reserve index” was used in our study for the ratio of \( K_1 \) during stress to \( K_0 \) at rest. Finally, the first-pass studies used by Jerosch-Herold’s team have yielded impressive results when compared with coronary flow reserve measurements using Doppler wires (2). In truth, the best comparison would be to compare the nutritive perfusion measurements obtained with positron emission tomography (PET), because coronary flow reserve and regional nutritive perfusion can differ. Nevertheless, although technically demanding, their first-pass technique looks promising, particularly if the imaging artefact problems are overcome and validation against PET can be achieved. The Kety model approach needs further research, but it may prove to have some advantages for the reasons already outlined.

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REFERENCES


Explaining the Race Paradox of Coronary Calcium Prevalence and Survival

Doherty et al. (1) report on the apparently paradoxical observation that, in a cohort of asymptomatic adults, baseline prevalence of coronary calcium was lower in blacks than in whites, whereas blacks suffered a greater number of events over the follow-up. According to the investigators, these findings indicate that coronary calcium has a “different pathobiologic significance in blacks and whites.”

In fact, rather than surprising, these findings are quite consistent with a very fundamental epidemiologic principle that relates to the approximate relationship between prevalence (\( P \)) and incidence (\( I \)):

\[
P = I \times D
\]

where \( D \) is the duration (survival) after disease onset.

Thus, the prevalence ratio obtained in a cross-sectional study (e.g., their baseline examination) will have the following approximate relationship with the incidence ratio (relative risk):

\[
\frac{P_{\text{blacks}}}{P_{\text{whites}}} \approx \frac{I_{\text{blacks}}}{I_{\text{whites}}} \times \frac{D_{\text{blacks}}}{D_{\text{whites}}}
\]

If the duration in blacks and whites is not equal, the prevalence ratio will be a biased estimate of the incidence ratio, the so-called prevalence-incidence bias inherent to many cross-sectional studies (2). The substantially higher co-morbidities, levels of risk factors, and lower access to health care treatment and preventive practices may determine that survival after onset of coronary artery disease is shorter in blacks than in whites, that is what Doherty and co-workers found in their prospective analysis (1). Thus, \( D_{\text{blacks}} < D_{\text{whites}} \) and this may explain why the observed prevalence of coronary calcium is lower in blacks (i.e., \( P_{\text{blacks}}/P_{\text{whites}} \)) even if their risk (incidence) of coronary disease is higher (see also Fig. 1).

The findings by Doherty et al. are analogous to an earlier survey showing that tuberculosis was less prevalent in American blacks than in whites (3). Was this an indication of blacks having lower risk of tuberculosis? As subsequent prospective studies demonstrated (3), tuberculosis incidence was indeed much higher in blacks, while their case-fatality rate was also higher. Thus, the earlier baseline finding was simply a product of the incidence-prevalence bias.

Large prospective studies of the natural history and progression of subclinical atherosclerosis in different ethnic groups, such as the ongoing Multi-Ethnic Study of Atherosclerosis (MESA), will provide answers to some of these questions. In the meantime, however, caution should be taken in interpreting complex racial/ethnic differences as “biological” simply because an observed difference persisted after adjustment for standard risk factors and/or surrogates of socioeconomic status. Residual confounding stemming from imperfect or incomplete adjustment (e.g., imperfect measures of socioeconomic status) is an important limitation. In addition, as discussed in numerous publications (4–6), the use of the biological construct “race” defined solely on the basis of skin color is of questionable validity. The marked genetic heterogeneity within groups such as “blacks,” “whites,” or “Hispanics” explains why this practice has been abandoned by anthropologists, even though biomedical scientists persist in ignoring these calls for caution.

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REFERENCES

REPLY
We thank Drs. Nieto and Blumenthal for their thoughtful and intriguing comments regarding our recent article (1). The major findings in our study were that asymptomatic black subjects had a lower prevalence of coronary calcium compared to white subjects, but nevertheless suffered more coronary heart disease events during a 70-month follow-up period. After adjusting for age, gender, and coronary risk factors, black race was associated with an odds ratio of 2.16 for a coronary event (95% CI limits, 1.34–3.48). Drs. Nieto and Blumenthal advance two possible explanations of our findings:

1. Blacks suffered higher rates of co-morbid conditions, risk factors, and diminished access to health care treatment, collectively impacting event-free survival deleteriously.

2. The duration from disease onset to event occurrence differed in blacks compared to whites, secondary perhaps to a higher case-fatality rate among our black subjects (incidence-prevalence bias).

Drs. Nieto and Blumenthal suggest that our findings may at least in part be explained by higher co-morbidities and risk factors in blacks, combined with lower access to health care. This possibility cannot be excluded, as we stated in our article. Blacks underwent revascularization at rates similar to whites, yet it could conceivably be argued that the rates of revascularization should have in fact been higher in blacks, commensurate with their event rate. Blacks in our study had roughly equivalent coronary risk factors to whites; however, it is not at all clear that standard coronary risk factors derived from epidemiologic investigations comprised almost exclusively of white subjects are applicable to blacks to the same extent that they are to whites. In fact, as we pointed out, there is evidence that some risk factors such as smoking, hypertension, and cholesterol have a different impact on black subjects compared to white subjects. Although black and white subjects in our study had equivalent overall Framingham risk, black subjects had significantly higher systolic blood pressure and body mass index and a higher incidence of diabetes mellitus and a history of hypertension. Conversely, white subjects were older, and they had a higher incidence of positive family history of coronary heart disease. As we pointed out, it is possible that the variable impact of standard risk factors on differing ethnic groups could have affected our results.

Drs. Nieto and Blumenthal suggest that the inverse relation between incidence ($I$) and disease duration ($D$) might explain the lower prevalence of calcification and the higher incidence of clinical events. If the proposed relation $\text{Prevalence} = \frac{I}{D}$ were valid, $I$ could be higher for blacks even though Prevalence was lower only if the disease duration, $D$, were much shorter for blacks. However, this was not the case: the duration between screening and events was the same for both ethnic groups (Table 1).

In addition, prevalence of calcification at the time of screening is not the same as prevalence of clinical disease or even of atherosclerosis. Calcification is only imperfectly related to atherosclerosis—and the latter only imperfectly related to clinical events. Our findings regarding higher coronary event rates but lower prevalence of calcium in blacks thus cannot be explained in the manner proposed by Drs. Nieto and Blumenthal, and they pose intriguing and important questions for further investigation.

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REFERENCE

Table 1. Duration to Events in Black Subjects Compared to White Subjects

<table>
<thead>
<tr>
<th>Race</th>
<th>Mean Time (in Months) to Event [SD]</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Event†</td>
<td>White 46.7 [24.8]</td>
<td>0.52</td>
</tr>
<tr>
<td></td>
<td>Black 43.9 [26.2]</td>
<td></td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>White 49.7 [26.8]</td>
<td>0.52</td>
</tr>
<tr>
<td></td>
<td>Black 56.6 [32.7]</td>
<td></td>
</tr>
</tbody>
</table>

Table 1. Duration to Events in Black Subjects Compared to White Subjects.