EDITORIAL COMMENT

Blood Pressure and the Therapy of Advanced Heart Failure*

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In the 1960s, when we initially introduced the concept of vasodilator therapy for the failing heart (1), we had to overcome skepticism about the safety and efficacy of this approach. Health care workers were focused on auscultatory blood pressure (BP), which often was falsely reduced in sick patients (2), and vasoconstrictor drugs frequently were administered to restore perceived low pressure, which was thought to be harmful. The idea that vasodilator drugs, which are designed to lower pressure, would be safe in such an individual was anathema.

Our early experience convinced us of the wisdom of this approach even when the directly measured arterial pressure was low. One of our first patients was in severe pump failure after an acute myocardial infarction. Our bedside hemodynamic assessment (3) revealed a brachial arterial pressure of 90/70 mm Hg and a cardiac output of 2.3 l/min. Having already demonstrated the favorable effects of sodium nitroprusside on cardiac output in such patients (4), we initiated an infusion which, as expected, doubled cardiac output and produced dramatic clinical improvement while reducing arterial pressure to 84/60 mm Hg. Because we were satisfied with our titration and it was now 2 AM, I left orders with the nursing staff to maintain systolic pressure <90 mm Hg by adjusting the dose of nitroprusside. When I returned at 7 AM, the nurse informed me apologetically that she had adjusted the dose of nitroprusside. When I returned at

Despite the clarity of this physiologic principle, clinicians still often focus on BP in their management of sick patients, perhaps because it is easy to measure and generates a number that people think they understand. And because of that number, patients may be deprived of effective therapy, such as angiotensin-converting enzyme inhibitors and beta-blockers. Indeed, nurses often withhold these drugs, even when they are prescribed, if the BP is low in a hospitalized patient. Hypotension can of course be a concern when it is associated with cerebral, cardiac, or renal evidence of inadequate perfusion. But in the absence of such signs or symptoms, the therapeutic goal is to maintain treatment with drugs that lower impedance, improve flow, and slow left ventricular (LV) structural remodeling.

Systolic BP is a product of the stroke volume and the impedance to ejection. When the heart is healthy, impedance does not affect stroke volume but rather determines pressure. In the failing heart, however, impedance controls stroke volume (5). The neurohormonal and vascular consequences of HF (6) raise impedance, and stroke volume then becomes a measure of the severity of LV dysfunction. Under these circumstances, hypotension is a consequence of reduced contractile function of the heart. The hypotensive patient with HF, therefore, should be at high risk because of the severity of HF and should be a candidate for the most aggressive therapy to lower impedance and slow the progression of structural and functional disease.

The study by Rouleau et al. (7) in this issue of the Journal is a welcome reminder of the fallacy of the concern with low BP in administering carvedilol. As the authors point out, low BP is often cited as a reason for not administering a beta-blocker in HF despite the impressive data supporting its long-term efficacy. The vasodilator action of carvedilol related to its alpha-blocking effects should in fact be beneficial in such patients, just as it was in our early patient experience. As nicely documented by Rouleau et al. (7), low entrance BP in the Carvedilol Prospective Randomized Cumulative Survival (COPERNICUS) trial was a powerful mortality risk factor and identified patients in particular need for aggressive therapy.

It is important to reiterate an often-disregarded principle in the management of HF. Symptoms of decompensated HF are a consequence of long-term structural remodeling of the heart complicated by short-term and often reversible dysfunction related to heightened impedance and acontractile disorder. Lowering the impedance or increasing the contractility can reverse the functional disorder (8) but not necessarily the long-term structural disorder. Beta-blockers deal with the structural disorder (9). Vasodilators correct the functional disorder, and some vasodilators (e.g., nitrates, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers) also favorably affect the structural disorder (10–12). Alpha blockers are not among these (10), so the alpha-blocker activity of carvedilol may be important in restoring LV function in these hypotensive patients with HF, but it probably does not contribute to the long-term structural benefit of the beta-blocking activity of carvedilol.

The message of the Rouleau et al. study (7) should be

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See page 1423
Hypotension in severe HF is grave and helps physicians identify patients who are in need of aggressive therapy to improve emptying of the LV and, long-term, to correct its structural remodeling. Vasodilator therapy can usually be tolerated by such patients and indeed perhaps should be mandated. Low BP should not preclude a trial with such drugs, and a fall in BP not accompanied by hypotensive signs or symptoms should not necessarily lead to a discontinuation of the therapy.

Carvedilol is dual therapy: Its vasodilator effect supports LV function, whereas its beta-blocking effect exerts long-term benefits. One could alternatively use a vasodilator, such as a nitrate (often combined with hydralazine to preserve the generated nitric oxide) (13) and a purer beta-blocker to obtain the same effect. The latter combination would have the benefit of separate titration to optimal doses of the vasodilator and beta-blocker and would also have the benefit of additional antiremodeling properties of the nitrate (14). In the meantime, however, the experience with carvedilol in COPERNICUS suggests that it is safe and effective in this patient population.

**REFERENCES**