Cardiorenal Syndrome: Introduction

Andrew A. House

Introduction

One hundred years ago, in November of 1913, Thomas Lewis from University College Hospital, London, delivered a lecture entitled “Paroxysmal Dyspnoea in Cardio–Renal Patients,” in which he provided his clinical observations on a number of patients with dyspnea related to advanced heart and kidney disease, referred to as cardiac and uraemic asthma respectively, and expounded his theories on the inter-relationship between the two organ systems (1). For anyone interested in cardiorenal syndromes as we understand them today—where advanced diagnostic techniques, imaging to precisely characterize the structure and function of both organ systems and novel biomarkers threaten to replace careful and methodical bedside history and clinical examination, microscopic examination of the urinary sediment, thoughtful clinicopathologic correlation, and other remnants of a simpler time in our history—the transcript of this lecture is well worth combing through one’s local medical library archives (or as I did, a quick perusal of our University library electronic archives) (1). Although some of the dyspnea associated with the uremic state was attributed to acidosis, Lewis (1) also recognized the important contribution of kidney disease to cardiac dysfunction and vice versa. The description by Lewis (1) of the “renal heart,” with significant dilatation and hypertrophy, and the role of venous engorgement, where “stasis” is accompanied by a reduction in urine output and the appearance of urinary albumin and casts, provides an early attempt to understand the complex pathophysiology underlying the bidirectional signaling between these organs. The recognition by Lewis (1) that even the postmortem examination cannot always with certainty point “to one or other organ as the seat of the chief mischief” mirrors our own current attempts to categorize patients as suffering primarily from cardiorenal versus renovascular syndromes (2).

In this Moving Points series, we fast forward 100 years to the current day and focus our attention on acute and chronic cardiorenal syndromes, where the failing heart, either acutely decompensated or in a more chronic state of dysfunction, is believed to be “the seat of the chief mischief,” leading in some causative manner to AKI and/or more progressive CKD. The work by Anand (3) provides an overview of the prevalence and incidence of these types of cardiorenal syndromes, highlighting some of the risk factors and showing the grim prognosis of either disorder.

Then, after briefly touching on the importance of various putative nonhemodynamic factors, it provides a comprehensive review of the role of hemodynamics in the development of renal dysfunction, challenging our preconceived ideas about arterial underfilling and exploring the response of the kidneys to venous congestion. This work concludes by trying to answer the question of whether kidney dysfunction is potentially reversible, or whether intrinsic kidney damage makes progressive kidney disease an inevitability. This question ties in nicely with the observation by Lewis (1) that “nothing is clearer than the frequent discrepancy between the degree of functional impairment in these organs and the amount of structural change in them.”

In terms of treatment options for cardiorenal syndromes, it is noteworthy that evidence-based advances in the past 100 years have been relatively limited, in part because of exclusion of patients with significant renal dysfunction from clinical trials, and patients suffer an extremely high level of morbidity and mortality, particularly those patients with acute cardiorenal syndrome. In Lewis’ time, the patient with acute decompensated or advanced chronic congestive heart failure was offered bed rest, dietary restriction, diuretics, digitalis, supplemental oxygen, and of course, morphine. The work by House (4) examines some recent trials of age-old remedies, specifically loop diuretics, for the management of acute decompensated heart failure and tries to put these results into perspective vis-à-vis management or prevention of acute cardiorenal syndrome. Although there is no shortage of discouraging negative trials of vasoactive or natriuretic peptides for acute decompensated heart failure in recent memory, a recent positive trial of recombinant human relaxin-2, called serelaxin, is also reviewed. House then looks at pivotal trials of renin-angiotensin-aldosterone blockade for chronic congestive heart failure and points out the limitations of renal outcome data in these studies, while also highlighting some recent promising results of a study using an agent that combines angiotensin receptor blockade with nephrisin inhibition (enhancing endogenous natriuretic peptide action) in a single molecule.

Finally, in terms of nonpharmacologic approaches to management of the severe and often refractory volume overload that so often accompanies advanced acute decompensated heart failure, an area that has seen significant advances from the time of Southey tubes and venesection is the use of extracorporeal...
ultrafiltration. Kazory (5) reviews the significant shortcomings of current medical therapies and the issue of unresolved congestion during hospitalization for acute decompensated heart failure. He then provides a nice background on the proposed mechanistic advantages of ultrafiltration and some of the early uncontrolled observations and takes us through the history of ultrafiltration for heart failure, with its technical challenges. Kazory then brings us to the new era of ultrafiltration, with newer generation devices that greatly broaden the generalizability and applicability of this therapy, and reviews the recent clinical trials that have been conducted. His thoughtful review of the subject helps to make sense of the seemingly contradictory results of two of the largest and most recent ultrafiltration trials, the Ultrafiltration Versus Intravenous Diuretics for Patients Hospitalized for Acute Decompensated Congestive Heart Failure Trial (6) and the Cardiorenal Rescue Study in Acute Decompensated Heart Failure Trial (7), by providing important similarities and differences in the populations studied, cointerventions, timing, etc. He finishes this review by examining some of the practicalities of cost, vascular access, and rate of fluid removal and questions about long-term kidney function and other important clinical outcomes.

We hope that this Moving Points series challenges your thoughts about cardiorenal syndromes, helps to make sense of a burgeoning literature on the topic, illustrates some of the advances that have been made in our understanding of the pathophysiology and treatment of these disorders over the past 100 years, and inspires interest in furthering research into these complex disorders. Most important, we hope that the reviews herein will improve your ability to optimize the care of your patients with cardiorenal syndromes while the search for innovative and more effective therapies continues.

Disclosures

A.A.H. reports receiving honoraria from Gambro and research support from Pfizer. No financial support was received for the preparation of this text.

References

1. Lewis T: A clinical lecture on paroxysmal dyspnoea in cardiorenal patients: With special reference to “cardiac” and “uraemic” asthma: Delivered at University College Hospital, London, November 12th, 1913. BMJ 2: 1417–1420, 1913

Published online ahead of print. Publication date available at www.cjasn.org.