Letters

TO THE EDITOR

Heart Failure and Comorbidities

The timely and well-structured presentation concerning the burden of comorbidities and functional and cognitive impairments in elderly patients with heart failure by Murad et al. (1) and the accompanying thought-provoking editorial by Shaffer and Maurer merit an additional point of concern regarding mortality. The comorbid statistical assessment of factors contributing to greater total mortality risk included diabetes, kidney disease, cerebrovascular disease, depression, impairment of activities of daily living, and cognitive impairment. The comorbidities of hypertension, coronary heart disease, atrial fibrillation, and obstructive pulmonary disease were not associated with mortality (at least, not directly). Noteworthy was the fact that hypertension was the most common comorbidity (82% of patients), a not unexpected fact. We now arrive at the point of possible consternation: hypertension versus cognitive impairment. If it is accepted that antihypertensive drug therapy may have an adverse influence on cognition in “normal” as well as in those patients who already have such dysfunction, the possibility that guideline therapy for hypertension can be contributing to or associated with the increased mortality, as noted in the statistical analysis and conclusion.

The consideration of drug therapy being involved in the causation of increased mortality in the cognitively impaired patients in this study is further confounded by the fact that the drugs used to treat heart failure are the same as those used in treating hypertension: beta-blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and hydrochlorothiazide. Therefore, treated hypertension would be the unappreciated catalyst of the association of increased mortality in the patients with cognitive impairment.

Severe forgetfulness in a young woman caused by methyldopa was described 39 years ago (2). Callender et al. (3) reported memory deficits in patients taking nicardipine and propranolol. Two years later, Callender (4) reported that patients on atenolol were noted to have highly significant impairment of short-term memory. A significant study by Heckbert et al. (5) described the presence of greater cerebral white matter changes on magnetic resonance imaging in patients taking calcium-channel blockers or loop diuretics and correlated these findings with deficits on the Mini-Mental State Examination. Many years of careful clinical observation leads me to conclude that impairment of rapid recall is the most frequently overlooked side effect of all classes of antihypertensive drugs.

As usual, the practicing clinician is faced with a trek through the therapeutic quagmire of who to treat, what to treat, when to treat, and how to treat, all based on guidelines for each particular condition or disease. The patient who will fare best is the one whose physician has appropriately synthesized a therapeutic program which adjusts for the presence of multiple comorbidities. This may at times include the philosophy of “less is more”.

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REFERENCES

REPLY: Heart Failure and Comorbidities

We thank Dr. RuDusky for his interest in our recent report describing the burden of comorbidities and functional and cognitive impairments in elderly patients with heart failure by Murad et al. (1) and remembering to credit the philosophy of “less is more”.

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Please note: Dr. RuDusky has reported that he has no relationships relevant to the contents of this paper to disclose.
patients with incident heart failure (HF) and their impact on outcomes in the Cardiovascular Health Study (1). Our purpose was to use this established, National Institutes of Health–funded population database to provide a detailed, comprehensive examination of the impact of patient characteristics in these key domains that have not been traditionally accounted for in HF research. Our data confirmed and significantly extended other emerging data indicating that these patient characteristics may affect outcomes as strongly as or even stronger than (at least in elderly patients) traditional measures such as cardiac anatomy and function.

We appreciate the writer’s comments reiterate evidence in other reports suggesting a relationship between antihypertensive medications and cognitive impairment, mainly rapid recall. However, to our knowledge, this hypothesis has not been tested in patients with HF, in whom, as we showed in our study, cognitive impairment is highly prevalent. We might expect that any potential burden created by antihypertensive medications would be mitigated by their benefit for patients with HF. This hypothesis could be a focus of future studies. The large, multicenter National Institutes of Health–funded SPRINT (Systolic Blood Pressure Intervention Trial), which recently released its preliminary overall results, has an ongoing component (SPRINT-MIND) that is likely to provide the most definitive test to date of the effect of hypertension and its treatment on cognitive function (2).

Dr. RuDusky’s letter seems to misinterpret some findings from our study. We did not find an association between hypertension and mortality in either direction (both unadjusted and adjusted hazard ratios were neutral or not statistically significant). Our study showed that cognitive impairment was associated with increased mortality in both unadjusted and adjusted analysis. The lack of association in analyses adjusting for hypertension or use of antihypertensive drugs would generally exclude hypertension as a confounding factor. We did not test specifically for an association between hypertension or the use of antihypertensive medications and cognitive impairment because this was not pertinent to the study question. We defined hypertension as elevated systolic and/or diastolic blood pressure or active use of blood pressure–lowering medication.

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