Chapter 9

Epidemiology of Chronic Dialysis Patients in the Intensive Care Unit

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Additional information is available at the end of the chapter

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1. Introduction

The incidence and prevalence of end-stage renal disease (ESRD) is rising worldwide, in part due to increasing rates of diabetes, hypertension and an ageing population [1,2]. Incidence rates of patients commencing renal replacement therapy (RRT) are estimated at 109 and 354 per million population (pmp) per year in the UK and US respectively [1,2], with the highest incidence seen in patients over 75 years of age.

Shifting demographics over the past two decades have resulted in an older and sicker long-term dialysis population, burdened with multiple and significant co-morbid conditions. ESRD patients experience higher rates of hospitalisation, cardiovascular events and all cause mortality when compared to patients with normal renal function, and are more likely to require admission to the intensive care unit (ICU) [3,4]. It has been estimated that 2% of all dialysis patients will require admission to ICU every year [5]. The presence of pre-existing end-stage organ failure, and often numerous co-morbidities, can impact on medical decisions regarding appropriateness of escalation of care and ICU admission. For a long time, it was thought that patients requiring long-term dialysis would have similarly poor ICU outcomes to those with acute kidney injury (AKI), however emerging evidence suggests otherwise.

This chapter aims to review the epidemiology, patient characteristics and short and long-term outcomes of critically unwell chronic dialysis patients, who require admission to ICU. Risk factors for early mortality, ICU prognostic scoring systems and end of life care planning will also be discussed in relation to the critically ill hemodialysis patient.

2. Characteristics on admission to ICU

Chronic dialysis patients have higher critical care admission rates than the general population; however there is a significant variation in estimates between published studies. This may reflect differences in referral rates, ICU admission policy and resource availability on a national and local level as well as the demographics of the surrounding population.

The largest cohort of critically ill ESRD patients studied derives from the Intensive Care National Audit & Research Centre (ICNARC) Case Mix Programme Database which records data of patients admitted to more than 200 ICUs across England, Wales and Northern Ireland. Analysis of this database showed that from 1995 to 2004 there were 270,972 admissions to ICU, of whom 1.3% were chronic dialysis patients [4]. The authors of the study projected that this was equivalent to six ICU admissions or 32 ICU bed days per 100 dialysis patient-years. When compared to annual ICU admission rates of 2 per 1,000 of the general population, this represents a 30-fold difference in critical care requirements. A more recent study using the same UK ICNARC database with data from 1995-2008, similarly found that ESRD patients accounted for 1.4% of all ICU admissions [6].

Other studies have proposed much higher estimates for admission rates of chronic dialysis patients to the ICU; however these are mostly single centre and involve significantly smaller study cohorts than Hutchinson et al [4]. A French prospective observational single-centre study admitted 92 chronic dialysis patients over a 3 year period, which gives a calculated admission rate of 8.6%, significantly higher than the UK database study [7]. Of note, this study was based at a teaching hospital which served as the sole critical care unit able to provide RRT to its large surrounding population.

Strijack and colleagues [8] report that 3.4% of all admissions to 11 adult ICUs in Winnipeg, Canada over a 6 year period were chronic dialysis patients, with crude admission rates for the ESRD population significantly higher than for those without ESRD (15.6 admissions per 100 prevalent patients with ESRD per year vs. 0.58 per 100 prevalent patients without ESRD per year). An American single-centre study conducted in Pittsburgh, and involving medical, surgical, trauma, neurological/neurosurgical, coronary and cardiothoracic ICUs found a similar admission rate for chronic dialysis patients of 3.6% [9]. In contrast to the 30-fold increase in critical care admissions for ESRD patients reported by Hutchinson et al [4], a multi-centre Australian study based on 3 months of data demonstrated a significantly lower 4-fold annual risk of ICU admission in dialysis patients compared to the general population [5].

Although ICU admission rates for the ESRD population vary from 1.3% - 8.6%, it is evident that patients with chronic renal disease are at higher risk of requiring critical care than the general population. Whether this is related to the underlying renal disease or associated co-morbidities remains to be seen. The decision to admit a patient to critical care is based on multiple factors, including the patient's and relatives' wishes, local admission policy, judgement of the clinicians involved and capacity.

Epidemiological data has shown that ESRD patients admitted to ICU are younger and more likely to be male in comparison to the general population [4,6-8,10]. The proportion of male admissions to the ICU is in keeping with the male preponderance in the dialysis population; however the reason for the lower mean age seen in critically ill ESRD patients requires further analysis.

3. Characteristics of critically ill dialysis patients

3.1. Severity of illness scores

Chronic dialysis patients requiring intensive care admission are more critically unwell and have a greater number of co-morbidities than the general population. Strijack et al [8] found they had significantly higher rates of diabetes (52.3% vs. 21.7%, $p<0.0001$) and peripheral arterial disease (29.7% vs. 12.3%, $p<0.0001$) than those without ESRD on admission to the ICU. Rates of coronary artery disease, stroke and cancer were comparable between the two groups.

Several studies have used ICU mortality and prognostication models such as the Acute Physiology and Chronic Health Evaluation II (APACHE) score [11] to attempt to quantify the severity of illness of dialysis patients admitted to critical care. Hutchinson et al [4] reported that both the APACHE II (24.7 vs. 16.6, $p < 0.001$) and Simplified Acute Physiology Score (SAPS) (17.2 vs. 12.6, $p < 0.001$) were significantly higher in dialysis patients when compared to those not requiring long-term renal replacement. Both scoring systems include physiological variables assessing cardiovascular, respiratory, biochemical, haematological and neurological status, within the first 24 hours of admission to ICU; however the APACHE II score places more emphasis on age and medical history than the SAPS. Strijack and colleagues [8] found a similar trend in their Canadian historical cohort study where patients with ESRD had a higher APACHE II score than those without ESRD (24 vs. 15, $p < 0.0001$), a finding that persisted even after removal of the renal component (serum creatinine and presence of AKI) of the score (20 vs. 14, $p < 0.0001$).

The fact that ESRD patients are more critically unwell on admission to ICU than the general population is an interesting concept. Certainly, this cohort is not being denied treatment based on illness severity, and it may reflect the differing admission diagnoses between the groups. However it does raise the possibility of whether there exists a higher threshold for seeking intensive care intervention in chronic dialysis patients, resulting in delayed referral, or whether patients need to be more critically unwell before being accepted into the ICU. It is also possible, that the commonly used scoring systems to assess severity of illness are not valid in chronic dialysis patients.

3.2. Reasons for admission to ICU

Dialysis patients are more likely to be admitted to ICU with a medical diagnosis than the general population (66.7% vs. 56.2%) [4]. Data shows that whilst there is a significant difference in critical care admissions after elective surgery (7.4% vs. 19%, $p< 0.0001$) between the two groups, with ESRD patients much less commonly admitted post operatively, the figures for admission after emergency surgery are comparable [8].

Interestingly, among patients with ESRD, admission after cardiopulmonary resuscitation (CPR) is a more frequent reason for ICU admission compared to other patient populations (13.6% vs. 7.3%, $p < 0.001$) [4]. Senthuran and colleagues [12] similarly found that 12% of their cohort of chronic dialysis patients were admitted to a single Australian ICU having survived a cardiac arrest. Epidemiological data from the US suggests that hemodialysis patients have a 10-fold increased risk of dying from cardiac arrest than the general population [2]. The fluid and electrolyte shifts experienced during and in between dialysis sessions may contribute to this increased risk in conjunction with left ventricular hypertrophy/dysfunction, ischaemic heart disease, autonomic dysfunction, hypertension, diabetes, and being male [13]. The fact that dialysis patients are more likely to have had CPR in the 24 hours prior to ICU admission is consistent with the finding that these patients are more critically unwell when they arrive in the ICU. Again whether this is an indirect consequence of delayed referral or acceptance or a direct consequence of the unphysiological fluid and electrolyte shifts experienced during hemodialysis is uncertain.

Cardiovascular disease and sepsis are the leading causes of death in patients with ESRD [1,2], and it is therefore not unexpected that these constitute two of the most common reasons for admission to ICU. Dialysis patients are particularly susceptible to infections due to uraemia related immune deficiency, defective phagocytic function, older age, and co-morbidities including diabetes mellitus. In addition, repeated vascular access for the purpose of hemodialysis increases the risk of bacteraemia. The annual percentage mortality rates secondary to sepsis for dialysis patients have been estimated at 100- to 300-fold higher than rates seen in the general population [14]. Between 5.6%-46% of chronic dialysis patients are admitted to ICU with a diagnosis of sepsis [4,7,8,10,12,15-18]. Strijack et al [8] found that significantly more ESRD patients were admitted to ICU with a diagnosis of sepsis compared to those without renal failure (15.8% vs. 6.5%, $p< 0.0001$), however the source of sepsis was not detailed, and whether this was related to vascular access infections cannot be determined. A small Brazilian study reported that the lung was the most frequent source of sepsis in the critically ill dialysis population, followed by soft tissue, catheter related/blood-stream and abdominal sources [17].

As well as having traditional cardiovascular risk factors, chronic kidney disease patients have associated non-traditional risk factors such as increased levels of inflammatory markers, left ventricular hypertrophy, anaemia, endothelial dysfunction, increased arterial calcification and stiffness, abnormal apolipoprotein levels, high plasma homocysteine and enhanced coagulability [3]. These factors are thought to put patients with renal dysfunction at a higher risk of adverse cardiac events including myocardial ischaemia, pulmonary oedema, cardiogenic shock, arrhythmias and sudden cardiac death. Studies have estimated that the proportion of ESRD patients admitted to ICU with a cardiac diagnosis (including pulmonary oedema) ranges from 5.1%-31% [4,7,8,10,12,15-17].

A recent study conducted in a single French ICU specifically analysed chronic dialysis patients admitted to their unit with acute pulmonary oedema [19]. Out of 102 patients with ESRD and pulmonary oedema admitted to ICU over an eight year period, they reported 41% could be attributed to an underlying cardiac cause, 26% to bronchopneumonia, 25% to excessive interdialytic weight gain and 23% secondary to an inappropriate dialysis prescription and incorrect assessment of dry weight. Interestingly they noted a distinct pattern to the ICU admissions related to patients‘ dialysis schedules; those dialysed on Monday-Wednesday-Friday were commonly admitted on Sunday and those on a Tuesday-Thursday-Saturday timetable were more likely to be admitted on Monday. The authors speculated that this may reflect a reduced tolerance to fluid overload in patients‘ with cardiac dysfunction and/or poor compliance with salt and water restriction over the weekend.

Gastrointestinal bleeding is the third most common reason for chronic dialysis patients to require critical care. Dara et al [10] report that between 1997 – 2002, 20% of their ESRD cohort had an ICU admission and the most common ICU admission diagnosis was gastrointestinal haemorrhage. However other studies have slightly lower estimates of 2.7%-15% [7,16,17].

It is difficult to ascertain precisely how often ESRD patients require critical care intervention for hemodialysis related complications, including pulmonary oedema, arrhythmias, hyperkalaemia or vascular access related septicaemia. Hutchinson and colleagues [4] report from their large UK database analysis that the most common ICU admission diagnosis for long-term dialysis patients is ‘chronic renal failure' (8.6%), which they define as volume overload or electrolyte disturbance. Hyperkalaemia was recorded as the admitting diagnosis for 4.3% [7] and 3% [12] of ESRD patients admitted to single ICUs in France and Australia respectively. Clearly, these statistics depend not only on patients’ severity of illness but also ICU admission policy, capacity, patients’ wishes and whether a renal unit is on-site or not.

In summary, patients admitted to critical care on long-term dialysis are more likely to have multiple co-morbidities and have a higher severity illness score on admission than the general population. They more frequently present having had a cardiac arrest and CPR prior to admission and are more commonly admitted for medical rather than surgical reasons [18].

4. Short term outcomes of chronic dialysis patients admitted to ICU

4.1. Mortality

During the last ten years, numerous studies have focussed on the outcomes of critically ill long-term dialysis patients admitted to ICU (Table 1). Prior to this, it was believed that ICU mortality in this population was high, and comparable to those admitted with AKI. Reliable data on prognosis are necessary to enable patients and clinicians looking after critically ill dialysis patients to make well-informed and timely decisions regarding escalation of care.

Clermont et al [9] were among the first to attempt to evaluate ICU outcomes in ESRD patients admitted to eight American ICUs over a 10 month period. They reported an observed ICU mortality of 11% for ESRD patients compared to 5% in patients without renal failure. Numerous other studies have reported ICU mortality rates of 9-44% for chronic dialysis patients [4,5, 7,9,10,12,15-18,20-22].

Study	Country	Type of RRT	No of patients (n)	Mean age (years)	Mean severity score	ICU mortality (%)	Hospital mortality (%)	30-day mortality (%)	ICU LOS (days) Mean±SD or Median [range]	ICU readmission rate (%)
Clermont [9] 2002	USA	IHD, CVVHD	57	58	64 (APACHE III)	11	14	-		-
Uchino [5] 2003	Australia	CRRT	38	45	22 (APACHE II)	22	38	-	6	-
Dara [10] 2004	USA	N/A	93	66	64 (APACHE III)	9	16	22	2	-
Manhes [7] 2005	France	IHD	92	63	49.4 (SAPS II)	28	38	-	6.2±9.9	-
Bagshaw [22] 2006	Canada	IHD, CRRT	92	66	29.7 (APACHE II)	16	34	-	-	-
Hutchinson [4] 2007	UK	N/A	3420	57	24.7 (APACHE II)	26	45	-	1.9 [0.9-4.2]	9
Ostermann [21] 2008	UK and Germany	IHD, CRRT, PD	797	55	8 (SOFA)	21	35	-	2 [1-64]	-
Senthuran [12] 2008	Australia	IHD, CVVHDF, CAPD	70	57	26.1 (APACHE II)	17	29	-	2 [1-27]	-
Strijack [8] 2009	Canada	IHD, CVVHDF	619	62	24 (APACHE II)	-	16	-	4.3	12
Chapman [20] 2009	UK	N/A	199	59	27.6 (APACHE II)	44	56	-	7.5±10.1	-
Rocha [17] 2009	Brazil	IHD, CRRT, SLED	54	66	43.9 (SAPS II)	20	24	-	5 [3-11]	-
Juneja [16] 2010	India	IHD, CRRT, SLED	73	54	27.1 (APACHE II)	27	-	41	2 [1-20]	-
Sood [18] 2011	Canada	N/A	578	61	19 (APACHE II, renal adjusted)	13	-	-	-	-

Study	Country	Type of RRT	No of patients (n)	Mean age (years)	Mean severity score	ICU mortality (%)	Hospital mortality (%)	30-day mortality (%)	ICU LOS (days) Mean±SD or Median [range]	ICU readmission rate (%)
Walcher [24] 2011	USA	CRRT	28	58	-	36	39	39	9±8	-
O'Brien [6] 2012	UK	N/A	8991	59	24.6 (APACHE II)	24	42	-	2 [0.9-4.7]	-
Bell [37] 2008	Sweden	CRRT, IHD	245	-	-	-	-	90 day mortality 42%	-	-

Abbreviations: APACHE, Acute Physiology Assessment and Chronic Health Evaluation; SOFA, sequential organ failure assessment; SAPS, Simplified Acute Physiology Score; ICU, intensive care unit; LOS, length of stay; RRT, renal replacement therapy; CRRT, continuous renal replacement therapy; IHD, intermittent hemodialysis; CVVHDF, continuous hemodiafiltration; CVVHD, continuous hemodialysis; SLED, slow extended dialysis; CAPD, continuous ambulatory peritoneal dialysis; PD, peritoneal dialysis

Table 1.

Analysis of the UK ICNARC database showed an ICU mortality rate of 26.3% in patients with ESRD compared to 20.8% in those without ESRD ($p < 0.001$) [4]. This significant increase in mortality is however not surprising, given the higher illness severity scores of ESRD patients on admission to ICU. In 199 dialysis-dependent patients requiring support of two or more organ systems (including RRT) in ICU between 1999 - 2004, ICU mortality was 44% [20], which is similar to ICU mortality for patients with multi-organ failure which can range from 20-95% depending on number of organs involved and underlying comorbitdity [23].

Factors that are commonly associated with ICU mortality in chronic dialysis patients are age, number of non-renal organ system failures, an abnormal serum phosphorus level (high or low), higher mean APACHE II or SAPS II score and duration of mechanical ventilation [7,9,12]. There is clearly some overlap between these factors as confirmed by multivariate analyses [7]. The importance of abnormal serum phosphorus levels is unclear. Manhes et al [7] hypothesise that a low phosphate level can signify malnutrition and be related to severity of illness, where as hyperphosphataemia may be an indicator of inadequate renal replacement and a risk factor for cardiovascular disease in long-term dialysis patients, although the relevance of this to acute illness is uncertain.

4.2. Length of stay

Epidemiological data consistently show that chronic dialysis patients have comparable lengths of stay in ICU to the general population [4,7-9]. Mean length of stay ranged from 1.9 to 9 days [4,6-9,12,17,20,24], with Manhes [7] reporting a trend towards longer admissions in patients without ESRD. Clearly, the decision to discharge patients from ICU is influenced by the capabilities and staffing of the receiving ward which may explain some of the discrepancies between different studies. In hospitals with renal units offering level two care, safe discharge of patients may be possible earlier compared to hospitals without dedicated step-down units.

4.3. Re-admission to ICU

Studies have shown that ESRD patients have a higher rate of readmission to ICU during the same hospital stay than patients with normal renal function [4,8], with quoted figures of 9-12% [4,8,12]. Strijack et al [8] found a significant difference in readmission rates (12% vs. 4.9%, $p < 0.0001$) between those on chronic dialysis and the general population and reported twice the frequency of readmissions to ICU within three days in the former. A recent Canadian study explored ICU readmission rates even further by evaluating the impact of dialysis modality and vascular access. They found a significant reduction in readmission rates to ICU for hemodialysis patients using arterio-venous (AV) fistulae as opposed to central venous catheters (4.7% vs. 16.4%, $p < 0.05$) [18], but acknowledged that this finding was open to confounding as central venous catheters may be simply a surrogate for poor performance status. The same group also reported that dialysis dependence was independently associated with two-fold higher odds for ICU readmission in the elderly (> 65 years) population even after adjustment for case mix and illness severity variables [25].

Therefore, the literature suggests that sicker chronic dialysis patients have shorter stays in ICU but experience almost twice the number of readmissions. Readmission to ICU is associated with poor outcomes and while many renal units have considerable experience in managing unwell dialysis patients, careful planning for a timely and safe discharge from ICU to a suitable destination is paramount.

5. Longer term outcomes of critically ill dialysis patients

Having been discharged from ICU it is essential to know how an episode of critical illness impacts on the medium and long-term outcomes of patients requiring chronic dialysis. Several studies have attempted to quantify hospital and 30-day mortality rates for this cohort and report figures of between 14-56% [4-10,12,16,17,20,24] and 32-41% [10,16,24] respectively. Hospital mortality rates were significantly higher in chronic dialysis patients compared to the non-ESRD population after ICU discharge (45.3% vs. 31.2%, $p < 0.001$) [4]. The wide range seen in these figures can in part be attributed to differences in case-mix as well as variations in illness severity between the studies.

Chapman et al [20] reported the highest hospital mortality rate of 56% for their 199 chronic dialysis patients after discharge from ICU, but emphasised that their patient cohort had a longer length of stay in ICU and higher APACHE II score than other studies, suggesting that they were a sicker group of patients. Two year survival was 29%. Interestingly they reported that a medical admission reason to ICU was associated with a relative risk of death of 2.1 when compared to patients with surgical diagnoses. 61% of medical patients died, in contrast to 19% of surgical admissions to ICU. The effect remained significant even after discharge. Age, dialysis vintage and APACHE II score did not appear to significantly affect mortality in this cohort. The majority of deaths in critically ill dialysis patients occurred within the first month, and Chapman calculated that if a patient survived to one month or hospital discharge, then long-term survival reverted back to that of chronic dialysis patients who had not been admitted to ICU.

A large Swedish nationwide cohort study involving 32 ICUs followed up 245 ESRD patients who had been admitted to critical care [15]. 90-day mortality of ESRD patients was 42%. Diabetes and heart failure were significant predictors of 90-day mortality in this population with age adjusted odds ratios of 1.9 and 2, respectively. The long-term mortality in critically unwell ESRD patients was 25 times higher than expected from mortality rates in the general population (Standardized mortality ratio 25; 95% Confidence Interval 20-31), with the highest number of deaths occurring in the first year after ICU discharge, as might be expected. This is in contrast to the work of Chapman and colleagues who reported that on leaving hospital, mortality rates for ESRD patients reverted back to normal [20]. This discrepancy may be explained by different statistical methods used, for instance, Bell and team [15] did not exclude patients who had died in ICU from their calculations.

Dialysis access and modality have been found to impact on long term mortality rates in ESRD patients admitted to critical care. Sood and colleagues [18] evaluated the 6 and 12 month outcomes of 619 ESRD patients admitted to 11 Canadian ICUs. More than 80% of admission diagnoses were medical, most commonly sepsis, and 6 and 12 month mortality were 38% and 48%, respectively. Interestingly they reported that hemodialysis patients with central venous catheter access had higher crude mortality rates at both 6 and 12 months than those who dialysed with AV fistulae. Central venous catheters remained independently associated with death even after adjustment for baseline and ICU admission characteristics as well as comorbidities. Again, this finding is open to confounding, given that tunnelled lines are more commonly used in patients with a poor performance status, and pose an increased risk of infection. Two additional cohort studies have reported similar 6 and 12 month survival rates for critically ill chronic dialysis patients [7,22]. Bagshaw et al [22] found that chronic dialysis patients had a similar 1-year mortality rate to those with no kidney dysfunction after adjustment for age, severity of illness and admission type, a finding confirmed by Strijack and coworkers [8]. These studies suggest that although ESRD identifies a cohort with a worse ICU outcome than the general population, the prognosis is related to illness severity and comorbidities rather than lack of renal function itself.

In addition to a medical admission diagnosis [4,20], diabetes, heart failure [15], and central venous catheter use [18], there are further factors which are associated with an increased mortality risk after discharge from ICU. Studies showed that older age, admission after emergency surgery, chronic health problems, CPR in the 24 hours preceding admission to ICU, having been in hospital for at least 7 days prior to ICU and the number of non-renal organ failures significantly affect outcome of ESRD patients post ICU [4,9,10,17]. As expected physiological and biochemical disturbances including hypotension, bradycardia, tachypnoea, hypoxia, reduced GCS, hyponatraemia, leucopenia and sepsis within the first 24 hours of ICU admission exert a significant impact on hospital mortality, too [4]. Mechanical ventilation and need for inotropic support are also significantly associated with mortality at 30 days [16]. Whilst many of these variables are risk factors for mortality in ICU patients in general, their impact on the ESRD population appears to be greater, perhaps due to a lack of physiological reserve in this group.

An important long-term outcome after ICU admission is quality of life and functional status. Unfortunately, to date this area has not been explored in detail in chronic dialysis patients but certainly deserves attention.

6. ICU outcomes in AKI compared to ESRD

Acute kidney injury is extremely common in critically ill patients and a frequent reason for admission to the ICU. A significant proportion require RRT and have a high associated mortality rate which can vary from 25-90% depending on patient characteristics and defining AKI criteria. Several studies have compared outcomes in patients with AKI to outcomes in critically ill chronic dialysis patients.

Clermont and colleagues [9] were among the first to examine ICU mortality in patients with AKI, ESRD and those with normal renal function. In spite of similar illness severity scores in the AKI and ESRD populations, ICU mortality rates were five times higher in the dialysis-requiring AKI group than those on chronic dialysis and ten times higher when compared to those with normal renal function (57% vs. 11% vs. 5%, respectively). There was no reported difference between patients with AKI on admission to ICU and those who developed AKI during their stay in ICU.

Similarly a small case-control study conducted in Brazil compared the outcome of AKI patients on RRT with ESRD patients, two cohorts characterised by loss of renal function. They reported double the ICU and hospital mortality rates in AKI patients compared to ESRD patients when matched for age, severity of illness and number of organ dysfunctions (42% vs. 20% and 50% vs. 24%, respectively) [17]. Length of stay in both ICU and hospital was also significantly increased in the AKI group. Having excluded patients admitted to ICU for post-operative monitoring and fluid overload or electrolyte imbalance secondary to inadequate dialysis, sepsis was the main reason for admission in both cohorts. In this study however they reported that patients with AKI were more likely to require mechanical ventilation and vasopressors than those on chronic dialysis, even when matched for severity of illness.

The largest comparison of outcomes in these two groups has come from a retrospective analysis of the Riyadh Intensive Care Program database, which recorded over 40,000 ICU admissions to nineteen units in the UK and three units in Germany over a 10 year period [21]. 1847 patients with AKI on RRT were compared to 797 ESRD patients. ICU and hospital mortality in addition to ICU length of stay were significantly increased in the cohort with AKI requiring RRT. ESRD patients had approximately half the ICU and hospital mortality rates of AKI patients on RRT (20.8% vs. 54.1%, $p < 0.0001$ and 34.5% vs. 61.6%, $p < 0.0001$, respectively). As expected, increasing ICU mortality was seen with an increasing number of organ failures in both cohorts,

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however the group of AKI patients on RRT had a significantly higher proportion with more than two non-renal organ failures (75.4% vs. 25.6%) and needed mechanical ventilation more often (91.3% vs. 60.9%, $p<0.0001$). The strongest independent risk factors for ICU mortality were mechanical ventilation, maximum number of organ failures and non-surgical reason for admission.

Walcher et al [24] also reported that significantly more AKI patients were mechanically ventilated than critically ill dialysis patients, even when well matched for illness severity scores and controlled for mode of RRT (89% vs. 57%, $p = 0.0003$). Mechanical ventilation was the single factor associated with increased hospital mortality with an odds ratio of 3.1. ICU, hospital, 30- and 60-day mortality rates as well as length of stay in ICU were higher in the AKI cohort compared to ESRD patients, when both received continuous renal replacement therapy (CRRT).

Although the majority of published literature indicates that ICU and hospital outcomes are significantly worse for AKI patients requiring RRT than critically ill chronic dialysis patients, one small Australian study reported comparable ICU and hospital mortality rates for diagnosis and severity-score matched AKI and ESRD patients receiving CRRT [5].

Most outcome studies are hampered by the difficulty in assessing severity of illness correctly in patients with ESRD. The commonly used ICU prognostic scoring systems are often applied to patients with ESRD despite the fact that they are not fully validated in this patient population and may over-estimate mortality rates. What is evident from the literature is that the requirement for mechanical ventilation appears to be significantly increased in patients with AKI and that this is independently associated with an increased mortality rate.

7. Validity of ICU severity scores in ESRD

ICU illness severity and organ dysfunction scoring systems are primarily used within critical care as research and audit tools to enable comparison between observed and predicted mortality and controlled matching between study cohorts. Whilst these scoring systems have been validated in a wide variety of different subspecialties, their application and accuracy in the ESRD population remains controversial.

The Acute Physiology and Chronic Health Evaluation (APACHE II and III) [11,26], SAPS II [27] and Sequential Organ Failure Assessment (SOFA) [28] scores are commonly used in critical care literature. The first two scores assess up to 20 physiological variables within 24 hours of admission to ICU, while the SOFA score is used to track progress between subsequent 24 hour periods in ICU. As might be expected all scoring systems have a renal component, taking into account urine output, urea, serum creatinine, serum potassium and bicarbonate to varying degrees. Application of these tools to chronic dialysis patients and their accuracy in predicting mortality in this group is therefore uncertain.

Several studies have attempted to assess the validity of different scoring systems when used in the ESRD population, with differing results. Hutchinson and co-workers [4] used the

APACHE II score and reported an area under the receiver operating curve (ROC) of 0.721 for their ESRD cohort, compared to 0.805 in the non-ESRD group, indicating that it is less accurate in predicting mortality in chronic dialysis patients. When using a modified renal-adjusted APACHE II score especially for dialysis patients the ROC improved to 0.817. Uchino [5] and Juneja [16] also reported a ROC of 0.81 and 0.86 respectively for the APACHE II score, using a much smaller cohort of long-term dialysis patients. The APACHE III score is an extension of its predecessor and takes into account twenty physiological variables as well as major disease categories and treatment location prior to ICU admission to provide risk estimates for hospital mortality for individual ICU patients. Two small studies have demonstrated that this score over-estimates 30-day mortality in ESRD [9,10]. Similarly, Strijack [8] found that the APACHE II score over predicted mortality in dialysis patients by a factor of 2.5.

The SOFA score assesses degree of dysfunction of six organ systems, including respiratory, cardiovascular, renal, hepatic, neurological and coagulation system. Data on its validity in patients with ESRD are conflicting. One study reported a ROC of 0.92 (although not significantly different from the APACHE II score) [16] whereas Dara et al [10] found the SOFA score to be less accurate than the APACHE III with a ROC of 0.66. Notably the patients in the first study were sicker than those included in the latter with an increased number of organ failures and greater need for mechanical ventilation and inotropes.

Therefore at present there is limited and conflicting information regarding the validity of commonly used scoring systems in chronic dialysis patients. The majority of studies have used too small sample sizes to make any reliable claims. As mentioned previously ESRD patients have similar illness severity scores to patients with AKI on admission to ICU, but have significantly better outcomes indicating that these prognostic tools over-estimate mortality in dialysis patients. The application of these tools in their current form to a population of anuric patients with chronically deranged biochemistry on long-term RRT is at best limited.

A group in Belgium have developed a renal specific prognostic score to predict outcomes in patients with AKI [29]. The Stuivenberg Hospital Acute Renal Failure Scoring System (SHARF II) is based on eight parameters; age, serum albumin, bilirubin, prothrombin time, respiratory support, sepsis, hypotension and heart failure and consists of two scores at AKI diagnosis and 48 hours later. ROC was 0.82 at diagnosis and 0.83 at 48 hours in a cohort of 293 patients admitted to the ICU with AKI. As with other prognostic tools, this system has limited clinical application because of its complexity and remains a research and audit tool. It has yet to be assessed in critically ill long-term dialysis patients and it would be interesting to investigate whether it is a more accurate predictor of mortality than current scoring systems.

8. End of life planning in critically ill dialysis patients

Advance care planning varies widely between institutions, regions and countries. The study to understand prognoses and preferences for outcomes and risks of treatments (SUPPORT) was published in 1995 and highlighted the shortcomings in end-of-life decision making practices [30]. The authors described issues with communication, frequency of intensive interventions and the way in which patients died. Less than half of physicians knew whether their patients wanted to avoid CPR, 46% of do-not-resuscitate (DNR) orders were signed within 2 days of death, and 38% of those who died had spent at least 10 days in ICU. More recently significant efforts have been made to try and improve end-of-life care for patients with chronic and terminal disease.

Critically ill patients in the ICU frequently lack the capacity to make decisions regarding life-saving and life-prolonging interventions [31]. Instead the burden falls to the family to act as surrogate decision makers in conjunction with the multi-disciplinary team. Good communication between health professionals and relatives in this scenario is essential in order to ascertain the patient's values and beliefs, as well as impart key information regarding prognosis, probability of survival and future quality of life. Decisions to withdraw active life sustaining therapies in ICU appear to be comparable between dialysis and non-dialysis patients [4].

A large retrospective mortality study using the US Renal Data System found that chronic dialysis patients over the age of 65 years experienced very high rates of medical intervention in the last month of their lives; 76% were hospitalized, 48.9% were admitted to ICU and 29% underwent at least one intensive intervention (mechanical ventilation, CPR or feeding tube placement) [32]. Unfortunately patients' preferences related to ICU admission and interventions were not explored.

With an increasingly elderly and unwell hemodialysis population advance care planning before an episode of critical illness or ICU admission is key [33]. Nephrologists have frequent contact with their patients and are in an ideal position of trust to explore any religious or cultural beliefs and discuss limitations of treatment. Advance care planning is known to address fears, prepare patients for death, and allow them to exert some control over their life as well as strengthen interpersonal relationships. Many physicians are reluctant to initiate such important discussions either through lack of adequate training or belief that patients will initiate any discussion when they are ready. In fact qualitative research has shown that ESRD patients prefer earlier physician initiation of end-of-life discussions and would welcome more information on prognosis and potential outcomes of their disease than is currently delivered [34]. These discussions are infinitely better suited to an outpatient environment rather than on a critical care unit.

A group in Saudi Arabia carried out a survey of 100 primarily Muslim dialysis patients on their views regarding advance care planning [35]. More than 95% had little knowledge of CPR, intubation or ventilation, however interestingly more than half of those surveyed had been admitted to ICU within the last 2 years. It was generally believed that CPR was effective in 50-90% of cases and the majority of patients opted to have CPR in the event of cardiac arrest. When informed about the more realistic success rates of CPR and potential ventilator dependency, brain injury and coma, the proportion of respondents agreeing to CPR fell to 35%. This study emphasises the importance of effective doctor-patient communication regarding prognosis and quality of life, supporting patients to make informed decisions.

Similarly a British study found that 76% of hemodialysis patients surveyed wished to receive CPR in the event of an in-hospital cardiac arrest not related to dialysis [36]. The patients who opted to receive CPR were significantly younger (59 ± 16 vs. 74 ± 10 years, $p < 0.01$) and had a significantly higher albumin level than those who declined or who were undecided, perhaps indicating a better chronic health status. Gender, comorbidity, dialysis vintage, proportion of patients with adequate dialysis and mean haemoglobin level were not associated with the decision.

It is evident that a large proportion of chronic dialysis patients experience an admission to ICU before they die. End-of-life discussions often fall to the family and health professionals caring for the patient. Research indicates that dialysis patients want to be involved in advance care planning at the earliest opportunity and the onus rests on the physician to enable patients to make well informed and timely decisions regarding end-of-life care.

9. Conclusion

Critically ill patients with ESRD are frequently admitted to the ICU, and although they display worse outcomes than those with normal renal function, their prognosis is better than that of ICU patients with AKI. Mortality is related primarily to the severity of the underlying illness and their co-morbidities rather than to lack of renal function itself. Having survived an episode of critical illness, data on longer-term outcomes remains conflicting and little is currently known about quality of life and performance status after discharge from ICU. Prognostic scoring systems used in critical care appear to over-estimate mortality in the chronic dialysis population and should be used with caution. There is a need for ESRD-specific tools to score severity of illness and predict mortality in the critically ill and enabling accurate research and audit in this population. Current evidence suggests that long-term dependence on dialysis should not prejudice against prompt referral or admission to ICU.

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