COMMENTS AND RESPONSES

Prediction of Mortality Using Measures of Cardiac Autonomic Dysfunction in the Diabetic and Nondiabetic Population: The MONICA/KORA Augsburg Cohort Study

Response to Salvi et al.

We thank Salvi et al. (1) for their interest in our study (2). While there is no doubt that a number of diseases and drugs may contribute to corrected QT (QTc) interval prolongation, cardiac autonomic neuropathy (CAN) has been identified as one of these contributing factors. CAN is 2.3 times (95% CI 1.9–2.7) more likely to be present in diabetic patients with than in those without QTc prolongation (2). Recently, a reasonable sensitivity of 76.5%, specificity of 75%, and positive predictive value of 81.3% of QTc prolongation for the diagnosis of CAN were reported in type 2 diabetic patients (3). In a population-based study, diabetic patients with QTc prolongation but without prior physician-diagnosed heart disease had a threefold increased risk of primary cardiac arrest after accounting for autonomic and electrocardiogram characteristics (4), suggesting that risk stratification by measurement of the QTc interval may be useful in subjects with diabetes.

Because the prevalence of CAN increases with the severity of peripheral neuropathy (5), a concomitant QTc prolongation and reduction in heart rate variability (HRV) would be expected. Therefore, it is surprising that such a gradient was not seen in the studies by Salvi et al. for both QTc (6) and HRV in diabetic patients with and without peripheral neuropathy. However, it remains unclear how peripheral neuropathy was defined and assessed in their study. Moreover, possible selection bias cannot be excluded, as these patients originated from two phase II studies.

We disagree with the view of Salvi et al. that defining a cutoff value for HRV would have made our observations clinically more relevant. We have not defined abnormal ranges for the measures of HRV used in our study because we computed HRV from relatively short 20-s resting electrocardiogram recordings for epidemiological purposes rather than for the use clinical practice. However, we previously demonstrated that 22% of type 2 diabetic patients have definite CAN (7). Thus, using the lowest quartile is compatible with the expected percentage of HRV abnormalities.

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DOI: 10.2337/dc08-1136

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