ICU

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Quality

PLUS

Biomarkers in Heart Failure

Difficult Intubation

Emergency Intraosseous Access

Pain Assessment and Management

Dexmedetomidine, Delirium & Sleep

Early Mobilisation: From Concept to Reality

What Can Psychologists Do in Intensive Care?

Clinical Pharmacist Role

Social Media: Blessing or Curse?

Learning to Lead an ICU

Renal Replacement Therapy for Acute Kidney Injury

Country Focus: UK

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RENAL REPLACEMENT THERAPY FOR ACUTE KIDNEY INJURY

QUESTIONS REMAIN

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What should be the definition of "early" renal replacement therapy in your opinion?

There is no agreement currently. The demand for initiation of renal replacement therapy (RRT) is driven by severity of acute kidney injury (AKI), but also by severity of illness, co-morbidity, volume overload and other factors

Two major studies published this year addressed the timing of initiation of renal replacement therapy (RRT). The Early vs Late Initiation of Renal Replacement Therapy in Critically Ill Patients With Acute Kidney Injury (ELAIN) trial (Zarbock et al. 2016) used KDIGO/AKI severity stage 2; the AKIKI trial (Gaudry et al. 2016) used stage 3 AKI. That shows that this is a field that's not so clear. Both trials had divergent outcomes. The ELAIN trial showed benefits for early initiation started at stage 2 AKI, while the AKIKI trial did not show the benefits of starting RRT early. Both trials used increases of serum creatinine and decreases of periods of oliguria and AKI staging as a timing tool. Perhaps that's not really how clinical practice is at present, because when you decide in daily practice to initiate RRT or not of course it is the severity of AKI that's the driver for this decision as well as other factors such as the severity of the patient's illness, volume overload etc. Maybe looking only at kidney variables is a bit too narrow and we need to look at a broader picture of the patient.

There is another trial coming up—the Standard vs. Accelerated Initiation of RRT in Acute Kidney Injury (STARRT- AKI) trial, led by Ron Wald and Sean Bagshaw (clinicaltrials.gov/ct2/show/NCT02568722). It's an ambitious worldwide trial that aims to enrol 2866 patients, and it is aimed at investigating the timing of RRT. Inclusion of patients in the trial will be when they are at AKI stage 2 or 3, so that is similar to previous trials. However, an important aspect is that patients can only be included when the physician thinks there is a window for waiting or early initiation, delayed or not. If the physician thinks the patient needs an immediate start or thinks this patient needs to wait a little the patient cannot be included and of course the decision of the physician will be triggered by other factors then AKI severity stage.

In addition, an eagerly awaited French trial, the Initiation of Dialysis EArly Versus deLayed in Intensive Care Unit) (IDEAL-ICU) (clinicaltrials.gov/ct2/show/NCT01682590) has started recruiting 800+ patients this year, and it will also address the question of early or delayed RRT initiation.

What are the most important considerations in deciding which patients should receive RRT?

The first question always is whether there is consensus amongst the staff and the patient's family to initiate RRT. It is often considered a sign of being very severely ill. Needing RRT is sometimes a step too far for family members or patients themselves. As clinicians you have to inform your patient and make sure that you have a clear mindset to offer this to patients who will receive the benefits or who still have a prognosis. For septic and liver failure patients the consideration is what kind of modality to use. Typically, septic shock and severely haemodynamic unstable patients, or liver failure patients, are initiated on a continuous modality. Because it is better haemodynamically tolerated especially in acute liver failure patients there may be an issue of encephalopathy caused by brain oedema and in these patients you don't want the volume shifts associated with intermittent therapy. We also have volume-overloaded patients, in which we want to remove volume, which is not always well tolerated when you do it on a four-hour basis. These patients are also initially on continuous or sustained low-efficiency dialysis (SLED) therapy, and we review during a 12-hour or 24-hour period.

What criteria should ICUs use to decide on continuous or intermittent renal replacement therapy?

There is no data to support the superiority of continuous over intermittent or vice versa. How

familiar you are with the technique is important. In expert hands intermittent therapies, using 6-hour duration or 8-hour treatment duration, are also tolerated in haemodynamically unstable patients, but that's in expert hands. The nurses need to be able to do this. It has been demonstrated very elegantly in several studies, especially in France, by Christophe Visonneau and Fréderique Schortgen, that you can also treat severe septic shock patients with intermittent therapies (Visonneau et al. 2006; Schortgen et al. 2000). However, not all units are able to do this. If most of your patients are severe septic shock patients, mechanically ventilated and on vasopressors, then continuous or hybrid blood therapies are preferable. If your patients are less severely ill, intermittent therapies are equally effective and can be used. It's your expertise that really drives the decision.

How should the most appropriate anticoagulation strategy be identified?

There are two possibilities—unfractionated heparin and citrate. Unfractionated heparin was the standard up till a few years ago and is now gradually being replaced by citrate in many units. Citrate is associated with longer filter life and less bleeding, so in that respect citrate has replaced unfractionated heparin. There are typical patients who are at risk for systemic bleeding, such as trauma or cirrhosis patients, who probably are better treated with citrate.

Perhaps a third option is also possible and that's something we also tend to do with SLED, which is using heparin-coated membranes and no anti-coagulation at all. That is also an option if the treatment duration is intermittent and not too long.

When and how should renal support be stopped?

It is a big question mark. I don't think there is data out to support a clear statement on that, but typically when the patient is passing urine again continous RRT is stopped for 12 hours or a day to see how things are going and if the patient tolerates the discontinuation of CRRT. Adequate urine volume is the main driver for stopping renal replacement support as well as adequate clearance, creatinine clearance above 10. Of course you can only measure the clearance when you stop the therapy.

> "we should move on and look at specific subgroups"

Is there good evidence on risk factors for persistent dialysis dependency of AKI patients who receive RRT? Your 2015 study (Oeyen et al. 2015) found that a quarter of long-term AKI-RRT survivors have persistent dialysis dependency. What is needed to improve this?

There is observational data from cohort studies that suggests that continuous RRT patients compared to intermittently treated patients have lower risk for persistent need for RRT (Schneider et al. 2013). But it is still not shown in prospective trials, and it's still an open question. It's strongly suggested, but has yet to be proven. Hybrid therapy with a longer duration of intermittent therapy has probably the same outcomes as continuous RRT so it should be regarded as similar. Other risk factors are the risk factors that can't be altered, such as pre-existing chronic kidney disease. That is one of the most important risk factors and associated with that is hypertension and diabetes, as these patients also tend to have chronic kidney disease. The definitive word on modality is not out but it is suggested and the data have suggested that continuous therapy or hybrid therapies are associated with less persistent need for RT.

What should be the priorities for further research into renal replacement therapy for AKI patients?

Timing is the number one priority, and data on this are being generated at the moment. The elements that may decrease persistent AKI or persistent need for chronic renal replacement therapy are also very important, because they have a huge impact on the patient and society, as well as an economic impact. Currently all our studies on AKI patients are as a group. I think we should move on and look at specific subgroups, because it doesn't make sense that patients who develop AKI following cardiac surgery are put in the same basket as septic shock patients. Probably the timing of initiation and choice of modality etc —all these questions have different answers for different subgroups. I see this as an important research question. Hybrid therapies are not well studied yet and should be evaluated in more detail.

Should variation in practice at ICU level on initiation of RRT etc. be addressed at a national or European level?

There is already variation in practice within one unit. When I am on call I will have a different opinion on it than my colleague. I think it should be addressed on a global level or even better a European level because there are so many opinions and there is no good data at present. ■

Conflict of Interest

Eric Hoste declares a speaker's fee from Alexion and a study grant from Bellco for a study on ECCO2R.

Abbreviations

AKI acute kidney injury
CRRT continuous renal replacement therapy
RRT renal replacement therapy
SLED sustained low-efficiency dialysis

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