Abete et al.) having been reported. This variation in life span is not unique to the rabbit, and it underscores a crucial caveat: life span or age is, in itself, a poor predictor of the aging process (4). Thus, evaluation of established biomarkers of aging (4)—rather than attempts to equate, from maximum life spans, relative ages among species—may represent a more germane approach in addressing this question.

We observed significant myocyte hypertrophy and myocardial fibrosis—the morphologic hallmarks of cardiovascular aging—in four-year-old versus young adult rabbits (1). For example, left ventricular collagen content was 10.8 ± 0.5% (SD 1.8%) versus 6.2 ± 0.3% (SD 1.2%), respectively—a mean 1.7-fold increase (range: 1.2- to 2.5-fold, computed from the SD values) in fibrosis. Abete and colleagues contend that our results are qualitatively, but not quantitatively, similar to those observed in the ~2-year-old rat, an accepted model of senescence. We find, however, that despite methodologic differences among studies, our results fall within the range of data reported for rats (5,6)—including those from Anversa et al. (5), in which collagen volume fraction was 16 ± 4% (mean ± SD) versus 8 ± 2% in 29- versus 4-month-old animals, corresponding to a twofold increase (range: 1.2- to 3.3-fold) in fibrosis. (Of note, the values of 7% and 22% cited by Abete et al. correspond to a twofold increase (range: 1.2- to 3.3-fold) in fibrosis.)

There is an emerging consensus that, in isolated buffer-perfused rat heart, the efficacy of infarct size reduction with PC wanes with increasing age (8,9). In contrast—and contrary to the correspondents’ interpretation of our data—we found sustained, 49%, 58% and 50% reductions of infarct size in PC rabbits versus age-matched adult, two-year-old and four-year-old controls (1). Does this difference in outcome make the four-year-old rabbit, exhibiting definitive biomarkers of cardiovascular aging, the “wrong” model? We believe this disparity is not a question of “right” versus “wrong” models. Indeed, recent preliminary evidence from isolated human myocardial samples—arguably a “right” model—revealed persistent PC-induced protection even in cohorts aged 70 to 90 years old (10). Rather, this may reflect underlying mechanistic difference(s) among models/species that warrant resolution.

REFERENCES


Revascularizing Chronic Total Occlusions: What About the Coronary Collaterals and Myocardial Viability Story?

With reference to the study by Suero et al. (1), I wish to make the following comments:

1. Although there was a 10-year survival advantage in patients who had a successful percutaneous coronary intervention (PCI) to a chronic total occlusion (CTO), this study did not look at the relation of such a survival advantage following a successful revascularization to the presence of viability of infarcted myocardium in the 54% with a previous myocardial infarction (MI). This relationship is expected.

2. It may not be correct to state that all CTOs benefit from revascularization. I suspect that the survival advantage in this cohort came mainly from improvement in left ventricular (LV) function following improvement in contractility of viable infarcted myocardial segments (2). In support, there is data from some uncontrolled surgical series to show that improved survival in patients with LV dysfunction correlates with the presence of myocardial viability in several LV segments (3).

3. The role of collaterals in this situation has always been an area both of controversy and interest. This would perhaps be a good opportunity to review the data to see whether the survival advantage reported in this study correlates with the presence of angiographic collaterals, especially as there is now data to show that collateral flow assessed invasively (5) does correlate with viability.

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PII S0735-1097(02)01819-3
infarcted myocardium, as was first proposed in Chugh’s hypothesis (6).

An important relevant observation is that the study population had a mean duration of occlusion of the CTO vessel of 12 ± 20 months. This study is therefore more likely to be able to answer the often asked question about the role of angiographic collaterals in predicting myocardial viability. This is because it is believed that CTOs such as these give adequate time for collateral development, unlike the recent occlusions studied using contrast echocardiography soon after acute MI (7).

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REPLY
Dr. Chugh's comments regarding our chronic total occlusion (CTO) experience are well stated and germane to our findings. Our intent for this project was to investigate the association between long-term survival and successful recanalization of a CTO. In order to demonstrate this association, a matched cohort was developed using a propensity-scoring model. Thus, the comparison groups were remarkably similar with respect to baseline covariates that are known predictors of long-term survival. In fact, the survival curves for the matched cohort and the CTO group were markedly similar. Only those patients with a successful recanalization of a CTO demonstrated a survival benefit. This link persisted following multivariate adjustment and was identified in the failed percutaneous coronary intervention (PCI) cohort in whom successful surgical recanalization of the CTO was performed.

In our opinion, this body of work clearly identifies a group of patients in whom successful PCI is associated with improved long-term survival. There is no question that further work needs to be performed on the mechanism of survival. Two leading theories are certainly collateral flow and viability. Other plausible explanations that are worthy of future investigation include the effect of successful recanalization upon the incidence of sudden cardiac death, left ventricular remodeling, and identification of certain clinical patient subsets that are associated with an improved survival following CTO and recanalization. For example, patients with a history of diabetes mellitus have been demonstrated to have a decreased incidence of collateral vessel formation despite abnormal coronary atherosclerosis. However, patients with a history of diabetes mellitus derived substantial benefit from a successful recanalization of a chronic total occlusion in our study (data not shown). To further our understanding of this cohort, we have identified 558 patients from our nuclear database with a periprocedural radionuclide perfusion study. We are hopeful that this additional information will result in an enhanced understanding of the survival benefit of successful recanalization of a CTO.

Finally, Dr. Chugh's comments are insightful and, it is hoped, will prompt future investigation into the mechanism of survival benefit associated with a successful recanalization of a CTO.

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Is a High Hematocrit Level Good for Patients With Heart Failure?

We were interested to read the article by Al-Ahmad and colleagues (1) regarding the prognostic value of impaired renal function and anemia in patients with left ventricular (LV) dysfunction, published in the Journal of the American College of Cardiology. The investigators report that reduced kidney function and a low hematocrit are independent risk factors for increased all-cause mortality in patients with LV dysfunction, with there being a synergistic relationship between the two parameters. The results from this study, together with other work in the field (2), may have important clinical implications for the management of patients with chronic heart failure (CHF). However, we believe several points deserve further consideration.

The prognostic benefits of treating anemia in CHF and whether there is an optimal range of hematocrit for survival are not known. In the Framingham study, the impact of hematocrit on all-cause death as well as morbidity and mortality due to cardiovascular disease was shown to follow a U-shaped curve (3). Other prospective epidemiological studies of healthy populations have shown that the lowest mortality rate correlates with a mid-range hematocrit level in both genders and at all ages (4). Al-Ahmad et al. (1)