Editorial – ADQI Consensus

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The 17th Acute Disease Quality Initiative International Consensus Conference: Introducing Precision Renal Replacement Therapy

John A. Kellum[a] Claudio Ronco[b]

[a]Center for Critical Care Nephrology, CRISMA, Department of Critical Care Medicine, University of Pittsburgh School of Medicine, Pittsburgh, Pa., USA; [b]Department of Nephrology, Dialysis and Transplantation, International Renal Research Institute of Vicenza, San Bortolo Hospital, Vicenza, Italy

In August 2000, we convened the first international consensus conference under the banner of the Acute Dialysis Quality Initiative [1]. The focus of the conference was on continuous renal replacement therapy (CRRT) and 46 questions were evaluated covering the broad domains of definitions/nomenclature, patient selection, solute control, membranes, operational characteristics, access and anticoagulation and fluid composition and management. Of the 46 questions, consensus was identified for 20, the existence of evidence but no consensus for 5 (concerning membranes, catheters, modality and dose) and insufficient evidence for the remaining 21. A detailed research agenda was proposed to address these knowledge gaps.

Over the years, since the publication of these findings, much has changed. We recommended the development of standard criteria for diagnosing acute kidney injury (AKI) and then these criteria were defined [2], and subsequently refined [3, 4] and validated in multiple studies [5]. Since 2002, large randomized trials [6, 7] have provided evidence by which to base clinical recommendations and the first clinical practice guideline was published on AKI in 2012 [4]. However, much controversy remains and the practice of CRRT continues to be variable across centers. New trials exploring the timing of initiation [8–10] of RRT and large observational studies exploring the effects of modality on renal recovery after AKI [11, 12] have provided much evidence but no definitive conclusions. Thus, practice variation continues and may in fact be warranted.

These heterogeneous results underscore a fundamental limitation for randomized trials. A single best solution may not exist for all or even most patients. Lack of a 'one-size fits all' answer to complex medical problems is not uncommon. There is no 'best' dose of insulin to treat diabetes and no 'best' antibiotic. Treatments must be tailored to the specific patient or specific disease condition. The search for one dose, modality and time for initiation of RRT that is 'best' for all patients will never be fruitful.

Given these considerations, the 17th Acute Disease Quality Initiative (ADQI) International Consensus Conference sought to revisit CRRT 16 years later and to focus on the development of core concepts to advance 'precision renal replacement therapy'. Precision medicine is an innovative approach that takes into account individual differences in people's genes, environments and lifestyles. It allows targeting specific treatments of illnesses by selecting different drugs and doses that do not just work for the average patient but are chosen specifically for an individual. Precision RRT therefore is the use of specific

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E-Mail karger@karger.com
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Prof. John A. Kellum, MD
Department of Critical Care Medicine
Center for Critical Care Nephrology, University of Pittsburgh School of Medicine
604 Scaife Hall, 3550 Terrace Street Pittsburgh, PA 15261 (USA)
E-Mail kellum@pitt.edu

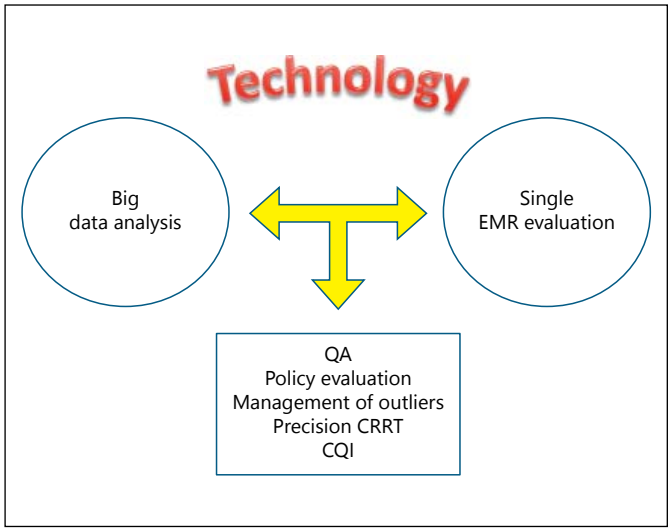

Fig. 1. The interaction between big data analysis and single case evaluation will allow to establish consistent CRRT policy for the average population and precision CRRT for the single individual resulting in significant improvements in QA and CQI programs. Reprinted with permission from www.ADQI.org. EMR = Electronic medical record; QA = quality assurance; CQI = continuous quality improvement.

information about the patient to personalize the use of RRT and the RRT prescription to the patient. This information would include measures of solute load, fluid balance and residual renal function. It might also include information on the inflammatory response, oxidative stress and even genetic make-up of the patient. It would definitely include hemodynamics and comorbidities and consider the medications the patient needs. Most of these factors would be changing over time; so measurements would need to be dynamic even to point of continuous monitoring for some variables. Using this framework, we would no longer speak of an optimal dose or modality for RRT but rather these aspects of renal support would be tailored to the specific patient and change over time. For this reason, recommendations on new technologies (membranes, techniques etc.) are based more on expert experience and opinion rather than on stringent evidence gathered from large trials. At the same time, the rationale for application of peculiar devices and the pathophysiological foundations of the mechanisms involved in the syndromes to be treated represent the suitable basis to recommend personalized approach for single individuals or selected group of patients. Somehow we are facing a kind of paradox in modern medicine, moving in the direction of single patient approach and on the other side advancing in the world of big data and pragmatic trials derived from huge data collection systems. In reality, the paradox is only apparent and the 2 approaches tend to be integrated generating precision medicine as an individual vertical progress for single patients starting from a well-established horizontal standardized basis of knowledge. This allows to change policy in case of unsatisfactory results for the average treated population, but also to deal with outliers that may require precision and personalized approach. In the area of critical care nephrology [13–24], recent reports have provided new insights and suggestions for the application of large databases and big data [25–28]. The tendency to gather big data from large databases composed of millions of electronic medical records require a remarkable effort to harmonize and standardize terminology and nomenclature. This has emerged as a priority among all groups and a specific recommendation to utilize recently published nomenclature has been made [29–33].

The practice of medicine is only just coming to grapple with data requirements (acquisition and management) for precision medicine and precision RRT will be no less data intensive (fig. 1). We also require more knowledge concerning the precise interactions between the therapy and these various parameters. Beyond this, however, there is also the need for a broad conceptual framework to base the practice of precision RRT. In general, consensus was reached on the fact that a continuous balance between patient's demand and treatment capacity should be made. Adequacy of renal replacement therapy cannot be a number any longer. It should be a comprehensive recipe of components, each of them being essential for the final outcome of the patient. The purpose of ADQI 17 was to develop this framework where possible and to set a research agenda to answer key questions needed to refine the framework for clinical use. It is our hope that the reports from this initiative will guide clinical thinking now and serve to catalyze new research in the future.

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