LETTERS TO THE EDITOR

Why Is Chronic Kidney Disease the “Spoiler” for Cardiovascular Outcomes: An Alternate Take From a Generalist

In a recent report (1), and the accompanying editorial (2) in the Journal, the excess mortality among acute coronary syndrome (ACS) patients with reduced creatinine clearance (CrCl) was mostly attributed to chronic disease of the kidneys and to related alterations in vascular biology and drug metabolism. The CrCl more appropriately represents the collective functional status of all the nephrons, and their capacity to adjust to stressful physiologic situations (the organ reserve of kidneys), rather than a “disease” state. Only a few of those with mild to moderate reduction in CrCl ever develop any obvious renal disease (3,4). The age-related decline in CrCl is also associated with a decline in the average functional reserves in all other organ systems (maximal organ reserve). It has been estimated that a healthy young adult has a maximum reserve capacity that is 7 to 11 times that of the average demand, and by the age of 85 years, less than 50% of the original organ reserve remains in humans.

Illnesses cause severe alterations in the overall physiological state of the individual (homeostasis). The maximal organ reserve at any age determines the ability of an individual to restore homeostasis and maintain it within narrow confines necessary for preservation of life. The lower the organ reserve, the higher the chance of fatality, as is the case with older people when they face common illnesses like pneumonia. However, the level of maximal organ reserve does not necessarily correlate with chronological age, because both the onset and the progression of the decline in general organ reserve show profound individual variations (5,6). I hypothesize that the CrCl is a crude representation of the maximal organ reserve of an individual at any given age. Hence, CrCl predicts mortality in ACS independent of age and other factors related to individual organ systems.

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REFERENCES

REPLY

The concept of impaired “organ reserve” as a determinant of cardiovascular and all-cause survival proposed by Dr. Manhapra is an important one. Through normative aging, data from the National Health and Nutrition Examination Survey indicated that the estimated glomerular filtration rate (eGFR) does not dip below 60 ml/min/1.73 m² through age 85 (Fig. 1). Hence, an eGFR <60 ml/min/1.73 m² indeed represents impaired renal organ reserve, and remnant nephrons must pick up a higher filtration and metabolic workload. Thus, at this level, we can expect a different

metabolic milieu that accelerates atherosclerosis, valvular disease, heart failure, and arrhythmias, which invariably leads to higher rates of cardiac and noncardiac death. Having recognized chronic kidney disease (or impaired renal organ reserve) as an independent cardiovascular risk state, the real challenges now are to develop new diagnostic and therapeutic targets to better care for this rapidly growing segment of our cardiovascular population.

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Heart Rate Recovery After Exercise
Is Not Demonstrated as a Predictor of Mortality: Maybe After Treadmill-Exercise

Regarding the elegant and innovative study by Vivekananthan et al., entitled “Heart Rate Recovery After Exercise Is a Predictor of Mortality, Independent of the Angiographic Severity of Coronary Disease” recently published in JACC (1), I must object that the title of such a good report is substantially wrong. In fact, the word “exercise” should have been more precisely substituted with the words “treadmill-exercise.” This is definitely not a trivial correction, for no study has ever demonstrated that heart rate recovery (HRR) after any type of exercise other than treadmill has any relation with mortality. My group has completed a study of 1-min HRR after cycleergometer-exercise test as a predictor of mortality in a cohort of 1,420 real-life exercise-test candidates; we found substantial differences compared to the treadmill-derived parameter. I can surely state that no evidence has ever been published in the peer-reviewed medical literature linking HRR and mortality using any exercise modality other than treadmill-exercise. This should be emphasized, as many clinicians could be tempted to apply these results to other clinical exercise settings.

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REPLY
Dr. Gaibazzi is correct in stating that current evidence linking heart rate recovery with death has been derived from cohorts of patients undergoing treadmill-exercise testing. As previous work has shown that heart rate responses during exercise are different when using a bicycle (1), it will be important to perform future research involving very large cohorts of patients undergoing this type of test modality. Of note, recent work has shown that vagal activity plays an important role in heart rate recovery after mental stress (2), suggesting that the concept linking heart rate recovery with prognosis may transcend the type of stress.

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Pulmonary Venous Flow by Doppler Echocardiography: Usefulness of Diastolic Wave Deceleration Time in Predicting Filling Pressures

I read with great interest the study by Tabata et al. (1), which reviews all the current applications of measuring pulmonary venous flow by Doppler echocardiography. As reported by the investigators, measurement of pulmonary capillary pressure and left ventricular end-diastolic pressure may utilize either the systolic fraction or the difference between pulmonary venous atrial reverse-wave duration and mitral inflow atrial-wave duration. Noninvasive assessment of filling pressures with Doppler methods represents a promising tool in diagnosing and monitoring heart failure (2); thus, it appears of interest to point out the clinical usefulness of the deceleration time of the pulmonary venous diastolic flow, which has been well correlated to invasive pulmonary capillary pressure in several studies regardless of left ventricular systolic function and rhythm (3–7). Furthermore, a recent work by Kinnaird et al. (8) has reported its better accuracy than the pulmonary artery occlusion pressure in predicting left atrial pressure. At present, the usefulness of the deceleration time of pulmonary venous diastolic flow is limited in practice by the difficulty to record the pulmonary venous flow from apical windows in critically ill patients (7); nevertheless, the steady improvement of the quality of Doppler echocardiographs will increase its feasibility in the coming years.

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