

Heartbeat: can cardiogenetics reduce adverse events due to catecholaminergic polymorphic ventricular tachycardia?

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Catherine M Otto 

A genetic diagnosis is of increasing importance in prevention of adverse events in patients with cardiovascular disease.¹ For example, catecholaminergic polymorphic ventricular tachycardia type 1 (CPVT1) is usually due to a pathogenic variant in cardiac ryanodine receptor 2 (RYR2) and is inherited in a familial autosomal dominant pattern, but sporadic cases also have been reported. In this issue of *Heart*, Shimamoto and colleagues² compared 24 probands with familial inheritance of CPVT1 to 58 patients with de novo variants. In both groups, almost ½ the probands presented with syncope or cardiac arrest before a genetic diagnosis was known. Symptom onset occurred earlier in those with a de novo variant compared with those with familial inheritance (figure 1). In addition, symptoms occurred in only 37.5% of genotype-positive parents versus 66.7% of siblings with the pathogenic variant. The authors conclude: 'Because two-thirds of the genotype-positive parents were asymptomatic and inheritance could not be predicted by their symptoms, genetic screening of parents and siblings in all CPVT1 cases may enable early diagnosis and prophylactic therapeutic intervention to prevent sudden cardiac death.'

In the accompanying editorial,³ Postema and van der Werf point out that although CPVT is rare, with an estimated prevalence of 1 in 10 000 individuals, this arrhythmias syndrome is a cause of sudden cardiac death in children and young adults who are otherwise healthy (figure 2). They conclude that this study provides 'new insights in CPVT showing that de novo pathogenic or likely pathogenic RYR2 variants are of very common occurrence in CPVT, often locate to the RYR2 C-terminus, and that these associate with a more malignant CPVT phenotype. In addition, this study once again shows that national and international collaborations are essential to perform valuable studies

in such rare and malignant arrhythmia syndromes.'

In this issue of *Heart*, the joint British Societies guidelines⁴ for cardiac multidisciplinary team meetings (MDMs) are published online and accompanied by an summary editorial by Lindman and Goel.⁵ MDMs are recommended for patients being considered for myocardial

revascularisation, aortic valve disease, mitral and tricuspid valve disease and endocarditis. Many patients can be rapidly triaged by the MDM but some will require detailed review. Ideally, MDMs should be virtual (or hybrid) to include all members of the team and allow participation by referring clinicians. The principles of patient-centred

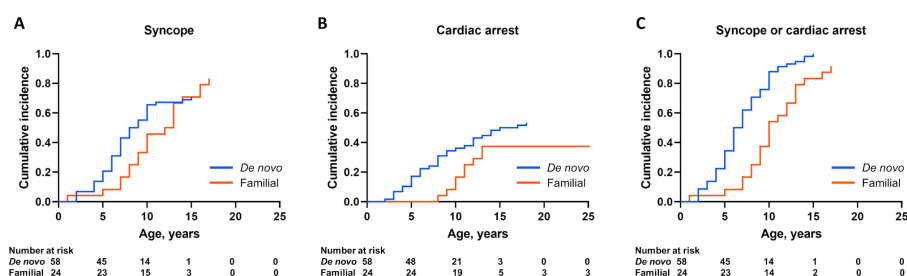


Figure 1 Cumulative cardiac incidence before diagnosis of CPVT in probands with RYR2 variants. Cumulative cardiac events of first syncope (A), first CA (B) and any of the first cardiac event (C) in probands harbouring RYR2 variants inherited from the parent or those with de novo cases. CA, cardiac arrest; CPVT, catecholaminergic polymorphic ventricular tachycardia.

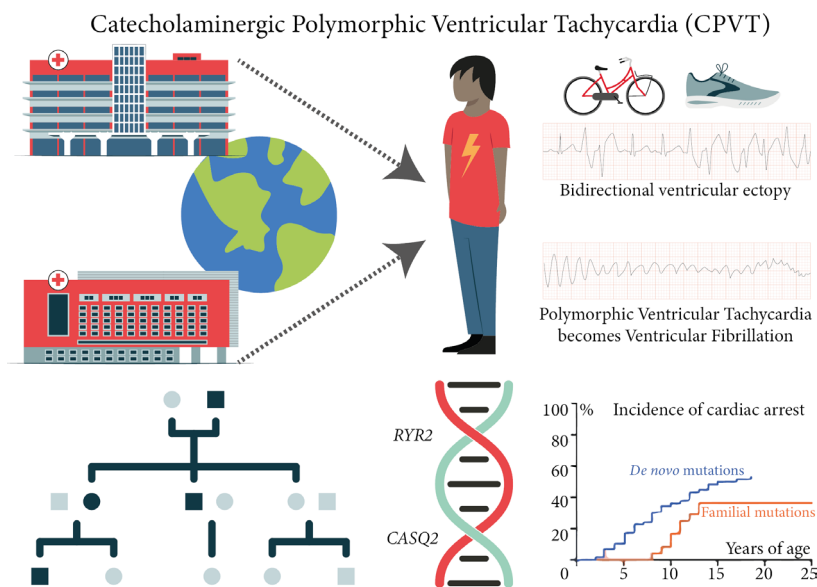


Figure 2 Overview of CPVT. Illustrated are the international collaborations (shown by the hospitals and globe) that are essential to perform valuable studies in a rare and malignant arrhythmia syndrome where catecholaminergic triggers such as exercise may result in bidirectional ventricular ectopy and potentially in polymorphic ventricular tachycardia and ventricular fibrillation. CPVT may well inherit in families but there is an important number of patients with de novo mutations. Importantly, it appears that patients with de novo mutations have a worse outcome compared with patients with familial mutations (survival curve illustration adjusted from Shimamoto and colleagues (2) in this issue of *Heart*). CPVT, catecholaminergic polymorphic ventricular tachycardia.

Division of Cardiology, University of Washington, Seattle, Washington, USA

Correspondence to Professor Catherine M Otto, Division of Cardiology, University of Washington, Seattle, WA 98195, USA; cotto@uw.edu

British Society Recommendations

Heart Team Multidisciplinary Evaluation

Myocardial Revascularization	Aortic Valve Disease	Mitral and Tricuspid Valve Disease	Endocarditis
<p>Rationale</p> <ul style="list-style-type: none"> Rapid evolution of treatment options and guidelines Disease complexity and concomitant disease may influence treatment options and approach Optimal treatment approach (transcatheter, surgical, hybrid) requires multidisciplinary expertise Informed and shared decision making requires that the patient be informed with accurate and up-to-date information on treatment approaches and risk/benefits 	<p>Key Principles</p> <ul style="list-style-type: none"> Single, disease-specific, point of entry rather than referral to an individual surgeon or cardiologist ("one front door") All relevant expertise (transcatheter, surgical, cardiac imaging, clinical) informs the evaluation Multidisciplinary meetings are the focal point of the review process Clear documentation of the decision-making process and rationale for it Joint clinics (staffed by cardiologist and surgeon) can be very useful in the evaluation of patients Flexibility in the review process is needed to accommodate review of elective and non-elective cases The patient must be informed of all treatment options with their goals and preferences elicited for shared decision making 	<p>Anticipated process variation</p> <ul style="list-style-type: none"> The process by which key principles are implemented in different countries and regions will be influenced by resources and personnel available and healthcare system and policy Core members of the heart team may vary based on the availability of personnel and certain types of procedures Whether and when (before or after an MDM) patients are seen in a joint clinic may depend on several factors How referring providers and/or centers are linked to tertiary centers for MDMs What testing is done at the referring versus tertiary center 	

Heart Team Multidisciplinary Meetings (MDMs)

- MDM is a meeting of members of the multidisciplinary team convened for the purpose of reaching consensus on the optimal management of a particular patient
- MDM chair (senior clinician) is critically important to the effective functioning of the meeting
- MDM coordinator is responsible for which patients are discussed and when, documenting discussion, and communicating decisions to others
- Participation in the meeting should be open and encouraged and attendance of core members recorded; core members will differ depending on the disease focus
- Complex decisions or those for which there is equipoise require prioritized discussion
- A minimum dataset (e.g., history, relevant diagnostic testing, cardiac imaging) should be available for review to inform discussion and decision making
- MDMs for elective cases should occur at least weekly and a mechanism should be in place to allow for ad hoc or daily MDMs to address urgent cases
- Output of the MDMs should be clearly documented and communicated to relevant parties
- A feedback and auditing process should be in place to evaluate, refine, and improve team decision making and processes

Figure 3 Overview of the British Societies' recommendations for multidisciplinary Heart Team evaluation and meetings.

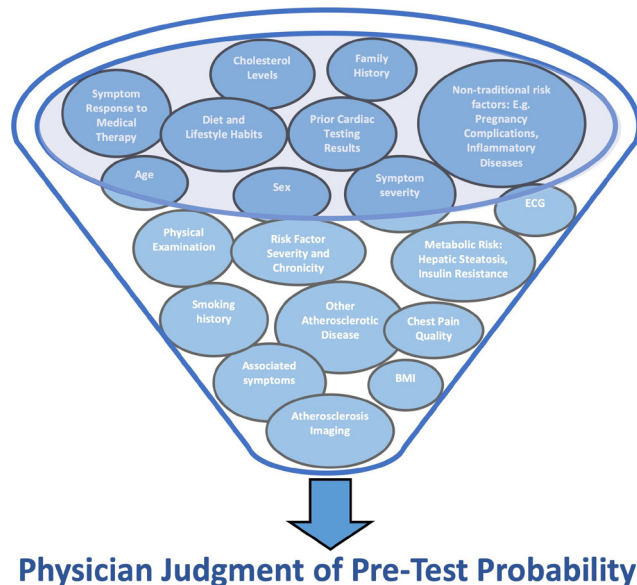


Figure 4 Clinical input for physician estimation of pretest probability of obstructive coronary artery disease in patients with stable chest pain. BMI, body mass index.

care and shared decision making are core to the MDM process, which should be documented in the medical record. As Lindman and Goel⁵ conclude: 'With a multidisciplinary Heart Team evaluation now widely recommended and

no longer a novel concept, the British working group has provided helpful guidance for how the Heart Team does its work. Other countries should follow suit in a way that incorporates regional particulars relevant to the optimal

implementation of foundational principles (figure 3). And, in all locations, further studies and efforts are needed to refine, update and disseminate best practices in multidisciplinary Heart Team evaluation motivated by the overarching objective to treat the right patient at the right time with the right therapy.'

Adding to the evidence that aortic stenosis (AS) is more common than previously recognised, Stewart and colleagues⁶ report data from Australia on over 90 000 men and women with a mean age about 60 years who had two echocardiograms at least 2 years apart. Overall, 6.9% developed AS within 5 years. In addition, there was a higher risk of all-cause mortality with any degree of AS, ranging from 1.42-fold for mild AS to 2.27-fold for severe AS (median follow-up 7.7 years), emphasising the importance of periodic surveillance once AS is diagnosed.

Despite the wide-spread use of numeric scores to estimate risk in patients presenting with chest pain, we should not underestimate the value of physician judgement. In an analysis of 4533 patients from the PROMISE (Prospective Multi-center Imaging Study for Evaluation of Chest Pain) Trial, Fordyce and colleagues⁷ found that physician risk estimated correlated poorly with Diamond-Forrester and European Society of Cardiology (ESC) pretest probability (PTP) estimates. However, only the physician estimates were associated with a higher incidence of adverse cardiovascular outcomes. Villines and Weber⁸ suggest it is 'time to move on from pretest probably scores for stable chest pain' (figure 4). As they succinctly conclude: 'In the future, it is likely that artificial intelligence will improve PTP estimates, harnessing the sizeable amount of clinical and imaging information available on many patients. For now, we believe that the field of cardiovascular medicine should consider moving beyond rigid pretest probability approaches that anchor primarily on age, sex and classifications of angina typicality and trust the power in physician judgement.'

The *Education in Heart* article⁹ in this issue provides an overview of cardiac resynchronisation therapy (CRT) including indications, effect on clinical outcomes, and optimisation of patient benefit. They conclude that although biventricular CRT provides benefit in heart failure patients with a wide QRS due to left bundle branch block, CRT has a less clear role with other QRS morphologies. Alternate approaches under investigation include delivering CRT via the His or left bundle to provide conduction system pacing.

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ORCID iD

Catherine M Otto <http://orcid.org/0000-0002-0527-9392>

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