diagnostic criteria for ARVC after further evaluation or experienced adverse events during the 2-year follow-up.

These findings by Malhotra et al. (1) extend the previous observations on the benign clinical course of anterior T-wave inversions in young adults and athletes. However, contrary to what the investigators state in their paper, the prevalence and prognostic significance of T-wave inversions in right precordial leads V_1 to V_3 have been previously reported in white adults in >10,000 Finnish middle-aged subjects from the general population (3). In the Finnish study, the prevalence of anterior T-wave inversions was also 0.5%, with a surprisingly similar distribution between men (0.1%) and women (0.9%) as Malhotra et al. (1) reported. T-wave inversions normalized during the course of the study in only 20% of the subjects. During the mean follow-up of 30 years, no increase in mortality was observed among those with anterior T-wave inversions. In contrast, T-wave inversions beyond leads V_1 to V_3 were associated with increased risk of mortality and sudden cardiac death. Therefore, it should be emphasized that all T-wave inversions in chest leads may not be benign, even in young athletes.

Together, these data will help to reassure subjects with isolated anterior T-wave inversions about the benign nature of this finding. However, decisions about the need for further evaluation of patients with this electrocardiographic pattern need to be individualized based on the extent of T-wave inversions and other electrocardiographic and clinical features, as well as the estimated prevalence of ARVC in the specific geographic region.

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http://dx.doi.org/10.1016/j.jacc.2017.01.079

Please note: The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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REPLY: Are T-Inversions in Chest Leads Always Benign?

We are grateful to Dr. Aro and colleagues for their interest in our paper (1). They cite their study of 10,899 middle-aged subjects, including 52% of males, that investigated the presence of anterior T-wave inversion over a substantial mean follow-up of 30 ± 11 years (2). The prevalence of T-wave inversion in leads V_1 to V_3 was 0.5% and similar to that reported in our study. There was no increase in mortality among this group, contrary to T-wave inversion in leads other than leads V_1 to V_3, which was associated with an increased risk of cardiac and arrhythmic death. This study supports our findings that T-wave inversion in the anterior leads may be a physiological variant among white individuals in the absence of symptoms or a concerning family history. Both studies suggest that electrocardiographic criteria used by the Task Force recommendations for arrhythmogenic right ventricular cardiomyopathy (ARVC) may be nonspecific in the general population (3). However, we did emphasize that the benign pattern pertained to T-wave inversion limited to leads V_1 to V_2, and that extension beyond this may warrant further investigation. We entirely agree that T-wave inversion in territories other than an anterior territory should be investigated further, particularly as these may be harbingers of cardiomyopathy (4).

We would like to highlight that our study included 14,646 young white athletes and nonathletes, aged between 16 and 35 years. The mean age of these subjects was 21.7 ± 5.4 years, which was significantly lower than the middle-aged Finnish subjects (mean age: 44.0 ± 8.5 years). It is important to note that a similar prevalence of anterior T-wave inversion seems to persist among individuals in the third to fifth decades. However, we do maintain that the rarity of T-wave inversion beyond lead V_2, especially in men (<0.3%), warrants further investigation. This is particularly relevant to the electrocardiograms of young athletes in light of recent studies that have suggested that exercise increases age-related penetrance and arrhythmic risk in ARVC (5).

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http://dx.doi.org/10.1016/j.jacc.2017.03.612

Please note: The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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Infective Endocarditis, Gentamicin, and Vestibular Toxicity

I applaud the recent paper by Cahill et al. (1), in which they comment that aminoglycosides (AGs) may be causing harm without clear clinical benefit.

With regard to their reference to AG toxicity, it is perplexing that only nephrotoxicity was cited but not AG-induced ototoxicity. The former is reversible in most cases and can be prevented with judicious monitoring of urine protein and serum creatinine concentrations from baseline (i.e., day zero). AG-induced nephrotoxicity is defined as an increase in serum creatinine of 0.5 mg/dl from baseline (i.e., day one). Importantly, this includes levels within normal ranges. Because serum creatinine concentrations can lag behind proximal tubular damage by 72 h, trending of creatinine concentrations is a key strategy in preventing nephrotoxicity. The incidence of AG-induced nephrotoxicity is often cited as 10% to 25%. Perhaps we should question the high incidence of nephrotoxicity because monitoring parameters are relatively straightforward? Maybe the reason is simply lack of clinician adherence to monitoring parameters?

AG-induced ototoxicity can cause irreversible cochlear and vestibular toxicity (2). A specific genetic mutational defect is responsible for hearing loss associated with AGs. In contrast, AG-induced vestibular toxicity can occur after 1 dose, during or after completion of therapy, and despite therapeutic AG concentrations. Of equal concern is the fact AG-induced vestibular toxicity often goes unrecognized by physicians and pharmacists (3,4) who incorrectly advise patients that troublesome vertigo or dizziness will dissipate once drug therapy has been completed. For these reasons, patients should be provided with clear and detailed informed consent about the possibility of AG-induced vestibular toxicity before initiation of therapy, when possible. Any patient complaints related to changes in hearing acuity or balance dysfunction is cause for immediate discontinuation of AGs and referral to neurology or otolaryngology physicians to rule out AG-induced vestibular toxicity.

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http://dx.doi.org/10.1016/j.jacc.2017.03.613

Please note: Dr. McGarity has reported that he has no relationships relevant to the contents of this paper to disclose.

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REPLY: Infective Endocarditis, Gentamicin, and Vestibular Toxicity

We are grateful to Dr. McGarity for elaborating on the risks of aminoglycoside therapy as raised in our State-of-the-Art Review (1). Aminoglycoside-induced nephrotoxicity and ototoxicity are potentially preventable causes of harm in patients with infective endocarditis and require increased focus.