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Extracorporeal Blood Purification in the Context of Multiorgan Support: Current Role and Best Practices

Announcer:
Welcome to *KDIGO: Conversations in Nephrology.* This episode titled, "Extracorporeal Blood Purification in the Context of Multiorgan Support, Current Role and Best Practices," is provided by KDIGO and supported by Baxter Healthcare.

Here's your host, Dr. Kathleen Liu.

Dr. Liu:
Hello and welcome to KDIGO Conversations in Nephrology. I'm Dr. Kathleen Liu, Professor of Medicine and Anesthesia in the Divisions of Nephrology and Critical Care Medicine at the University of California, San Francisco. Joining me to discuss extracorporeal blood purification in the context of multiorgan support, current role and best practices, is Professor Claudio Ronco. Professor Ronco is the Director of the Department of Nephrology in the International Renal Research Institute of San Bortolo Hospital in Vicenza, Italy, and his clinical and research interests include critical care nephrology and related technology. I want to note that there are differences in nomenclature and the terms Continuous Kidney Replacement Therapy and Continuous Renal Replacement Therapy are often used interchangeably. For the purposes of this conversation, we will be using the term Continuous Renal Replacement Therapy.

Professor Ronco, welcome to the program.

Prof. Ronco:
Thank you very much for the invitation. It is my pleasure to be here with you today.

Dr. Liu:
So, we'll get started. So, Professor Ronco, we have a number of clinical trials suggesting that there is not benefit to early renal replacement therapy in the setting of AKI in critically ill patients. Do you think that these studies apply in patients with multiorgan failure? If not, why not?

Prof. Ronco:
First of all, rather than saying no benefit, I would say that it is controversial whether early or late application of renal replacement therapy in AKI is of any benefit for the patient. However, when you move from acute kidney injury alone to multiple organ failure conditions, you have to analyze the endophenotype of the patient, and describe the totally different conditions where renal replacement is only part of this concept, and we have to expand the concept of extracorporeal blood purification to other organ support. As a matter of fact, we sometimes have been speaking about most multiple organ support therapy, or ECOS - extracorporeal organ support – and today, these all fit in the family of extracorporeal blood purification therapy. There is no sufficient evidence to define the early versus late application, but we have understood perfectly that every patient is a single entity, and personalization is probably the most accurate approach for each patient, once you have defined the endophenotype and the characteristic of its condition. We have to remember that every patient in the ICU changes quite rapidly, and therefore the continued surveillance of the patient may impose rapid origin or emergency application of extracorporeal blood purification therapies. That may include ultrafiltration, may include removal of uremic toxin, may include removal of bilirubin, may include removal of CO2, and may include possibly removal of other mediators in condition of cytokine release syndrome or sepsis.

Dr. Liu:
Great. And you've touched on it a little bit, but maybe you can share with us a little bit more. Beyond the kidney what other organ systems do these extracorporeal therapies directly support in the context of multiorgan failure, or how should we think about that?

Prof. Ronco:
Well, we have to consider the condition of multiple organ failure as a situation where there is a kind of endothelial failure, often caused by an underlying condition of sepsis. And when several organs are failing rather than trying to support uniquely the function of this or that organ, you probably need to better understand the pathophysiology of that condition, and possibly try to treat the underlying mechanism, that is a final common pathway for different organ system failure. Certainly today, we have one thing in common, of every organ in the body, when it is failing and it is blood. And blood is a target for potential therapy and removal of conditions that may affect the different organ system function. I am meaning specifically about the possibility to re-equilibrate the blood in terms of fluid and electrolytes, removing toxin and factors that may affect organ function, and finally, possibly removing the condition of disruption of the immuno-response that lead to presence of DAMPS and PAMPs into the circulation, leading to subsequent kidney, lung, liver, and heart failure. In this situation, different extracorporeal organ support system can be applied in sequence or in parallel.

Dr. Liu:
For those just tuning in, you're listening to KDIGO Conversations in Nephrology on extracorporeal blood purification in the context of multiorgan support. I'm Dr. Kathleen Liu, and I'm speaking with Professor Claudio Ronco. Maybe you can tell us a little bit about the role of both current CRRT technology and other types of extracorporeal therapies, with regards to the removal of inflammatory mediators which you alluded to as being very important in multiorgan failure.

Prof. Ronco:
Well, the discussion that arose recently on what is the current role of technology in extracorporeal blood purification therapies has to be seen in light of a long history and development of dialysis techniques, membranes, and recently sorbents and new techniques. First of all, we are perfectly aware that the first observation that CRRT could remove some of the mediators of inflammation during sepsis and multiple organ failure goes back to 1992, when Grootendorst demonstrated that the ultrafiltrate of septic patients may reproduce sepsis in an animal model. At this point, it is clear that there is a humoral component that can be removed.

But this component can hardly be removed by diffusion in continuous hemodialysis, and it is always likely, removed by continuous hemofiltration or hemodiafiltration, where the permeability of membranes are improved. More recently, we have available mass separation by sorbents, which include the term "hemoadsorption" and may allow the removal of molecules in a wide spectrum of molecular weights – things that cannot be done with classic extracorporeal blood purification therapies. So, we are facing a new era in this, let's say, area of study and investigation, that is probably seeing sorbents as the new frontier.

Dr. Liu:
Great. And, Professor Ronco, are there any specific things about some of those sorbents that you would want to share with the audience?

Prof. Ronco:
Well, I think that adsorption was originally used for intoxication and this goes back to the last century. However, today we have understood that porosity and structure of these sorbents, including electrical charges, hydrophobic or hydrophilic size, can be modified in order to target specific molecules. For example, we have the sorbents capable of removing viral particles or bacteria. We have sorbents capable of removing from the circulation activated leukocyte or endotoxin. And finally, we have sorbents that are capable of removing cytokines. In this case, we have to divide sorbents between selective and nonselective, and among the nonselective sorbents, cytokine removal, according to the peak concentration hypothesis may be beneficial because you are not only remove proinflammatory mediators, but you also remove anti-inflammatory mediators, reconstituting somehow a kind of immunohomeostasis. The highest is the concentration of the cytokine in blood. The highest is the removal. I think that in the future, we might have some kind of smart sorbents that can target specific molecules, and this is where our research today is oriented.

Dr. Liu:
Wow. I think that sounds very exciting and a great future frontier. Before we come to the end of our conversation, Professor Ronco, are there any final messages you'd like to leave with our listeners?

Prof. Ronco:
Yes, I think that we cannot be satisfied from the results we have achieved so far. We need to do research, research, research. And our research agenda should be a mixture of rigorous attention to potential design of randomized controlled trials, but at the same time, we should consider endophenotype and personalization of patients to which we want to apply specific techniques. In this context, I think it's very important to achieve levels of evidence that are step by step, rather than targeting one ultimate endpoint which is survival. We have biological endpoints, we have biochemical endpoints, we have clinical and pathophysiological endpoints. Survival is only at the end, when the right population is being identified and the right methodology is clearly applied in a way that we can standardize our results and better understand the results.

Dr. Liu:
Great. Well, that's a great way to round out our discussion. I want to thank Professor Claudio Ronco for joining me today. Claudio, as always, it was a pleasure speaking with you.

Prof. Ronco:
And it is a pleasure speaking to you.

Dr. Liu:
I'm Dr. Kathleen Liu. If you'd like to listen to this episode, or other episodes in our series, please visit kdigo.org/podcasts. Thanks for listening.