Risk stratification in Hypertrophic Cardiomyopathy

Dr. Andrés R. Pérez Riera

About the risk stratification in HCM, this work is key to the understanding of the subject. In addition, the major risk factors for sudden death in HCM are listed.

O'Mahony C, Jichi F, Pavlou M, et al.; Hypertrophic Cardiomyopathy Outcomes Investigators.A novel clinical risk prediction model for sudden cardiac death in hypertrophic cardiomyopathy (HCM risk-SCD). Eur Heart J. 2014 Aug 7;35(30):2010-20.

O'Mahony et al presented the first validated risk prediction model for SCD e diverse, and well characterized population of patients followed at six different European centers and provides accurate, individualized estimates for the probability of SCD using readily collected clinical parameters. The broad patient inclusion criteria of the study mean that the model can be used in the majority of adult patients with HCM, including those with mild disease identified during family screening. Current clinical guidelines for HCM in the USA and Europe recommend SCD risk algorithms based on a simple summation of a limited number of binary clinical parameters (NSVT, severe hypertrophy, unexplained syncope, family history of SCD, and abnormal BPRE).(**Eur Heart J 2003;24:1965–1991; Circulation 2011;124:2761–2796**.) Even though this approach has been used in clinical practice for more than a decade, it provides only a very crude estimate of relative risk of SCD and fails to account for the different effect size of individual risk factors. (**Heart 2013;99:534–541**.) Moreover, some risk factors such as hypertrophy are considered as binary variables when in fact they are associated with a continuous increase in SCD risk. (**Lancet 2001;357:420–424**.) As a result, existing algorithms have a low positive predictive accuracy for SCD that results in the unnecessary treatment of patients who are at intrinsically low risk. .(**Heart 2013;99:534–541**.) The usefulness of this model lies in providing accurate prognostic information that aids clinical decision making. The model achieved this by showing good agreement between the predicted and observed hazards of SCD and by demonstrating the ability to separate patients with regard to their 5-year risk of SCD.(**Steyerberg EW. Clinical Prediction Models. A Practical Approach to Development, Validation and Updating, 1st edn. New York: Springer Science+Business Media; 2009.**) The C-indices indicated that the proposed risk prediction model has superior discrimination compared with the model of conventional risk factors used in contemporary clinical practice. The sensitivity analysis demonstrated that the relationship between the predictors and SCD remains unchanged with the inclusion of

center in the model and the risk model without center is proposed for general clinical use. The risk prediction model has the potential to improve the management of patients with a solitary and multiple risk factors by simultaneously reducing unnecessary and potentially harmful ICD implants in patients who do not suffer SCD and correctly identifying the majority of those who suffer SCD and are most likely to benefit from an ICD. Currently, patients without conventional risk factors are reassured and reassessed and are not routinely offered ICD therapy. However, approximately one-third of all SCD come from this subgroup of patients, and contemporary management strategies fail to address this problem. The risk prediction model may help identify a small proportion of SCD in this group which represents an improvement when compared with current clinical practice, but the performance of the model in this patient subgroup is not optimal. The probability of SCD at 5 years is derived from a range of readily available clinical parameters, each with a unique contribution to risk. For example, consider the management of two patients with NSVT, maximal wall thickness of 23 mm, and LA diameter of 44 mm. One is aged 24 years with a resting LVOT Gmax of 64 mmHg and the other is 64 years old with an LVOTG max of 36mmHg.Current guidelines treat these two patients identically as they each have a single risk factor (NSVT). By applying the clinical risk prediction model in this clinical this level of risk might have different implications in an otherwise well 20-year-old compared to a 70-year-old patient with significant comorbidity. When deciding on device treatment, physicians and patients have to balance the benefits of protection from SCD against the potential hazards of therapy. Approximately one-third of ICD recipients experience implant complications or inappropriate shocks after 5 years, and while the majority of ICD-related adverse events are not life threatening, they often require hospitalization and additional invasive procedures.(***Heart 2012;98:116–125***.) In addition, the impact of ICD therapy on employment, driving, and recreational activities has to be considered. Ultimately, the decision on treatment rests on the relative weightsof the risks and benefits of ICD therapy in individual patients. **Steyerberg EW. Clinical Prediction Models. A Practical Approach to Development, Validation and Updating, 1st edn. New York: Springer Science+Business Media; 2009.**

Risk factors associated to sudden death in HCM and conditioning factors for a worse prognosis

Risk markers used to assess the magnitude of risk

- Ø Extreme increase of septal thickness: extreme left ventricular (LV) hypertrophy (> 30 mm) in young patients
- Ø Very increased estimation of myocardial mass
- Ø Progression of the disease to LV wall thinning and decrease of EF
- Ø History of recovery from SCD
- Ø Recurrent syncope in young people

Ø Unexplained (not neurally mediated) syncope, particularly in young patients

Ø Nonsustained ventricular tachycardia in Holter electrocardiographic recording

Ø Significant bradyarrhythmia or concealed conduction

Ø Blood pressure decrease or inadequate increase during upright exercise.

Ø Hereditary genetic defect, associated to unfavorable prognosis.

Ø Multiple risk factors convey a definite increase in risk. However, a single risk factor such as family history of multiple sudden deaths, massive LV hypertrophy in a young patient, or frequent and/or prolonged runs of nonsustained ventricular tachycardia on Holter, may also justify consideration of a prophylactic ICD.

Ø **Type I HCM:** with genetic alteration with mutations in locus 1q of the long arm of chromosome 14, which alters the heavy chain of cardiac b-myosin (b-MyHC), high penetrance, severe hypertrophy and sudden cardiac death present in approximately 50% of affected patients.

Ø The locations Arg403 (substitution of the amino acid arginine by glycine in position 403), Arg453Cys (substitution of the amino acid arginine by cysteine in position 453), and Arg719Trp (substitution of the amino acid argynine by tryptophan in position 719) are considered malignant.

Ø **Type II HCM:** (15%) alteration in chromosome 1: locus 1q3. It modifies cardiac troponin T (cTnT). These patients present little hypertrophy and high arrhythmic mortality in young people under 30 years old. To this moment, 8 mutations have been described.

Ø **Note:** in patients in whom a genetic diagnosis has been made of malignant form, even in absence of symptoms and hypertrophy, implantable cardioverter defibrillator is indicated.

Ø Atrial fibrillation;

Ø Presence of NS-VT in Holter in patient with alteration of conscience;

Ø S-VT induction in electrophysiological study;

Ø History of associated infarction;