Intravascular Volume Expansion Before Primary Angioplasty for Prevention of Acute Kidney Injury
Hydration or Dilution?

Charanjit S. Rihal, MD; Kianoush B. Kashani, MD

A number of points regarding this important trial bear emphasis. First, patients with STEMI are at particularly high risk of CI-AKI, as evidenced by the 27% incidence of CI-AKI observed in the control group of this trial. Operators are frequently performing high-risk procedures among these patients, without full knowledge of baseline renal function and other important clinical data, given the clinical urgency to reperfuse occluded arteries as rapidly as possible. Third, a significant prevalence of risk factors for the development for CI-AKI, such as low ejection fraction, low estimated GFR, and diabetes mellitus, exist in this population. Particular care and attention must be given to intraprocedural factors that may influence the subsequent development of CI-AKI. Rapid treatment of cardiogenic shock, minimization of contrast volume administered, treatment of dehydration, and, ostensibly, early and rapid hydration are all important. When taken at face value, the results of the trial would suggest that early rapid hydration continuing for 12 hours to a mean volume of almost 1200 mL would appear to be indicated (the trial does not provide informational value as to whether this should be sodium bicarbonate or isotonic saline infusion). Of note, the early hydration group not only received earlier intravenous hydration but also received a different type of fluid in comparison with the late group; thus, any observed differences or similarities between the 2 groups cannot automatically be attributed to early versus late hydration only.

A critical appraisal of these data, of the pathophysiology of CI-AKI, and of our methods for detecting CI-AKI might suggest an alternative interpretation of these data. Creatinine is a metabolite of creatine; and when 24-hour urinary creatinine clearances are performed, more precise estimates of true renal function may be obtained. Measurement of urinary creatinine clearance, however, is typically not performed nor practical in routine clinical practice, and clinicians rely on fluctuations in serum creatinine to gauge renal function. A number of equations, including the Cockcroft-Gault (with age, sex, weight, and serum creatinine as inputs) and the modification of diet in renal disease (with age, race, sex, and serum creatinine as inputs), have been developed to estimate the true GFR. These formulas are developed from regression equations and provide good correlations with 24-hour creatinine clearance when applied to populations, but, when applied to individual patients, must be considered only a rough estimate of GFR. The modification of diet in renal disease underestimates GFR, particularly in individuals with normal baseline kidney function. Moreover, these formulas were developed for steady-state conditions and are not applicable to acutely ill patients with fluctuating renal function. In CI-AKI, 3 things can influence estimates of renal function. These include the true underlying GFR, fluctuations in creatinine production, and fluid balance. Jelliffe and Jelliffe have published a formula specifically designed for fluctuating renal function, which, when modified for fluctuations in fluid balance, provides the most accurate estimates of GFR. It is important to consider the role of dilution and the volume of distribution of serum creatinine when interpreting...
the results of the current study. Hemodilution can reduce serum creatinine, and cumulative daily fluid balance (input/output) directly affects the concentration (ie, dilution) of serum creatinine values.\(^2\) Adjusted serum creatinine (sCr) can be calculated for volume balance as

Adjusted creatinine = sCr × correction factor


correction factor = [hospital admission weight (kg) × 0.6 + (sum of daily fluid balance)] / hospital admission weight × 0.6

As evident, what matters is the volume balance and not the net volume intake. Unfortunately, the cumulative volume balance data are usually not provided in most studies. Close scrutiny of Figure 2 shows an acute reduction in mean serum creatinine values among patients undergoing systemic hydration by day 1 followed by a slow rise thereafter—which exactly parallels the control group. This suggests that much of the observed putative benefits may, in fact, be due to dilution of serum creatinine because we can safely assume that creatinine production did not change among these patients. Of course (and as the authors conclude), these differences could also be due to true differences in GFR; but 2 further points argue against this. First, the parallel nature of the curves in Figure 2 suggest an underlying similarity of true GFR; and clinically important major adverse cardiac events were not significantly different between the 3 groups, even though patients who had CI-AKI had overall higher rates of events than those who did not have CI-AKI. If serum creatinine is only a rough marker of CI-AKI, what, then, should be brought to the field to improve our diagnostic capabilities?

The answers may lie in the development of biomarkers of AKI, of which a number are currently available and in various stages of clinical evaluation. Markers of tubular damage under investigation include neutrophil gelatinase-associated lipocalin, kidney injury molecule-1, monocyte chemotactic peptide-1, liver-fatty acid binding protein, Netrin-1, and interleukin-18.\(^3,5\) Of course, we must remember that serum creatinine is also a biomarker. Cystatin C is a 122-amino acid, low-molecular-weight protein that is produced at a constant rate by all nucleated cells in the body that may be a particularly useful marker to estimate GFR in CI-AKI.\(^7\) It has a short half-life (1.5 hours) and a much smaller volume of distribution than serum creatinine (extracellular fluid versus total body water). Cystatin C does not undergo tubular secretion and is excreted by filtration alone.\(^7\) These factors may make it a particularly useful early marker for changes in true GFR for whatever reason (prerenal, renal, postrenal) closer to real time. Such biomarkers would add considerable informational value to trials evaluating CI-AKI but, in general, have not been incorporated into study designs.

What, then, can we conclude from the study of Maioli et al? First, it is safe to conclude that patients presenting with STEMI and treated with primary PCI are at high risk for CI-AKI, with an incidence of more than 20%. In comparison, patients undergoing elective PCI generally have an incidence of CI-AKI of less than 5% in most series (in both cases undoubtedly multifactorial rather than attributable to any one factor, such as contrast type). Second, we can conclude that hydration with either isotonic saline or sodium bicarbonate infusion over a 12-hour period is safe because no episodes of acute pulmonary edema or heart failure were precipitated. Third, such hydration does not appear to affect the incidence of major important cardiac outcomes, such as death, recurrent myocardial infarction, repeat emergent PCI, or stroke in the short term. It is safe to say there would be no argument that treatment and prevention of dehydration is crucial in preventing CI-AKI. What is unclear is the role of superhydration (or dilution). Even though the incidence of rises in serum creatinine was significantly lower among patients undergoing early and continuous hydration, it is unclear whether this represents true differences in GFR, a dilutional effect, or some combination of both. Therefore, the data are not yet convincing that early and continuous hydration should be the new standard of care for all STEMI patients undergoing primary PCI. For hospitals that incorporate such a protocol, it should not interfere with early and rapid reperfusion therapy; patients should be watched for signs of congestive heart failure, and it will be contraindicated in most patients presenting with pulmonary edema and in many patients presenting with cardiogenic shock. Early assessment of left ventricular ejection fraction should be performed if aggressive hydration protocols are to be used. Finally, the authors are to be congratulated for the execution of this study in a patient subset that is notoriously difficult to study in prospective trials. The results bring us a step closer toward understanding how best to prevent CI-AKI, but, unfortunately, there still is a long road to go.

Disclosures

None.

References


Key Words: Editorials  angioplasty  intravascular volume
Intravascular Volume Expansion Before Primary Angioplasty for Prevention of Acute Kidney Injury: Hydration or Dilution?
Charanjit S. Rihal and Kianoush B. Kashani

Circ Cardiovasc Interv. 2011;4:405-406
doi: 10.1161/CIRCINTERVENTIONS.111.964304
Circulation: Cardiovascular Interventions is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2011 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-7640. Online ISSN: 1941-7632

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circinterventions.ahajournals.org/content/4/5/405

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation: Cardiovascular Interventions can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation: Cardiovascular Interventions is online at:
http://circinterventions.ahajournals.org//subscriptions/