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A dynamic risk management approach to reduce harm in hypertrophic cardiomyopathy

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ABSTRACT

Hypertrophic cardiomyopathy (HCM) is thought to be a leading cause of sudden cardiac death (SCD) in athletes, and while SCD is the most dramatic and feared of all HCM presentations, its exact incidence remains unclear. Current expert opinion and consensus panels that formulated exercise recommendations in HCM to reduce the risk of sudden death by avoiding competitive sport are based on scant, observational, often circumstantial, and sometimes conflicting evidence. These recommendations rely on multiple cross-referencing of few original papers from a limited number of research groups. At the same time, there is accumulating data that recommendations to avoid competitive exercise in HCM come at the price of avoidance of all physical activity which carries its own risks and complications. Consequently, physicians are challenged when asked by concerned parents and children to justify overly restrictive clinical judgements and guidance about permitted exercise levels in HCM. In this manuscript, we review the strength of the evidence underlying current sport recommendations in HCM. We propose that developing a working risk management approach to assist anxious parents and children is imperative and must be customized to the needs of the child and their parents. Rather than a blanket recommendation to avoid competitive sport, we believe that HCM patients deserve to have a robust and real-world risk assessment strategy that is tailored to the individual needs, discussed with the child and their parents, and updated as the child grows and matures.

1. Risk Management Approach Towards HCM

When parents of children with HCM seek medical care, they entrust their health and wellness to us. While life expectancy is generally good in hypertrophic cardiomyopathy (HCM), premature mortality can occur unexpectedly via three modes: heart failure, stroke and sudden cardiac death (SCD). Of these, SCD is the most dramatic and feared of all presentations, especially as it occurs seemingly without warning in young, healthy appearing, and athletic individuals. The response to these rare events is often further fueled by sensationalist media attention. The hypothesized mechanisms underlying SCD in HCM are diverse and powerful, including arrhythmia, ischemia and hemodynamic mechanisms, but none are specific and all are unproven [1]. So, have we really made significant progress in better understanding the 'interlocking factors' that lead to SCD in HCM?

Traditionally, risk has been seen as exposure to potentially injurious events that may threaten or damage the individual or an organization [2]. The variability in risk tolerance by patients and clinicians in medicine is complicated and not well understood. There is a pervasive and troubling belief among advocates of the patient safety movement that all adverse events in a health system are discoverable and preventable. The belief is primarily that having more information at hand will be sufficient to improve health systems and prevent all risk from leading to harmful outcomes [3]. Fortunately, more sensitive analyses based on expertise in accident investigation acknowledges that 'adverse events should be characterized as emergent properties of complex systems, and they cannot always be predicted' [4]. Perhaps our 'explanatory hypotheses' need revision in HCM in order to take into consideration our evolving knowledge about the role of risk mitigation and help to make better observations of SCD and how best to prevent these extraordinary outcomes? Our central hypothesis proposed by the paper is that the affordances of the environment of children with HCM and the thinking it entails resists reduction to stable and standardized risk identification and management methods.

The historical context of the everyday experiences of clinicians treating HCM with children and their parents is not adequately captured by statistical measures employed in evidence-based medicine. The clinical experience with HCM is more nuanced and dynamic than

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the simple cause and effect sequences constructed in observational studies and investigations. This situation warrants a co-production care model [5] which entails open and frank discussions with parents and other clinicians in order to identify more effective models of inquiry and a more robust risk management and mitigation approach to help prevent SCD in these patients [6].

Developing an understanding of the unexpected events in the lives, of children with HCM and their parents, requires a different approach, sets of tools and mental models [7]. We explicitly define the "rare events problem" as a situation where only a small proportion of patients are at comparatively "high risk" of experiencing an event. How can we identify these children at risk? We hasten to reinforce a conceptual distinction: the goal of risk classification is not predicting precisely who will live or die. Rather, the goal is identification of a small subset of high-risk patients.

The lives of parents of children with HCM are not conducted as a controlled experimental environment and the risks are ambiguous, constantly emerging and unpredictable. Risks in the lives of these children are situational and context-specific. The needs of children with HCM might be better understood in their temporal context where managing constraints and negotiating the boundaries of safe and joyful living is a matter of collective expertise and experience [8]. This requires us to reflect on optimal judgement and decision-making by parents and their children when faced with questions about exercise levels and risk exposure. When clinical teams are faced with the complexity of a past SCD or near death event in an HCM child, there is no experimental control, nor any assurance that their recommended actions will reduce the risk of recurrence of the event in the future in these or other children with HCM.

Achieving optimal outcomes in children with HCM, while preventing harm requires a comprehensive and dynamic risk management strategy that includes [1] *identifying risk*—finding out what is going wrong; [2] *analyzing risk*—collecting data and using appropriate mixed-methods to understand what it means; and, [3] *controlling risk*—devising and implementing strategies to better detect, manage, and mitigate the harmful events from occurring [9,10]. This begs the question, do we understand where and when the child with HCM is most at risk?

Essentially, risk is defined as the chance of something happening that will have a negative impact on key elements. It can be measured in terms of consequences and likelihood of outcomes (see Fig. 1). Clinical risk management addresses the culture, process, and structures that are directed towards the effective management and prevention of potential harmful opportunities and adverse events [11]. We measure risk in terms of the likelihood and consequences of something going wrong, which is in contrast to how we measure quality (i.e., the extent to which a service or product achieves a desired result or outcome). The task of the clinician trying to tailor an optimal risk management approach that helps the parents and their children with HCM appreciate the risk management, which is all about having the wherewithal to balance the consequences of risks against the costs of risk reduction.

In general, a risk management model takes into consideration the probability of an event occurring, which is then multiplied by the potential impact of the event. Fig. 1 illustrates a risk management model adapted to HCM that considers the probability of an adverse event (low, medium, or high) and the impact of the consequences on the child (limited/minor, moderate, or significant). Assigning an event in one of the cells is not an exact science, but the matrix offers guidance for clinicians in advising parents and their children a workable approach towards assessing the risk to the child. In the end, the parents, as guardians of their children, are ultimately responsible for accepting the risk. The risk/benefit discussion with the physician should therefore provide the family with as much information as possible, enabling them to make the best decision if they wish to assume the risk and responsibility of rare injurious outcomes.

The most recent available guidelines concerning the recommended risk management approach towards children with HCM related to permissible levels of activities in HCM are from the American Heart Association (AHA)/American College of Cardiology (ACC) in 2015 where the general statement regarding exercise in cardiac disease is that: "hypertrophic cardiomyopathy being the most common (cause of sudden cardiac death (SCD)), accounting for at least one-third of the mortality in autopsy-based athlete study populations" [12]. Indeed, the guidelines preamble goes on to say that the three Bethesda, Maryland Conferences 16 (1985), 26 (1994), and 36 (2005), published and used over a 30-year period; and the current 2015 AHA/ACC scientific statement was driven by the tenet that "young trained athletes with underlying cardiovascular abnormalities are likely at some *increase in risk* for sudden cardiac death usually on the athletic field [4–8]". [12] We will subsequently review the supporting literature for those statements. However, the intuitive logical risk management inference from such a tenet is that avoidance of any vigorous activities or competitive sports in young patients with HCM will reduce the risk of SCD. Do we know that to be true?

The recommendations of all three Bethesda evidence-based conferences over a 30-year period, and the recommendations of the most recent 2015 AHA/ACC guidelines are that: "Athletes with a probable or unequivocal clinical expression and diagnosis of HCM (i.e. LV hypertrophy on echocardiography) should *not participate* in most competitive sports, with the exception of low intensity class IA sports such as golf and yoga. (Class III; Level of Evidence C)" [13]. This recommendation is independent of age, sex, magnitude of LV hypertrophy, sarcomere mutation, or absence of LV outflow obstruction (at rest or with exercise), prior cardiac symptoms, late gadolinium enhancement on CMR, surgical myectomy or alcohol ablation. A class III recommendation generally indicates that an intervention is not recommended. This inherent confusion in the meaning of the recommendation itself adds to the widespread ambiguity among clinicians on how best to advise parents and children regarding sport participation. A level C evidence statement indicates expert consensus, as opposed to the stronger evidence of data derived from evidentiary sources such as randomized or controlled clinical trials. This recommendation is at the lowest strength level and based on the lowest level of evidence raises important and troubling implementation questions about how best to support the request of families for expert guidance.

Participation in competitive athletics, for asymptomatic, genotype-positive HCM patients, without evidence of LV hypertrophy by 2-D echo and CMR, is stated as reasonable, particularly in the absence of a family history of HCM-related sudden death (Class IIa; Level of Evidence C) [13]. The European Society of Cardiology guidelines from 2014 have a Class 1, level of evidence C recommendation to parents and their children to avoid most competitive sports in HCM [14]. This recommendation is supported by a single reference, itself a consensus document statement, rather than any original evidence, that recommends avoidance of all sports in patients with HCM [15]. The document states that: "Sports participation increases the risk for SCD in HCM patients and this disease is the most common cause of athletic field death in young athletes in the USA". Again, this implies that avoidance of sports is protective and only two references are provided to support this over-reaching statement. One of these references is a literature review that aims to clarify and summarize the relevant clinical issues and to offer an overview of the rapidly evolving concepts regarding HCM [16]. The authors performed a 'systematic analysis of the relevant HCM literature, accessed through MEDLINE (1966-2000), bibliographies', and extensive 'interactions with investigators'. They assimilated the data into a 'rigorous and objective contemporary description of HCM, affording the greatest weight to prospective, controlled, and evidence-based studies'. The conclusions of the study based on review of the literature were that: a) HCM is the most common cause of cardiovascular sudden death in young people, including trained competitive athletes. b) Sudden death occurs most commonly during mild exertion or sedentary activities but *is not infrequently* related to vigorous physical exertion. c) Intense physical exertion constitutes a