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Predictors of outpatient kidney function recovery among patients who initiate hemodialysis in the hospital

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Abstract

Background—Recent policy clarifications by the Centers for Medicare and Medicaid Services have changed access to outpatient dialysis care at end stage renal disease (ESRD) facilities for individuals with acute kidney injury in the United States. Tools to predict “ESRD” and “acute” status in terms of kidney function recovery among patients who previously initiated dialysis in the hospital could help inform patient management decisions.

Study Design—Historical cohort study

Setting & Participants—Incident hemodialysis patients in the Mayo Clinic Health System who initiated in-hospital RRT and continued outpatient dialysis following hospital dismissal (2006 to 2009)

Predictor—Baseline estimated glomerular filtration rate (eGFR), sepsis/surgery acute tubular necrosis (ATN), heart failure, intensive care unit, and dialysis access.

Outcomes—Kidney function recovery defined as sufficient kidney function for outpatient hemodialysis discontinuation.

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Disclosure

The authors have no conflict of interest to disclose.

Contributions: research idea and study design: LJH, SC, ADR, SMN, AWW, BT, JTM, JRG, RCA, JJD; data acquisition: LJH, SC, SMN, AWW; data analysis/interpretation: LJH, ADR, SMN, SC, AWW, BT, JTM, JRG, RCA, JJD; statistical analysis: LJH, ADR; supervision or mentorship: ADR, SMN, AWW. Each author contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved. LJH takes responsibility that this study has been reported honestly, accurately, and transparently; that no important aspects of the study have been omitted, and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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Results—Cohort consisted of 281 patients with mean age 64 years, 63% men, 45% heart failure, and baseline eGFR ≥30 mL/min/1.73m^2 in 46%. Over a median 8 months, 52 (19%) recovered, most (94%) within 6 months. Higher baseline eGFR (Hazard Ratio 1.27 per 10 ml/min/1.73m^2; 95% CI 1.16–1.39; p<0.001), ATN from sepsis or surgery (HR 3.34; CI 1.83- 6.24; p<0.001), and heart failure (HR 0.40; CI 0.19–0.78, p=0.007) were independent predictors of recovery within 6 months while first RRT in the intensive care unit and a catheter dialysis access were not. There was a positive interaction between absence of heart failure and eGFR≥30 ml/min/1.73m^2 for predicting kidney function recovery (p<0.001).

Limitations—Sample size.

Conclusions—Kidney function recovery in the outpatient hemodialysis unit following in-hospital RRT initiation is not rare. As expected, higher baseline eGFR is an important determinant of recovery. However, patients with heart failure are less likely to recover even with higher baseline eGFR. Consideration of these factors at hospital discharge informs decisions on “ESRD” status designation and long-term hemodialysis care.

Keywords

acute kidney injury; heart failure; chronic kidney disease; hospitalization; risk factors; renal recovery

Introduction

Acute kidney injury (AKI) in hospitalized patients has become increasingly common with reported prevalences of 3% to 20% [1–3] and occurs at an even higher frequency within the intensive care unit (ICU) population, 22% to 67%[4,5]. Patients with severe AKI requiring initiation of renal replacement therapy (RRT) have the highest in-hospital mortality rate ranging from 45% to 70%[6–10]. Among survivors of this high-risk event, as many as 13% to 32% require dialysis at the time of hospital discharge[7,11–13]. Limited data are available regarding recovery of sufficient kidney function to allow discontinuation of dialysis following hospital discharge in patients with severe AKI[14] yet patients initiating in-hospital RRT comprise a significant proportion, 39% to 64%, of the incident dialysis population each year [15–17].

Kidney function recovery from perceived end stage renal disease (ESRD), following 30 or more days of dialysis, has been studied in a heterogenous manner[18–26]. From these investigations, the occurrence is rare (1–5%) but a recent study in Medicare patients by Mohan et al[26] reported rates above 5% and suggested an increasing recovery rate over time. The reason for this observation is unclear but may reflect improved patient survival after severe AKI episodes, changes in practice patterns such as timing of RRT initiation, or an overall change in patient case-mix. Among incident hemodialysis patients, a substantial proportion initiate RRT in the hospital, primarily due to 1) severe AKI episodes of varying etiologies or 2) unprepared or suboptimal dialysis starts for advanced renal failure[27]. In such patients faced with a potentially lifelong illness, concern over the possibility of recovery is paramount. This concern is shared by dialysis providers facing the difficult task of determining the prognosis for kidney function recovery, balancing timely kidney

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transplantation referral, and avoiding more permanent dialysis access placement in patients who will eventually recover.

In July 2012, the Centers for Medicare and Medicaid Services (CMS) clarified policy on coverage for outpatient dialysis services provided to AKI patients in the United States[28,29]. This clarification prohibited ESRD facilities from furnishing acute dialysis to hospital outpatients, restricting dialysis care to continued treatment in the hospital or locations qualifying for provider-based departments of the hospital. As such, these locations may not be convenient or readily accessible to patients and caregivers. Subsequently, hospital nephrologists indirectly receive added pressure to categorize renal failure events at hospital discharge as either “ESRD” or “AKI.” Unfortunately, readily available clinical prediction tools for kidney function recovery in the outpatient setting are lacking. Gaining an understanding of potential predictors of recovery following hospital discharge may further aid in early clinical decision making in the care of incident hemodialysis patients. In this study, we examined the likelihood of recovery of sufficient kidney function to discontinue outpatient hemodialysis and predictors of such recovery among incident hemodialysis patients who initiated in-hospital RRT.

Methods

Patient selection

The Mayo Clinic Health System provides a comprehensive integrated health care network in an area with 395,000 residents in Southeast Minnesota, Northern Iowa, and Southwest Wisconsin. Mayo Clinic Dialysis Services (MCDS) provides all hemodialysis in the Mayo Clinic Health System through eight community-based outpatient hemodialysis facilities and is staffed solely by Mayo Clinic nephrologists who also provide the inpatient hemodialysis care. All adults (age ≥18 years; n=470) in the Mayo Clinic Health System initiating outpatient in-center hemodialysis from January 1, 2006 through December 31, 2009 with Minnesota Research Authorization were identified. Only patients whose RRT initiation occurred in the hospital just prior to transitioning to outpatient in-center hemodialysis were included in this study (n=281). Long term acute care facilities were not utilized and following hospital discharge all patients transitioned directly to outpatient in-center hemodialysis within 1–3 days. Patients receiving home dialysis therapies as their first treatment (peritoneal or hemodialysis) were not included in this study. The primary outcome was recovery of sufficient kidney function to completely discontinue outpatient hemodialysis. Patients were followed for recovery through December 08, 2010. The Mayo Clinic Institutional Review Board approved this study.

Data collection

Baseline characteristics, comorbidities, and laboratory tests were collected through review of the electronic medical records. The Charlson Comorbidity Index score, consisting of 19 comorbid conditions, was obtained by a previously validated automatic note search strategy (automated digital algorithm)[30]. Charts were reviewed to determine the cause of kidney failure, baseline kidney function, dialysis access, dialysis location, and duration of hospital stay. Baseline kidney function (n=253) was determined from the last available stable serum

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creatinine within 1 year prior to hospitalization or lowest inpatient creatinine prior to renal failure event if outpatient creatinine values were unavailable. Heart failure included the diagnoses of congestive or systolic heart failure, diastolic heart failure, or cardiomyopathy based on manual review of medical records at the time of hospitalization. For patients hospitalized and/or receiving medical care at a non-Mayo institution at time of RRT initiation, outside records were reviewed to obtain baseline serum creatinine values. The estimated glomerular filtration rate (eGFR) was calculated using the CKD-EPI creatinine based equation[31].

Patients were divided into four groups based on ***baseline eGFR*** available within 1 year prior to the kidney failure episode that precipitated hemodialysis during hospitalization: acute kidney injury (AKI), acute kidney injury on chronic kidney disease (AoCKD), chronic kidney disease stage 5 (CKD5), and acuity unknown. **AKI** was defined as loss of baseline normal renal function (eGFR ≥60 ml/min/1.73m^2) requiring dialysis. **AoCKD** was defined as loss of renal function precipitating initiation of dialysis in patients with impaired renal function (eGFR ≥15 and <60 ml/min/1.73m^2) at baseline. **CKD5** was defined as loss of baseline advanced renal disease (eGFR <15 ml/min/1.73m^2) requiring initiation of dialysis in-hospital. **Acuity unknown** consisted of patients with no known baseline creatinine to calculate baseline eGFR. In addition to eGFR cutoffs, ***clinical and pathological causes*** of acute and chronic kidney injury were defined for each patient based on kidney biopsy (performed prior to or at time of hospitalization), supportive laboratory testing, and clinical judgement at time of kidney failure episode. Acute clinical and pathological etiologies included: infection/sepsis-induced AKI, postoperative AKI, glomerulonephritis/ tubulointerstitial disease (GN/TIN), drugs, and other/unknown. For the purpose of this study, infection/sepsis and postoperative AKI were later combined to encompass a diagnosis of acute tubular necrosis (ATN). Sepsis/postoperative ATN classification was further supported by the common presence of urinary renal tubular epithelial cells, muddy brown casts or granular casts, though renal biopsy confirmation was not usually performed. Chronic clinical and pathological etiologies included: diabetes mellitus (DM), hypertension, GN/TIN, polycystic kidney disease, refractory acute tubular necrosis, failing kidney transplant, and other/unknown. First dialysis access was categorized as arteriovenous fistula, arteriovenous graft, or central venous catheter. Catheters were further classified as temporary (non-tunneled, non-cuffed) or tunneled (cuffed).

For each incident patient, recovery events were collected during follow up. Kidney function recovery was defined as the development of sufficient kidney function allowing for complete discontinuation of outpatient hemodialysis.

Statistical analysis

Continuous variables were reported as mean ± standard deviation or median with inter-quartile ranges (IQRs) for non-normally distributed variables. Categorical variables were expressed as count (percent). Comparison of proportions between groups was made using the Chi square test. Recovery rate was estimated using the Kaplan-Meier method. Since there were very few recovery events after 6 months, Cox models were developed to predict the risk of kidney function recovery within 6 months of starting outpatient hemodialysis.

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Multivariable hazard regression models for kidney function recovery considered only variables that were statistically significant in the univariate model and readily available to the practicing clinician. Kaplan-Meier survival curves (plotted for failure) were generated to characterize the timing of recovery by level of eGFR and presence of heart failure. Subjects were censored at time of transfer to a non-MCDS dialysis facility, study period end (December 08, 2010), or at death. Patients who discontinued in-center hemodialysis due to kidney transplantation or transitioned from in-center to home dialysis therapies (peritoneal or hemo- dialysis) were assigned maximum follow up time under the assumption that they did not recover kidney function. A ***subgroup analysis*** was also performed restricted to patients with a baseline eGFR>15 ml/min/1.73m^2 (n=225). The purpose of this analysis was to exclude patients with CKD stage 5 since they are often deemed "ESRD" and unlikely to recover kidney function. A ***sensitivity analysis*** was also conducted assigning the maximum follow-up time to patients who died (n=97) as these patients may not have recovered kidney function had they lived. Statistical analyses were performed with JMP 9.0 (SAS Institute Inc, Cary, NC). .0

Results

From January 2006 to December 2009, there were 470 new patients who started outpatient hemodialysis in the MCDS. Our study was limited to the 281 (60%) patients who initiated and continued RRT in the hospital prior to transitioning to outpatient hemodialysis. The mean follow up of hospital starters in this study was 15±16 months (median 8; IQR 2, 26). Baseline characteristics and recovery events by *baseline kidney function subgroups* are shown in Table 1. Mean age overall was 64±16 years (median 66; Interquartile range (IQR): 54, 77), 63% were men, 89% were Caucasian, 49% had DM, and 45% had heart failure. A Charlson comorbidity score was ≥8 in 49%. Baseline serum creatinine was available in 253 patients (90%) and median eGFR was 26 mL/min/1.73m^2 (IQR: 16, 48). Baseline eGFR was ≥30 mL/min/1.73m2 in 43% with known eGFR.

Within baseline kidney function subgroups, the distribution of patients included AKI (15%), AoCKD (55%), CKD5 (20%), and Acuity unknown (10%). The AKI group was generally younger and had less comorbidity, more ICU starts, and longer hospital stays. Besides classification by baseline eGFR, the acute and chronic *clinical and pathological etiologies* of kidney failure as obtained from chart review are shown in Table 2. Acute causes precipitating dialysis initiation were found in 211 (75%) patients while chronic cases of kidney failure were identified in 221 (79%). Overall, the most common acute etiologies were infection/sepsis or a complication of surgery, and together these comprised the category of sepsis/postoperative ATN (32% of entire cohort studied). The most common causes of chronic injury were diabetes, glomerulonephritis/tubulointerstitial nephritis, and hypertension. A kidney biopsy was performed either at the time of hospitalization or historically in 71 (25%) patients.

Kidney function recovery

A total of 52 patients recovered. At 6 months, the cumulative recovery rate was 21%, Figure 1. Most recovery (73%) occurred within the first 3 months of RRT initiation (n=38).

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Thereafter, 11 patients (21%) recovered between 3- to 6-months and only 3 (6%) beyond 6 months. Notably, the last recovery event occurred at 12 months.

Kidney function recovery by 6 months

The majority (94%, n=49) of recovery events occurred within 6 months. Notably, 52% of patients with AKI recovered kidney function within 6 months while no patients with CKD5 recovered kidney function. Table 3 shows the association between baseline characteristics and kidney function recovery by 6 months. On univariate analysis, factors predictive of 6-month recovery were absence of heart failure, lack of prior outpatient nephrology evaluation within 1 year, lower Charlson comorbidity index score, ICU initiation of RRT, later calendar year (2007–2009 vs. 2006), catheter dialysis access, AKI (eGFR-based) subgroup, sepsis/postoperative ATN, and higher baseline eGFR. Multivariable Cox models intentionally considered clinically relevant and readily available variables to practitioners: ICU initiation, catheter dialysis access, heart failure, sepsis/postoperative ATN, and baseline eGFR. In multivariable analysis only 3 variables (higher baseline eGFR, sepsis/postoperative ATN, and heart failure) were independent predictors of recovery.

In a *subgroup analysis* (n=225) that excluded patients with CKD5, ICU initiation and catheter access were no longer predictors of recovery in the unadjusted models. In multivariable analysis, heart failure, sepsis/postoperative ATN, and eGFR continued to be independent predictors of 6-month recovery (Table 3). As a *sensitivity analysis*, we assigned the full 6 months follow-up for all patients who died (n=97), but this did not meaningfully change the multivariable analysis findings (Hazard Ratio (HR) =0.39 for heart failure, HR=2.85 for sepsis/postoperative ATN, and HR=1.22 for eGFR per 10 ml/min/1.73 m2).

Baseline eGFR

Baseline eGFR was an important determinant of 6-month recovery. In the unadjusted model, patients with an eGFR ≥30 mL/min/1.73m^2 had a 7.5-fold higher likelihood of recovery. Following adjustment for ICU initiation, catheter access, sepsis/postoperative ATN, and heart failure this relationship was preserved [HR=5.86; p<0.001]. The relationship between baseline eGFR, heart failure, and 6-month recovery is illustrated in Table 4. With eGFR <30 mL/min/1.73m^2 as the reference group, eGFR 30–44 mL/min/1.73m^2 trended toward a higher likelihood of recovery (HR=2.63; p=0.09). However, patients with eGFR 45–59 mL/min/1.73m^2 and eGFR ≥60 mL/min/1.73m^2 had a significantly higher likelihood of recovery (HR=8.19 and HR=9.45; p<0.001 for both).

Heart failure and baseline eGFR

To determine the predictive utility of two important and readily available clinical variables for providers, the interaction of heart failure and baseline eGFR was also explored. In Table 4 a baseline eGFR ≥30 mL/min/1.73m^2 and no history of heart failure was associated with a higher likelihood of recovery compared to patients with eGFR<30 mL/min/1.73m^2 and a history of heart failure (HR=8.00; p<0.001). Among patients with heart failure, the probability of recovery at 6 months for an eGFR<30 mL/min/1.73m^2 was 9% and eGFR ≥30 mL/min/1.73m^2 was 13%. Among patients without heart failure, the probability of recovery for an eGFR<30 mL/min/1.73m^2 was 3% and for an eGFR ≥30 mL/min/1.73m^2 was 49%.

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Those with higher baseline eGFR subcategories were most likely to recover in either heart failure or non-heart failure group, Figure 2. However, heart failure appeared to be an effect modifier of the relationship between eGFR≥30 and kidney function recovery ($p<0.001$ test for interaction in adjusted and unadjusted models). In particular, eGFR≥30 mL/min/1.73m^2 was a weaker predictor of recovery in patients with heart failure than in patients without heart failure, Figure 3.

Other Patient Outcomes

Over a mean study period of 15±16 months, 227 (81%) of 281 incident cohort patients discontinued outpatient in-center dialysis at MCDS. Fifty-two of 227 (23%) recovered kidney function. Other reasons for discontinuation of outpatient in-center dialysis included: death (43%), transfer to a non-MCDS dialysis center (24%), kidney transplantation (8%), and transfer to home dialysis therapies (2%).

Discussion

Among incident outpatient in-center hemodialysis patients directly transitioning from RRT that was started during a preceding hospitalization, kidney function recovery was not uncommon. Despite a high prevalence of comorbid conditions, we found a cumulative recovery rate of 21% at 6 months. Recovery most often occurred within the first 3 months of RRT start. However, the 3- to 6-month period remained an important time frame for further recovery events. Predictors associated with recovery within 6-months were ICU initiation, ATN in the setting of sepsis or surgery, higher baseline eGFR, later time period, lower Charlson comorbidity score, catheter as first dialysis access, lack of prior outpatient nephrology evaluation within 1 year, and absence of heart failure. Baseline eGFR was a strong and independent predictor of recovery. However, the association was modified by the presence of heart failure. Taken together, these data fill an important knowledge gap and provide a working platform from which providers may estimate the likelihood of recovery, plan scheduled monitoring for recovery when transitioning patients at hospital discharge, and arrange permanent access placement or transplantation referrals in those who are unlikely to recover.

Care of the incident dialysis population can be challenging. Approximately 50%–65% of our incident outpatient hemodialysis patients had first initiated in-hospital RRT [16]. This experience is common across the U.S. and other regions[15,17,27,32]. Based on USRDS reporting, 32% of incident ESRD patients in 2011 initiated RRT without prior nephrology care[32]. Among our cohort, only 48% of incident patients initiating RRT in the hospital had been under the care of a nephrologist within 12 months prior to dialysis initiation. Many of these patients have normal baseline eGFR, hence there may have been no prior reason for nephrology referral before the hospitalization. For individuals with evidence of CKD, early nephrology referral is routinely promoted given the survival benefits of advanced planning, education, and permanent access creation for long-term dialysis[33]. Even among those with early nephrology referral, AoCKD frequently leads to unplanned hospital RRT starts as illustrated by O'Hare et al. In the 2 year period before dialysis initiation in 5,606 U.S. veterans, there were heterogenous patterns of kidney function loss enhanced by AoCKD

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contributing to suboptimal hospital starts[15]. An AKI episode occurred during hospitalization in 53% and 64% of the total veteran cohort initiated in-hospital RRT. At the time of hospital discharge, patients carry additional burdens of physical debility, infection or wound management, re-hospitalization risk, and/or loss of independence, especially among elderly patients[16,34,35]. As such, the complexity of new outpatient hemodialysis patients who started RRT in the hospital is often overwhelming for both patients and the providers who manage them

During the transition from hospital discharge to outpatient hemodialysis, the possibility of recovery remains a significant concern, and hope, for patients and their families. One important area for improvement in communication may be through early discussions regarding the potential for recovery of kidney function. By understanding the predictors of recovery in hospital starters, providers can more appropriately identify which patients should be more closely monitored for kidney function recovery and minimize unnecessary dialysis and healthcare costs or patient harm. In our study, we identified several variables which were predictive of recovery. Over half of the patients with AKI (defined as eGFR ≥60 mL/min/1.73m^2) recovered kidney function while no patients with eGFR <15 mL/min/1.73m^2 were free of dialysis support by study end. Patients who had an eGFR <15 mL/min/1.73m^2 and only chronic pathology at baseline have little to no chance of recovery since there is no reversible acute component to their kidney failure.

In multivariable analysis, higher baseline eGFR, ATN from sepsis or surgery, and absence of heart failure were independent predictors of recovery. Similar to other studies, those with normal baseline kidney function and less comorbidity represent a group more likely to recover[36–39]. In an attempt to provide specific cut points regarding recovery within 6 months, we found that patients with a baseline eGFR ≥30 mL/min/1.73m^2 had a 6-fold higher likelihood of recovery that was independent of other predictors (heart failure and ATN following sepsis or surgery). Comorbid conditions contribute to the prediction of poorer outcomes; however, calculation of Charlson scores can be cumbersome in busy day-to-day practice. Therefore, we chose to evaluate heart failure in combination with eGFR as two readily available clinical factors. In our study, patients with no heart failure and with eGFR ≥30 mL/min/1.73m^2 had a much higher likelihood of recovery than with either factor alone. Overall, heart failure predicted a lower risk of recovery in the outpatient setting. This finding is relatively intuitive given the interrelationship of acute and chronic cardiorenal pathophysiology, difficulties in volume management, and potential for hemodialysis-induced myocardial injury[43–45]. Once heart failure patients require RRT, they are much less likely to recover kidney function even with a higher baseline eGFR.

This study has several potential limitations. First, the sample size may have been too small to detect all the characteristics that predict kidney function recovery. The predominantly white population limits the generalizability of the results to other groups. Nonetheless the integrative practice allowed for population-based estimates of kidney function recovery for the Midwest population which has been shown to be reasonably similar to the general U.S. population[46]. Second, baseline kidney function was often determined by a single serum creatinine measurement in the previous 12 months and in some cases (10%) was not even available. Although less optimal, we believe this to be consistent with the realities of clinical

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practice wherein baseline serum creatinine data are not always available. In addition, we did not assess recovery in peritoneal or home hemo- dialysis patients in whom the likelihood and predictors of recovery may differ from in-center hemodialysis patients. Third, we did not study patients who started RRT in the hospital but either died or had kidney function recovery prior to outpatient hemodialysis. The subset of new kidney failure patients in the hospital who survive their hospitalization but need to continue dialysis as an outpatient is a population of particular clinical interest that deserves separate study. Lastly, we did not have cardiac physiologic data (e.g., echocardiograms) in all patients which may have led to under-reporting of heart failure.

In conclusion, given that AKI has a likelihood of kidney function recovery not present with "true" ESRD[26], identification of new outpatient hemodialysis patients who started RRT in the hospital and who may recover kidney function is important. In particular, higher baseline eGFR is a potent predictor of recovery in the absence of heart failure. Since we lack biomarkers to distinguish acute reversible from chronic irreversible renal injury[47,48] uncertainty in the designation of "end stage renal disease" in such patients should be recognized not only by patients and providers but also by payers. Close monitoring for kidney function recovery is warranted. Conversely, in patients with low baseline kidney function (eGFR<30 mL/min/1.73m^2) or heart failure, psychosocial support, education regarding alternative RRT modalities including transplantation and home dialysis modalities, and early more permanent dialysis access placement should be pursued.

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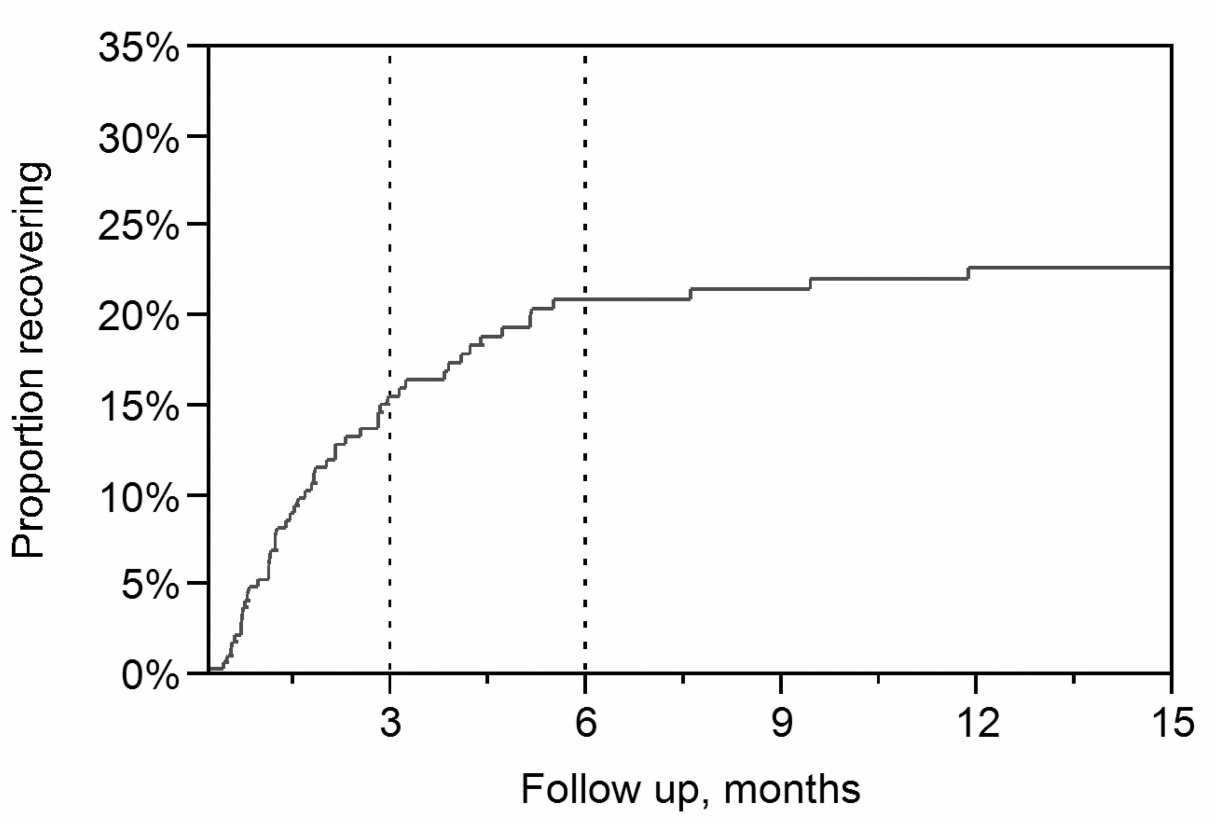

	Time Zero	3 mo	6 mo	9 mo	12 mo	15 mo
Total no. renal recovery events	0	38	49	50	52	52
No. at risk	281	186	147	138	124	106

Figure 1.
Outpatient kidney function recovery events following in-hospital initiation of renal replacement therapy.

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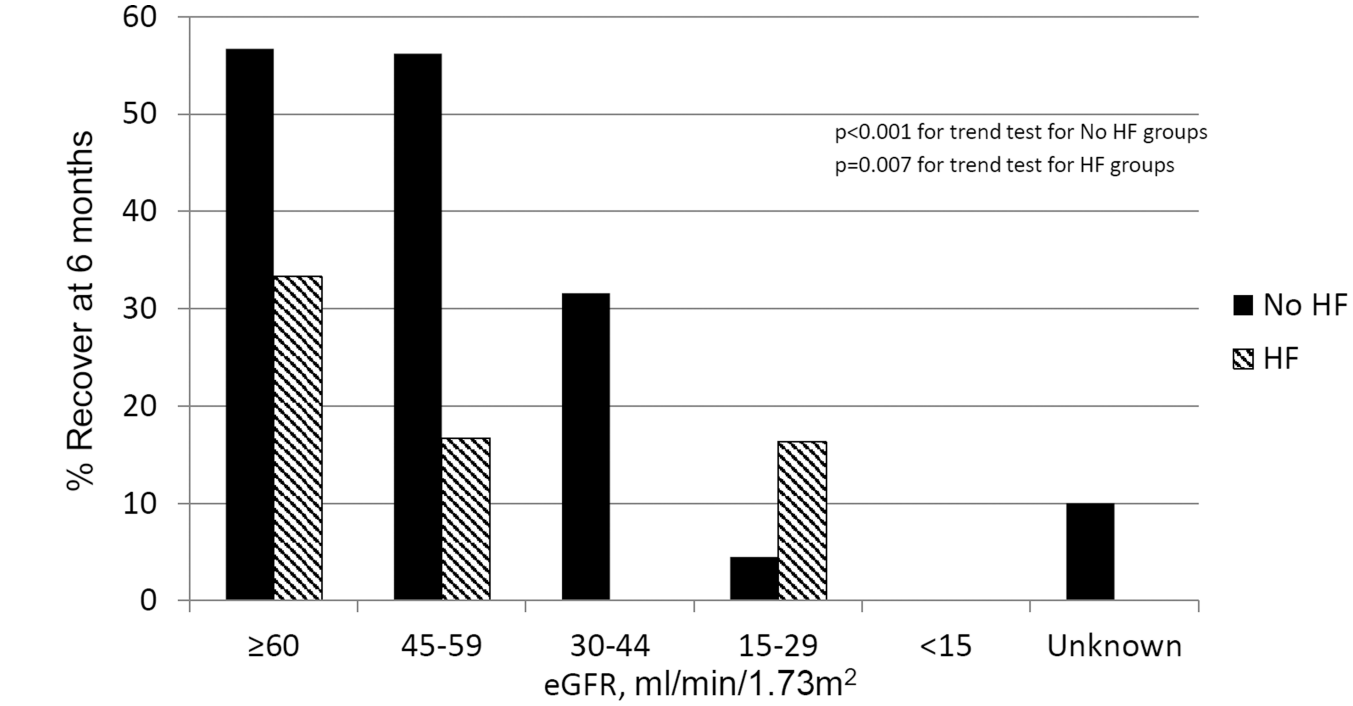

Number of patients per subgroup:						
No HF	30	16	19	44	25	20
HF	12	12	21	43	31	8

Figure 2.

Outpatient kidney function recovery at 6 months stratified by baseline estimated glomerular filtration rate (eGFR) and heart failure (HF). **A**. Patients without HF (n=154). **B**. Patients with HF (n=127).

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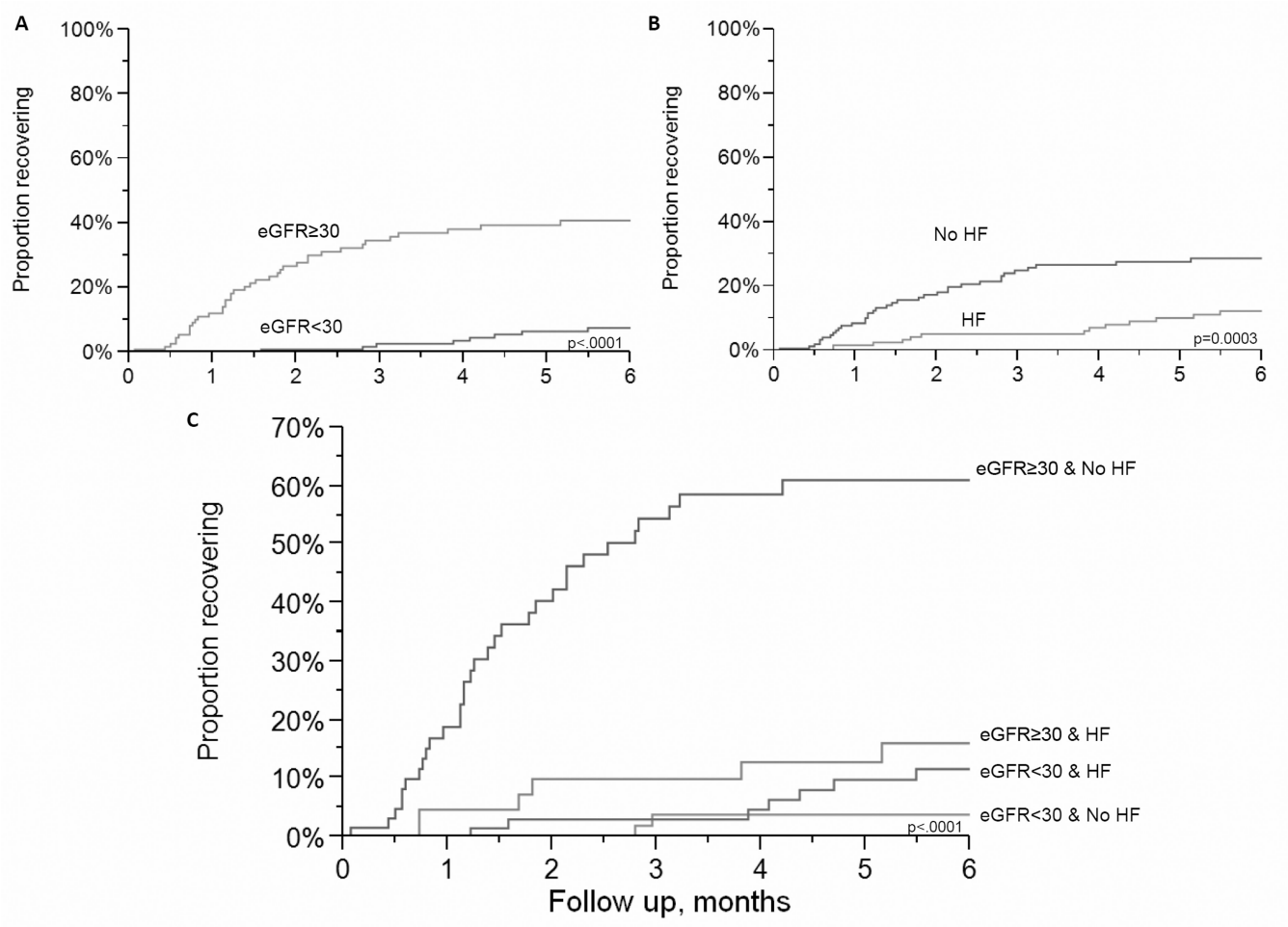

Figure 3.

Outpatient kidney function recovery stratified by estimated glomerular filtration rate (eGFR) and heart failure (HF). **A**. Stratified by eGFR<30 or ≥30 mL/min/1.73m^2. **B**. Stratified by HF status. **C**. Stratified by eGFR <30 or ≥30 mL/min/1.73m^2 and HF status.

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Table 1

Comparisons of baseline demographics, comorbid conditions, and kidney function recovery by baseline kidney function among incident hemodialysis patients with in-hospital initiation of renal replacement therapy.

Baseline demographics, comorbid conditions, and kidney function						
		All (n=281)	**Acute Kidney Injury (n=42)**	**Acute on CKD (n=155)**	**CKD stage 5 (n=56)**	**Acuity Unknown (n=28)**
Age, years	Mean ±SD	64 ± 16	59 ± 16	66 ± 14	68 ± 16	55 ± 19
	Median (IQR)	66 (54,77)	61 (46, 73)	68 (58,77)	72 (57,81)	55 (43,71)
	Age ≥75	81 (29%)	9 (21%)	44 (28%)	23 (41%)	5 (18%)
	Age 70 to <75	36 (13%)	3 (7%)	24 (15%)	7 (12.5%)	2 (7%)
	Age 65 to <70	35 (12%)	4 (10%)	24 (15%)	6 (11%)	1 (4%)
	Age 60 to <65	26 (9%)	6 (14%)	15 (10%)	3 (5%)	2 (7%)
	Age 55 to <60	30 (11%)	1 (2%)	18 (12%)	7 (12.5%)	4 (14%)
	Age 50 to <55	26 (9%)	5 (12%)	14 (9%)	2 (4%)	5 (18%)
	Age 45 to <50	14 (5%)	4 (10%)	5 (3%)	4 (7%)	1 (4%)
	Age 40 to <45	14 (5%)	5 (12%)	5 (3%)	1 (2%)	3 (11%)
	Age <40	19 (7%)	5 (12%)	6 (4%)	3 (5%)	5 (18%)
Gender						
	Male	176 (63%)	28 (67%)	95 (61%)	34 (61%)	19 (68%)
	Female	105 (37%)	14 (33%)	60 (39%)	22 (39%)	9 (32%)
Caucasian race		249 (89%)	38 (90%)	142 (92%)	49 (88%)	20 (71%)
Diabetes mellitus		137 (49%)	10 (24%)	85 (55%)	28 (50%)	14 (50%)
Coronary artery disease		122 (43%)	10 (24%)	74 (48%)	30 (54%)	8 (29%)
Heart failure		127 (45%)	12 (29%)	76 (49%)	31 (55%)	8 (29%)
Prior outpatient nephrology evaluation (n=276)		133 (48%)	4 (10%)	79 (52%)	46 (82%)	4 (15%)
Charlson comorbidity index score (n=272)						
	Mean ±SD	7 ± 4	5 ± 3	8 ± 3	9 ± 4	4 ± 3
	Median (IQR)	7 (4,10)	4 (3,7)	8 (6,10)	8 (6,11)	4 (2,7)
	Charlson score ≥8	133 (49%)	9 (21%)	87 (58%)	33 (60%)	4 (15%)
First dialysis location in hospital						
	Intensive care unit	99 (35%)	22 (52%)	57 (37%)	10 (18%)	10 (36%)

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Baseline demographics, comorbid conditions, and kidney function

	All (n=281)	Acute Kidney Injury (n=42)	Acute on CKD (n=155)	CKD stage 5 (n=56)	Acuity Unknown (n=28)
Non-Intensive care unit	176 (63%)	18 (43%)	95 (61%)	46 (82%)	17 (61%)
Outside hospital	6 (2%)	2 (5%)	3 (2%)	0 (0%)	1 (3%)
First dialysis access utilized					
Non-cuffed, temporary catheter	150 (53%)	36 (86%)	88 (57%)	14 (25%)	12 (43%)
Cuffed tunneled catheter	110 (39%)	6 (14%)	61 (39%)	30 (54%)	13 (46%)
Arteriovenous fistula/graft	21 (7%)	0 (0%)	6 (4%)	12 (21%)	3 (11%)
Hospital duration, days					
Total (Median, IQR)	9 (5,17)	20 (10,31)	11 (6,17)	5 (4,9)	7 (3,13)
Prior to RRT	2 (1,6)	6 (1,11)	2 (1,6)	1 (1,3)	1 (0,3)
Following RRT	6 (3,12)	12 (6,23)	7 (3,12)	4 (2,7)	4 (3,8)
Baseline kidney function	n= 253	n= 42	n= 155	n= 56	n= 0
Creatinine, mg/dL					
Mean ±SD	2.6 ± 1.6	0.9 ± 0.2	2.2 ± 0.8	4.9 ± 1.3	- -
Median (IQR)	2.2 (1.4,3.5)	0.9 (0.8,1.1)	2.1 (1.5,2.8)	4.6 (3.9,5.7)	- -
eGFR, ml/min/1.73m^2					
Mean ±SD	37 ± 29	85 ± 32	32 ± 13	11 ± 2	- -
Median (IQR)	27 (17,52)	77 (66,93)	28 (21,42)	12 (10,13)	- -
eGFR ≥60	42 (15%)	42 (100%)	0 (0%)	0 (0%)	- -
eGFR <60 and ≥45	28 (10%)	0 (0%)	28 (18%)	0 (0%)	- -
eGFR <45 and ≥30	40 (14%)	0 (0%)	40 (26%)	0 (0%)	- -
eGFR <30 and ≥15	87 (31%)	0 (0%)	87 (56%)	0 (0%)	- -
eGFR<15	56 (20%)	0 (0%)	0 (0%)	56 (100%)	- -
eGFR unknown	28 (10%)	- -	- -	- -	28 (100%)
Kidney function recovery during follow-up	n= 281	n= 42	n= 155	n= 56	n= 28
6 months	49 (17%)	21 (50%)	26 (17%)	0 (0%)	2 (7%)
Overall	52 (19%)	22 (52%)	27 (17%)	0 (0%)	3 (11%)

*Baseline kidney function classifications include: Acute kidney injury (baseline eGFR ≥60 mL/min/1.73m^2); Acute on chronic kidney disease (baseline eGFR≥15 and <60); Chronic kidney disease stage 5 (baseline eGFR <15); Acuity unknown (baseline eGFR unknown within 12 months prior to dialysis initiation). CKD: chronic kidney disease; eGFR: estimated glomerular filtration rate. Values expressed as

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Mean± Standard deviation, Median (IQR: interquartile range), or Number (%) unless otherwise specified. Charlson score: Carlson comorbidity index score; ICU: intensive care unit; RRT: renal replacement therapy; AVF/G: arteriovenous fistula or graft; eGFR: estimated glomerular filtration rate calculated from the CKD-Epi equation.

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Table 2

Comparisons of clinical and pathological kidney failure etiologies by baseline kidney function classification among incident hemodialysis patients with in-hospital renal replacement therapy initiation.

Clinical and pathological diagnoses of kidney failure by baseline kidney function classification*	All (n=281)	Acute Kidney Injury (n=42)	Acute on CKD (n=155)	CKD stage 5 (n=56)	Acuity Unknown (n=28)
Acute clinical and pathological etiologies#					
Infection/Sepsis	56 (20%)	13 (31%)	39 (25%)	2 (4%)	2 (7%)
Postoperative	33 (12%)	8 (19%)	22 (14%)	3 (4%)	0 (0%)
Glomerulonephritis/Tubulointerstitial nephritis	30 (11%)	7 (17%)	17 (11%)	2 (4%)	4 (14%)
Drugs	16 (6%)	5 (12%)	8 (5%)	2 (4%)	1 (4%)
Other/Unknown	76 (27%)	9 (21%)	48 (31%)	9 (16%)	10 (36%)
None	70 (25%)	0 (0%)	21 (14%)	38 (68%)	11 (39%)
Chronic clinical and pathological etiologies#					
Diabetes	77 (27%)	2 (5%)	46 (30%)	23 (41%)	6 (21%)
Hypertension	21 (7%)	0 (0%)	6 (4%)	10 (18%)	5 (18%)
Glomerulonephritis/Tubulointerstitial nephritis	37 (13%)	2 (5%)	22 (14%)	10 (18%)	3 (11%)
Polycystic kidney disease	5 (2%)	0 (0%)	2 (1%)	3 (5%)	0 (0%)
Refractory acute tubular necrosis	5 (2%)	2 (5%)	3 (2%)	0 (0%)	0 (0%)
Failing kidney transplant	19 (7%)	0 (0%)	16 (10%)	2 (4%)	1 (4%)
Other/Unknown	57 (20%)	3 (7%)	40 (26%)	8 (14%)	6 (21%)
None	60 (21%)	33 (79%)	20 (13%)	0 (0%)	7 (25%)

*Baseline kidney function classifications include: Acute kidney injury (baseline eGFR ≥60 mL/min/1.73m^2); Acute on chronic kidney disease (baseline eGFR≥15 and <60); Chronic kidney disease stage 5 (baseline eGFR <15); Acuity unknown (baseline eGFR unknown). CKD: chronic kidney disease; eGFR: estimated glomerular filtration rate calculated from the CKD-Epi equation.

#Patients could have either acute, chronic, or both (acute and chronic) clinical and pathological etiologies for kidney injury.

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Table 3

Association between kidney function recovery and baseline features.

Unadjusted associations between baseline characteristics and Kidney function recovery at 6 months					
		Entire Cohort (n=281)		Subgroup excluding CKD5 (n=225)	
Predictors of Kidney function recovery at 6 months*		**Hazard Ratio (95% CI)**	**p**	**Hazard Ratio (95% CI)**	**p**
Age, per 5 year		0.93 (0.85–1.01)	0.1	0.94 (0.87–1.03)	0.2
Female gender		1.43 (0.80–2.50)	0.2	1.39 (0.78–2.44)	0.3
Caucasian race		2.19 (0.80–9.02)	0.1	2.11 (0.78–8.67)	0.2
Diabetes mellitus		0.64 (0.36–1.12)	0.1	0.58 (0.33–1.03)	0.06
Coronary artery disease		0.67 (0.37–1.18)	0.2	0.70 (0.39–1.24)	0.2
Heart failure		0.36 (0.19–0.67)	**<0.001**	0.39 (0.20–0.71)	**0.002**
Prior outpatient nephrology evaluation		0.21 (0.09–0.41)	**<0.001**	0.31 (0.14–0.61)	**0.004**
Charlson comorbidity score					
	Charlson score, per 1 point	0.84 (0.77–0.91)	**<0.001**	0.85 (0.78–0.93)	**<0.001**
	Charlson score ≥8	0.37 (0.19–0.68)	**<0.001**	0.41 (0.21–0.75)	**0.004**
Hospital					
ICU vs. non-ICU first dialysis location		1.96 (1.11–3.44)	**0.02**	1.59 (0.90–2.79)	0.1
	Time between admission and RRT start, per 1 day	1.02 (0.98–1.06)	0.3	1.01 (0.96–1.05)	0.8
	Time between RRT start and discharge, per 1 day	0.99 (0.98–1.01)	0.8	0.99 (0.98–1.00)	0.4
	Length of hospital stay, per 1 day	1.00 (0.99–1.01)	0.9	1.00 (0.98–1.00)	0.5
Incident HD year	Incident HD year 2006	1.0 (REFERENT)		1.0 (REFERENT)	
	Incident HD year 2007	2.87 (1.15–8.12)	**0.02**	3.11 (1.25–8.79)	**0.01**
	Incident HD year 2008	3.45 (1.43–9.57)	**0.005**	3.20 (1.33–8.86)	**0.009**
	Incident HD year 2009	2.64 (1.02–7.58)	**0.04**	2.91 (1.13–8.37)	**0.03**
First Dialysis access					
Catheters vs. Arteriovenous fistula/graft		4.95 (1.08–87.55)	**0.03**	2.76 (0.61–48.93)	0.2
	Arteriovenous fistula/graft	1.0 (REFERENT)		1.0 (REFERENT)	
	Cuffed tunneled catheter	1.33 (0.23–25.07)	0.8	0.85 (0.15–16.11)	0.9
	Non-cuffed, temporary catheter	8.22 (1.79–145.75)	**0.003**	4.11 (0.90–72.91)	0.08

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Unadjusted associations between baseline characteristics and Kidney function recovery at 6 months				
	Entire Cohort (n=281)		Subgroup excluding CKD5 (n=225)	
Predictors of Kidney function recovery at 6 months*	**Hazard Ratio (95% CI)**	**p**	**Hazard Ratio (95% CI)**	**p**
Renal failure type subgroups				
Acute kidney injury	1.0 (REFERENT)		1.0 (REFERENT)	
Acute on chronic kidney disease	0.25 (0.14–0.45)	**<0.001**	0.25 (0.14–0.45)	**<0.001**
Chronic kidney disease stage 5	0.00 (0.00–0.04)	**<0.001**	Not included	
Acuity unknown	0.09 (0.01–0.31)	**<0.001**	0.09 (0.01–0.31)	**<0.001**
Sepsis/Postoperative ATN vs. other AKI & non-AKI	3.33 (1.90–5.93)	**<0.001**	2.57 (1.46–4.58)	**0.001**
Acute and chronic pathology subgroups				
Sepsis/Postoperative ATN pathology	1.0 (REFERENT)		1.0 (REFERENT)	
Non-Sepsis/Postoperative ATN pathology	0.51 (0.28–0.89)	**0.02**	0.53 (0.30–0.92)	**0.03**
Chronic pathology only	0.00 (0.00–0.07)	**<0.001**	0.0 (0.00–0.00)	**<0.001**
GFR Measurements: n= 253			**n= 197**	
eGFR, per 10 ml/min/1.73m^2	1.30 (1.21–1.40)	**<0.001**	1.24 (1.15–1.34)	**<0.001**
eGFR ≥30 ml/min/1.73m^2	7.50 (3.78–16.56)	**<0.001**	4.40 (2.22–9.71)	**<0.001**
Multivariable-adjusted# associations between baseline characteristics and Kidney function recovery at 6 months				
Predictors of Kidney function recovery at 6 months with acute and acute on chronic	**Hazard Ratio (95% CI)**	**p**	**Hazard Ratio (95% CI)**	**p**
Variable (n=253)			(n=197)	
ICU location of first dialysis	0.83 (0.44–1.56)	0.6	-	-
First dialysis access was a catheter	1.74 (0.36–31.34)	0.6	-	-
Heart Failure	0.40 (0.19–0.78)	**0.007**	0.38 (0.19–0.74)	**0.004**
Sepsis/Postoperative ATN pathology	3.34 (1.83–6.24)	**<0.001**	2.78 (1.54–5.13)	**<0.001**
eGFR, per 10 ml/min/1.73m^2	1.27 (1.16–1.39)	**<0.001**	1.21 (1.11–1.32)	**<0.001**

*Subgroup analysis excluded CKD5 patients (n=56) with baseline eGFR<15 mL/min/1.73m^2;

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CKD: chronic kidney disease; eGFR: estimated glomerular filtration rate calculated from the CKD-Epi equation; Charlson score: Charlson comorbidity index score; AKI: acute kidney injury; HD: hemodialysis; ICU: intensive care unit; RRT: renal replacement therapy.

Sepsis/Postoperative ATN pathology includes all patients (AKI or Acute on Chronic injury) with sepsis or postoperative clinical or pathological etiologies.

[#]Adjusted for each other variable in the model, excluding patients with unknown baseline eGFR in the subgroup analysis.

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Table 4

Association between kidney function recovery, estimated glomerular filtration rate (eGFR), and heart failure (HF) at baseline.

Adjusted association between eGFR, HF, and kidney function recovery in the entire cohort					
eGFR subgroups*			eGFR & HF subgroups		
Variable#	Hazard Ratio (95% CI)	p	Variable##	Hazard Ratio€ (95% CI)	p
eGFR ≥60	9.45 (4.05–23.97)	**<0.001**	eGFR ≥30 & no-HF	8.00 (3.60–20.54)	**<0.001**
eGFR <60 and ≥45	8.19 (3.13–22.17)	**<0.001**	eGFR ≥30 & HF	1.02 (0.32–3.20)	0.9
eGFR <45 and ≥30	2.63 (0.86–7.58)	0.09	eGFR<30 & no-HF	0.33 (0.05–1.37)	0.1
eGFR <30	1.00 (REFERENT)		eGFR<30 & HF	1.0 (REFERENT)	

*eGFR: estimated glomerular filtration rate in mL/min/1.73m calculated from the CKD-Epi equation; HF: heart failure. Patients without baseline eGFR (Acuity unknown group, n=28) were excluded from the analysis.

#Adjusted for ICU location, first dialysis access catheter, heart failure, sepsis/postoperative ATN.

##Adjusted for ICU location, first dialysis access catheter, sepsis/postoperative ATN.

€There was an interaction of heart failure with eGFR≥30 in predicting kidney function recovery (p<0.001 in adjusted and unadjusted models).