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Cardio-Electrophysiological Balance Index in Cardiovascular Diseases

Abstract

More information regarding ventricular arrhythmogenesis is provided by the heart's electrophysiological balance index (iCEB) than other electrocardiography (ECG) indices, such as ventricular repolarization (VR) (QT, corrected QT [QTc], etc.). Malignant ventricular arrhythmia has been linked to iCEB. Drug-induced arrhythmias have been linked to a novel risk marker known as the iCEB (QT interval divided by the QRS duration), which was recently tested in an animal model. The effective refractory time (ERP) multiplied by the conduction velocity was assumed to be the cardiac wavelength iCEB, and an increase or reduction in iCEB might indicate an increased risk of VT/VF caused by TdP or non-TdP. One of the most often used methods for assessing the cardiac waveform is iCEB (QT/QRS). Increases in iCEB are associated with TdP, whereas decreases in iCEB are associated with non-TdP mediated VT/VF. Since it is noninvasive and easily measured, iCEB may serve as an indicator of arrhythmia risk.

Keywords: cardiac wavelength, effective refractory time, electrocardiography, index of cardio-electrophysiological balance

Introduction

Sudden cardiac mortality from drug-induced arrhythmias, heart illness acquired over time, or a genetic predisposition to the condition is hard to predict. There is currently no risk marker that is comprehensive, straightforward to quantify, and widely accessible. Arrhythmia risk may be assessed by measuring the QT interval, an ECG indicator of action potential length [1]. TdP (torsades de pointes, VT or VF in the setting of prolonged QTc) may be diagnosed by looking at the length of the QT interval, which is often used to identify those who are at risk of developing VT or VF. QTc alone cannot identify patients at risk of developing nontorsadogenic VT/VF, underscoring the need of other biomarkers [2].

An important element in ventricular arrhythmias, the invasive electrophysiological (EP) technique of measuring the cardiac wavelength, is the iCEB (EP). According to previous studies, iCEB might be a simple way to detect people who are at higher risk of developing an arrhythmic rhythm [2]. Recent studies have shown that the iCEB (index of cardio-electrophysiological balance) may be used to predict the development of drug-induced ventricular arrhythmias [3].

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The QT interval divided by the QRS duration (QT/QRS) is used to calculate it. Non-invasive iCEB measures the risk of drug-induced ventricular tachycardia. Repolarization dispersion and aberrant conduction velocity are significant indicators in the etiology of arrhythmia and may be used to detect anomalies in the action potential's repolarization and depolarization phases. Cardiac wavelength λ (λ = effective refractory period (ERP) × conduction velocity) has been shown to be linked to arrhythmias of the malignant kind. Several investigations have shown this correlation. An animal model was utilized by Aidonidis et colleagues to explore ventricular tachycardia and atrial fibrillation (AF) [4].

Animal studies have shown a correlation between the QT interval and the ERP, as well as between changes in the QRS duration and changes in conduction velocity [3]. Robyns et al [2] recently shown that the ERP recorded invasively during EP investigation corresponded with the QT interval. According to the research, the iCEB (QT/QRS) and the cardiac wavelength – ((ERP – conduction velocity) – are similar since they both measure the repolarization and depolarization of action potentials.

iCEB and iCEBc parameters in cardiovascular disease were examined for the first time, to the best of our knowledge. Determining the risk of proarrhythmia may be as easy and noninvasive as checking for changes in the cardiac action potential's balance (iCEB and iCEBc), which measures the ratio of depolarization to repolarization in the heart. We wrote this review to highlight the link between these alterations in electrophysiology and ventricular arrhythmias.

Malignant arrhythmias

Changes in iCEB levels may be a predictor of greater vulnerability to malignant ventricular arrhythmias. TdP was seen in rabbit ventricular wedge samples after the treatment of dofetilide, an IKr blocker, which enhanced the QT, Tp-e intervals and iCEB [3]. Encainide, an INA blocker, had no influence on QT or Tp-e intervals, but it did diminish iCEB levels and cause VT that was not TdP-like, according to the research. That iCEB can predict drug-induced non-TdP like ventricular arrhythmia better than Tp-e and QT intervals. If you have a paroxysmal supraventricular arrhythmia, you should avoid sotalol because it raises iCEB and flecainide because it reduces iCEB [2].

LQTS patients had considerably higher levels of iCEB and iCEBc compared to their genotype-negative relatives, but BrS patients have much lower levels of iCEBc. LQTS

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patients were shown to have a greater iCEB, which was linked to a longer QT interval. By inhibiting IKr, class III drugs raise phase 3 of the action potential and ERP [5].

QT interval lengthens as a result of loss of slow (IKs) or fast (IKr) IK function in LQTS [6]. The blocking of fast Na+ channels may reduce the iCEB (QT/QRS) in the treatment of class IC medicines. Reduced sodium current is the primary cause of iCEB decrease in BrS, which results in the dysfunction of the cardiac sodium channel. It follows that phase 0's upstroke velocity reduces [7]. As the surface ECG shows, this results in an extended QRS [2].

Amiodarone had the greatest Tp-e and iCEBc values in the Afsin et al. research, whereas propafenone had the lowest Tp-e and iCEBc values. iCEBc values for patients with TdP-mediated VT and those with non-TdP-mediated VT were also significantly different. If these alterations in electrophysiology are linked to ventricular arrhythmias, more research is required. The iCEB readings of amiodarone patients were also comparable to those of healthy controls. It is possible that the QT/QRS ratio will not be changed since amiodarone is a multiple ion-channel blocker. As cardiac wavelength () is equivalent to iCEB, this parameter may be used to detect abnormal heart rhythms. The iCEB and iCEBc durations are increased by antiarrhythmic drugs (AADs) that lengthen the QT interval, while the iCEB and iCEBc durations are lowered by AADs that prolong the QRS duration. Because of this, iCEBc lengthening and shortening may indicate an elevated risk for malignant arrhythmia (figure-1) [8].

Data on cardiac wavelength as a risk stratifier is few in vitro because of the difficulty in measuring it [9,10]. These restrictions necessitated the development of the "ICEB" (QT/QRS) as an easily measured, local approximation of cardiac wavelength. QRS duration, in absence of a clearly defined bundle branch block, is often inversely related to cardiac conduction velocity [7]. The QT interval and ERP have been linked since the 1970s, when the first studies were conducted. QT and ERP had comparable impacts on increased right ventricular pacing rates during EPS in Guss and colleagues, but no formal association test was done [11].

Olsson et al. [12] found similar findings when they plotted QTc vs ERP in 14 individuals and found "a definite but weak link," but no formal association test was conducted. There was no statistically significant connection between ERP and the uncorrected or rate adjusted QT interval in 19 healthy canines by Voss et al. [13]. Over the last two decades,

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medication-induced arrhythmia has been the primary focus of drug research in the pharmaceutical sector. It is recommended by current recommendations to do a complete QT clinical research to assess the cardiac risk of new medicines. However, the exclusive use of the QT interval as a risk factor for drug-induced arrhythmias has raised some questions [14]. If a medicine prolongs the QT interval, it doesn't always mean that it's going to cause ventricular arrhythmias [15]. Because of this, new or improved risk indicators are being sought.

In contrast to other putative risk indicators like Te-Tp, which is only raised in LQT2, iCEB is considerably greater in LQTS patients, regardless of genotype [16]. Because of this, it's still a mystery why LQTS and sotalol-treated patients with increased iCEB (or) were more likely to develop TdP, whereas BrS and flecainide-treated patients with reduced iCEB were more likely to develop ventricular fibrillation. It is likely that these medications' cellular actions and the underlying genetic causes of the particular hereditary heart disease might be the reason of this. Sotalol is a betablocker and a class III antiarrhythmic agent all in one pill. If IKr (the delayed rectifier potassium current) is blocked, then phase 3 of the action potential and ERP are prolonged, resulting in class III features [17].

Defects in either the slow or fast components of delayed rectifier potassium current (LQT1; KCNQ1 gene; IKs) or gain of function of the cardiac sodium channel represented by the SCN5A gene are the most prevalent causes of congenital LQTS (LQT3; SCN5A gene; INa). An increase in iCEB may be the underlying mechanism of action potential duration lengthening. When it comes to sodium channel blockage, flecainide is widely recognized [18]. Patients with (perhaps) pathogenic mutations in SCN5A were included in the BrS group in this investigation, which had a lack of cardiac sodium channel function. For example, SCN5A mutations, as well as therapy with flecainide and BrS, result in decreased sodium channel function, decreased sodium current, and hence decreased upstroke velocity of the action potential [7]. ECG data show an increase in QRS length as a result of this condition. The drop in iCEB is most likely due to this impact on the cardiac sodium channel and action potential [2].

Patients with coronary slow flow (CSF) had considerably higher levels of ICEB and iCEBc, according to Askin et al. The higher QTc time may be to blame [19].

Limitations

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Measurement of the QT interval at the commencement of the EPS technique verified that ERP was measured noninvasively. Under order to correctly quantify T wave amplitude at the conclusion of each QT interval, we used a steady isoelectric line at the beginning of each EPS in resting circumstances [20].

Due to LQTS and BrS's low penetrance and varied expression, one can argue that the notion of increased arrhythmia risk due to a positive genotype is not totally valid. However, it seems that bearers of a harmful mutation that does not manifest any symptoms are at greater risk [21]. iCEB defined as QT/QRS is currently not a rate-independent factor. But even in healthy people, there is some QRS rate dependency (QRS shortening at higher heart rates) [22]. As a result, the influence of heart rate fluctuations on iCEB is reduced. For Class I antiarrhythmic medicines, rate-dependent effects are well-known [18]. A rate-dependent broadening of the QRSduration is proof of this. Bazett's heart rate correction method is less accurate in LQTS and BrS patients because QT rate dependency is extremely individual and is notably affected in these patient groups [23-25].

Conclusion

Finally, we recommend iCEB as the best feasible ECG substitute for and provide data on this parameter for the first time in humans in this preliminary investigation. iCEB rises in the presence of conditions like sotalol usage and congenital LQTS, both of which have been linked to an increased risk of TdP. Flecainide and BrS usage raises the likelihood of non-TdP-mediated VT/VF, as shown by a reduced iCEB. As a result, iCEB may be a universal marker for ventricular arrhythmias since it may identify both higher risk of TdP and nonTdP driven VT/VF. It is imperative that further studies with suitable power be conducted in order to validate our review.

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Figure legends:

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Figure-1: iCEB diagram. The QRS duration and QT interval of cardiac electrophysiology. Changes in the index of electrophysiological balance (iCEB): significant increases/decreases in the QT interval or QRS duration may be proarrhythmic for TdP-mediated and non-TdP-mediated VT/VF (imbalance of cardiacelectrophysiology). VT = ventricular tachycardia; VF = ventricular fibrillation