such as hypokalemia and heart failure, patients with ERP may be at increased arrhythmic risk. Recent studies support the important role of additional proarrhythmic triggers in the pathogenesis of ER, especially in the case of acute myocardial ischemia (2–5). A prospective study composed of patients at high coronary risk could add some robustness to these theses in the event that a higher arrhythmic risk was detected in those with ERP. Moreover, inclusion of low-risk coronary patients only, eventually based on Framingham risk stratification, could help us better evaluate the potential intrinsic arrhythmogenic nature of ER.

Although the authors highlighted that increased transmural heterogeneity of ventricular repolarization may be the mechanism involved, it is of note that some researchers have reported that repolarization abnormality markers, such as T-wave alternans and QT dispersion, do not differ between patients with and without J-waves, whereas the incidence of late potentials (a depolarization abnormality marker) in idiopathic ventricular fibrillation J-wave groups is higher than in non–J-wave groups (6). The contribution of various pathophysiological mechanisms in ER syndrome seems as likely as in the Brugada syndrome.

In the first 2 forest-plots, the I² is more than 90%, illustrating a very high heterogeneity. Interpretation of data arising from pooling of such a heterogeneous group of studies may compromise the overall validity of the meta-analysis. Moreover, the fact that there are no funnel-plots provided makes us wonder about a potential publication bias in this meta-analysis.

Although physicians should be aware of the potential arrhythmogenic role of ERP, there is no evidence to support different primary prevention strategies for patients with ER. Nevertheless, prevention of arrhythmic triggers, such as acute myocardial ischemia, through more aggressive prevention of coronary artery disease might mitigate the apparent association between ER duration and arrhythmic mortality.

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REFERENCES


Reply

The early repolarization pattern (ERP), which is characterized by an elevation of ≥0.1 mV of the QRS-ST junction (J point) with either QRS slurring or notching in the inferior and/or lateral leads on 12-lead electrocardiography (ECG), has recently been associated with vulnerability to ventricular fibrillation in case-control studies. However, the prognostic significance of ERP in the general population remains controversial. We conducted a meta-analysis to summarize all published prospective studies and case-control studies to date on the risk and incidence of cardiac death, arrhythmia death, and all-cause death in the general population with ERP. The results from our meta-analysis showed that ERP was associated with increased risk of arrhythmia death (risk ratio: 1.70; 95% confidence interval [CI]: 1.19 to 2.42; p = 0.003) but not with cardiac or all-cause death. At the same time, we found that the absolute risk differences of the patients with ERP were 70 cases of arrhythmia death per 100,000 patients per year (1).

Although our meta-analysis included large sample sizes, long durations of follow-up, and well-established prospective studies or case-control studies and our pooled estimates were based on prospective analyses with detailed adjustment for confounding variables, there were some limitations. First, the relatively small number of studies limited our ability to identify which subgroups were at higher risk for reported events. Second, the small number of studies also limited our ability to determine whether heterogeneity in summary estimates was explained by factors related to study quality. Heterogeneity among studies was formally assessed using Q and I² statistics, and risk ratios and 95% CIs were pooled in random-effects models in our meta-analysis because of big I² values. Third, we cannot exclude the possibility of patient confounding and publication bias due to miscategorization, although there was no evidence of publication bias (p = 0.22) in the patient risk estimates for arrhythmia death. At the same time, sensitivity analysis in our study showed that none of the individual studies substantially influenced the pooled risk ratios for any of the outcomes.

How the ERP increases the risk of arrhythmia death is unclear. Experimental studies have shown that a prominent transient outward current (I∞)-mediated action potential notch in ventricular epicardium, but not endocardium, causes a transmural voltage gradient during early ventricular repolarization that produces J-point elevation on the ECG. An increase in net repolarizing current, due either to a decrease of inward currents or augmentation of outward currents, accentuates the action potential notch and leads to augmentation of the J-point elevation. The prominent I∞ responsible for the ERP may facilitate the development of ventricular fibrillation (2–5). The genetic basis for ERP remains unclear.

We consider ERP to have a cardiac electrophysiological unstable and potential intrinsic arrhythmogenic nature that increases the
vulnerability to ventricular fibrillation in the presence of some provocative factors. Although primary prevention strategies for patients with ERP are not necessary, it may be important for future researchers to understand the genetic basis and ECG characteristics of the ERP subgroups with a higher risk for arrhythmia death.

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REFERENCES