RRF).<sup>8-10</sup>

Residual renal function is the capacity of native kidneys to remove water and uremic toxins in patients with ESRD undergoing renal replacement therapy.<sup>11</sup> Measuring the daily urine volume is the simplest way to evaluate RRF. Many

studies have shown that residual urine output (RUO) correlates with residual glomerular filtration rate (GFR).<sup>12–14</sup> Other methods of assessing RRF require laboratory testing, including isotope, inulin, creatinine and urea clearance analysis. Additionally, measuring plasma concentration of solutes that are too large to be removed by dialysis, such as cystatin C or beta-2 microglobulin, can be used as surrogate markers of kidney function.<sup>11,15–17</sup>

Medline indexes over 5000 articles on RRF. Many studies underline the importance of its preservation in ESRD patients undergoing dialysis. Residual renal function has been shown to correlate directly with higher survivability.<sup>8,16–20</sup> One of the most significant benefits of RRF is middle molecule clearance, such as B2-macroglobulin,<sup>21</sup> reducing the likelihood of dialysis-associated amyloidosis.<sup>22</sup> Furthermore, it helps to control the hydration status, blood pressure and reduces the risk of left ventricular hypertrophy, improves cardiac index and reduces the total peripheral resistance index.<sup>16,17,19,20,23–27</sup> Anuric patients have a greater risk of developing secondary hyperparathyroidism, vascular calcifications, and arterial stiffening, as well as hyperkalemia and hyponatremia.<sup>14,16,17,19,20,24,28,29</sup> They are also more prone to restless leg syndrome.<sup>30</sup> On the other hand, patients with preserved RUO benefit from less profound inflammation,<sup>31–34</sup> malnutrition,<sup>35,36</sup> anaemia and present with fewer hypotensive episodes during HD procedures.<sup>18,28,34,37</sup> As shown above, RRF has a positive impact on reducing many of the morbidity and mortality risk factors in ESRD patients.<sup>16</sup>

Patients treated with dialysis suffer from declining renal function.<sup>8,10,36</sup> The loss of RRF progresses more rapidly in patients undergoing maintenance haemodialysis than in those on peritoneal dialysis.<sup>38</sup> Preserving RUO should be an important goal for physicians involved in the care of patients on dialysis. It can be achieved in many ways, including using biocompatible dialysis membrane and ultra-pure dialysate, avoiding nephrotoxins, prescribing ACE inhibitors and/or calcium blockers, avoiding volume depletion and hypotension. Incremental treatment starting with fewer HD sessions per week can also be a viable method of preserving residual renal function.<sup>21,37</sup>

This study aims to show how the presence of RUO impacts the frequency of CV events, CV and all-cause mortality, as well as other variables influencing the prognosis of ESRD patients undergoing maintenance haemodialysis.

## Materials and Methods

### Study Design

We gathered a group of 485 patients 18 years and older (191 females, 294 males) suffering from ESRD and undergoing maintenance HD with renal replacement therapy vintage lasting at least 4 weeks. This was a prospective, observational, multicentric study conducted in 7 separate dialysis centers located in western part of Poland. The period of recruitment lasted 5 years. Patients with temporary HD catheter access were not eligible for participation. We also excluded subjects with poor short-term prognosis, implantable cardioverter defibrillators and other subcutaneous devices, amputees, and patients with prosthetic joint replacement. Each patient was informed about the risks and benefits of participating in the study and signed a consent form. The study protocol was approved by the Poznan University of Medical Sciences Bioethical Committee (approval number 423/13) and complies with the Declaration of Helsinki. The study was initiated with the qualification, which included medical history analysis, blood sampling, physical examination, and hydration assessment. Then the follow-up started, which lasted for 24 months or was concluded earlier in case of a kidney transplant, HD therapy disqualification, conversion to peritoneal dialysis or death. In cases of patients receiving a kidney transplant the medical centers that carried through the procedure adhered to the highest ethical standards, and the transplants were conducted with the utmost consideration for patient well-being and informed consent, and in accordance with the principles outlined in the Declaration of Istanbul.

The main objective of the study was to assess the impact of residual urine output on cardiovascular and overall prognosis in patients with ESRD undergoing maintenance HD. The secondary objective was to evaluate the influence of residual urine output on other parameters that have a direct or indirect impact on the prognosis and wellbeing in patients with ESRD, such as electrolyte balance, hydration status, occurrence of malnutrition, mineral-bone disorders, anaemia and markers of cardiovascular damage.

### Residual Renal Function Assessment

In our analysis, we used residual urine output (RUO) as a measure of RRF. To evaluate the volume of urine output, every patient was asked to perform three 24-hour urine collections during non-dialysis days; then, the results were averaged.

## Fluid Overload Assessment

For hydration assessment, whole-body bioimpedance spectrum analysis (BIA) was conducted using Body Composition Monitor (BCM, Fresenius Medical Care Deutschland GmbH, Bad Homburg, Germany). The measurements were performed shortly before the mid-week HD session in the supine position using four disposable electrodes attached to a patient's hand and foot contralateral to the location of the arteriovenous shunt (when present), as per the device manual.

## Bloodwork

Blood samples were taken before the mid-week HD session. The panel included: a complete blood count with *haemoglobin* [Hb, g/dL], *albumin* [Alb, g/dL], *total cholesterol* [TC, mg/dL], serum *N-terminal pro-brain natriuretic peptide* (NT-proBNP, Elecsys<sup>®</sup> assay, Roche Diagnostics, Basel, Switzerland) and *cardiac troponin T* (cTnT, Elecsys<sup>®</sup> Troponin T fourth generation assay, Roche Diagnostics, Basel, Switzerland). HD efficacy was assessed with *Kt/V*, *ultrafiltration rate* (UFR, [mL]) and *weekly HD dose* expressed as the total weekly timespan of HD (HDD, [h/week]).

## Subgroups

The entire cohort (n=485) was divided into four groups based on the RUO volume. The first group (n=121) consisted of anuric patients (defined as less or equal to 100mL per day). The second group consisted of patients with daily RUO higher than 100mL up to 500mL (n=118), the third group contained patients with daily urine volume from over 500mL up to 1000mL (n=121) and the fourth group was made up of patients with RUO over 1000mL (n=125) respectively. The threshold between subgroups was chosen based on previous publications on this matter.<sup>8,9,18,23,24,28,29,33,34</sup>

## Statistical Evaluation

Statistical analysis was performed using StatSoft, Inc. (2014) STATISTICA (data analysis software system) version 12 ([www.statsoft.com](http://www.statsoft.com)). Since most of the data did not show normal distribution (assessed with the Shapiro–Wilk test), the analysis employed non-parametric tests only. The presence of statistically significant differences between the studied groups was tested using the Kruskal–Wallis test. The chi-square test ( $\chi^2$ ) was employed to test qualitative data, whereas the significance of correlations was verified with the Spearman test. Survival analysis was based on Kaplan–Meier curves which were tested with long rank test. A p-value lower than 0.05 was considered significant. The values throughout the paper are presented using medians (first quartile–third quartile) unless noted otherwise.

## Results

### Group Characteristics

The median age of the entire cohort was 67.2 (58.2–76.3) years. The most common cause of ESRD in the studied cohort was diabetic kidney disease (n=111, 22.9%), ischemic nephropathy (n=57, 11.6%), chronic glomerulonephritis (n=54, 11.1%) and hypertensive nephropathy (n=53, 10.9%). Patient demographics and median values for studied parameters in the entire cohort can be found in [Table 1](#). The median observation time lasted 24.0 (11.0–24.0) months, with a median HD therapy vintage of 52.2 (33.0–78.8) months. During the study, 223 patients (46.0%) reached one of the designed endpoints: 171 of them died (35.3%), 34 received kidney transplants (7.0%), 4 subjects were disqualified from HD therapy (0.8%), 12 patients (2.5%) were transferred to another HD centre, and 2 patients (0.4%) were converted to peritoneal dialysis. Residual urine output was not correlated with age (Spearman  $r=0.046$ ,  $p=0.310$ ) but was significantly lower in patients with longer HD vintage (Spearman  $r=-0.139$ ,  $p=0.002$ ).

### Subgroups

The median values of tested parameters in subgroups are also summarised in [Table 1](#). Statistical analysis showed no significant differences with respect to patients' age between the subgroups. There was a male dominance of patients with residual urine output above 500mL ( $p=0.0113$ ), but there were also more males in the entire cohort (298 vs 191). Electrolyte disturbances, including hyperkalaemia and hyperphosphatemia, were most significant in the anuric group. The patients with daily RUO volume under 100mL also had the highest concentration of cardiac damage markers (NTproBNP and cTnT). ECW/TBW and ICW/TBW ratio

**Table 1** Patient Demographics and Mean Values for Studied Parameters in the Entire Cohort and Urine Output Subgroups

Parameter	Cohort	<100	100–500	500–1000	>1000	P-value
Age, years	67.2 (58.2–76.3)	65.2 (53.9–73.8)	68.4 (60.2–77.7)	69.5 (60.7–78.2)	65.9 (57.6–73.8)	0.0044
Male sex, %	60.6	53.7	52.5	67.7	68.0	0.0113
HD vintage, months	52.2 (33.0–78.8)	67.1 (39.7–110.2)	46.1 (28.7–71.8)	44.7 (27.8–69.0)	54.1 (34.5–73.0)	0.0000
Observation, months	24.0 (11.0–24.0)	22.5 (9.8–24.0)	24.0 (6.2–24.0)	24.0 (11.8–24.0)	24.0 (19.9–24.0)	0.0061
RUO, mL	600 (120–1200)	0 (0–0)	450 (300–500)	1000 (1000–1000)	1700 (1500–2000)	0.0000
ECW/TBW, %	50.4 (48.1–53.0)	50.0 (47.6–53.0)	51.2 (49.3–53.0)	50.4 (48.1–53.0)	49.6 (47.4–52.0)	0.0033
ICW/TBW, %	49.6 (47.1–52.0)	50.0 (46.7–52.0)	48.8 (46.6–51.0)	49.6 (46.9–52.0)	50.5 (48.4–53.0)	0.0011
NTproBNP, pg/mL	6284 (2013–21,651)	10,389 (5587–35,000)	4989 (1884–21,143)	5803 (1681–20,600)	4026 (1012–15,660)	0.0000
cTnT, ng/L	50 (30–89)	72 (40–122)	49 (30–88)	49 (31–84)	42 (24–67)	0.0012
K+, mmol/L	4.90 (4.49–5.45)	5.30 (4.80–5.80)	4.83 (4.20–5.40)	4.80 (4.30–5.10)	4.86 (4.40–5.40)	0.0000
PO <sub>4</sub> , mg/dL	5.20 (4.19–6.30)	5.80 (4.54–7.00)	5.00 (4.19–6.14)	5.10 (4.05–6.00)	5.01 (4.00–6.15)	0.0080
Smoking, %	33.8	27.7	28.4	36.0	43.0	0.0724
All-cause mortality, %	24.2	35.5	24.6	22.5	14.4	0.0016
CV mortality	16.2	25.7	16.8	16.2	7.0	0.0026

**Note:** Data presented as medians (quartile 1–3).

**Abbreviations:** CV, cardiovascular; cTnT, cardiac troponin T; ECW, extracellular water; HD, haemodialysis; ICW, intracellular water; NT-proBNP, N-terminal pro-brain natriuretic peptide; RUO, residual urine output; TBW, total body water.

was most favourable in the group with the highest RUO and most detrimental in the second group (RUO volume between 100 and 500mL per day).

## Correlations

The correlation analysis has been performed on the entire cohort (n=485). The data showed a positive correlation between RUO and total cholesterol (p=0.0008), sodium (p=0.02757) and calcium levels (p=0.01096). There was a negative connection between RRF and overhydration (p=0.0295), NTproBNP (p<0.0001), TnT (p<0.0001), osteocalcin (p=0.00477), potassium (p=0.00037) and phosphates (p=0.00144) levels (for more details see Table 2).

**Table 2** Correlations Between Studied Parameters and Residual Urine Output

Parameter	R	P-value
HD vintage	-0.139	0.0023
Observation	0.166	0.0002
ECW/TBW	-0.109	0.0171
ICW/TBW	0.123	0.0075
NTproBNP	-0.297	<0.0001
cTnT	-0.239	<0.0001
K+	-0.177	0.0004
Na+	0.110	0.0276
PO <sub>4</sub>	-0.159	0.0014

**Abbreviations:** cTnT, cardiac troponin T; ECW, extracellular water; HD, haemodialysis; ICW, intracellular water; NT-proBNP, N-terminal pro-brain natriuretic peptide; TBW, total body water.

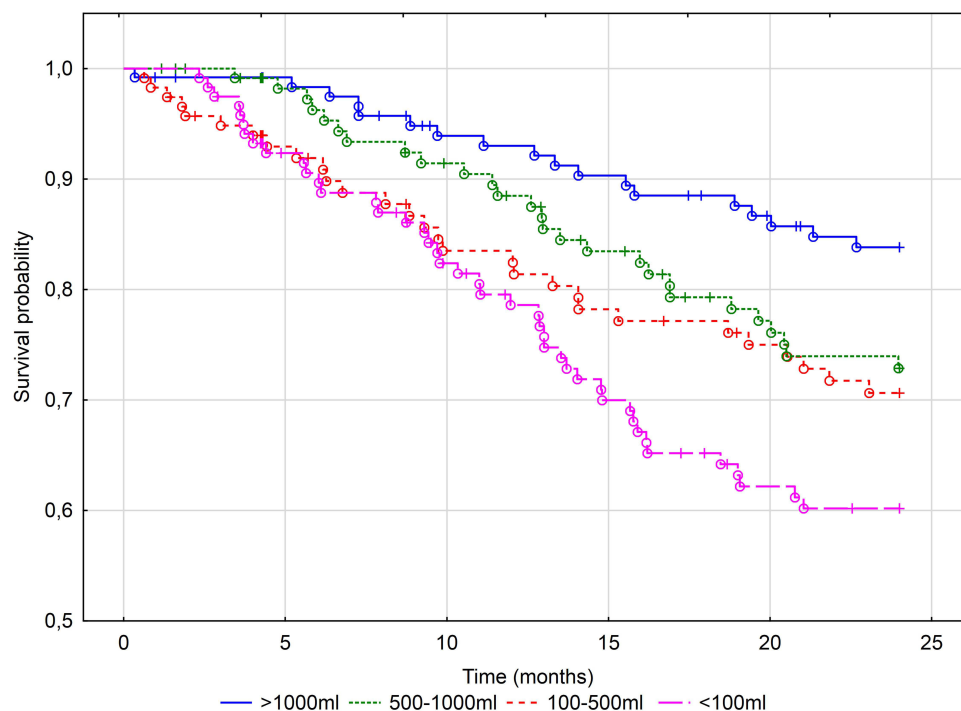
## Mortality

During the 2-year follow-up, 171 patients died (35.3%), and the remaining 262 patients (54%) were still under observation at the end of the study. During the first year of observation, 61 patients died, which sets the mortality rate at 12.6%; in the second year, the mortality rate reached 22.9% (n=111). Most fatalities occurred secondary to cardiovascular events (60.7% of all deaths). The mortality rate was significantly higher in groups with lower RRF ( $p=0.00163$ ). The highest all-cause mortality has been noted as expected in the first – anuric group (total mortality rate of 35.5%). There were no evident differences between the second (22.5%) and the third group (24.6%). The lowest mortality rate was present in the group with the highest RUO (14.4%). For more details, see [Table 1](#). For Kaplan-Meier survival analysis, see [Figures 1 and 2](#).

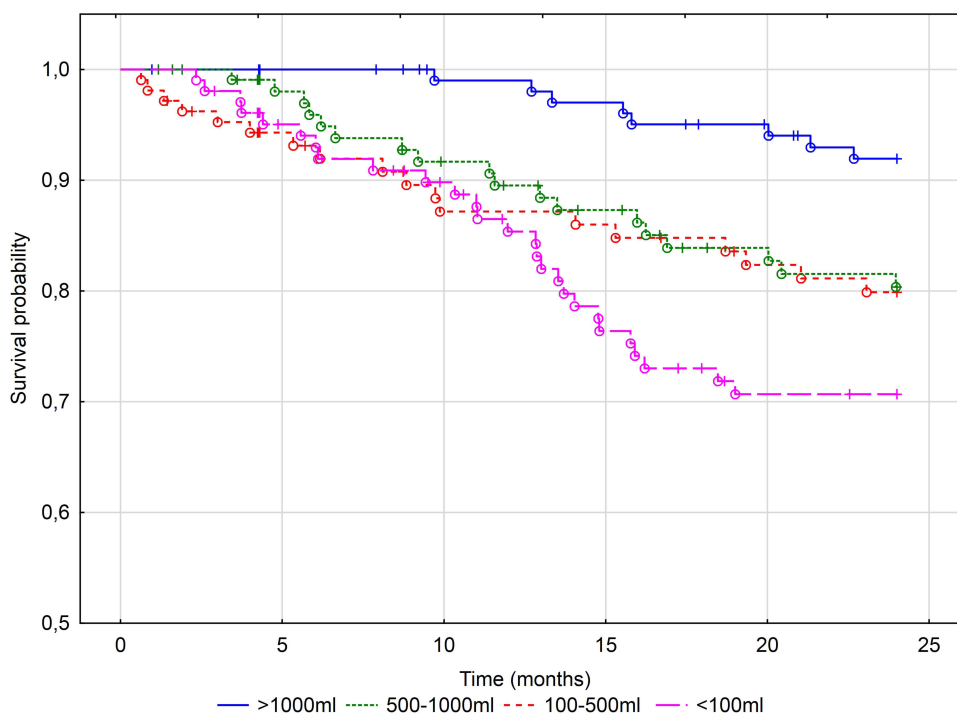
## Discussion

Preserving residual renal function plays an important role in achieving therapeutic goals in ESRD patients undergoing RRT and reducing their morbidity and mortality rates. Many studies conducted thus far prove multiple positive results of maintaining RUO. Our study showed a significant mortality rate increase following the reduction of RUO volume. Other authors ended up with similar results.<sup>8,16–20</sup> In their study, Shafi et al<sup>18</sup> analysed the difference in mortality rate in patients starting their HD treatment based on urine output preservation during a one-year observation. They proved that baseline urine output was not associated with a lower mortality rate, but the presence of RUO at one year mark, meaning RRF preservation, correlated significantly with lower mortality. Shemin et al<sup>8</sup> highlighted an interesting fact of a more rapid decline in residual renal function in women compared to men.

CV events are the most common cause of death in ESRD patients, as was proven multiple times. In their article, Ma and Ding<sup>24</sup> presented the negative correlation between RUO and the concentration of serum BNP, homocysteine and left ventricular hypertrophy in patients undergoing maintenance HD. The results also indicated that patients with preserved RRF have better left ventricular function. Similar conclusions could be found in the article by Araujo et al,<sup>23</sup> where they described a negative correlation between RUO and the total peripheral resistance index and stated that patients in the group with preserved residual urine output (RUO+) exhibited a significantly higher cardiac index. Similarly, our results showed that RRF was negatively correlated with both serum NTproBNP and TnT. The highest concentration of both of those markers was present in the anuric subgroup. In their study, Wang et al<sup>39</sup> assessed the efficacy of 10 biomarkers in



**Figure 1** Kaplan-Meier curves for all-cause mortality in the studied cohort. Long rank  $p<0.00039$ .



**Figure 2** Kaplan-Meier curves for cardiovascular mortality in the studied cohort. Long rank  $p < 0.00067$ .

predicting mortality and major cardiovascular events in a cohort of around 3000 individuals monitored for up to 10 years. They observed that the most informative biomarker for both predicting death and major cardiovascular events was B-type natriuretic peptide. What is also interesting from a nephrological point of view is that one of the most informative biomarkers in both groups was the urinary albumin-to-creatinine ratio. Daniels et al investigated the predictive significance of detectable cardiac troponin T (TnT) and elevated N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels in a sample of older adults. In the examined cohort, higher TnT was associated with higher NT-proBNP levels and the concentration of both those markers was positively correlated with reduced creatinine clearance. Subjects who exhibited detectable cardiac troponin T (TnT) levels had a higher mortality rate. Elevated levels of N-terminal pro-B-type natriuretic peptide (NT-proBNP) were found to be predictive of both all-cause mortality and cardiovascular mortality. Notably, participants with both high NT-proBNP levels and detectable TnT levels experienced the most significant increase in mortality risk.<sup>40</sup> In their works, de Lemos et al, de Filippi et al, and Saunders et al came to similar conclusions. They showed that cTnT detected with a highly sensitive assay in the general population was associated with structural heart disease, incident heart failure, incident coronary heart disease, the subsequent risk of cardiovascular death and all-cause mortality.<sup>41–43</sup>

Hyperphosphatemia is considered to be one of the risk factors for increased cardiovascular mortality among dialysis patients. Iwasawa et al,<sup>14</sup> in their study conducted on a group of HD patients with preserved RRF, presented evidence that urinary phosphate excretion strongly correlated with GFR, which in turn correlated with urine volume. They also showed that mean serum phosphate and FGF-23 were significantly lower in the group with higher GFR. Furthermore, serum intact PTH, urine phosphate, tubular reabsorption of phosphate and tubular maximum reabsorption for phosphate corrected for GFR were more elevated in the group with lesser RRF. Penne et al<sup>28</sup> made similar observations where patients with RRF suffered from hyperphosphatemia significantly less often despite using lower doses of phosphate-binding agents. Ma and Ding<sup>24</sup> showed that patients with RUO had lower serum phosphate and parathormone levels while maintaining higher serum calcium levels. In their study Almeida et al<sup>29</sup> also showed that patients with RRF have lower phosphatemia values. Moreover, they presented that the group without RRF had significantly higher potassium levels increase during the long interdialytic interval. Those patients also exhibited lower sodium levels, and a greater percentage of patients with natremia below 137 mmol/l was present in the anuric group. Almeida et al<sup>29</sup> also suggested

that patients without RRF are more likely to have lower bicarbonate levels and inadequate respiratory response to metabolic acidosis. These patients also showed higher interdialytic weight gain, which could be an explanation for the inadequate respiratory response. In our study, patients with preserved RUO had lower serum phosphate levels with higher calcium concentration. The group with daily urine output over 1000mL had the lowest PTH values; however, the correlation analysis between RUO and PTH levels showed no statistical significance. On the other hand, the negative correlation between RRF and serum potassium concentration was very strong. Not as strong, but still significant, was the positive correlation with serum sodium levels. The patients with the highest RUO also showed the highest sodium concentration compared to the three other groups. In other studies, lower sodium levels were associated with higher mortality.<sup>44</sup> We have not examined the correlation of acid-base balance in our patients. However, similarly to other authors,<sup>29</sup> we found that patients without RRF suffered from more severe overhydration. We have no statistically significant correlation between RUO and blood pressure values. However, a group of Polish authors<sup>45</sup> described an elevated level of serum norepinephrine in haemodialysed patients, especially anuric ones, which in turn led to higher blood pressure values. Interestingly, de Sequera et al<sup>34</sup> showed that patients with RRF suffered from fewer hypotensive episodes. They found no correlation between hypotensive episodes and intradialytic weight gain, the patients' hydration status or the ultrafiltration amount during HD sessions. That is why in their opinion, the possible explanation for fewer hypotensive episodes may be the better condition of the vascular system in patients with RUO.

Patients with ESRD have elevated levels of inflammation markers which are independent predictors of increased mortality. Pecoits-Filho et al<sup>31</sup> conducted a study on a group of patients with stage 5 chronic renal failure shortly before initiating RRT. The entire cohort was divided into 2 groups: the first included patients with GFR lower than 6.5mL/min/1.73m<sup>2</sup>, while the second included patients with GFR ranging from 6.5 to 16.5mL/min/1.72m<sup>2</sup>. They found that the first group had significantly greater hsCRP, neopterin and hyaluronian levels, while differences in S-albumin, IL-6 and TNF- $\alpha$  were not statistically significant. They also described significant negative correlations between GFR and hsCRP, IL-6, hyaluronian, and neopterin. Borges et al<sup>33</sup> and de Sequera et al<sup>34</sup> presented similar results, showing that patients with RRF undergoing haemodialysis had lower hsCRP levels. In our study, there were no significant differences in CRP levels between the groups as well as no significant correlation between RUO and CRP.

In nearly all research studies that have assessed the nutritional status of individuals with end-stage renal disease (ESRD), a consistent finding has been the presence of malnutrition to varying degrees.<sup>46</sup> Malnutrition has been found to be linked with various negative consequences, including apathy, depression, fatigue, and diminished motivation to recover. Furthermore, the decline in muscle strength resulting from malnutrition can adversely affect respiratory function, making individuals more vulnerable to chest infections. Additionally, malnutrition can negatively impact cardiac function. Furthermore, impaired immune function associated with malnutrition raises the risk of infections. Ultimately, these complications contribute to a higher incidence of illness and death.<sup>47,48</sup> RUO positively impacts nutritional status in ESRD patients undergoing maintenance haemodialysis, as shown in a study by Suda et al.<sup>34</sup> In a group of over 100 patients, they proved that serum albumin was positively correlated with RRF and was not associated with dialysis Kt/V urea. Furthermore, they described a positive connection between RUO and body fat percentage and normalised protein catabolic rate, indicating an overall better nutritional status. In our group of patients, there was no significant correlation between serum albumin and RRF. However, RUO was positively associated with higher lean tissue mass ( $p=0.007629$ ) and lean tissue index ( $p=0.048465$ ). Several authors stated in their studies that lower LTI is correlated with higher morbidity and mortality in ESRD patients undergoing maintenance haemodialysis. On top of that, Marcelli et al showed that not only LTI but likewise FTI falling within the 10th–90th percentile range of a healthy population matched for age and sex were associated with the most favourable survival outcomes. Conversely, individuals with low FTI and low LTI, particularly when both conditions were present together, exhibited higher mortality rates. Interesting observations were made by Trimarchi et al,<sup>49</sup> who, in their study, stated that higher BMI correlated with higher urinary output and a slower decline in urine output. Subjects with high BMI displayed higher urine output, albumin, leptin and insulin levels. There was a notable relationship between higher urinary outputs and lower levels of cardiac biomarkers, specifically troponin T and pro-B-type natriuretic peptide. Moreover, there was an inverse and significant correlation between albumin levels and TnT and Pro-BNP levels. Naturally, in the studied cohort, insulin levels increased in parallel with BMI. They proposed that the ability of insulin to retain salt and water may trigger pressure-diuresis and a maintained urinary output.

It is possible that higher levels of albumin further enhance this effect. On the other hand, Drechsler et al<sup>50</sup> showed that during their observation of patients through the first 18 months after the initiation of dialysis therapy, obesity and overweight significantly increased the decline in kidney function. Kalantar-Zadeh et al, in a review article, stated that overweight (BMI: 25–30) or obesity (BMI: >30) in patients with chronic kidney disease undergoing maintenance hemodialysis or high BMI, in general, is associated with improved survival.<sup>51</sup>

Many authors also explored the connection between RRF and anaemia management in the ESRD patients undergoing RRT. It was proven that patients with RUO have lower requirements for erythropoiesis-stimulating agents.<sup>28,34</sup> We found no significant correlation between RUO and haemoglobin levels or any other marker of the iron economy like serum Fe, ferritin, TIBC and TSAT.

Numerous approaches have been documented on how to preserve RUO in patients undergoing maintenance haemodialysis, including avoiding nephrotoxins, maintaining euvolemia and avoiding volume depletion and managing blood pressure. Medication such as angiotensin-converting enzyme inhibitors (ACE inhibitors) or angiotensin receptor blockers (ARBs), and calcium blockers may be prescribed to help manage blood pressure and preserve kidney function. Other important examples are using biocompatible dialysis membrane and ultra-pure dialysate and optimising dialysis prescription, including dialysis duration, frequency, and dose.<sup>21,37</sup>

## Study Limitations

The main factor that could disturb the reliability of the measurements is the fact that the daily urine collections were performed by the patients themselves, without any medical supervision, which is considered a standard routine practice. However, this could lead to measurement errors and improper allocation of some patients into specific groups. Moreover, there was no re-assessment of the urinary output during the study's follow-up period. The lack of correlation between RUO and inflammation in our study may be caused by the fact that the evaluation of systemic inflammation was limited to CRP and complete blood count.

## Conclusions

The preservation of residual urine output in ESRD patients undergoing maintenance haemodialysis is invaluable in achieving therapeutic goals, reducing morbidity, and lowering mortality rates. Multiple studies have demonstrated the positive outcomes associated with maintaining RRF. RUO has shown beneficial effects on various aspects of cardiovascular health. It has been linked to lower levels of cardiac biomarkers, such as troponin T and pro-B-type natriuretic peptide, indicating improved cardiac function. Patients with preserved RRF have been found to have better left ventricular function and less frequent left ventricular hypertrophy. Hyperphosphatemia, a common risk factor for increased cardiovascular mortality in dialysis patients, has been less prevalent among individuals with RRF. These patients exhibited lower serum phosphate levels as well as higher serum calcium levels. Furthermore, RRF has been correlated with improved potassium and sodium homeostasis. Maintaining RRF has shown positive effects on nutritional status, anaemia management and limiting chronic inflammation. Overall, the evidence strongly supports the importance of preserving residual urine output in ESRD patients undergoing RRT.

## Acknowledgments

We would like to extend our sincere gratitude to Dr Tomasz Paciorkowski for language editing.

## Disclosure

The authors declare no conflicts of interest in this work.

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