Reviewer’s report

Title: The association of spatial T wave axis deviation with incident coronary events. The ARIC cohort.

Version: 1 Date: 28 July 2004

Reviewer: Lennart Bergfeldt

Reviewer’s report:

General

General comment
According to the author and this reader’s opinion this is the 4th large scale attempt to test the prognostic value of the spatial T wave axis. This study focuses on future coronary events. Although I fully understand the authors’ attitude to look at the results from a positive perspective this is basically a negative study. However, this does not make the study less important, and its background deserves some comments.

It is correct that ventricular repolarization abnormalities play an important role for the occurrence of potentially life threatening ventricular arrhythmias, both as trigger and for sustenance of the arrhythmia (substrate). It is equally clear that myocardial repolarization is extremely dynamic and is altered in many conditions, such as in myocardial hypertrophy of any cause, acute ischemia, congenital and acquired long QT syndromes etc. Recent studies (referred to by the authors) have shown that hypertension is accompanied by repolarization abnormalities as reflected by e.g. the QRS-T angle. There is, however, hitherto, very little available information regarding stable coronary artery disease (CAD). Unfortunately, the authors do not take the opportunity to compare the spatial T wave axis in individuals with and without signs and symptoms of CAD in their large cohort. Instead they exclude 790+162 patients with such evidence (page 4, 3rd paragraph) who they could have studied to shed light on the crucial issue of the discriminative power of this parameter. This is a major concern. It becomes even more important to solve this issue because it’s a major point in the comparison of the present study with the positive Rotterdam and CHs studies (page 13, 3rd paragraph).

The shortcomings of the scalar QT interval and its dispersion in relation to CAD are well-known, although this negative attitude probably should be modified in other settings such as hypertension induced left ventricular hypertrophy, and also in the congenital LQTS. So it is perfectly rational to try, as the authors have, other non-invasive techniques for assessing ventricular repolarization both for epidemiological purposes and for monitoring the effects of interventions. The authors have previously presented data in support of a reasonably good repeatability (or rather reproducibility) in healthy individuals (ref. 22). This is important methodological information, which, if included in this report (because it is hitherto only published as an abstract) would strengthen it. It is as important as the quality measures of the ECG recording and analysis procedure. This reader agrees with the statement on page 3, 3rd paragraph, that limited time-dependent variability is a methodological asset, especially when it comes to following interventions. However, if the method cannot separate individuals with a disease from those without the method has no place in population studies. Therefore the first step after showing a good reproducibility should have been to make a comparison as mentioned above between people with and those without the disorder of interest. It is not too late because it can be added as another post hoc analysis. It is, however, also reasonable to do as the authors have done i.e. to test a method which has shown some promise in 2 out of 3 previous studies (ref. 23-25). To this there is no objection.

Based on the studies of hypertensive patients (ref. 18-19) it would have been perfectly rational to hypothesize that hypertension would have a significant – confounding - impact, and it is unclear why the authors didn’t include this issue as one secondary objective. They definitely confirmed its
importance, which could be stressed. My basic criticism of this manuscript is, however, that the authors do not apply as critical an attitude towards the spatial T wave axis as at least one of them have criticized QT dispersion (ref. 3-4). In fact the spatial T wave axis is not only reconstructed from the ECG instead of constructed from a anatomically 3-dimensional vectrocardiographic recording e.g. according to Frank, overcoming some of the limitations correctly discussed on page 15, 1st paragraph, but only and probably more importantly it is only a measure of direction and therefore at least for theoretical reason contains much less information than the T wave vector or vector loop, as suggested by Badilini et al. referred to by the authors (ref. 13). Again and having presented this criticism I find it perfectly reasonable to use what has been collected by enormous and well appreciated efforts when collecting this important database.

When assessing the value of a procedure or test in qualitative rather than quantitative terms a scale of “mild, moderate, and severe/strong” is accepted. In the first part of the Discussion the authors use “modestly” to describe the predictive value of the spatial T wave axis assessed according to the authors. I firmly believe that the authors have data to prove that is not a useful parameter neither on the group nor on the individual level (and in fact we treat individuals). They would best serve the scientific community by stating that this parameter should be put aside, and that the attention should be directed towards the evaluation of other potential non-invasive measures of ventricular repolarization, which we badly need.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
Rewrite the manuscript in line with the basic criticism. Page 2, 4th paragraph: The conclusion should be rewritten.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
Page 6, 2nd paragraph: The method for measuring the QT interval should be included.

Page 9, 1st paragraph: It is unclear why the authors at this point introduce “the mean T wave axis in the frontal plane”. If no clear reason can be provided it should be deleted.

Page 9, 3rd paragraph: The writing in this paragraph gives the impression that age and height have any impact on the T wave axis, while Table 1 seems to imply that weight is what matters. This should be clarified.

Page 13, 2nd paragraph: Was the QT interval measured in the same way in the present and the Rotterdam study? This issue should be clarified.

Page 13, 3rd paragraph: It is stated that CHD was not present in the ARIC and MRFIT studies, although in the same paragraph “subclinical coronary artery disease” certainly exists. It is more than likely that among a population of individuals aged 45 to 64 years, some with hypertension and/or diabetes, there is a significant number of persons with coronary artery disease, a disease that starts already in the teens. Therefore both the methods and this part of the discussion should be modified with regard to the ARIC population. My understanding is that in this study of the ARIC population there were no clinical or ECG evidence of coronary artery disease. This issue should be clarified.

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Discretionary Revisions (which the author can choose to ignore)
Page 6, 1st paragraph: The spatial T-wave axis is neither a well established nor an intuitive parameter and should be described in more detail, because it is the main method of the study.

Page 15, 1st paragraph: The authors would find support for their results also from
vectorcardiographic analysis with Frank leads. In a comparison of CAD patients and healthy controls the T vector axis assessed as T azimuth and T elevation could not separate the groups. (Rubulis A, Jensen J, Lundahl G, Tapanainen J, Wecke L, Bergfeldt L. T vector and loop characteristics in coronary artery disease and during acute ischemia. Heart Rhythm, in press. Accessible through the Heart Rhythm Society, formerly NASPE).

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

None.