Review Article

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From the armchair to contemporary cardiac rehabilitation: the remarkable ongoing journey of exercise training in ischemic heart disease

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Abstract Exercise is an important physiological activity with several health benefits. In the setting of ischemic heart disease (IHD), the view toward exercise has greatly evolved throughout the years, concurrently to several major advances in the management of this complex entity. Currently, exercise training has broad applications across the IHD continuum as a powerful tool in its overall management, being a core component of comprehensive cardiac rehabilitation programs. Beyond this, exercise has also been incorporated as an integral part of contemporary methodologies aiming to provide diagnostic and prognostic data, such as cardiopulmonary exercise stress testing or stress echocardiography. In this article, we provide a pragmatic overview concerning the role of exercise in IHD, with a focus on its incorporation in cardiac rehabilitation frameworks, while also discussing some of the challenges and unmet needs concerning these interventions.

Keywords: cardiac rehabilitation, exercise, exercise training, ischemic heart disease, preventive cardiology

Introduction

Throughout the ages, physical exercise has played a key role in different civilizations, with its health impact being described across various settings.[1] These range from the early depictions attributed to Sushruta in the Indus valley thousands of years ago, to reports from the Yellow river civilizations or those by physicians from ancient Greece such as Hippocrates and Heraclius.[1-3] Interestingly, the notion that, in its prescription, factors related to the individual and general setting were to be considered also emerged early on.[1,2]

Cardiovascular disease is a major cause of morbidity and mortality.[4,5] While encompassing a broad and complex group of pathologies, often having intricate links with other entities (such as cancer, autoimmune, or infectious disorders), ischemic heart disease (IHD) has been a particularly relevant health care burden.[4-8] Although sometimes referred to as a "modern" disease, namely given the profound influence of lifestyle factors (including dietary patterns, tobacco exposure, or sedentarism) and ensuing cardiovascular risk factors in its expression, studies have progressively shown that this too may have been a challenge since ancient times.[9,10] This is elegantly illustrated by data derived from the study of mummies from diverse world regions by computed tomography, showing atherosclerotic disease (in different vascular beds) already in these bygone eras.[9]

Over the past century, groundbreaking improvements have been made in IHD, across its continuum from acute presentations to chronic settings.[11,12] These span its prevention, diagnosis, and treatment and have heralded major reductions in mortality while also greatly affecting morbidity.[4,6,8] As detailed below, data have highlighted the importance of exercise in both the prevention and management of IHD.[6,8,13] Indeed, exercise training has been incorporated as a core component of cardiac rehabilitation (CR) programs, one of the central strategies in the management of IHD as underscored by current guidelines.[6,8,14,15] Furthermore, exercise has also been coupled with various tests (such as the electrocardiogram and echocardiogram), being used for both diagnostic and prognostic assessments (Fig. 1).[14,16,17]

In this review, we present an overview concerning the role of exercise in IHD, while also pragmatically reviewing its incorporation in CR and briefly exploring some of the unmet needs and future challenges concerning these interventions.

A brief review concerning the interplay between exercise and the cardiovascular system

A plethora of pathways have been described when analyzing the benefits of exercise.[13,18,19] Although beyond the scope of this article, having been previously extensively explored, different mechanisms have been linked to its positive effects.[13,18-20] In this

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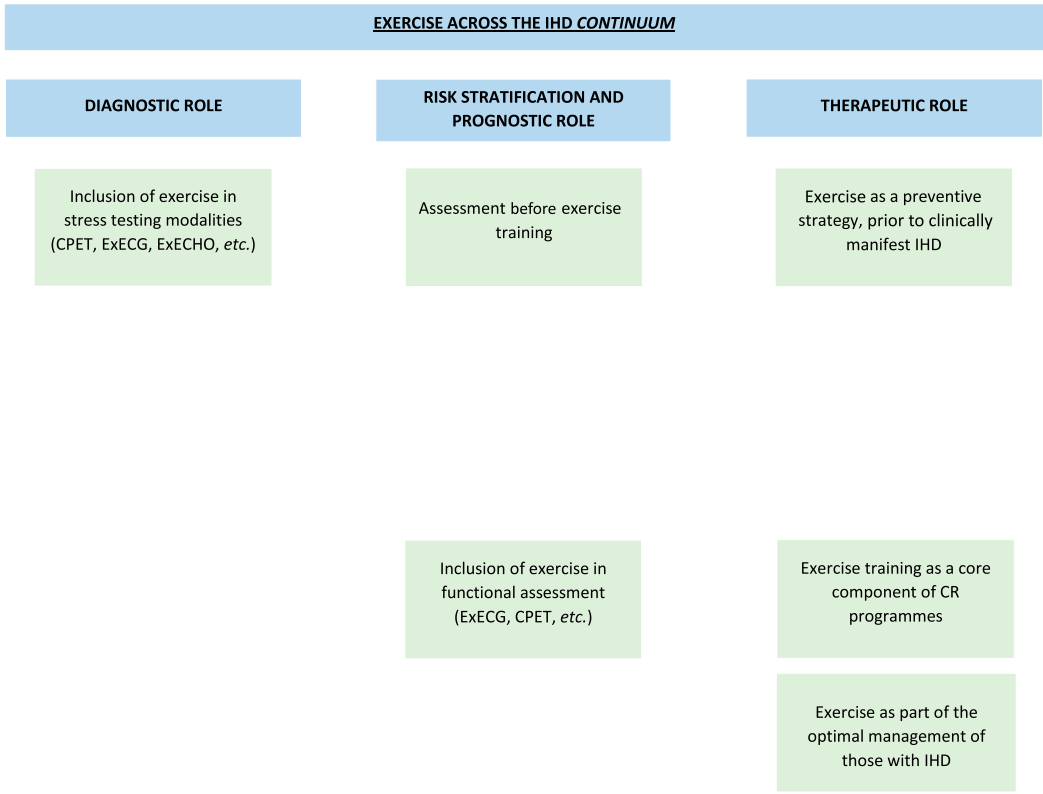

Figure 1. Overview of some of the potential applications of exercise across the continuum of ischemic heart disease. CPET, cardiopulmonary exercise stress testing; CR, cardiac rehabilitation; ExECG, exercise stress testing with electrocardiographic monitoring; ExECHO, exercise stress echocardiography; IHD, ischemic heart disease.

regard, not only effects specifically related to the cardiovascular system but also those in other systems have been under the spotlight.[14,18,21,22] Among the former, both structural and functional adaptations (including some assessed by readily available noninvasive tests such as echocardiography and others needing ancillary methodologies to be fully ascertained) are a mainstay of the effects of exercise.[14,23,24] These encompass not only the heart but also the peripheral vasculature, with improvements in cardiac contractility, chronotropic reserve, and endothelial function.[18,20,21] For the latter, some effects include those elicited in the musculoskeletal system where the release of myokines can modulate the cardiovascular response, as well as in the respiratory and autonomic nervous systems, and overall metabolic response.[13,14,21,22,25,26] These far-reaching effects resonate with the manifold components of physical fitness, while concurring with the benefits of exercise beyond cardiovascular disease, where its role has progressively garnered center stage in areas ranging from lung diseases (being incorporated in respiratory rehabilitation programs) to cancer.[27-32] Moreover, its place at the intersection between cardiovascular disease and other pathologies should also be considered, as in chronic kidney disease.[33,34]

Notably, it should be emphasized that although cardiopulmonary function is a critical part of physical fitness, other determinants are also paramount to its overall expression.[14] Importantly, data derived from frameworks such as cardiopulmonary exercise stress testing (CPET) can allow a dynamic assessment of several components of the response to exercise (providing relevant data in several scenarios).[16,35] Moreover, methodologies such as invasive CPET or exercise magnetic resonance imaging have also been reported, further improving knowledge and perspectives on this complex and expanding field.[36,37]

Another point worthy of mention relates to the fact that, albeit associated with various benefits, there could also be deleterious effects related to exercise.[38,39] Some of those reported range from phenomena such as elevated cardiac biomarkers or increased risk of atrial fibrillation (where long-term high-intensity endurance training has been associated with this arrhythmia, albeit the possible effects of sex, cardiovascular risk factors, and other factors should be considered, namely given that the mechanisms for this finding remain to be fully characterized), to potential adverse effects in terms of plaque remodeling or atherosclerotic burden.[38-46] These reinforce the need for a careful risk stratification, particularly when considering exercise in individuals with IHD or at increased risk (including those with more advanced age or with a high cardiovascular risk undergoing high-intensity activities).[14,47] Once more, when addressing exercise across the IHD continuum, an integrated view is of pivotal relevance.[14]

It should also be recalled that, although acknowledging areas of overlap, concepts concerning physical activity and exercise have specificities which should be noted.[14,48] As detailed in the European Society of Cardiology (ESC) guidelines, exercise may be defined as physical activity which is structured and performed in a repetitive purposeful manner to maintain or improve one or more components of physical fitness.[14] On the other hand, any bodily movement which results in energy expenditure and was produced by skeletal muscle could be within the scope of physical activity.[14] These concepts are also relevant when analyzing the settings in

which these take place, as data have shown that this may also affect the cardiovascular response.[49-51] Some examples encompass changes in atmospheric conditions (such as temperature but also pollution) and differences between occupational and recreational activities, in terms of their cardiovascular profile.[19,49-52]

Exercise and ischemic heart disease

A journey from the armchair to contemporary guidelines

The interplay between exercise and IHD has been an evolving topic across timeframes.[53-56] Although depictions suggesting angina pectoris were already mentioned in the Papyrus Ebers dating back millennia, as well as those of epicardial artery narrowing by renaissance master Leonardo Da Vinci, the portrayal of this entity would be greatly refined in the eighteenth century.[57-59] At this point, William Heberden provided a seminal and (especially at a time when much of the pathophysiology of IHD was yet to be unraveled) remarkably eloquent description of the clinical features of angina pectoris, the prototypical manifestation of IHD.[57] Of note, he also described an individual who improved his symptoms by exercising (in the case by sawing wood).[53,56] Although the depiction of typical anginal symptoms has (with subsequent adaptations) to some extent stood the test of time, the case for exercise in IHD would still be a point of discussion.[53,55,56,59]

At the dawn of the twentieth century, prolonged bed rest and immobilization were the norm after a myocardial infarction.[11,53,54,56] It should be recalled that at this time major leaps were being undertaken into the understanding of some of the mechanisms leading to myocardial infarction, spearheaded by James Herrick's now classical depiction of coronary thrombosis.[11,54,60] These initial insights (such as the emphasis on the development of scar tissue), however, coupled with the lack of effective and widespread therapeutic interventions, lead to a restrictive view in terms of exercise (and "stress" in general as recalled years later by Eugene Braunwald, recollecting on what could be described as an "expectant" phase in the management of myocardial infarction).[11,56] Nonetheless, already at this time the value of long bed rest periods, as well as their potential adverse effects, would be put into question.[54,55] During the first half of the past century, pioneering works such as those by Samuel Levine (who in 1944 expressed several concerns regarding these strict regimens, illustrated by clinical cases) paved the way, in many respects, to deep paradigm shifts in rehabilitation strategies.[53,55,61] Among these a special mention should be given to the so-called "armchair" treatment (also recalled as the "cardiac chair treatment"), an approach in which patients were sited with feet dependent early on in their clinical course.[54,62] Albeit extraordinarily simple and plain by current standards, this innovation proved central in ushering in an era of early mobilization and rehabilitation.[54-56,63] Concurrently to these developments, some the first CR programs were being introduced, a milestone which would profoundly affect the care of myocardial infarction survivors (and several other cardiovascular diseases).[64-66] As previously alluded to, when assessing exercise in IHD, careful considerations should be made in terms of the overall context in which it is inserted. In this background, it should be recalled that several strategies, nowadays commonplace, were yet to be developed and generalized, as illustrated by the (at the time) much publicized management of US president Eisenhower's myocardial infarction.[56,67]

Since the inception of the first CR programs, exercise has been a core component of these interventions.[68,69] Although the management of IHD has remarkably evolved (to name a few, with the advent of coronary care units, revascularization strategies including percutaneous coronary intervention, and a myriad of pharmacological agents), CR has along this journey continuously shown its relevance.[55,70,71] In this regard, meta-analyses have shown the benefits of CR across several time points and profiles.[71,72] Although care should be taken when analyzing and interpreting different studies (namely given the differences in design or patient characteristics), these are reinforced by an updated meta-analysis reporting on the benefits of CR in cardiovascular mortality and recurrent myocardial infarction and hospitalizations.[69,72-75] These data have led to the incorporation of CR at the center of IHD management, as illustrated by the high levels of recommendation provided in guidelines by different societies such as the ESC and the American College of Cardiology/American Heart Association (both endorsing CR as a class I, level A recommendation in these settings).[6,8,15,76] Of note, these programs can be of interest in a range of patient characteristics.[77-81] Albeit different responses have been reported across populations under study, the potential benefits of these interventions reinforce their usefulness.[79,80,82-84]

Cardiac rehabilitation frameworks

Since its first iterations, CR has matured substantially to provide a comprehensive intervention addressing the many facets of IHD.[53,68,69,83,85] Although the multilayered nature of CR should be underscored (encompassing areas such as nutritional counseling, psychological support, smoking cessation, and others), exercise training is an integral component of these programs.[68,83] Beyond its therapeutic role, exercise also forms a key part of risk stratification and prescription optimization and in assessing the (functional) impact of the program.[14,35,68,86] This concept is clearly displayed by its incorporation in stress testing [such as in exercise stress testing with electrocardiographic monitoring (ExECG) or CPET], providing highly important inputs for these components.[17,35,86]

Although there are many particularities concerning exercise prescription in IHD, stemming from both patient characteristics (including functional capacity, osteoarticular limitations, and other comorbidities or the presence of risk features such as residual ischemia and left ventricular dysfunction) and availability, an individualized approach is essential to harness the full breadth of this intervention.[14,83,86] In parallel to the approach used in pharmacological interventions, an adequate and personalized exercise prescription is paramount.[86,87] This notion is expressed for both aerobic and resistance training, where different methodologies may be applied according to specific contexts.[83,86,87] In aerobic training, assessing ventilatory thresholds (by CPET) can provide an invaluable window with which to tailor prescription, whereas peak heart rate and maximal load attained, as well as the Borg scale, can also inform on specific regimens.[86-88] Notably, beyond continuous moderate training, different modes of exercise training such as those using high-intensity interval training have also been reported.[8,83,86,89-91] For resistance training, this too has been shown to be a relevant component of regimens.[8,86,92] As for aerobic training, in resistance training an individualized assessment for risk (taking into consideration factors such as diabetes and retinopathy) and aspects such as the type of equipment to be used and intensity to be employed (namely with the definition of repetition maximums)

should be considered.[92] When structuring the exercise training program, the presence of cardiac implantable electronic devices is another important factor.[87,92,93] In these patients, an integrated assessment of not only background disease but also issues related to the device (such as programming or the risk of trauma) should be performed, to appropriately couple safety considerations with optimal benefits.[93]

Assessing the functional impact of the program is an important part of current CR.[68] This can also inform on prognosis, as variations in peak oxygen consumption have been associated with outcomes such as mortality.[78,94,95] Thus, from preintervention to training sessions and finally postintervention assessments, exercise (whether with a predominantly therapeutic intent or as a component of tests such as CPET) forms one of the pillars of CR across different moments.[35,68,86]

Role of exercise beyond therapeutic effects

Beyond its role with a primarily therapeutic intent, exercise can also be a useful tool for diagnostic, risk stratification, and prognostic evaluations (Fig. 1).[14,16,17,35,96] Although much research has in recent years focused on settings such as heart failure, cardiomyopathies, and cancer, these capabilities also extend to the global assessment of IHD.[14,28,35,96-99] In this capacity exercise has been discussed, although with marked methodological and technical variations, for several decades.[17,100,101]

As mentioned above, since some of the first descriptions of IHD, exertion has been regarded as having a leading role in eliciting symptoms (whether chest discomfort or dyspnea).[8,59,102] Beyond these clinical manifestations, electrocardiographic changes associated with exercise were also reported early on.[103] These would lead to the incorporation of exercise as part of the workup of IHD with examples such as the Master two-step test (in which patients climbed two steps, each with 22.86 cm) lavishly illustrating the resourcefulness of some of the early frameworks employed, aiming to standardize its application.[103-105] As recalled decades after its inception in a review by Arthur Master (one of its codevelopers and the namesake for the test), its predominant focus, however, was the assessment of myocardial ischemia and not overall fitness.[100,106,107] Although with limitations, this was one of the precursors of what would later become the contemporary ExECG.[103] This technique would be subsequently refined and streamlined by American cardiologist Robert Bruce, leading to the eponymous and now ubiquitous Bruce protocol.[17]

As imaging methodologies continue to improve, showing increasing accuracy in the assessment of suspected IHD, the use of the ExECG with a diagnostic aim has progressively been superseded.[7,8] However, beyond its role in electrocardiographic changes appraisal with a focus on ischemia assessment for diagnostic purposes, this test can also provide data on several other dimensions such as symptom status, functional capacity, blood pressure, heart rate, rhythm, and conduction disturbances.[8,17,108] Indeed, its utility in the assessment of these parameters has been reported in distinct scenarios.[17,108] As for additional applications, several of the principles used in ExECG also form a core part of CPET. [16,35] Finally, applying exercise beyond these examples is another hallmark of its resolute enduring relevance.[8,102,109,110] This can be distinctly seen in stress echocardiography where exercise has been advised as a first-line stressor in the setting of coronary artery disease but also by its use in modalities such as myocardial perfusion scintigraphy.[8,102,109] Concurrently to these, the role of cardiorespiratory fitness as a powerful predictor of events across several populations should also be recalled.[94,96,111,112]

Future perspectives—cardiac rehabilitation in a changing world

As discussed above, the prominent role of exercise in IHD is currently well established.[6,8,68,73] Albeit this, there are still several hindrances concerning its application.[69,73] For CR (and secondary prevention in general), a gap between recommendations and overall implementation should be considered as several studies have described suboptimal patient participation in these programs.[64,113,114] Many barriers affecting diverse links have been identified, including those related to health care systems as well as patient-specific and clinician-specific issues, reflecting the complex nature of this matter.[113] Some of the proposed avenues to address these unmet needs range from strategies such as providing different models of CR (versus classical center-based programs) and incorporating automatic referrals, to improving patient education on this issue and further expanding health care provider training.[113,115] In addition, as digital platforms and technological innovations become ever more intertwined with day-to-day activities, their use to leverage CR has also been an area of increasing interest.[113,116,117] From possible roles in allowing more individualized regimens (by taking into consideration data on different parameters, namely with inputs derived from devices such as smartwatches or wearable sensors) to their incorporation in home-based or hybrid programs, outlooks on the use of digital technologies have progressively been under the spotlight.[116-118] Notwithstanding their major potential in improving CR, pitfalls such as how to best apply different technologies, patient preferences, and selection issues, among others, should still be taken into consideration.[53,119]

Another point worthy of mention relates to the distinct profiles encompassed by IHD.[6,8] These reflect also the progressive shift from the prior classical view of IHD centered on epicardial obstructive disease to one where both macrocirculation and microcirculation (with anatomical and functional specificities) are increasingly recognized as having prominent roles in health and disease.[8,59,120,121] This notion, coupled with the multitude of different patient characteristics (in terms of comorbidities, the presence of frailty, prior physical activity, among others) leads to the need to integrate several components when assessing the individual patient.[8,14,83,86,87,122,123] As with other areas of cardiology, the possible incorporation of novel and transformative frameworks such as those related to artificial intelligence and machine learning may also improve the application of these interventions.[124,125] Beyond this, these could also allow enhancements in the interpretation and scope of tests such as CPET, by providing novel insights and potential applications.[82,126,127]

Conclusion

Exercise represents a unique and fundamental strategy across the continuum of IHD. Robust data support its role in the management of IHD, namely when incorporated in contemporary CR programs. Moreover, the use of exercise as part of frameworks such as CPET or stress echocardiography provides relevant information for diagnostic purposes, risk stratification, and prognostic assessment. Although having accompanied several major paradigm changes in IHD over the years, exercise has maintained its prominence, having a leading role in this continuously and rapidly evolving field.

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