

## Challenges of Exercise Recommendations and Sports Participation in Genetic Heart Disease Patients

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Physical activity has been shown to have many health benefits in the primary and secondary prevention of noncommunicable chronic diseases, including cardiovascular disease, diabetes mellitus, and certain cancers.<sup>1-3</sup> Physical activity also has a positive effect on psychological well-being, reducing the risk and severity of depression and anxiety and improving stress levels and mood.<sup>4,5</sup> Physical activity includes activities undertaken as part of occupational and household duties, or for transport, as well as sporting and other recreational activities.<sup>6</sup> Exercise is a major component of physical activity, distinct in that it is generally planned, structured, repetitive and has an objective of improved physical fitness and health.<sup>6</sup> With physical activity providing so many health benefits, it follows that physical inactivity should be a major concern for health professionals and the population as a whole. Physical inactivity is the fourth leading cause of death worldwide and has been identified as a pandemic requiring global attention.<sup>7</sup> In addition, physical inactivity has been deemed responsible for nearly 10% of premature deaths worldwide.<sup>8</sup>

Although exercise is beneficial for all age groups for both healthy people and those predisposed to chronic medical conditions, such as coronary artery disease, the role of exercise in the setting of patients with genetic heart diseases is more complex. A well described association between high-intensity exercise and sudden cardiac death (SCD) has been established,<sup>9,10</sup> and this has historically led to blanket sport and exercise restrictions for any patient meeting diagnostic criteria for a genetic heart disease. The increased understanding of the beneficial effects of even low intensity exercise has called in to question whether current exercise and sports restrictions are too strict, and more importantly whether we are doing enough to actively encourage patients to undertake low to moderate intensity exercise. Negotiating a balance between avoiding high-intensity exercise and at the same time encouraging low-to-moderate intensity exercise for the purpose of general health is a real challenge for clinicians when discussing lifestyle advice with patients. This review focuses on the current issues related to exercise recommendations in genetic heart disease patients, with an emphasis on current recommendations, specific subgroups of patients, such as gene carriers

or those who have an implantable cardioverter-defibrillator (ICD), and how this information can be integrated to provide the best possible advice about exercise in the setting of genetic heart diseases.

### Genetic Heart Diseases

Exercise plays an important role in the management of all patients with genetic heart diseases. Genetic heart diseases include the inherited cardiomyopathies, such as hypertrophic cardiomyopathy (HCM) and arrhythmogenic right ventricular cardiomyopathy (ARVC), and primary arrhythmogenic disorders, including long QT syndrome (LQTS), Brugada syndrome, and catecholaminergic polymorphic ventricular tachycardia. Over 90% of genetic heart diseases are inherited in an autosomal dominant fashion,<sup>11</sup> and all are characterized by both genetic and clinical heterogeneity. Over 100 genes have been implicated in various genetic heart diseases,<sup>12</sup> and there is vast diversity of clinical outcomes, from asymptomatic to severe complications, including heart failure and SCD.

Although the benefits of exercise are numerous at both an individual and a population level, individuals with genetic heart diseases are discouraged from participating in high-intensity, vigorous activities, including competitive sports, for fear of triggering sudden death events as a result of the underlying arrhythmogenic nature of these diseases.<sup>8,13</sup> Table 1 provides examples of activities and their intensity, as well as the corresponding metabolic equivalent value (METs). The recommendation to avoid high-intensity activity (METs >6) and competitive sports is often a difficult issue for many patients. The unique and complex issues that genetic heart disease patients must face have been previously described<sup>17,18</sup> and often relate to individuals being diagnosed in adolescence and early adulthood, many of whom have minimal cardiac limiting symptoms, though must come to terms with having a potentially life-threatening heart condition. In this setting, advising a young person that they cannot continue to engage in high-intensity or competitive sports, even though they may not have any functional limitations, can be a sensitive discussion point. Although difficult at first, most patients will adapt their lifestyle accordingly, though there are a small number who ignore

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**Table 1. Recommendations for HCM and LQTS for a Selection of Exercise Activities**

Sport	Intensity (METS)	Recommendation	
		HCM	LQTS
Horse riding (walk)	Low (3.2)	Assess on individual basis	Assess on individual basis
Brisk walking (5 km/h)	Low (3.2)	Probably permitted	Probably permitted
Snorkeling (light)	Low (4)	Probably permitted	Not advised
Golf (pulling cart)	Low (3–4)	Probably permitted	Probably permitted
Cycling (10–15 km/h)	Moderate (4.8–5.9)	Probably permitted	Probably permitted
Jogging/Walking (7 km/h)	Moderate (5.3)	Assess on individual basis	Assess on individual basis
Swimming (laps)	Moderate (4.3)	Probably permitted	Not advised
Free weights	Moderate (3–7)	Not advised*	Not advised*
Soccer	High (10.3)	Not advised	Not advised
Squash	High (8–12)	Not advised	Assess on individual basis
Ice hockey	High (12.9)	Not advised*	Not advised*
Skiing (cross-country)	High (7.7+)	Assess on individual basis	Assess on individual basis
ICD patient-specific recommendations			
No contact sports			
Restriction from sports involving ipsilateral arm movements, for example, swimming and tennis <sup>14</sup>			

Adapted from Maron et al.<sup>15</sup> Authorization for this adaptation has been obtained both from the owner of the copyright in the original work and from the owner of copyright in the translation or adaptation.

METS values from Jette et al.<sup>16</sup>

Low intensity, <4 METS.

Moderate intensity, 4–6 METS.

High intensity, >6 METS.

HCM indicates hypertrophic cardiomyopathy; ICD, implantable cardioverter-defibrillator; LQTS, long QT syndrome; and METS, metabolic equivalent value.

\*Involves potential for traumatic injury, especially during times of impaired consciousness, for example, because of ICD shock.

the advice and continue to engage in high-intensity exercise and competitive sports, accepting the small but significant risk of an SCD event. The bigger issue, however, is whether the patients will become overly cautious and restrict themselves from undertaking low to moderate intensity exercise. Finding a balance and conveying this to the patient is a real challenge, and currently there is limited data regarding exactly how this patient group interpret and respond to these recommendations.

### Exercise as a Trigger for Sudden Cardiac Death

Although exercise is associated with many health benefits, for those with genetic heart diseases, it may predispose to an increased risk of SCD or cardiac arrest.<sup>13</sup> Specifically, high-intensity and competitive exercise can trigger malignant ventricular arrhythmias, leading to cardiac arrest and SCD among at-risk individuals. There is data from around the world that reports on the issue of SCD during exercise, particularly in athletes. A 21-year prospective study from Italy showed that participation in sports was associated with an increased risk of SCD in people aged 12 to 35 years,<sup>19</sup> and the incidence was over

2-fold higher in athletes compared with nonathletes, with ARVC being the most common cause.<sup>20</sup> Data from a large study in the United States identified a total of 1866 athletes over a period of 27 years who died suddenly (or were resuscitated) during exercise, equating to an incidence of <100 per year.<sup>10</sup> In contrast to the Italian study, HCM was the most common cause of death accounting for approximately one third of all deaths recorded.<sup>10</sup> Many other smaller studies exist. A study of male joggers from Rhode Island, USA, found a 7-fold increased risk of SCD compared with those involved in less strenuous activities.<sup>21</sup> Similarly, a study by Siscovick et al<sup>22</sup> found the relative risk of sudden cardiac arrest during exercise in those with high levels of habitual activity (ie, athletes) to be 5-fold higher than sustaining a sudden cardiac arrest at other times. Interestingly, the relative risk increased over 50-fold for those who were not habitually active but sporadically engaged in high-intensity exercise.<sup>22</sup>

Several other studies have been conducted examining the rates of SCD and cardiac events in young cohorts, particularly in athletes, highlighting the relationship between exercise and increased risk of cardiac events for individuals with genetic heart disease.<sup>23–25</sup> However, other studies have suggested SCD in athletes may be comparable to SCD rates in nonathletes. Most recently, a 3-year nationwide study in Denmark failed to identify any significant difference in SCD rates in noncompetitive compared with competitive athletes.<sup>26</sup>

Collectively, these studies suggest high-intensity exercise (be it at the competitive or recreational level) likely confers an increased risk of sudden death events, particularly in young individuals who may have an underlying predisposition to development of potentially lethal cardiac arrhythmias. This increased risk exists because of the nature of the underlying predisposition, including genetic heart diseases in the young, and the effect of exercise on the heart. A common mechanism is the presence of a trigger such as exercise and a substrate such as myocardial fibrosis, necrosis, and hypertrophy. Exercise induces physiological changes, including increased catecholamine levels, acidosis, dehydration, and electrolyte imbalance, all of which can act as triggers and promote generation of arrhythmias.<sup>27</sup>

For individuals with normal hearts, these physiological changes do not generally form an insurmountable challenge to the heart. However, in patients with an underlying condition, such as HCM, these triggers act on the substrate inducing arrhythmias and even SCD. In terms of the primary arrhythmogenic disorders, LQT1 has been shown to confer a higher risk of cardiac arrest during exercise because of mutations in cardiac potassium ion channels. Schwartz et al<sup>28</sup> hypothesized that the abnormal potassium current within the heart, as a result of a mutation in potassium channels, impedes the physiological protection (shortening of ventricular repolarization) usually activated by presence of fast heart rates and catecholamines (such as during exercise). These effects can be magnified with an increase in intensity, duration, and frequency of exercise.

### Current Exercise Recommendations for Genetic Heart Disease Patients

#### General Exercise Recommendations

Based on the available but limited data, as well as expert consensus, exercise recommendation guidelines have been developed

advising restrictions on certain physical activities depending on the underlying genetic heart disease. Both the American College of Cardiology (ACC) in conjunction with the American Heart Association (AHA) and the European Society of Cardiology (ESC) have sought to address this issue and have released various recommendation documents, a summary of which is provided in Figure 1.<sup>14,15,29</sup> Although there is a paucity of strong evidence to guide these recommendations, there is a consensus view that maintaining low to moderate intensity activity is important to avoid health burdens associated with physical inactivity.

The ACC/AHA recommendations seek to address the conflict between the risk of high-intensity exercise and the risk of a sedentary lifestyle, although also acknowledging the desire of patients to participate in exercise.<sup>15</sup> They specifically focus on patients involved in recreational sports (ie, noncompetitive athletes) and reinforce that patients with a genetic heart disease can still gain some benefit from exercise and sports participation, highlighting the importance of maintaining physical and psychological well-being in this young patient group. Furthermore, an additional recommendations document has focused specifically around competitive athletes engaged in systematic training and competition, where there is emphasis on achievement.<sup>30</sup> An underlying difference is assumed between competitive athletes and recreational participants that necessitates separate recommendations, namely, that nonathletes have greater opportunity to exert reasonable control over their level of exercise and therefore are more likely to reliably detect cardiac symptoms and wilfully terminate physical activity.<sup>15</sup>

The ACC/AHA recommendations for those involved in noncompetitive activities categorize a selection of common sports based on the degree of physiological exertion,

measured in METS. Recommendations are made for HCM, LQTS, ARVC, and Brugada syndrome patients for each sport, taking into account the characteristics of each condition. Table 1 illustrates a selection of sports and activities, their corresponding intensity measured in METS (categorized according to low, moderate, and high MET values) and the recommendation regarding participation for individuals with HCM and LQTS. The core principle underlying this document is that patients with genetic cardiovascular disease can safely participate in most forms of recreational exercise judged to be of moderate or low intensity.<sup>15</sup> Avoidance of several activities and environmental factors that may increase the likelihood of an adverse cardiac event is recommended, for example, burst activities, such as sprinting, extremely adverse environmental conditions, such as extreme heat, and activities that result in a gradual increase in levels of exertion such as running.

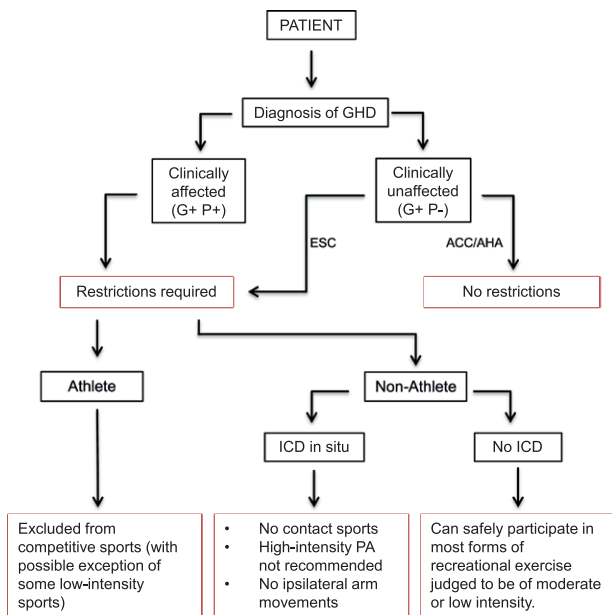
Some gene-specific recommendations are also considered. For example, in patients with LQT1 (eg, mutations in *KCNQ1*), evidence suggests physical exertion particularly in the form of swimming is a common trigger<sup>31</sup>; therefore, water-based activities are not recommended. This is shown in Table 1 with LQTS individuals advised against participating in activities, such as snorkelling and lap swimming, despite their low-moderate intensity. Similarly, LQT2 patients with *KCNH2/HERG* mutations may be more susceptible to auditory triggers,<sup>31</sup> such as a gunshot, which may preclude participation in certain sports, such as shooting. A third example is catecholaminergic polymorphic ventricular tachycardia patients with an *RYR2* mutation. These individuals are susceptible to exercise-induced ventricular tachycardia or fibrillation because of catecholamine release during exercise, and avoidance of all forms of vigorous activity is recommended in all patients, particularly those with a known *RYR2* mutation.<sup>15,32</sup>

The ESC also provides recommendations regarding exercise in the genetic heart disease setting that overall are similar to those of the ACC/AHA recommendations represented in Table 1.<sup>14,29</sup> Individuals with cardiomyopathies, such as HCM and ARVC, are restricted from competitive and high-intensity and contact sports with participation in low and some moderate intensity sports, such as golfing, tennis (doubles), and in some cases, jogging or swimming, permitted.<sup>29</sup> For individuals with arrhythmogenic disorders, the overarching recommendation is exclusion from competitive sports but to allow participation in low to moderate intensity leisure sports and physical activities, with some provisions.<sup>14</sup>

Although the importance of allowing a certain level of exercise is at the core of both sets of recommendations, neither strongly encourages or promotes exercise in this patient population. Both recommendations, perhaps understandably, concentrate more on providing a safe limit for exercise for patients with a genetic heart disease, rather than promoting and encouraging low to moderate intensity exercise that will allow them to potentially gain the many health benefits of being physically active.

### Exercise Recommendations in Genotype-Positive, Phenotype-Negative Patients

Although the similarities between the ACC/AHA and ESC recommendations are considerable, with many common



**Figure 1.** Flowchart of decision-making for exercise recommendations in genetic heart disease. Based on American College of Cardiology/American Heart Association (ACC/AHA) and European Society of Cardiology (ESC) expert consensus documents for athletes and nonathletes (clinical action points marked in red boxes). GHD indicates genetic heart disease; G+ P-, genotype positive, phenotype negative; and ICD, implantable cardioverter-defibrillator.



themes, one major and contentious difference exists regarding individuals who carry the gene mutation, but who have no phenotypic evidence of disease, so called genotype-positive, phenotype-negative (G+ P-) individuals. These G+ P- individuals present a completely new spectrum of patients in all of the genetic heart diseases, with relatively little known about the natural history and outcomes in these patients.<sup>33-35</sup> The issue of exercise recommendations in this subgroup remains controversial and unresolved. Indeed, the ACC/AHA and ESC guidelines are completely opposed in their recommendations for competitive athletes, as highlighted in Table 2.

The ACC/AHA recommendations state, "at present, it is unresolved as to whether genotype-positive, phenotype-negative individuals warrant any restrictions from either recreational or competitive sports."<sup>15</sup> In their 36th Bethesda recommendations for competitive athletes, it is maintained that although a resolution has not yet been achieved, no compelling data exists, which would preclude G+P- patients from either recreational or competitive sports.<sup>37</sup> In contrast, the ESC recommends the same restrictions for G+P- individuals (referred to as silent gene carriers) as for clinically affected individuals. The ESC bases this recommendation on the fact that the natural history of G+P- individuals is at present relatively unknown and that regular exercise training could lead to alterations in heart structure similar to the HCM phenotype.<sup>36</sup>

Because the ACC/AHA and ESC recommendations were released in 2004 and 2006, respectively, further studies have added to the pool of knowledge regarding G+P- individuals

and exercise. A study by Gray et al<sup>34</sup> followed a cohort of 32 G+P- HCM patients for a mean period of 4 years, and in this time-period, no G+P- individuals aged over 18 years developed clinical HCM or any adverse outcomes during the follow-up period. Maron et al presented a further 4 HCM families in which the challenges of decision-making related to exercise recommendations among G+P- HCM individuals were presented and discussed.<sup>33</sup> A more recent study examined a cohort of 353 patients with LQTS of which 130 continued to participate in competitive sports (above the recommended intensity) after diagnosis. Of these 130 patients, 70 were identified as G+P- patients and, as such, were participating in competitive sports against the recommendations of the ESC but in line with the ACC/AHA Bethesda recommendations.<sup>38,39</sup> No adverse events were observed in the follow-up period of  $\leq 10$  years. Collectively, these studies provide some evidence that G+P- adults may have a relatively benign clinical course, and elite-level sports participation should be permitted in some cases. These studies highlight the need for larger studies in G+P- individuals with various genetic heart diseases to evaluate the effect of high-intensity exercise and elite-level sports participation on clinical outcomes.

### Exercise Recommendations for Patients With Implantable Cardioverter-Defibrillator Devices

Although ICD therapy is established as a life-saving device in selected genetic heart disease patients at highest risk of SCD,<sup>40</sup> how this therapy affects exercise recommendations regarding what patients can and cannot do remains less clear. In terms of exercise recommendations, the presence of an ICD creates an additional layer of complexity for several reasons. First, both arrhythmias and associated ICD shocks may lead to a temporary loss of consciousness which, depending on the situation, may be dangerous not only for the individual, for example, while swimming, but those around them, for example, while driving a car. Second, the effectiveness of ICD shocks under the conditions of exercise is less well studied.<sup>41</sup> Third, there is the potential for lead displacement and damage to the ICD through direct force.<sup>27</sup> Finally and importantly, exercise may increase the likelihood of inappropriate ICD shocks because of sinus tachycardia, other supraventricular arrhythmias, T-wave oversensing, or noise caused by lead failure, which may lead to significant subsequent psychological distress.<sup>27,42</sup> Taking into account all these considerations, it is not surprising that the current exercise recommendations for those with an ICD are restrictive.

The specific and important subgroup of genetic heart disease patients with an ICD is highlighted in both the ACC/AHA and ESC recommendations. The recommendations regarding exercise are significantly more restrictive because of the potential additional risk of bodily trauma, resulting in damage to the ICD or lead placement or an inappropriate shock. Furthermore, specific recommendations are made regarding involvement in sports with potential for body contact with restriction to low intensity noncontact sports recommended.<sup>14,15</sup> The ESC also includes a recommendation regarding activities with ipsilateral arm movements, such as tennis and swimming, which are considered higher risk because of potential for lead dislocation or fracture with avoidance suggested.<sup>14</sup>

**Table 2. Comparison of Guideline Recommendations for Competitive Athletes With Selected Cardiovascular Abnormalities**

	Clinical Criteria and Sports Permitted	
	ACC/36th Bethesda	ESC
Gene carriers without phenotype (HCM, ARVC, DCM, ion channel diseases*)	All sports	Only recreational sports
LQTS	>0.47 s in male subjects	>0.44 s in male subjects
	>0.48 s in female subjects	>0.46 s in female subjects
	Low-intensity competitive sports	Only recreational sports
Premature ventricular complexes	All competitive sports when no increase in PVCs or symptoms occur with exercise	All competitive sports when no increase in PVCs, couplets, or symptoms occur with exercise
Nonsustained ventricular tachycardia	If no CV disease, all competitive sports	If no CV disease, all competitive sports
	If CV disease, only low-intensity competitive sports	If CV disease, only recreational sports

ACC indicates American College of Cardiology; ARVC, arrhythmogenic right ventricular cardiomyopathy; CV, cardiovascular; DCM, dilated cardiomyopathy; ESC, European Society of Cardiology; HCM, hypertrophic cardiomyopathy; LQTS, long-QT syndrome; and PVC, premature ventricular complex.

Modified from Pelliccia et al.<sup>36</sup>

\*Long-QT syndrome, Brugada syndrome, catecholaminergic polymorphic ventricular tachycardia.

As with all patients, the risks of playing sports with an ICD in place need to be balanced with the potential health gains and general psychological well-being of the patient. Interestingly, Heidbuchel and Carre<sup>27</sup> proposed that although the current recommendations do not allow for intensive sports participation for ICD patients, recent studies suggest that more leniency may be considered in some competitive athletes and is often possible in those who want to perform low- to moderate-intensity recreational activities.<sup>27</sup>

An important recent study used a prospective ICD registry and followed a cohort of 372 athletes with ICDs participating in organized or high-risk sports, such as basketball and running.<sup>43</sup> Although a total of 77 individuals recorded 121 shock episodes, there were no occurrences of tachyarrhythmic death, externally resuscitated tachyarrhythmia during or after sports participation or severe injury as a result of syncope, or shocks during sports. The study found that more shocks did occur during sports than at other times. However, it was also observed that the majority of athletes who experienced an ICD shock during sports participation chose to continue playing. The authors suggest that the benefits of sport participation for these individuals outweighed the unpleasant experience of an ICD shock, and that although ICD shocks can decrease quality of life, so can sports restriction. The study suggests that some patients with ICDs may be able to safely engage in more vigorous competitive sports.<sup>43</sup>

Once again, the multifactorial nature of the clinical setting needs to be considered with the benefits and dangers of high-intensity exercise, the underlying risk of SCD, whether the patient is an adult or a child, and the psychosocial well-being of the patient all significant factors. McDonough<sup>44</sup> examined a sample of young (18- to 40-year-old) patients and found that some individuals experienced anxiety during exercise because of the potential for an ICD shock.<sup>44</sup> Interestingly, some individuals chose to reduce their level of exercise, despite physician advice permitting participation, because of fear of an ICD shock. Other studies have reported similar results, reporting that a fear of exercise is common among ICD patients and that this fear negatively influences quality of life.<sup>45</sup> Further, interventions aimed at addressing this have shown mixed results and mostly use a cardiac rehabilitation-type program to demonstrate to the patient their ability to do high-intensity exercise in a safe environment.<sup>46,47</sup> These studies highlight the importance of how we negotiate the most effective ways to communicate the risks and benefits of exercise to this patient group, so that they can safely gain quality of life improvements.<sup>44,45</sup>

The effect of functional capacity and general fitness on adjustment and anxiety levels of ICD patients has also been examined. In a sample of ARVC patients with an ICD, a reasonably good level of functional capacity (ie, ability to participate in activities, such as daily living, sports, recreational activities) was observed overall.<sup>48</sup> The study found that higher functional capacity, represented by a higher score on the Duke Activity Status Index, was a significant predictor of better device adjustment in these ICD patients, and higher anxiety scores were associated with reduced functional capacity.<sup>48</sup> As the Duke Activity Status Index score correlates with peak oxygen uptake and therefore fitness levels,<sup>48</sup> this study raises the

possibility that a higher level of fitness aids adjustment for patients with an ICD.

### Other Adverse Exercise-Induced Cardiovascular Effects

Intense exercise, such as prolonged participation in endurance sports, including ultramarathons, triathlons, and cycling, has been shown to have potential to trigger adverse cardiovascular effects.<sup>40,49-54</sup> In some situations, particularly in endurance athletes, chronic and sustained exercise can cause patchy myocardial fibrosis and other cellular changes creating a substrate for atrial and ventricular arrhythmias, as well as coronary artery calcification, diastolic dysfunction, and large artery wall stiffening.<sup>54</sup> Although these adverse effects were observed in endurance athletes not known to have a genetic heart disease, the intense repetitive stress for sustained periods has potential for adverse cardiac effects. The most pertinent example is found in ARVC.

ARVC is a structural genetic heart disease of particular interest when considering exercise. ARVC primarily affects the right ventricle, and it is characterized by myocardial atrophy and fibro-fatty replacement of right ventricular myocardium.<sup>55</sup> Exercise has been found not only to increase the risk of SCD in ARVC patients but can actually contribute to the development of disease.<sup>56</sup> A study by James et al<sup>56</sup> found that the amount and intensity of exercise could increase the likelihood of arrhythmias and also the development of heart failure among desmosomal mutation carriers. The study found that a reduction in exercise could decrease the risk of VT/VF and that symptoms of ARVC developed in endurance athletes at a younger age compared to nonendurance athletes (mean age 30 years versus 40 years).<sup>56</sup>

The findings of this study concur with previous studies in both murine models and humans,<sup>57,58</sup> which suggest that endurance exercise may lead to particularly high strain on the right ventricle of the heart and subsequent cell damage, even in individuals who are *not* genetically predisposed. The constancy of the right ventricular strain associated with the regularity and intensity of endurance activities is suggested to lead to changes in the heart that resemble ARVC, and thus the concept of exercise-induced ARVC has been introduced.<sup>50</sup> Heidbuchel et al studied a cohort of 46 elite-level endurance athletes referred for evaluation of potential arrhythmias.<sup>58</sup> They found the majority (86%) of the ventricular arrhythmias originated in the right ventricle and speculated that many of these athletes were showing aspects of ARVC. A further study examined a cohort of 47 athletes with ventricular arrhythmias originating in the right ventricle, with only 13% found to have desmosomal mutations, far less than would be expected if these athletes had genetic ARVC.<sup>59</sup> Exercise-induced ARVC has therefore been proposed as a different entity to genetic ARVC and can be regarded as one end of a continuous spectrum where myocardial integrity is perturbed owing to a mismatch of strain and desmosomal integrity.<sup>50</sup>

### Move to Patient-Centered Care

The current available literature, combined with the various guideline documents and recommendations, collectively

highlight the complexities of the decision-making process in advising genetic heart disease patients about exercise. Figure 2 highlights some of these factors and the delicate balancing act that is required when making recommendations for individuals with a genetic heart disease. There is a common thread throughout both the ACC/AHA and ESC recommendations of a need for individualization for the patient depending on these factors or patient-centered care. Patient-centered care involves consideration of the patients' experience of their condition, looking at the patient as a whole, forming a partnership of equal footing between patient and doctor, health promotion, and focus on a caring relationship.<sup>60</sup> Both sets of recommendations emphasize the current sparseness of evidence in the area of exercise and genetic heart disease and therefore the need for a patient-centered approach rather than the application of blanket restrictions across the board. However, again there is diversity of opinion regarding the decision-making process and the balance between physician recommendations and patient preference.

A survey-based study of physicians associated with the Heart Rhythm Society looked at how physicians managed their patients with ICDs, including those who wished to remain in competitive or vigorous sports and the incidence of cardiac events in their patients.<sup>61</sup> Results from the study showed that 76% of physicians recommended against contact sports, 45% recommended against competitive sports, and only 10% recommended against all activities more vigorous than golf or bowling.<sup>61</sup> The data showed that 70% of physicians reported patients in their practice were involved in some form of sporting activity. In 42% of practices,  $\geq 1$  patient with an ICD was competing in competitive sports, and of these, 22% had patients reporting ICD shocks during the activity.<sup>61</sup> The authors postulate that their results suggest the potential risks associated with more vigorous exercise in ICD patients, such as shock failure or damage to the ICD system, are not as substantial as the recommendations suggest.<sup>61</sup> Whether or not more vigorous exercise is beneficial for ICD patients, this study highlights an important point in that, although physicians recommended against participation in competitive

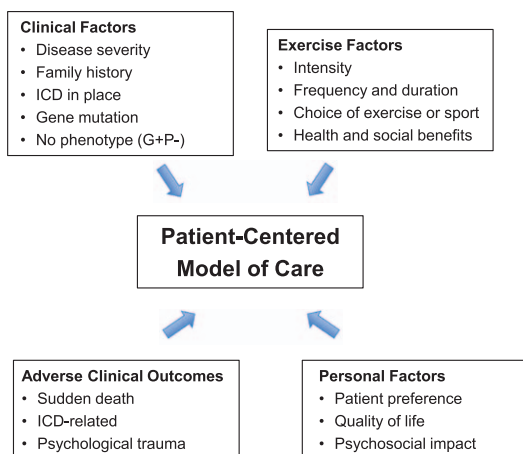
sports, there were several individuals who chose to compete regardless. This leads to the question who should have the deciding vote regarding a patient's participation in exercise—the physician or the patient?

The previously mentioned study by Johnson and Ackerman<sup>38</sup> provides evidence for an approach involving a higher level of patient input into the decision-making process after diagnosis. Although an adherence to the ACC/AHA 36th Bethesda recommendations for athletes in general is declared, the clinic at which the study took place encourages patient input into the decision-making process after significant patient and family education and counseling. The authors propose that future clinical concerns should primarily be the quality of life of the patient, rather than prevention of SCD, which in reality is a rare event.<sup>39</sup> This implies that if the patient has a strong desire to participate in exercise, be it competitively or recreationally, this should play a part in the clinical decision-making process.

The conclusions of this study raised concerns about the ability of young and adult patients with LQTS to make unbiased judgements when confounded by the potential for a sports career.<sup>62</sup> Pelliccia states that those involved in competitive sports are often entirely driven by participation in their chosen sport and the potential for status and economic return, and so to allow these patients input into decision making may be unwise.<sup>62</sup> This is supported by case-based evidence of athletes who continue to compete despite considerable risks, including Nicholas Knapp<sup>63</sup> and Dana Vollmer.<sup>64</sup> In summarizing the alternative to that proposed by Johnson and Ackerman,<sup>39</sup> Pelliccia states that "as long as professional sports generate immense public recognition and financial gain for fragile young individuals, physicians represent the ultimate shield to avoid ... adverse events," and therefore, physicians should make the final decisions regarding exercise participation.<sup>62</sup>

Although both views are primarily concerned with competitive athletes, the principles also need to be considered for individuals in the general population who may participate in various other forms of noncompetitive sport or recreational exercise. Although in the case of competitive athletes, there is a distinct drive to improve and achieve athletically, other individuals may still have a strong drive to participate in exercise for other reasons, particularly related to the beneficial health and social outcomes. In these patients, the benefits of limiting exercise need to be countered with the risks of restriction.

In addition to the needs and desires of the patient, there may be other factors at play in making recommendations to athletes in particular, such as the interests of sponsoring universities or colleges, sports organizations, and schools and the desire of physicians to minimize their liability. Numerous cases have been heard in the judicial setting<sup>65</sup> which highlight the issues, including the legal risk universities and schools may face in disqualifying athletes from competing based on discrimination and the legal risks physicians face in allowing participation. The case of Nicholas Knapp provides an example of a university prohibiting participation in a sporting team after diagnosis of a heart condition requiring implantation of an ICD.<sup>63</sup> Although Knapp initially fought and won a case against the school, an appeal later overturned the decision and upheld the universities' right to exclude Knapp based on



**Figure 2.** Multifactorial nature of decision-making for exercise recommendations in genetic heart disease patients. Factors to consider in the patient-centered model of care. G+ P- indicates genotype positive, phenotype negative; and ICD, implantable cardioverter-defibrillator.



medical justification after the consensus guidelines and recommendations available at the time.

Physicians may also face legal ramifications of making recommendations or not making a recommendation of exclusion when necessary. The case of *Hank Gathers v Loyola Marymount University* illustrates this issue as Gathers was permitted to continue participating in competitive basketball, despite having had a syncopal episode, although playing and exercise-related complex ventricular tachyarrhythmias had been identified.<sup>66</sup> Although this case was settled out of court, Paterick et al maintain that a finding of malpractice as a result of breach of the customary patient–physician relationship and failure to comply with expert consensus documents would have occurred.<sup>65</sup>

With such diversity of opinion about several aspects of exercise for genetic heart disease patients, the response of patients is of interest. As discussed, athletes often choose to compete counter to the recommendations and against physician advice.<sup>39,43,63,64</sup> Fewer studies have concentrated on the response of genetic heart disease patients in general to the burden of exercise recommendations and how the recommendations actually affect the patients' lives. However, those that have looked at the general population have reported interesting observations. A recent study of children with inherited arrhythmia syndromes (LQTS and catecholaminergic polymorphic ventricular tachycardia) reported on the level of intensity of exercise during free-living daily activities, that is, normal daily activities and playtime.<sup>67</sup> The study measured exercise through use of accelerometers over a period of 14 days and found that these children frequently exceeded the current recommended activity levels. Of particular interest in this study was the fact that this occurred during normal daily activities and not necessarily specific sports or exercise activities, highlighting the difficulties in limiting exercise outside organized or planned activities, particularly for children.

Another recent study was conducted by Reineck et al,<sup>68</sup> which concentrated on exercise in HCM patients. This study used survey-based methods to determine the exercise and health behaviors of a group of HCM patients. Although the HCM patients consumed less alcohol and had lower rates of smoking compared with the general population, the study found that the time spent being physically active was significantly less for the HCM patients. In addition, the study reported that many patients had a reduction in exercise after diagnosis and that the exercise restrictions had a negative effect on their emotional well-being. Alongside the patients who reduced their exercise after diagnosis, a group was described who lived counter to the recommendations and continued to participate in competitive sports. Interestingly, the study reported that >70% of these people were unaware of the recommendations restricting exercise, highlighting the need to clearly and accurately communicate the challenges of exercise in this patient group to both clinicians and patients.

### Clinical Implications

There are many benefits of exercise for the general population in terms of health and well-being. There is ample evidence that regular low to moderate intensity physical activity has numerous health benefits and that physical activity does not

have to be high intensity or vigorous to gain these benefits. This is an important consideration underpinning the clinical implications of current recommendations for exercise in genetic heart disease patients. Indeed, genetic heart disease patients need to be encouraged to undertake regular, low to moderate intensity exercise. However, some forms of high-level exercise come with an increased risk of an adverse cardiac event, such as SCD, for individuals with a genetic heart disease. Differences aside, the recommendations of both the ACC/AHA and ESC provide a starting point for discussion between the physician and patient. When considering lifestyle modification and the role of exercise in patients with genetic heart disease, an open discussion about the current knowledge in the field, the recommendations from guideline documents, and the areas where there are contention needs to carefully and sensitively be undertaken.

Discussion about the benefits and risks of different intensities of exercise needs to be addressed and tailored to the individual patient. Factors, such as the underlying disease, the clinical history, disease severity, knowledge about the gene mutation, presence of an ICD, age, sex, social setting, and psychological well-being, all need to be considered in making recommendations. A balanced discussion between the physician and patient about the beneficial health effects of exercise compared with the risk of adverse events during exercise, including SCD, is critical. Most importantly, the consultation needs to be performed in a patient-centered structure. Patients also need to be reminded that even in the setting of exercise restrictions in terms of high level exercise and competitive sports, regular low to moderate intensity exercise is strongly encouraged for overall health benefits. In the end, the unifying goal is to promote the best exercise recommendation for the individual genetic heart disease patient that will facilitate good general health, encompassing physical and mental aspects, and result in the most favourable clinical outcomes.

### Conclusions

There are many challenges and complexities regarding exercise and sports participation in people with genetic heart disease. Although helpful recommendation and consensus documents exist, there are many gray areas, including which sports or activities of different intensities may be performed, how much exercise is allowable, and the optimal recommendations for those who are in more contentious subgroups, such as those with an ICD, or who are G+P– individuals. These areas highlight the need for studies in larger cohorts of genetic heart disease patients, specifically focused on outcomes from patients adhering to different exercise recommendations. However, this is no simple task because of the clinical heterogeneity of genetic heart diseases, even within families, as well as the diversity in intensity of physical activities undertaken by patients and the low frequency of SCD events. Currently, patient management requires an integrated approach, which takes into consideration the available exercise data and recommendations, the individual circumstances of the patient, and a clear involvement of the patient in the decision-making process. These all represent fundamental aspects of care to facilitate the optimal management and outcomes in patients with genetic heart diseases.

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## Disclosures

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