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EDITORIAL

A heart job: predicting sudden cardiac arrest

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This editorial refers to 'Multiparametric models for predicting major arrhythmic events in Brugada syndrome: a systematic review and critical appraisal' by D. A. Gomes *et al.*, https://doi.org/10.1093/europace/euaf091.

'*It's tough to make predictions, especially about the future*'

Many authors, including Niels Bohr (1885–1962), Nobel laureate in Physics (for his investigations of the structure of atoms), and Yogi Berra (1925–2015), baseball player (and philosopher), are recognized for this famous sentence that should humble us still. This notwithstanding, we keep on trying to do exactly that, making predictions about the future. The weather forecast is already troublesome enough, let alone trying to predict the lightning strike of a sudden cardiac arrest. We are, however, quite experienced in making general assumptions on risk. An excellent example is the recognition in 1997 by Myerburg and colleagues on the high risk of sudden death in patients who had ventricular tachycardia or ventricular fibrillation in the setting of an acute myocardial infarction, after an out of hospital cardiac arrest, or in heart failure with an left ventricular ejection fraction below 30%.[1] It thus seemed reasonable to focus our energy on these patient 'archetypes' to try and prevent sudden death, as the incidence is so high and there possibly is a lot to gain. However, Myerburg *et al.* also indicated that in *absolute numbers*, these previous examples cause relatively few deaths. Much, much more sudden deaths are observed in patients without such clear characteristics. So, if we would want to go for numbers, we should focus on identifying risk outside those 'archetypes', albeit that the incidence of sudden cardiac arrests decreases substantially. Therefore, our aim should be to balance such realizations together with an idea on the potential of (qualitative) life years saved and to which costs (to society and to patients).

Fast forward to 2025. In the past decades, we have gained knowledge on specific patient populations in whom there is a clear risk of a premature sudden cardiac arrest/death due an inheritable arrhythmia syndrome or inheritable cardiomyopathy.[2–4] Importantly, in these syndromes we are often dealing with young patients with many decades of (qualitative) life to aim for: children, adolescents, and young to middle aged adults. In addition, we also know that the largest proportion of these patients will *not* develop malignant arrhythmias. Moreover, we know that physical harm from our interventions (let alone costs for society) can be impressive, and even letal.[5–7] It is not too surprising that not intervening, or intervening with only life style measures or (well titrated) anti-arrhythmic drugs appears to be good practice in experienced hands.[8,9] So, in the past years, we have tried to learn from previous experience and designed numerous risk models for patients with inheritable cardiomyopathies or arrhythmia syndromes, to treat exactly those who need it. Risk models in Brugada syndrome seem to be the pack leader in this field, which actually muddies the waters.[10,11] In this issue of *Europace*, Dr Gomes *et al.*[12] from London, Milan, and Lisbon, share with us their insights on why this is and provide us with lessons for future risk models in inheritable arrhythmia syndromes and cardiomyopathies.

A systematic review and critical appraisal of multiparametric models for predicting major arrhythmic events in Brugada syndrome

The review of Gomes *et al.* was well designed; a thorough bibliographic search with sufficient details provided in the supplementary tables for reproducibility. The quality of the studies was assessed through recognized instruments such as the Critical Appraisal and Data Extraction for Systematic Reviews of Prediction Modelling Studies (CHARMS) & Prediction Model Risk of Bias Assessment (PROBAST) checklists. In the end, they compared 16 studies including 11 unique multivariable scores (the other studies handled replications). A first essential remark is that they found the risk of bias to be high in all studies, and, thus, question the generalizability of these risk models for other cohorts and individual patients. In addition, the number of studies was still quite small (but evaluated >6900 patients), with an intermediate number of events (<600, <10%) and model performance measures were underreported, which further hampers comparisons. In addition, the number of patients and events were much lower in the most difficult patient population: those without previous malignant arrhythmias. This of course also relates to the value of the statistics that are inherent to such studies: wide confidence intervals combined with disputable applicability. This notwithstanding, for patients without previous malignant

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arrhythmia they found pretty good performance for the Brugada-Risk-model[13] [area under the curve (AUC) 0.81, 95% confidence interval (CI) 0.71–0.91; three studies], and fair performance for the Delise-model[14] (AUC 0.77, 95% CI 0.72–0.81, three studies), and Sieira-model[15] (AUC 0.73, 95% CI 0.64–0.82; I2 64%; five studies), all with high heterogeneity though. While the models performed worse than reported in the initial publications, their value still appeared in their (very) good negative predictive value when all risk variables were absent (ranging from 96% to 100%).

Discussion

As hard as risk prediction can be, our patients, their families and our society demand that we do our very best to do a good job. The multiparametric, or multivariable, models that have entered our field are designed for that purpose, but are still insufficient, heterogeneous and ill-validated outside the study cohorts. Moreover, they are not tested prospectively. Of course, we often lack the resources to do so, and there might be other (much more) important subjects for many around the world. Still, Gomes *et al.* elegantly shared with us their valuable insights in these models, which are not only relevant for Brugada syndrome, but also for other disease entities. And if I can make one prediction, we will improve our methodology of future research, with the goal of further improving our clinical tools to identify patients who probably will *and who probably will not* benefit from prophylactic interventions. Multiple groups around the world are currently working in this promise, including ours. The current power of computer modelling should then help us further[16] but will be practically useless when we will not be able to collect the necessary data.[17] Carefully collected and long-term data will be necessary, amongst cohorts from different parts of the world, with different characteristics (including critical elements such as sex and ethnicity[18–20]), with as much detail as possible (e.g. including digital electrocardiograms, raw format imaging, genetics, and homogeneous international definitions). In addition, these risk scores will also need to be reassessed in individual patients over time.

It will be a beautiful job and a heart job.

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Data availability

There is no original data in this editorial.

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