Can Ventricular Ectopics Save Patients from Sudden Cardiac Death?

Sudden Cardiac Death

Sudden cardiac death (SCD) is a major public health issue accounting for approximately 100,000 deaths in the UK and 400,000 in the USA per annum. The majority of SCDs are caused by life threatening arrhythmias (LTA) namely by monomorphic ventricular tachycardia (VT) degenerating into ventricular fibrillation.

Currently, predicting who is most at risk of SCD is a significant challenge and an area that remains unanswered. Primary prevention through risk stratification currently exists. Primary prevention trials reviewing patients with implantable-cardioverter defibrillator (ICD) therapy based on poor left ventricular ejection fraction (LVEF) showed only approximately a third had appropriate device therapy over 3-5 years follow-up. Conversely, and more worryingly, the majority of SCD victims are not known to have heart disease or have a LVEF of >40%. This demonstrates the difficulty of identifying those at highest risk of SCD.

Ventricular Ectopics

Ventricular ectopics (VEs) are a very common phenomenon described in 1% of the clinically normal population detected on a standard 12-lead electrocardiogram (ECG), and 40-75% of healthy people detected on a 24 or 48-hour Holter ECG. These are usually considered to be fairly benign, however increased frequency and complexity have been described to be associated with malignant arrhythmias particularly in the presence of structural heart disease. The Framingham study and Multiple Risk Factor Intervention Trial (MRFIT) studies suggested a similar correlation in healthy individuals. This was widely criticised for the lack of measures to exclude confounding by underlying heart disease.

Exercise Testing

Studies demonstrate that the subendocardial region of the myocardium is most sensitive to ischaemia in both ischaemic and non-ischaemic cardiomyopathies. This causes interruptions in the electrical conduction within the heart, leading to electrical delays. Consequently, distal activity can feedback and prematurely excite proximal tissue leading to premature VEs. Therefore one would postulate that increased VE during stress such as exercise, can identify those likely to suffer from future malignant arrhythmias. In 2000, Jouven et al. followed a cohort of 6,101 asymptomatic French men and concluded that those with frequent VEs (>10% of ventricular complexes in any 30 second period during exercise) had a 2.67 fold increased risk of cardiovascular death after 23 years. 3 years later, Frolkis et al. followed a larger cohort of 29,244 patients for a mean 5.3 years and demonstrated that frequent VEs during the recovery period of exercise is a better predictor of cardiac events with a hazard ratio of 2.4 versus 1.8 during exercise. In fact, once confounding was accounted for, only frequent recovery VEs were statistically significant with a hazard ratio of 1.5. Inadequate vagal reactivation post stress has been suggested to be the mechanism of arrhythmia formation as vagal activity is known to suppress ventricular arrhythmias. Although, this proposes exercise-associated VEs be used as an additional prognostic factor to ischaemia, it is
particularly difficult to carry out in patients with symptomatic cardiomyopathies. Can we obtain similar information from a resting ECG?

**Holter ECG**

Ruberman *et al.* studied a one-hour Holter ECG from a 1,739 man cohort of survivors of myocardial infarction (MI) for 5 years. The study suggested that the presence of frequent or complex VEs and runs of non-sustained VT during the one-hour recording were associated with around a 4-fold increased risk of sudden cardiac death. Cripps *et al.* describes a stronger association between heart rate variability (HRV) during 24-hour monitoring and risk of SCD with a HRV index of less than 25 corresponding to a 7-fold increased risk of SCD. Gallagher *et al.* had tested the use of VE QS interval (VEQSI) when examining 24-hour Holter ECGs to 2,332 patients of an unselected population and found that a large VEQSI duration (>170ms) predicts the presence of structural heart disease with a sensitivity of 41% and specificity of 83%. The number of VE morphologies predicts all-cause mortality with a 32% increased risk per additional morphology (p=0.02).

Most recently, Bastiaenen *et al.* studied a cohort of 189 patients with ischaemic heart disease. They demonstrated that the maximum VEQSI on 24-hour monitoring was longer in post MI patients suffering VT/VF (214±20ms) compared to normal patients (177±22ms; p<0.001). Additionally, a maximum VEQSI of >198ms gives rise to a 96% negative predictive value.

**Conclusions**

VE markers have shown to be useful at predicting malignant arrhythmias; be it on standard 12 lead ECG, exercise tolerance testing, or 24-hour Holter ECGs. Malignant arrhythmias are more likely to occur in patients with cardiomyopathies. The challenge lies in using these simple markers in identifying those patients with cardiomyopathies that are most vulnerable to SCD. VEQSI max described by Gallagher *et al.* and Bastiaenen *et al.* is the most recent variable to arise that not only can potentially predict risk of LTA, but also can identify patients with cardiomyopathies; even in the absence of symptoms. Another study carried out by Bastiaenen *et al.* showed that VEQSI max was a strong diagnostic predictor of ARVC even in the concealed phase, in the absence of visible fatty-fibrous deposits on cardiac magnetic resonance imaging. Although, large prospective studies are required to further assess the use of VEQSI max in risk stratification, it is currently a promising marker that is inexpensive and can potentially be used to save patients from SCD with early identification and appropriate device therapy.

**References:**


