Controversies in Clinical Nephrology:

Challenges of performing renal replacement therapy in the intensive care unit:

The intensivist perspective

Introduction

Since the 1960s, renal replacement therapy (RRT) has been used to treat the effects for acute renal insufficiency complicating major medical, surgical, or obstetric illness. In those early days, whether in an intensive care unit (ICU) or in a renal ward, RRT was invariably provided by renal specialists, reflecting the complexity of the dialysis technology of the time. Over-time, patients with acute renal failure in the context of multiple-organ dysfunction or major nonrenal illness were more rarely treated in renal wards, however, in many countries, RRT for the critically ill has remained prescribed and delivered by a nephrology service visiting the ICU. In other locales, including the United Kingdom, provision of RRT within the ICU has instead become the near-exclusive preserve of the intensive care specialist, delivered by ICU nursing staff with no requirement for specialist renal input or even the presence of a renal service in the hospital. The history of this change is interesting: In major UK hospitals in the 1970s, RRT in the form of hemodialysis or peritoneal dialysis (PD) was provided by the nephrology team to all patients, including those requiring mechanical ventilation in ICU [1]. Over-time, hemodialysis technology progressed, and by the early 1980s arteriovenous hemofiltration was being introduced for sicker ICU patients, still delivered largely by nephrologists [1]. Two things then occurred in the mid 1980s, firstly there was a significant expansion of the end-stage renal failure population with a five-fold increase in the UK chronic dialysis population from 1982 to 2002, shifting the focus of renal services to the management of CKD centralized in large regional renal units and away from acute renal failure. Secondly, around the same time, the introduction of microprocessor-controlled pumped veno-veno continuous renal replacement therapy (CRRT) devices greatly facilitated and simplified prescription and delivery of RRT to the sickest of patients. In the UK and Australia, the adoption of CRRT technologies was led by intensivist [2]. As a result, by the early 2000s, CRRT was the mainstay of therapy being used in > 90% of UK ICUs, solely under the direction of the intensivist in 89% of ICUs [3], and, by 2008, CRRT intermittent hemodialysis was only available at all in 10% of UK ICUs and rarely employed in those where it was technically available [4]. Thus, the UK provides a specific viewpoint to consider the benefits and drawbacks of the intensivist-led RRT provision for the critically ill.

The benefits and disadvantages of intensivist-led RRT in the critically ill

Intensivist-led provision of RRT involves the decision to commence, and all aspects of, RRT prescription being made by the attending intensivist with by line insertion and delivery of therapy by the ICU medical and nursing staff. This is the standard model of practice in countries such as the UK, Australia, and Sweden. The major advantage of this approach is that RRT just becomes another form of organ support applied by the ICU team to critically ill patients with multiple-organ failure. Thus, when RRT is clinically indicated, therapy can commence rapidly without additional consultation or the attendance of an external renal nurse. Importantly, RRT prescription can be integrated into a patients' hemodynamic, respiratory, nutritional, and pharmacological management, all coordinated by the intensivist. Furthermore, RRT can then be adjusted immediately to acute changes in clinical condition and integrated

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with other organ support by the bedside ICU medical and nursing team. While early commencement of RRT based on levels of serum creatinine is not clearly beneficial [5], serum creatinine is unlikely to be the best marker of the acute imbalance between renal functional capacity and the demand for renal function in critical illness. It is likely that prompt institution of RRT is beneficial in those with inadequate renal function in the context of their illness and its treatment [6], an evaluation that the intensivist, with a global view of the patient's critical illness, is best placed to make. Finally, provision of RRT in the ICU by intensivists and ICU nurses naturally favors the use of continuous modalities in step with the continuous nature of other organ support provided in the ICU. While definitive trial-evidence is of its superiority is lacking [7], the use of CRRT is recommended in hemodynamically unstable patients needing RRT [8] (the majority of those in the ICU). It is less associated with development of fluid overload [9] and is associated with better long-term outcomes in epidemiological studies [10]. Conversely, CRRT may be more difficult to implement by a visiting renal service both from a cost, human resources, and ease-of-prescribing point of view, leading to a potential bias toward use of intermittent hemodialysis (IHD).

While there are many potential benefits of embedding RRT provision within the ICU team, several disadvantages exist. In order to deliver safe and effective therapy by a broad-based clinical team without nephrologist input, in most ICUs, RRT is restricted to the sole use of continuous therapies with relatively inflexible protocols optimized toward the treatment of the sickest patients. While this is ideal for the management of early critical illness, continued use of conventional CRRT over many weeks of a prolonged recovery in the ICU may be more labor intensive, costly, and can restrict opportunities for rehabilitation. The flexibility to provide intermittent or extended intermittent treatment to these patients is a potential advantage of a specialist renal service. Other patient groups may also benefit from better-tailored prescription and wider modality choice, in particular patients with preexisting end-stage renal disease (ESRD) requiring ICU admission, and in circumstances where rapid clearance of a exogenous dialyzable toxin or resolution of an extreme electrolyte abnormality (such as profound hyperkaliemia) would benefit from the greater efficiency of online hemodialysis. Finally, the ease of institution of RRT in an intensivist-led model does run the risk that RRT may be implemented at too low a clinical threshold with the potential for increased cost and patient harm from unneeded treatment; in this context, the hand of an external nephrology consultation may be advantageous in tempering therapeutic overenthusiasm.

Other benefits from the involvement of a renal specialist may accrue that are not directly linked to the provision of RRT. For instance, cases of intrinsic renal disease presenting as critical illness, such as systemic vasculitis, may be more rapidly recognized and treated, and patients with preexisting chronic kidney disease or those developing CKD after RRT-requiring AKI can be seamlessly followed up and managed by the same service after ICU discharge and as outpatients. In the UK, patients requiring RRT in the ICU without previous renal history are rarely followed up, despite evidence of significant progression of CKD in this population [11], providing a significant challenge for intensivist-led care. However, while nephrology-led acute-RRT services provide the opportunity to achieve follow-up, this does not mean that this actually occurs [12] – too often the attitude amongst physicians has been that dialysis independence means continued nephrology involvement is no longer required, despite this being of significant potential benefit [13].

Given the pros and cons of these intensivist- and nephrologist-led approaches (Table 1), what is the optimum model for RRT provision in the critically ill? In my opinion, critically ill patients are united by severity of disease and the interplay of multiorgan dysfunction, and the ability to rapidly commence RRT and integrate therapy with demands of acute critical illness are the key features favoring embedding RRT provision within the ICU. However, no studies have compared organization of service provision for RRT in the ICU. Observational reports examining the transition from IHD toward CRRT in the early 90s suggested significant benefit [14], but these were not sustained in the highly-

Table 1.

Acute RRT providers	Intensivist/ICU nurse	Nephrologist/renal nurse
Timing	Rapidly after decision to initiate	Potentially delayed, requiring external consultation and nurse
Modality	Largely continuous with transition to IHD in ICU often not possible	Potentially biased against continuous therapy
Cost	High consumables with CRRT vs. IHD, but potentially lower nursing and physician costs using existing ICU resources	Lower consumables with IHD vs. CRRT, but potentially higher nursing and physician costs
"Integration with other" therapy	Well integrated with respiratory and hemodynamic management in multiorgan failure	Requires multi-professional team-working to integrate RRT into other aspects of critical illness
Individualized therapy	Simple, but inflexible protocols, well optimized for treatment in acute critical illness, but less suited to the recovery phase and for existing ESRD patients	Ability and expertise to tailor therapy to unusual clinical situations, facilitates management of the ESRD patient in the ICU.
Renal follow-up	Often neglected, requires renal consultation	Can be seamlessly continued after ICU discharge, new referral not required

CRRT = continuous renal replacement therapy; ESRD = end-stage renal disease; ICU = intensive care unit; IHD = intermittent hemodialysis; RRT = renal replacement therapy.

Table 2. Comparison of results and therapy in the VA/NIH ATN study and RENAL studies where similar groups of critically ill patients with AKI were treated in the USA and Australia & New Zealand, respectively [15, 16, 17].

	VA/NIH ATN study (USA)	RENAL study (Aus & NZ)
Number	1,124	1,465
Age, years	59.7	64.5
Percentage of males	70.6%	64.6%
CKD classification (of those with known eGFR)		
0 – 2	65.5%	42.0%
3a	22.7%	17.9%
3b	11.9%	19.2%
4	Excluded	20.9%
5	Excluded	Excluded
Sepsis	63.0%	47.9%
Mechanical ventilation	80.6%	73.9%
Illness-severity score	APACHE II: 26	APACHE III: 102.4
Cardiovascular SOFA	2.3	2.9
Modalities of RRT	CVVHDF, SLEDD, or IHD	CVVHDF
Commenced on CRRT	69.7%	100%
IHD in ICU at any time	63.1%	7.3%
Time from ICU admission to RRT	6.7 days (3.2 days from AKI diagnosis)	2.1 days
Urea at study enrolment	23.8 mmol/L	23.5 mmol/L
Survival at day 60	47.4%	Not reported
Survival at day 90	Not reported	55.3%
Alive and off RRT		
At day 28	25.8%	45.9%
At day 60	16.1%*	Not reported
At day 90	Not reported	47.7%

*Discharged alive off RRT. APACHE = Acute Physiology and Chronic Health Evaluation; CKD = chronic kidney disease; CRRT = continuous renal replacement therapy; ICU = intensive care unit; IHD = intermittent hemodialysis; RENAL = Randomized Evaluation of Normal vs. Augmented Level; RRT = renal replacement therapy; SOFA = Sequential Organ Failure Assessment; VA/NIH ATN = Veterans Affairs/National Institutes of Health Acute Renal Failure Trial Network.

selected patients randomized to trials examining intermittent vs. continuous modality. Some insights can be gained by examining the two largest randomized trials conducted to date examining RRT provision in the ICU, the VA/NIH ATN study [15] and the RENAL study [16]. These studies were respectively conducted in the USA and Australia & New Zealand where there were significant differences in practice of RRT management in the ICU, with predominantly intensivist-led treatment and 100% first use of CRRT in Australia & New Zealand, compared to a significant reliance on nephrology-delivered IHD in the USA. Thus, even though their primary clinical question regarding intensity of RRT was negative, interesting inferences can be gathered by comparing overall outcomes in the two studies. Despite comparable illness severity, level of uremia, and age, long-term survival free from chronic dialysis was much more common in the RENAL compared to the ATN study, 48 vs. 16% (Table 2). The major differences between these studies (Table 2) were more swift commencement of RRT from time of ICU admission and much lower exposure to IHD at any point in the ICU stay in the RENAL study (7 vs. 63%). While it is tempting to conclude that intensivist-led management led to the superior outcomes in the RENAL study, it is also possible that the renal specialists involved the ATN study were more selective at screening out patients who would survive without RRT, the group that have the best outcomes. Overall, side-by-side comparisons of these approaches are unlikely to be feasible as organization of RRT provision in the ICU is only one manifestation of differences in ICU culture between healthcare settings. However, this comparison does at least suggest that wider use of CRRT and earlier use in those with clinical indications may be features of an intensivist-led model, which could be most beneficial to patients.

Conclusion

In 2017, models of care in the best institutions around the world are no longer at the extremes discussed above. In the UK, intensivists with specialist renal interest and, not uncommonly, joint specialist training in nephrology are able to provide clinical expertise, devise more flexible RRT protocols, and provide liaison with specialist renal services without compromising speed and integration of RRT into integrated organ support. Similarly, in nephrology-led care, renal specialists are becoming more subspecialized, with acute nephrology physicians and nurses having a much greater presence in the ICU and integration with the ICU team during the management and follow-up of critically ill patients with advanced AKI. Thus, the answer to the challenges of performing best-quality RRT in the ICU may not be not to promote an exclusively intensivist- or nephrologist-led approach, but to take the best from each model into one's current practice with the aim of providing the best "critical care nephrology" service to our patients.

Conflict of interest

Dr. Prowle has received speaker's honoraria and travel costs from Nikkiso Europe GmbH and Baxter Inc. and institutional service development support from Nikkiso Europe GmbH.

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