Letters to the Editor

Editor's Note

Due to communication problems, several Letters to the Editor were misplaced and were not published in a timely fashion. We became aware of this recently when one of the authors contacted us as to the publication status. We have gathered those letters together and are now publishing them in this issue. In general, we believe that the letters and the replies are self explanatory. We apologize for this delay.

The CHARM of a Paradox

The paradox in the CHARM (Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity) study (1) needs to be explained if low brachial systolic pressure is perceived by physicians as a contraindication to the use of arterial dilator drugs such as nitrates, carvedilol, and candesartan in systolic heart failure. Meredith et al. (1) extended results of previous studies (AHeFT [African-American Heart Failure Trial (2)] and COPERNICUS [Carvedilol Prospective Randomized Cumulative Survival (3)]) in showing that an arterial vasodilator was at least as effective in trials of cardiac failure for improving outcomes in patients with systolic blood pressure (SBP) <100 mm Hg (whose left ventricular ejection fraction averaged 25%) as in those with normal or high SBP and without appreciable risk of causing symptomatic hypotension.

The paradox arises from exclusive consideration of brachial rather than central pressure (4) and from assuming that effects of dilator drugs on high-resistance arterioles dominate over effects on low-resistance conduit arteries. Arterial vasodilator drugs such as nitroglycerin reduce wave reflection (5,6) and "trap" reflected pressure waves in the peripheral circulation so that they do not summate with central systolic pressure, with this differentially reduced compared with brachial SBP (4,6). In patients with a low left ventricular ejection fraction and the ventricle contracting weakly and acting (in engineering terms) as a "pressure source" (6,7), reduction in aortic and left ventricular systolic pressure leads to increased left ventricular ejection from the heart (6,7). Such an increase in stroke volume can maintain or increase SBP in patients with cardiac failure due to systolic dysfunction.

The paradox described by Meredith et al. (1) is explicable. It explains why drugs that dilate muscular arteries and reduce wave reflection are very effective for reducing systolic pressure in hypertension when the heart is contracting normally (i.e., as a flow source) (6,7) and for increasing cardiac output in patients with heart failure when the heart's contraction is weakened, and it acts as a pressure source (6,7).

Consideration of blood pressure, cardiac output, and peripheral resistance is insufficient to explain the function of the pulsating heart and blood vessels. These comments are offered without any criticism of the excellent work of Meredith et al. (1).

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Please note: Dr. O'Rourke is the founding director of AtCor Medical, Sydney, Australia, maker of a pulse-wave analysis system.

REFERENCES

1. Meredith PA, Ostergren J, Anand I, et al. Clinical outcomes according to baseline blood pressure in patients with a low ejection fraction in the CHARM (Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity) Program. J Am Coll Cardiol 2008;52:2000–7.
2. Anand IS, Tam SW, Rector TS, et al. Influence of blood pressure on the effectiveness of a fixed-dose combination of isosorbide dinitrate and hydralazine in the African-American Heart Failure Trial. J Am Coll Cardiol 2007;49:32–9.
3. Rouleau JL, Roecker EB, Tendera M, et al. Influence of pretreatment systolic blood pressure on the effect of carvedilol in patients with severe chronic heart failure: the Carvedilol Prospective Randomised Cumulative Survival (COPERNICUS) study. J Am Coll Cardiol 2004;43:1423–9.
4. Agabiti-Rosei E, Mancia G, O'Rourke M, et al. Central blood pressure measurements and antihypertensive therapy: a consensus document. Hypertension 2007;50:154–60.
5. O'Rourke MF, Safar ME, Dzau V, editors. Arterial Vasodilation: Mechanisms and Therapy. London: Edward Arnold/Philadelphia, PA: Lea & Febiger, 1993.
6. Nichols WW, O'Rourke MF. McDonald's Blood Flow in Arteries. 5th edition. London: Arnold, 2005.
7. Westerhof N, O'Rourke MF. The hemodynamic basis for the development of left ventricular failure in systolic hypertension. J Hypertens 1995;13:943–52.

Cardiac Resynchronization in Mildly Symptomatic Heart Failure and Asymptomatic Patients

I read with interest the results of the REVERSE (REsynchronization reVErses Remodeling in Systolic left vEntricular dysfunction) trial in the paper by Linde et al. (1). The trial concluded that cardiac resynchronization therapy, in combination with optimal medical therapy, reduces the risk of heart failure hospitalization and improves ventricular structure and function in New York Heart Association functional class I and II patients with previous heart failure symptoms. I think that it is worth noting that the studied population was composed of patients having significantly prolonged QRS duration (average 156 ms) as well as quite severe