Don’t Throw the Baby Out With the Bath Water

Budoff et al. (1) have presented important information from the MESA (Multi-Ethnic Study of Atherosclerosis) trial about the interpretation of coronary artery calcium (CAC) scores. There has been some controversy as to how to interpret what constitutes a high-risk score. Is the age/sex/ethnicity adjusted percentile score or the absolute total score best? To me it seems to depend on what is your question about high risk. In the Budoff et al. (1) article, clearly the authors are interpreting high risk as the risk for a cardiac event in the short term (46 months). However, to the clinician and patient, it is of great importance to determine which individuals are at high risk in the longer term (i.e., decades).

The authors cite an example of a 50-year-old Hispanic woman who has a CAC score of 25, which places her in the 95th percentile for age/sex/ethnicity compared with an 83-year-old white man with a CAC of 1,572, which places him in the 72nd percentile for his age/sex/ethnicity. The main point of the article is that although the man has a lower percentile than the woman, he is at much greater risk for a short-term cardiac event. No argument, the greater the atherosclerotic burden the greater the short-term risk. However, I think it is important to recognize that the percentile score has clinically useful information that the absolute score does not. The fact that the 50-year-old woman’s score places her in the 95th percentile for age/sex/ethnicity means she will reach the high-risk score of 400 at a much earlier age, probably within 15 years (2), compared with many of her peers, who had the more likely score of 0 and will take 35 years or longer to achieve a high-risk score. I believe this is very useful information for the physician and the patient and will significantly impact decision-making about diet, lifestyle, and medications. In other words, I think we and our patients are interested in both the short- and long-term risk. If I am a 39-year-old white man with a score of 50, I certainly would want to know that I am likely to have a high-risk score within 10 years (3).

Knowing both short- and long-term risk is useful. The percentile score predicts the long-term risk and tells us how soon, untreated, we will reach a high-risk score. The absolute score represents the atherosclerotic burden currently present and therefore best predicts the short-term risk.

However, the Budoff et al. (1) article and the accompanying editorial seem to downplay the importance and value of the percentile score in their enthusiasm to identify the most powerful predictor of short-term risk. The data presented support their enthusiasm, but please don’t throw the baby out with the bath water.

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Reply

We completely agree with Dr. Brundage’s supposition that a more important marker for treatment targets may be lifetime risk. Data suggest that 67% of men and 50% of women over 40 years of age will develop chronic heart disease (1). The concept of lifetime risk was highlighted in the National Cholesterol Education Program Adult Treatment Panel III guidelines (2) and is especially important for individuals who are young to middle-aged.

However, most data with risk factors, C-reactive protein, and coronary artery calcium (CAC) have shorter-term follow-up and enable clinicians to match intensity of therapy to intensity of risk for near-term events. Lifetime lipid treatment or other antiatherosclerotic therapies may start shifting cost benefits and possibly even risk benefits away from treatment strategies.

Dr. Brundage correctly points out that while absolute scores are better short-term predictors, we cannot completely forgo percentile scores. From our standpoint, presence of “any” CAC, irrespective of percentile, especially in younger individuals is an indicator of significant intermediate-term and lifelong risk. The issues with using “only” percentiles for risk assessment pose problems at 2 levels. First, at each age group, women presenting with the same level of CAC scores as men are less likely to be considered as high risk and, thus, to be treated. Second, another risk of using the percentile scores is underestimation of risk, and, thus, there is potential for undertreatment of those persons with higher scores. Persons with scores as high as 1,500 may be deemed “normal” by age and sex cutpoints, but clearly have at least a 20-fold increased risk of future cardiovascular events (3). As participants with baseline calcium scores are followed up to 12 years, risk continues to diverge based upon baseline score, supporting the concept that CAC is a good predictor of lifetime risk (4).

One limitation of the MESA (Multi-Ethnic Study of Atherosclerosis) study is that there were no persons under age 45 years, so really assessing younger patients with advanced atherosclerosis is outside the scope of our study. Younger patients especially need to rely more heavily on percentile scores, as they rarely achieve scores >100, yet may be at increased risk. Taylor et al. (5) prospectively followed 2,000 persons (mean age 43 years) for 3 years, and the presence of any plaque was associated with an 11.8-fold increased risk of a cardiovascular event (5). Using a percentile to give patients a relative place compared with their age, sex, and ethnic/racial peers allows physicians to treat patients who are “ahead of the curve” with increased vascular age. By emphasizing both absolute and percentile scores, we can identify those at higher risk of lifelong cardiovascular disease by acknowledging presence of any CAC as a marker of subclinical disease.