

**THE AUTHORS REPLY:** Mascitelli and Goldstein suggest that screening athletes only once during adolescence will not identify some persons who are predisposed to cardiomyopathy because the overt disease phenotype may not develop until early adulthood. They advocate serial evaluation with annual ECG, as mandated in Italy. Six of the eight deaths in our study were attributable to a cardiac cause in athletes who had had normal results on ECG and echocardiography at 16 years of age. Although we did not perform serial evaluations to show the subsequent development of a cardiomyopathy, we agree that the concept of age-related penetrance of cardiomyopathies must be considered. Although these diseases are not expressed in many people during adolescence, intense exercise regimens may unmask the phenotype in susceptible athletes.<sup>1</sup> In light of our findings, the English Football Association recommends additional serial assessments with ECG at 18, 20, and 25 years of age.

Aengevaeren and colleagues highlight the need for timely recognition and management of sudden cardiac death during exercise. We agree that screening is not an alternative to providing essential emergency-response facilities or early CPR and defibrillation. Furthermore, we think that appropriate CPR training and AED maintenance are essential in organized sports.

Morita and Komuro raise the issue of family history and genetic analysis in the 6 athletes who died from inherited cardiac disorders despite a normal cardiac screening at 16 years of age. The English Football Association health questionnaire specifically asks about a family history of heart disease in persons younger than 50 years of age (Fig. S1 in the Supplementary Appendix of

our article, available at NEJM.org). Since our findings, the questionnaire has been modified to also include a family history of inherited cardiac disease. Molecular autopsies were not performed in these athletes, although they are playing an increasingly prominent role in investigating cases of sudden cardiac death in persons with a structurally normal heart.<sup>2</sup> Sheikh et al. recently evaluated 100 athletes with T-wave inversion typical of cardiomyopathy but without features of cardiomyopathy on ECG.<sup>3</sup> All the athletes underwent genetic analysis in addition to comprehensive clinical evaluation. Of these athletes, 21 received a diagnosis of cardiomyopathy on the basis of clinical assessment alone, and 10 of these 21 athletes had a disease-causing gene mutation. Of the remaining 79 athletes with a normal phenotype, genetic testing identified only 2 athletes with pathogenic variants, and the cost of genetic testing was three times that of a clinical evaluation alone. Therefore, our practice is to limit genetic testing in athletes to those who have an obvious disease phenotype or a family member with proven inherited disease and a recognized pathogenic variant.

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