Cardiorenal syndrome

(MAY 2006)

TO THE EDITOR: In their review of the challenges of cardiorenal syndrome (*Cleve Clin J Med* 2006; 73:485–491), Drs. Geisberg and Butler make several references to renal insufficiency and state that renal insufficiency is defined as a glomerular filtration rate (GFR) of less than 60 mL/minute/1.73 m^2.

In fact, the term *renal insufficiency* has become obsolete in modern medicine and has been replaced by the term *chronic kidney disease*. Rather than using vague terms such as mild or moderate renal insufficiency, a staging system has been developed based on the patient's calculated GFR, ranging from stage 0 to stage 5, with stage 3 representing the onset of chronic kidney disease and corresponding to a GFR of less than 60 mL/minute/1.73 m^2.

In recognition of the importance of the proper classification, the ninth revision of the International Classification of Diseases (ICD-9) coding system, published in 2005, included these stages and assigned codes 585.0 to 585.5 to represent the five stages. Furthermore, hospitals depend on accurate physician documentation to properly code the most accurate diagnosis-related group (DRG), and renal insufficiency is not a recognized term in the DRG system. Its use therefore deprives the hospital of the ability to properly assign kidney-disease-related comorbidities to the patient.

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IN REPLY: Dr. Hirsch is absolutely correct, and the nephrology community has adopted the staging system for chronic kidney disease. Even in the cardiology community, when chronic kidney disease is discussed as a risk factor for coronary artery disease, a similar classification is used.

The heart failure literature, however, continues to use the term *renal insufficiency*. The reason that we still hesitate to use the chronic kidney disease definition is that we are not sure to what degree the kidneys are actually diseased intrinsically vs how much of a change in glomerular filtration is related to extrarenal factors. In a patient with heart failure, a low GFR may be partially related to cardiac hemodynamics, and so the patient may not have intrinsic renal parenchymal disease. Or the problem may be dynamically mediated, related to heart failure therapy itself and, again, not intrinsically a renal issue completely. In addition, volume status and in turn GFR are likely to fluctuate more in heart failure than in other types of chronic kidney disease. Or the patient could have true parenchymal disease due to heart failure and ischemia or other associated comorbidities. In reality, all these factors may contribute simultaneously.

Perhaps for these and other reasons, the heart failure literature has not typically used the newer classification scheme, but several papers have, and as we understand this process further, perhaps it will be applied more uniformly.

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Postoperative septic shock

(SUPPLEMENT 1 TO VOLUME 73, MARCH 2006)

This letter concerns an article in a supplement to Cleveland Clinic Journal of Medicine *(Proceedings of the Perioperative Medicine Summit, March 2006) distributed to only a portion of the* Journal's *regular readership, owing to the terms of the grant supporting the supplement. The supplement is available to all online at* ***www.ccjm.org/toc/perioperative.htm.***

TO THE EDITOR: The review of postoperative septic shock by Dr. Ali Jahan[1] omits several important points about activated protein C and surgical patients.

First, surgical patients at the highest risk of bleeding were excluded from the Protein C Worldwide Evaluation in Severe Sepsis (PROWESS).[2]

Second, retrospective analyses of the surgical subgroup from PROWESS (28% of PROWESS cases) showed that, compared with placebo, activated protein C approximately doubled the bleeding risk in these patients (16.7% vs 7.7%, $P = .003$) and increased the risk of serious bleeding during the infusion from 0% to 3.1% ($P = .006$).[2,3] Six of seven serious bleeding events with activated protein C were procedure-related.[2,3] The authors concluded that these risks were acceptable,[3] noting that the absolute risk reduction conferred by activated protein C in high-risk patients was similar for the surgical subgroup (9.5% reduction) and the overall PROWESS population (12.8% reduction).[2] Because of the relatively small size of the surgical subgroup, however, the mortality benefit from activated protein C was statistically significant only for high-risk surgical patients who underwent intra-abdominal procedures.[2]

Third, the Administration of Drotrecogin Alfa (Activated) in Early Stage Severe Sepsis (ADDRESS) trial,[4] which randomized 2,613 septic patients with a low risk of death to either activated protein C or placebo, found no benefit from activated protein C. Notably, a subset of surgical patients suffered an increased risk of death with activated protein C therapy (20.7% vs 14.1% with placebo, $P = .03$; number needed to harm = 15).[4]

In light of these findings, consultants should recommend activated protein C only cautiously and after careful discussion of these concerns, whenever possible, with the patient, family, and surgeon.

Additionally, stress-dose corticosteroid therapy (ie, dosed to simulate endogenous steroid secretion under stressful situations) for septic shock has been supported by meta-analyses[5,6] and recommended in an international multispecialty consensus statement (the Surviving Sepsis Campaign guidelines),[7] in addition to the supportive seminal study by Annane et al[8] that Dr. Jahan cites. Rather than merely considering the use of stress-dose steroids, medical consultants should view them as the standard of care for vasopressor-dependent septic shock with[5] and perhaps without[6] inadequate adrenal reserve. Consultants can expect to save 1 in every 10 patients they treat with this intervention.[8]

Finally, surgeons are ideally suited to the task of source control, or the management of loci of infection such as pleural effusions, abscesses, and infected vascular access lines, etc. This vital, time-tested, and recommended[7] intervention deserves a mention in any discussion of perioperative sepsis.

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IN REPLY: I appreciate Dr. Jenkins' interest and agree that activated protein C must be used cautiously, particularly in postoperative patients, in light of the potential risk of bleeding. As stated in my article,[1] the Surviving Sepsis Campaign guidelines recommend use of activated protein C in those patients at high risk of death from sepsis, as identified by an Acute Physiology and Chronic Health Evaluation (APACHE) score of 25 or greater, whose risk of death would not further increase if bleeding were to occur (grade B recommendation).[7]

Furthermore, the use of steroids needs to be considered in the appropriate patient population, as supported by the Surviving Sepsis Campaign guidelines[7] and the Institute for

Healthcare Improvement's "Sepsis Management Bundle," a set of evidence-based goals to be achieved within 24 hours for patients with severe sepsis or septic shock.[9] Despite the support from meta-analyses,[6] which are significantly weighted by the landmark study by Annane et al,[8] many questions remain, including which patient populations would benefit from steroid use.

It is unclear whether or not patients without relative adrenal insufficiency should also be receiving steroid treatment. Post hoc analysis of the study by Annane et al revealed improved outcomes with steroid treatment only in patients with septic-shock-associated early acute respiratory distress syndrome (ARDS) who had relative adrenal insufficiency, not in patients without relative adrenal insufficiency and not in septic shock patients without ARDS.[10]

There is hope that the recently closed 800-patient Corticosteroid Therapy of Septic Shock (Corticus) trial by the National Institutes of Health[11] will shed light on this and other questions, such as long-term outcomes and how to taper steroid therapy.

Finally, I agree that surgeons clearly need to remain involved in the care of patients who require further intervention.

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