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CURRENT PERSPECTIVES

Hypertrophic cardiomyopathy: Paradigm shifts in the last 30 years (Part 2)

Miocardiopatia hipertrófica: mudanças de paradigma nos últimos 30 anos (Parte 2)

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''Half of what you are taught in medical school will be wrong in 10 years' time.''

– Sydney Burwell, 1944

Severe hypertrophic cardiomyopathy is untreatable and the prognosis is poor

Contemporary advances in the treatment of HCM have substantially modified its prognosis; this disease, previously considered untreatable and with high mortality,[1] is now treatable, with a similar mortality to that of the general population.

Risk stratification of sudden cardiac death (SCD) in the context of primary prevention identifies high-risk patients, who should receive an implantable cardioverter-defibrillator (ICD).[2] However, despite improved patient selection, there is still room to optimize the current algorithms, since the incidence of appropriate interventions in primary prevention is only 3–4%/year (versus 10%/year in secondary prevention[1,3]).

For a long time, the treatment of intraventricular obstruction was based on the use of beta-blockers and disopyramide, but surgical septal myectomy is currently a highly effective intervention with very low mortality.[1,4] Since 1995, percutaneous alcohol septal ablation has emerged as a less invasive alternative to surgery, with excellent results, low mortality, and similar outcomes, despite shorter follow-up times, delayed response and higher rates of permanent pacemaker implantation.[4]

Recently, a new drug class, myosin inhibitors, has been developed.[5] By reducing the excess actin–myosin cross-bridges in HCM, these drugs decrease the contractility of the interventricular septum, increasing left ventricular (LV) outflow tract dimensions, and thereby interrupting the pathophysiological cascade of obstruction.[5]

In heart failure with preserved ejection fraction (HFpEF), medical treatment involves the preservation of sinus rhythm to maintain atrial contraction. In addition, heart rate reduction to increase the duration of diastolic time and LV filling, and improvement of the 'diastolic environment',

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may also be useful. Recently, sodium-glucose cotransporter-2 inhibitors have also shown benefit in HFpEF. Some patients who are refractory to medical treatment evolve to a restrictive filling pattern, becoming candidates for heart transplantation.[6,7]

A small percentage of HCM patients progress to systolic dysfunction and heart failure with reduced ejection fraction (HFrEF). In the presence of intractability to medical therapy, advanced HF treatment and possible heart transplantation should be considered. HCM patients have excellent survival after transplantation (85% at one year, 75% at five years and 61% at 10 years), due to their younger age and fewer comorbidities.[6,7]

In patients with atrial fibrillation (AF),[7] it is important to try to preserve or restore sinus rhythm, using electrical or chemical cardioversion, usually with amiodarone, disopyramide or sotalol, and/or AF ablation. In cases where preservation of sinus rhythm is not predictable or feasible, a rate-control strategy should be adopted, with beta-blockers and/or calcium channel antagonists (verapamil or diltiazem). Radiofrequency ablation or, if there is concomitant myectomy, surgical ablation (Cox-Maze surgery) may be considered.[7]

The threshold for oral anticoagulation in HCM should be very low and independent of the CHA_2DS_2-VASc score, and novel oral anticoagulants or vitamin K antagonists should be used.[7]

Is severe HCM untreatable and is the prognosis poor? No, HCM is nowadays a treatable disease. Treatment exists, even for severe forms, and its prognosis, when appropriately treated, is overall similar to that of the normal population.

Competitive physical exercise is always contraindicated in these patients

HCM is an important cause of SCD in athletes <35 years of age and exercise may precipitate SCD. Based on these data, exercise has historically been contraindicated in HCM,[7–10] with only Mitchell class IA exercise being allowed.[7–10] Because of these restrictions (and rarely due to disease-related limitations), HCM patients are generally sedentary and inactive.

Over time, this formal contraindication to exercise in HCM has been questioned for several reasons[7–10]:

- Most HCM patients die of non-cardiac causes, and among cardiac causes the main etiology is coronary artery disease (not HCM), for which regular exercise is an integral part of prevention.
- Patients with HCM who regularly participate in sports have better exercise tolerance, higher peak oxygen consumption and better quality of life.
- In several small longitudinal studies (including about 500 HCM patients) with relatively long follow-up periods (nine years), physical exercise, even if vigorous, was not associated with an increase in cardiovascular events, including SCD.

Taking these findings into account, a more flexible approach is now recommended and the indication/contraindication for exercise in HCM should be individualized, based on multiple factors[7–10]:

- Individual risk stratification of SCD
- Patient's age (higher risk in younger individuals)
- Sport characteristics (recreational versus competitive) and intensity (light, moderate, or vigorous)
- Sports modality (greater risk in dynamic sports with frequent stop-and-go sequences, such as soccer and basketball)
- Shared decision-making, including the patient and family and never ignoring the importance of medical opinions from HCM experts and club/school/university physicians.

However, common sense and caution are always welcome[8] as there is also no clear scientific evidence with which to define the risk of all patients with a high degree of accuracy. A mature approach without generalizations is recommended. It is important to recall that the risk of SCD in patients with HCM is always higher than in the population without the disease, even in low-risk groups. Furthermore, it should be borne in mind that risk scores were not designed for athletes, as they do not consider hemodynamic and metabolic stress, or the sometimes adverse conditions of high-intensity competitive sports, particularly in obstructive forms, in which dehydration and extreme weather conditions are important.[8]

Accordingly, decisions should be individualized,[7–10] and risk should be reassessed regularly in all HCM patient-athletes (annually), and more frequently in those whose phenotype is evolving, such as adolescents and young adults (biannually). Supervised exercise in recreational areas and the availability of an automatic external defibrillator may increase safety.

This hot topic was also addressed in two important documents published in 2020: the ESC guidelines on sports cardiology[9] and the American College of Cardiology/American Heart Association guidelines on HCM.[10] Both of these guidelines, albeit cautiously and tentatively, open the door for the first time to the possibility of patients with HCM being able to exercise beyond Mitchell class IA – a milestone and a paradigm shift in the approach to these patients.

Is competitive physical exercise always contraindicated in these patients? No, a less rigid approach is now recommended, with individualized risk stratification, and, in selected low-risk individuals, participation in specific competitive sports may be considered.

Conclusion

Sydney Burwell's provocative and speculative statement fits HCM like a glove. Over the course of this work, we have shown how some 30-year-old concepts have substantially changed, due to major scientific advances in the knowledge of this fascinating disease.

Conflicts of interest

The author is an advisoy board member of Bristol Myers Squibb and Cytokinetics.

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