LETTER TO THE EDITOR

Disease-modifying medications in heart failure: more than ACE inhibitors and beta blockers

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To the editor,

I read with great interest the article entitled ''Predictors of low cardiac output in decompensated severe heart failure'' by Ochiai et al[1] in the Feb. 2011 issue of Clinics. This article analyzes factors predicting low cardiac output and mortality in systolic heart failure patients presenting with poor perfusion signs. Though the study design and findings are intriguing, I think there are some points that the authors may have missed.

First, the authors define compromised perfusion a priori as a combination of narrow pulse pressure, symptomatic hypotension, cool extremities, and impaired mental function. However, decreased urine output seems to be omitted as part of the presentation. Systemic hypoperfusion, by itself, can disrupt the way that vital organs work, and the brain and the kidney are both targets whose performance can be assessed at the bedside. Physiologic studies also demonstrate that blood pressure changes through variation in renal medullary perfusion[2] and proximal tubular sodium transport[3] affect urine output level in the same direction.[4] Thus, it is my opinion that decreased urine output should be listed as a sign of hypoperfusion.

In addition, Ochiai et al have elegantly shown the effect of medication on mortality, including the protective roles of angiotensin-converting enzyme inhibitors (ACEi) and beta-blockers (BB). However, while adjusting the variables in determining predictors of low cardiac output (CO), they seem to neglect this medication factor. In the long run, both BB and ACEi are beneficial for patients with systolic heart failure, but each also has a short-term hemodynamic effect, as BB causes negative inotropic effects while ACEi reduces peripheral vascular tone.[5] These effects will also influence the CO status if the distribution of these medications is imbalanced between groups. BB users will have a higher chance of being grouped into the lower CO category, while ACEi users have a higher chance of being grouped into the higher CO category because of the decreased likelihood of creatinine clearance <60 ml/min stratum (if physicians prescribe less ACEi in patients with advanced chronic kidney disease).

The authors also fail to report the percentage of digitalis usage in the population. Since the early 20th century, digoxin has been utilized in patients with systolic heart failure to improve symptoms and to reduce rates of hospitalization.[6] Though digoxin is shown to be neutral for overall mortality in pooled systolic heart failure patients, a higher serum digoxin concentration is associated with increased all-cause mortality.[7] In light of the elderly population described by Ochiai et al (average >60 years old) and the erratic pharmacokinetic profile of old patients using digoxin,[8] it is likely that elderly individuals who suffer from systolic heart failure will have a higher serum digoxin concentration if given digoxin. This contribution to overall mortality cannot be treated in the same way as in previous meta-analyses that focus on all digoxin users. Ahmed et al, in a post hoc analysis of the Digitalis Investigation Group (DIG) results, suggest that targeting lower serum digoxin concentration in all patients with a reduced left ventricular ejection fraction can reduce mortality.[9] The effect of digoxin and Chagas' cardiomyopathy, both of which may slow the heart rate because of an atrioventricular block, further complicates the clinical picture in heart failure patients.[10] Thus, the importance of reporting digoxin usage or even checking the serum concentration cannot be overemphasized in this context.

In conclusion, there are several aspects, most importantly the medication regimen for heart failure, that should be clarified in the article by Ochiai et al. The study results can only be refined further if these confounders are considered.

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