ment when they surely must have their own variability data? The claim that the differences seen in this study were greater than the variability published earlier gives the impression that readers are asked to accept apples and oranges as identical.

The third is relevance. The study reports values of QTc dispersion without QT duration, QT dispersion, and heart rate. Despite some probably appropriate criticism, Bazett's formula indicates that the duration of the QT interval depends on the heart rate. However, we fail to see why QT dispersion should depend not only on heart rate but also on the duration of QT interval in the same mathematical way. Heart rate itself is an important prognostic indicator in coronary artery disease.[5] If the authors were dealing only with measurement inaccuracy and effectively measuring not QTc dispersion but a random error (identical in all patients), the same results would still be achievable because in patients with faster heart rate this measurement error would be "corrected" into a higher "QTc dispersion." In other words, reporting QTc duration and dispersion without mentioning QT interval and dispersion and heart rate is as insufficient as reporting training induced changes in exercise capacity without describing subjects' physical state and age.

To summarise, the use of QTc dispersion in inappropriate situations makes the potential utility of this measure more complicated, especially if accepted prognostic indicators and serious technical problems and problems with data analysis are ignored.

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1 Darbar D, Luck J, Davidson N, Pringle T, Main G, McNeill G, *et al.* Sensitivity and specificity of QTc dispersion for identification of risk of cardiac death in patients with peripheral vascular disease. *BMJ* 1996;312:874-9. [With commentary by R Campbell.] (6 April.)
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QTc dispersion and vulnerability to ventricular fibrillation

EDITOR,—Dawood Darbar and colleagues report that QTc dispersion has a high degree of sensitivity and specificity for predicting cardiac death in patients with peripheral vascular disease.[1] In the accompanying commentary R Campbell expresses concern that, although it is an extremely useful non-invasive marker to identify patients at increased risk of cardiac death, protective strategies are extremely limited.[1]

Ischaemic preconditioning is one of the most powerful protective mechanisms in human myocardium.[2] Recent reports suggest that preinfarction angina improves inhospital mortality and the electrical stability of myocardium through the induction of ischaemic preconditioning.[3] We therefore investigated the association between acute myocardial infarction and QTc dispersion in 35 patients with or without preinfarction angina. All patients were admitted within six hours of the onset of symptoms and underwent coronary angiography 90 minutes after intravenous thrombolysis. Preinfarction angina was defined as new onset or worsening angina seven or less days before acute myocardial infarction. QTc dispersion was calculated from 12 lead electrocardiography on hospital admission and 24 hours later. Heparin treatment resulting in an activated partial thromboplastin time between two and three times the control value was continued for 24 hours. Preinfarction angina was reported in 16 patients.

Age, sex, delay in treatment, reperfusion time, and patency of the infarction related coronary artery at 90 minutes was similar in patients with or without preinfarction angina. However, QTc dispersion was less in the electrocardiogram on admission in patients with preinfarction angina (43 (15) ms) than in those with no preinfarction angina (77.3 (20) ms, P = 0.001). At 24 hours, this trend persisted between the two groups (62 (22) ms *v* 71 (22) ms, P = NS). The results show preinfarction angina is associated with reduced QTc dispersion, and this protection may be conferred by ischaemic preconditioning. Furthermore, ischaemic preconditioning has also been shown to reduce the incidence of ventricular arrhythmia in patients with acute myocardial infarction.[3]

As pointed out by Darbar and collleagues,[1] these studies show that strategies to reduce QTc dispersion and improve electrical stability of the myocardium are possible. In future, we may be able to use preconditioning mimetic agents to improve patient prognosis.[4]

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QTc dispersion also occurs in diabetes

EDITOR,—Dawood Darbar and colleagues showed a strong link between QTc dispersion and cardiac death in patients with peripheral vascular disease.[1] Their results have great importance because the risk of sudden unexpected death could easily be evaluated by a simple and non-invasive method. QTc dispersion was associated mostly with diffuse coronary disease, suggesting that myocardial fibrosis could be one of the most important causes of electrical heterogeneity leading to fatal arrhythmias. Chronic heart failure, ischaemic heart disease, and hypertrophic cardiomyopathy resulting in QTc dispersion might have a similar mechanism. I should like to add a further clinical condition to the list which perhaps has a different explanation for the QTc dispersion.

Cardiac autonomic neuropathy is a well recognised specific complication of diabetes mellitus. The clinical consequences of autonomic neuropathy include prolongation of the QT interval in diabetic patients.[2 3] It has been suggested that sympathovagal imbalance due to cardiac autonomic neuropathy might have resulted in prolongation of the QT interval in these patients. QT dispersion was also observed in diabetic patients,[4] and QT interval dispersion was an important predictor of mortality in patients with non-insulin dependent diabetes in a recent prospective study.[5] Regardless of the exact mechanism, measurement of QT dispersion could be a cheap but valuable tool for detecting patients at risk of sudden cardiac death, including diabetic patients with cardiac autonomic neuropathy.

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Authors' reply

EDITOR,—We agree with Nicholas J Linker and Adam P Fitzpatrick that a QTc dispersion of 60 $ms^{1/2}$ would be insufficient in clinical practice to alter the management of a patient with peripheral vascular disease. However, we chose this cut off point because it had optimal sensitivity and specificity in predicting cardiac death and was based on the receiver operating characteristic curve. All cut off points are artificial to some extent and highly dependent on the population studied. The risk of cardiac death is likely to increase as QTc dispersion increases, but our study was too small to show this. Clearly, a QTc dispersion of >100 $ms^{1/2}$ is much more meaningful in clinical practice and should alert a clinician to consider investigations and treatments in a patient. One further point that should be noted is that the QTc dispersion in the survivors (56.5 (25.4) $ms^{1/2}$) was in the same range as that established for healthy subjects in the study by Sylven *et al* (54 (27) $ms^{1/2}$).[1] In contrast, patients who died of probable cardiac causes showed a substantially greater and significant increase in QTc dispersion (86.3 (23.9) $ms^{1/2}$).

As Krishna Prasad and colleagues point out, the severity of coronary artery stenosis in patients with peripheral vascular disease influences prognosis. The crucial point is that coronary angiography, which is required to determine coronary anatomy is invasive and not applicable to all such patients. In contrast, QT dispersion is an easily obtained, non-invasive test that may be widely applicable. Nowhere do we claim that QT dispersion is the most accurate test, but it could be the easiest to apply in large populations of patients. In addition, as table 3 shows, there was a non-significant trend towards increased QTc dispersion with increasing severity of coronary stenosis. The mean ejection fraction showed no such association. As for other risk factors, hypercholesterolaemia and smoking were more common in the survivors while hypertension and diabetes were more prevalent in those dying of cardiac causes. QT dispersion and heart rate were not reported due to limitation of space; QT dispersion was significantly prolonged