ADQI Consensus on AKI Biomarkers and Cardiorenal Syndromes
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39 figures, 5 in color, and 21 tables, 2013
Contents

IX  Preface
McCullough, P.A. (Novi, Mich.); Kellum, J.A. (Pittsburgh, Pa.);
Mehta, R.L. (San Diego, Calif.); Murray, P.T. (Dublin); Ronco, C. (Vicenza)

1 Acute Dialysis Quality Initiative (ADQI)
Ronco, C. (Vicenza); Kellum, J.A. (Pittsburgh, Pa.); Bellomo, R. (Heidelberg, Vic.);
Mehta, R.L. (San Diego, Calif.)

5 Implementation of Novel Biomarkers in the Diagnosis, Prognosis, and
Management of Acute Kidney Injury: Executive Summary from the
Tenth Consensus Conference of the Acute Dialysis Quality Initiative
(ADQI)
McCullough, P.A. (Warren, Mich./Southfield and Novi, Mich./Madison Heights,
Mich./Detroit, Mich.); Bouchard, J. (Montréal, Que.); Waikar, S.S. (Boston, Mass.);
Siew, E.D. (Nashville, Tenn.); Endre, Z.H. (Christchurch); Goldstein, S. (Cincinnati,
Ohio); Koyner, J.L. (Chicago, Ill.); Macedo, E. (São Paulo); Doi, K. (Tokyo);
Di Somma, S. (Rome); Lewington, A. (Leeds); Thadhani, R. (Boston, Mass.);
Chakravarthi, R. (Albany, N.Y.); Ice, C. (Rotterdam); Okusa, M.D. (Charlottesville, Va.);
Duranteau, J. (Bicêtre); Doran, P. (Munich); Yang, L.;
Jaber, B.L. (Boston, Mass.); Meehan, S. (Chicago, Ill.); Kellum, J.A. (Pittsburgh, Pa.);
Haase, M. (Magdeburg); Murray, P.T. (Dublin); Cruz, D. (Vicenza); Maisel, A. (San Diego, Calif.);
Bagsah, S.M. (Edmonton, Alta.); Chawla, L.S. (Washington, D.C.); Mehta, R.L. (San Diego, Calif.);
Shaw, A.D. (Durham, N.C.); Ronco, C. (Vicenza); for the Acute Dialysis Quality Initiative (ADQI)
Consensus Group

13 Diagnosis of Acute Kidney Injury Using Functional and Injury
Biomarkers: Workgroup Statements from the Tenth Acute Dialysis
Quality Initiative Consensus Conference
McCullough, P.A. (Detroit, Mich.); Shaw, A.D. (Durham, N.C.); Haase, M. (Magdeburg);
Bouchard, J. (Montreal, Que.); Waikar, S.S. (Boston, Mass.);
Siew, E.D. (Nashville, Tenn.); Murray, P.T. (Dublin); Mehta, R.L. (San Diego, Calif.);
Ronco, C. (Vicenza); for the ADQI 10 Workgroup
30 **Differential Diagnosis of AKI in Clinical Practice by Functional and Damage Biomarkers: Workgroup Statements from the Tenth Acute Dialysis Quality Initiative Consensus Conference**
Endre, Z.H. (Sydney, N.S.W./Christchurch); Kellum, J.A. (Pittsburgh, Pa.);
Di Somma, S. (Rome); Doi, K. (Tokyo); Goldstein, S.L. (Cincinnati, Ohio);
Koyner, J.L. (Chicago, Ill.); Macedo, E. (São Paulo); Mehta, R.L. (San Diego, Calif.);
Murray, P.T. (Dublin); for the ADQI 10 Workgroup

45 **Use of Biomarkers to Assess Prognosis and Guide Management of Patients with Acute Kidney Injury**
Cruz, D.N. (Vicenza); Bagshaw, S.M. (Edmonton, Alta.); Maisel, A. (San Diego, Calif.);
Lewington, A. (Leeds); Thadhani, R. (Boston, Mass.); Chakravarthi, R. (Hyderabad);
Murray, P.T. (Dublin); Mehta, R.L. (San Diego, Calif.); Chawla, L.S. (Washington, D.C.);
for the ADQI 10 Workgroup

65 **Physiological Biomarkers of Acute Kidney Injury: A Conceptual Approach to Improving Outcomes**
Okusa, M.D. (Charlottesville, Va.); Jaber, B.L. (Boston, Mass.); Doran, P. (Dublin);
Duranteau, J. (Le Kremlin-Bicêtre); Yang, L. (Beijing); Murray, P.T. (Dublin);
Mehta, R.L. (San Diego, Calif.); Ince, C. (Rotterdam); for the ADQI 10 Workgroup

82 **Pathophysiology of the Cardiorenal Syndromes: Executive Summary from the Eleventh Consensus Conference of the Acute Dialysis Quality Initiative (ADQI)**
Müller, C. (Basel); Damman, K. (Groningen); Murray, P.T. (Dublin); Cruz, D. (Vicenza);
House, A.A. (London, Ont.); Schmidt-Ott, K.M. (Berlin); Vescovo, G. (Vicenza);
Bagshaw, S.M. (Edmonton, Alta.); Hoste, E.A. (Gent); Briguori, C. (Naples);
Braam, B. (Edmonton, Alta.); Chawla, L.S. (Washington, D.C.);
Costanzo, M.R. (Naperville, Ill.); Tumlin, J.A. (Chattanooga, Tenn.); Herzog, C.A. (Minneapolis, Minn.);
Mehta, R.L. (San Diego, Calif.); Rabb, H. (Baltimore, Md.);
Shaw, A.D. (Durham, N.C.); Singbartl, K. (Pittsburgh, Pa.); Ronco, C. (Vicenza);
for the Acute Dialysis Quality Initiative (ADQI) Consensus Group

99 **Pathogenesis of Cardiorenal Syndrome Type 1 in Acute Decompensated Heart Failure: Workgroup Statements from the Eleventh Consensus Conference of the Acute Dialysis Quality Initiative (ADQI)**
Haase, M. (Magdeburg); Müller, C. (Basel); Damman, K. (Groningen); Murray, P.T. (Dublin);
for the Acute Dialysis Quality Initiative (ADQI) Consensus Group

117 **Pathophysiology of Cardiorenal Syndrome Type 2 in Stable Chronic Heart Failure: Workgroup Statements from the Eleventh Consensus Conference of the Acute Dialysis Quality Initiative (ADQI)**
Cruz, D.N. (San Diego, Calif.); House, A.A. (London, Ont.); Schmidt-Ott, K.M. (Berlin);
Vescovo, G. (Vicenza); Kellum, J.A. (Pittsburgh, Pa.); Ronco, C. (Vicenza);
for the Acute Dialysis Quality Initiative (ADQI) Consensus Group
137 Cardiorenal Syndrome Type 3: Pathophysiologic and Epidemiologic Considerations

158 Cardiorenal Syndrome Type 4: Insights on Clinical Presentation and Pathophysiology from the Eleventh Consensus Conference of the Acute Dialysis Quality Initiative (ADQI)

174 Cardiorenal Syndrome Type 5: Clinical Presentation, Pathophysiology and Management Strategies from the Eleventh Consensus Conference of the Acute Dialysis Quality Initiative (ADQI)

195 Appendix 1: 10th Acute Dialysis Quality Initiative (ADQI) Consensus Group

197 Appendix 2: 11th Acute Dialysis Quality Initiative (ADQI) Consensus Group

199 Author Index

200 Subject Index
Preface

There are several important topics in modern medicine but only few of them have realized significant advancement in recent years as acute kidney injury (AKI). This field is one of the most attractive and sparkling due to new information on pathophysiology and new interesting links to other medical disciplines such as intensive care, cardiac surgery and cardiology. In particular, heart-kidney interactions and their clinical consequences have been a subject of debate for many years but it is only recently that they have been subjected to a systematic appraisal and a true multidisciplinary approach. Linked to AKI and to cardiorenal syndromes (CRS), the fascinating world of new biomarkers represent a popular area of investigation and a new opportunity for advancement of therapy.

Biomarkers of AKI and the CRS represent a sort of moving target for research and investigators and require frequent reviews of the literature to make possible the transfer of all available information and solid evidence into clinical practice. This represents the main task of a consensus organization called ADQI (Acute Dialysis Quality Initiative). Born in 2000, ADQI has been the motor for development of consensus conferences, confrontation among experts and definition of current unanswered questions in the area of AKI, leading to new research pathways, new clinical trials and landmark studies.

Just to mention a few examples, we may recall the Best Kidney Study derived from ADQI 1 conference on CRRT, the ATN study based on the CRRT dose question posed by the ADQI group in the same conference, and further, the several RIFLE validation studies derived from the ADQI 2 conference dealing with definition of AKI and related research. After the above-mentioned conferences, many others took place over the years, always responding to the most urgent unanswered questions in the field of AKI.

This book contains the resolutions of the ADQI delegates obtained during the 10th conference on Biomarkers in AKI held in Dublin, September 2011, and the 11th conference on CRS held in Venice, December 2012.
The Dublin conference was organized to answer specific questions about new biomarkers and their use and utility in AKI. What are the most suitable candidate molecules and physiologic measures, how solid and evidence-based is the discovery phase? How can we incorporate the new biomarkers in the AKI conceptual model describing the evolution from susceptibility to insult, decreased GFR and organ death? Even if we have a positive biomarker pattern and can identify patients at risk or patients with early or even subclinical AKI, how is this information affecting our clinical behavior and practice? All these questions were posed to the panel of experts and four workgroups were created to establish current evidence and built statements and recommendations. The first part of the book is dedicated to the collection of workgroup products from the Dublin ADQI conference on biomarkers and therefore the reader should be able to receive from the relevant papers the most updated information.

The second part of the book is dedicated to the results of the Venice ADQI conference on CRS with a similar structure. A significant step forward had been made in 2008 when an ADQI conference was organized to discuss several aspects related to the CRS and a new definition/classification was established and vetted among nephrologists, cardiologists, and critical care specialists around the world. The new definition/classification has been the basis for new interactions among specialists and a new spirit of multidisciplinary collaboration. From that moment in fact, an important series of papers and a new body of research appeared in the literature, filling at least in part the gap of the past and spurring new interest in bridging the knowledge of cardiologists, nephrologists, and intensive care physicians. It was suggested that a modern approach to CRS should be multidisciplinary and patient-centered rather than specialty-oriented; the wide acceptance of the new definition classification represented the basis for further trials and cooperative research. The 2012 Venice ADQI conference has been dedicated to the appraisal of the current knowledge about the pathophysiological mechanisms involved in different forms of CRS. Thus, the second part of this book is designed to collect a series of contributions on the state-of-the-art knowledge and practice of CRS particularly focusing on the pathophysiology of the five subtypes. Acute and chronic mechanisms of damage are explored in depth with particular attention to the primacy of organ involvement and the subsequent pathways of organ crosstalk. After the executive summary of the conference, five contributions describe in detail each single subtype with its pathophysiological mechanisms, clinical features and possible therapeutic approaches. The possibility of an early recognition of the syndrome through novel diagnostic biomarkers represents and interesting integration and a link to the previous ADQI conference. CRS types 1 and 2 are typical conditions encountered in the field of cardiology and especially in the area of heart failure. Both acute heart failure leading
to AKI and chronic heart failure leading to progressive renal insufficiency and chronic kidney disease represent conditions that may easily become interchangeable and sometimes it becomes very difficult to distinguish the two entities that often differ just for the time frame or the time window in the clinical history of the patient. Not only heart failure clinics are the stage for these disorders: acute heart failure may be induced by an acute coronary syndrome or by a sudden heart valve disease. Furthermore, CRS type 1 may be iatrogenically induced by an inappropriate use of diuretics and/or contrast media. So far, most heart failure trials excluded renal patients from enrollment and this has created a lack in knowledge for this category of patients. Therefore, CRS types 1 and 2 are frequently observed by cardiologists and a combined approach to these patients in conjunction with a nephrologist is strongly advised. CRS type 3 represents a totally different entity being a typical condition observed in critically ill patients admitted to the intensive care unit where AKI may induce a defective myocardial contractility and secondary heart failure. For this syndrome, the most appropriate case manager is probably the intensivist although a collegial evaluation of the patient and a multidisciplinary approach is recommended. CRS type 4 has been for many years defined as an increased cardiovascular risk in patients with chronic kidney disease. Today we know that even in the very early stages of chronic kidney disease, altered metabolism and gene expression may induce a complex derangement mediated by specific vitamin D receptors, oxidant stress, aldosterone receptors and so on. The fundamental role of the unfriendly milieu generated by uremia, hormonal dysregulation, and the combined effects of iron deficiency and anemia are explored in light of a significant combined damage. Further attention is placed in one contribution focusing on the delicate balance of organ crosstalk mediated by subclinical inflammation and a complicated network of mediators. The role of inflammation has been recently elucidated as an important mechanism for simultaneous heart and kidney damage and therefore sepsis has been taken as the prototype condition to study the pathophysiological mechanisms of CRS type 5.

Our intent as authors is to provide a compendium of the most recent research in the field of biomarkers, AKI and CRS. We hope the book will represent an important educational tool both for students and fellows, and for advanced investigators and clinical experts.

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