Between Scylla and Charybdis: The choice of inotropic agent for decompensated heart failure

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Then we entered the Straits in great fear of mind, for on the one hand was Scylla, and on the other dread Charybdis...

—The Odyssey, Book XII

Hospitalization for decompensated heart failure is a rapidly growing clinical problem, and optimal strategies for the management of these patients remain poorly defined. In patients for whom standard therapy with angiotensin-converting enzyme inhibitors, diuretics, and digoxin do not achieve clinical stabilization, short-term intravenous inotropic therapy is frequently used to improve hemodynamics and relieve symptoms. Inotropic therapy may be used as a temporary measure to achieve clinical stability (frequently with the guidance of invasive hemodynamic monitoring) or it may be continued as a bridge to a more definitive therapy such as cardiac transplantation. Despite the widespread use of these approaches, little data exist to demonstrate that they improve patient outcomes, especially the substantial morbidity and mortality associated with admission for decompensated heart failure, with a risk of short-term death or rehospitalization as high as 60%.1-3

If inotropic therapy is required in a patient with decompensated heart failure, the physician must typically choose between a catecholamine such as dobutamine or a phosphodiesterase III inhibitor such as milrinone. The choice between these agents is usually based on physician experience and preference because few quality data exist to guide the choice of first-line therapy. Although both drugs ultimately work by increasing intracellular levels of cyclic adenosine monophosphate, milrinone and dobutamine differ in their effects on hemodynamics, their pharmacodynamics, and their cost. Hemodynamic data suggest that milrinone causes a greater decrease in pulmonary pressures than does dobutamine and that milrinone is usually not associated with an increase in myocardial oxygen consumption, as can be seen with dobutamine.4,5 In patients treated with β-blockers, the hemodynamic effects of dobutamine are blunted, whereas milrinone retains its hemodynamic activity, suggesting that milrinone may be preferred over dobutamine for patients treated with long-term β-blocker therapy.6 Alternatively, the differences in hemodynamic effects between the agents are modest, and the cost of dobutamine is several fold less than that of equivalent doses of milrinone. Data directly comparing the 2 agents is sparse, and most such studies have compared the effects of these agents on hemodynamics rather than on clinical outcomes.4,5 A small randomized unblinded study of dobutamine and milrinone in 22 patients awaiting cardiac transplantation demonstrated similar clinical outcomes, although with an increase in arrhythmias in the dobutamine group and an increased cost with milrinone.7 Other nonrandomized retrospective data in patients being bridged to cardiac transplantation have suggested that milrinone use may be associated with a more stable clinical course and better outcomes than dobutamine.8,9

In this setting, the study by Yamani et al in this issue of the Journal represents a substantive addition to the data on this question. The authors present the results of a retrospective nonrandomized comparison of the use of milrinone and dobutamine for 329 patients with decompensated heart failure over a 4-year period at the Cleveland Clinic. This is the largest published experience to date comparing these 2 agents for this indication. Although milrinone therapy achieved better hemodynamic results (with significantly greater changes in pulmonary artery pressures and cardiac index than dobutamine), there were no differences in any of the clinical outcome measurements between the 2 groups. The authors conclude that dobutamine appears to be as efficacious as milrinone for this indication, at substantially less cost. Indeed, the cost difference seen in this study was quite dramatic, with direct pharmacologic costs (including the costs of other intravenous agents such as nitroprusside, nitroglycerin, and dopamine) for dobutamine-treated patients of $45 per day versus $1855 per day for milrinone. Although the authors did not perform a formal cost-benefit analysis, the similar clinical outcomes between the 2 groups would suggest that dobutamine therapy was extremely cost-effective for this indication. An additional conclusion of this analysis might be that better hemodynamics, as was seen in the milrinone-treated patients, do not necessarily translate into improved patient outcomes.

The current study has all the limitations inherent in
ards of chronic inotropic therapy are well known.10-13 With decompensated heart failure. The data on the hazards of chronic inotropic agents should be used at all for most patients randomized data directly comparing these 2 agents. At least as important as which agent to use is whether inotropic agents should be used at all for most patients with decompensated heart failure. The data on the hazards of chronic inotropic therapy are well known.10-13 Additionally, several lines of evidence suggest that even relatively short-term use of inotropic therapy may be associated with adverse outcomes. In the Flolan International Survival Trial (FIRST), treatment with intravenous dobutamine at the time of randomization was independently associated with increased mortality in patients with advanced decompensated heart failure.14 In the Outcomes of a Prospective Trial of Intravenous Milrinone for Exacerbations of Chronic Heart Failure (OPTIME CHF) study, the use of 48 hours of intravenous milrinone did not improve outcomes compared with placebo and was associated with a significantly greater incidence of hypotension and arrhythmias. Despite the evidence of the potential of inotropes to do harm in patients with heart failure, clinicians are faced with an ever-growing population of patients with severe advanced heart failure who are unresponsive to standard medical therapy and who have evidence of progressive end-organ hypoperfusion. Like Odysseus choosing between sailing toward the sea monster Scylla or the whirlpool Charybdis, the clinician faced with such patients may be forced to “choose his poison” in selecting a first-line inotropic agent for heart failure. The data from Yamani et al suggest that dobutamine is a reasonable and highly cost-effective option when this is the case. Further clarification of the role of these agents and inotropes in general in severe decompensated heart failure awaits the results of prospective randomized trials.

References