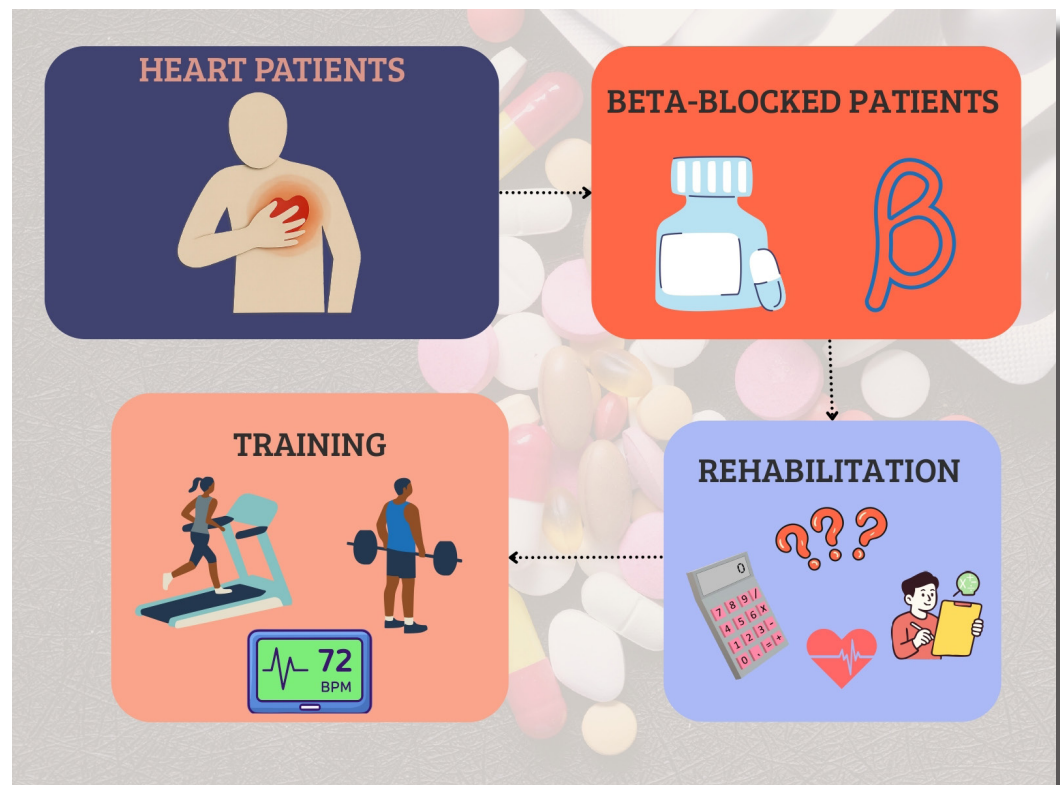


Exercise prescription for individuals using beta-blockers: a literature review

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Graphical Abstract



Highlights

- Reviews current formulas for heart rate prescription in individuals using beta-blockers.
- Beta-blockers alter the chronotropic response to exercise, impacting the target heart rate during training.
- The HR at optimal intensity should lie between VT1 and VT2 (ventilatory thresholds), aiming for greater safety and efficacy in cardiac rehabilitation.

Abstract

Exercise prescription for individuals using beta-blockers requires careful consideration of intensity, duration, and heart rate (HR). The present study aimed to identify formulas for calculating maximum heart rate (HR_{max}) and formulas used for adequate prescription of exercise intensity in patients on beta-blocker therapy. A literature review was conducted using the databases PubMed, PEDro, and SciELO, with the keywords “betablocker”, “exercises”, “heart rate”, “rehabilitation”, and “prediction equation”, combined using the Boolean operator “AND”. Inclusion criteria comprised: clinical trials, meta-analyses, and randomized controlled trials published in English or Portuguese, containing formulas for calculating HR_{max} and training HR for beta-blocked individuals. The search yielded 2,458 results, of which 4 articles were included. Two articles addressed HR_{max} formulas, one of which proposed formulas for patients with heart failure. The remaining two articles addressed training HR in beta-blocked individuals. The identified HR_{max} formula was $164 - (0.7 \times \text{age})$, and for specific situations involving stable patients with heart failure with reduced ejection fraction, the Keteyian formula ($114 + 0.5 \times HR_{rest} - 0.5 \times \text{age}$) and a new equation: $HR_{max} = 109 + (0.5 \times HR_{rest}) - (0.5 \times \text{age}) + (0.2 \times LVEF) - 5$ (if $Hb < 11 \text{ g/dL}$) were identified. For exercise prescription, the Karvonen HR formula [$0.6 \times (HR_{max} - HR_{rest}) + HR_{rest}$] or 80% of HR_{max} were found. For patients following acute myocardial infarction, the modified Karvonen formula was identified: $HR = 0.8 \times (HR_{max} - HR_{rest}) + HR_{rest}$.

Keywords: Adrenergic beta-Antagonists. Physical Exercise. Heart Rate. Cardiac Rehabilitation. Computational Prediction Methods.

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INTRODUCTION

Beta-blockers constitute one of the primary pharmacological classes in the management of cardiovascular diseases, including acute myocardial infarction, heart failure, arterial hypertension, and cardiac arrhythmias¹. Their mechanism of action is based on antagonism of beta-adrenergic receptors, promoting reductions in heart rate, myocardial contractility, and atrioventricular conduction². Although these effects are fundamental to cardiovascular protection, they also directly impact the physiological response to exercise, particularly with regard to the modulation of heart rate³.

In this context, chronotropic incompetence deserves particular attention — a condition characterized by the inability of the cardiovascular system to adequately increase heart rate (HR) in response to rising metabolic demands during physical exertion. From a pathophysiological standpoint, this condition is associated with attenuation of sympathetic activity mediated by beta-adrenergic receptors, resulting in a reduced chronotropic response⁴. In individuals using beta-blockers, this limitation is even more pronounced, leading to a decrease in the maximum heart rate achieved and, consequently, to alterations in the relationship between workload and cardiovascular response⁵.

This limitation imposes a significant clinical challenge in the prescription of physical exercise, particularly in cardiovascular rehabilitation programs, in which the adequate determination of exercise intensity is essential to ensure safety and effectiveness⁶. Traditionally, aerobic training prescription is based on percentages of estimated maximum heart rate. However, in patients under the effect of beta-blockers, this approach may be inaccurate, since the chronotropic response is pharmacologically modulated, potentially resulting in overestimation of the prescribed intensity and an increased risk of

adverse events⁷.

Several predictive equations have been proposed to estimate maximum heart rate (HR_{max}), including the classical “220 – age”, as well as more recent models such as the Tanaka equation (“208 – 0.7 × age”)⁸ and the Gellish equation (“206.9 – 0.67 × age”)⁹. However, these formulas were developed from heterogeneous populations composed predominantly of healthy individuals, and thus do not adequately address populations with pharmacological or pathophysiological alterations in the chronotropic response. Consequently, considerable variability has been observed among estimated values, along with limited accuracy when applied to patients on beta-blocker therapy¹⁰.

Additionally, although cardiopulmonary exercise testing is considered the gold-standard method for evaluating the cardiovascular response to exercise, its use may be limited by clinical, structural, or operational factors, particularly in certain clinical practice contexts¹¹. Consequently, predictive equations remain widely used despite their limitations⁶.

Given this scenario, a relevant gap in the literature is evident regarding the standardization of methods for estimating maximum heart rate and prescribing exercise intensity in individuals using beta-blockers¹². The absence of consensus, combined with the variability among equations and the pathophysiological particularities of this population, reinforces the need for a critical analysis of the strategies currently employed¹³.

Therefore, the present study aimed to identify and analyze the formulas used for calculating maximum heart rate and training heart rate (HR_{train}), as one of the methods employed for prescribing physical exercise intensity in patients on beta-blocker therapy, thereby contributing to a safer, more individualized, and evidence-based clinical practice.

MATERIALS AND METHODS

This is a secondary literature review study. Searches were conducted in the following databases: Physiotherapy Evidence Database (PEDro), US National Library of Medicine National Institutes of Health (PubMed), and Scientific Electronic Library Online (SciELO). The following keywords were used: “betablocker”, “exercises”, “heart rate”, “rehabilitation”, and “prediction equation”, combined using the Boolean operator “AND”, with the filters: Clinical Trial; Meta-Analysis; and Randomized Controlled Trial, spanning the last 25 years, in English, Portuguese, and Spanish. The bibliographic search was conducted from October 2024

through May 2025 as a continuous search to maintain the currency of the proposed subject matter. Inclusion criteria comprised articles presenting specific formulas for calculating maximum heart rate and the optimal training heart rate in patients with cardiac disease who were using beta-blockers. Exclusion criteria included articles not relevant to the topic.

Following record identification, results were exported in Research Information Systems (RIS) format and imported into the Rayyan software, a widely used digital platform for the organization and screening of studies in literature reviews. Rayyan facilitates

the reading and classification of titles and abstracts, making the selection process more efficient and standardized. Duplicate removal was performed. Thereafter, titles and abstracts were screened according to the pre-established inclusion and exclusion criteria. Potentially relevant studies were selected for full-text

reading, and the complete texts were subsequently assessed for eligibility. The synthesis of findings was conducted in a descriptive and interpretive manner, with the aim of ensuring critical integration of the main evidence, concepts, and gaps identified in the literature.

RESULTS

Searches using the descriptors “beta blockers” and “prediction equation” retrieved 3 articles; using “beta blockers” and “exercises”, 455 articles were found; “beta blockers” and “Rehabilitation” yielded 81 articles;

and “beta blockers” and “heart rate” returned 1,594 articles, totaling 2,133 articles (Figure 1). Of these, only four met the selection criteria and were included in the study, all retrieved from the PubMed database (Table 1).

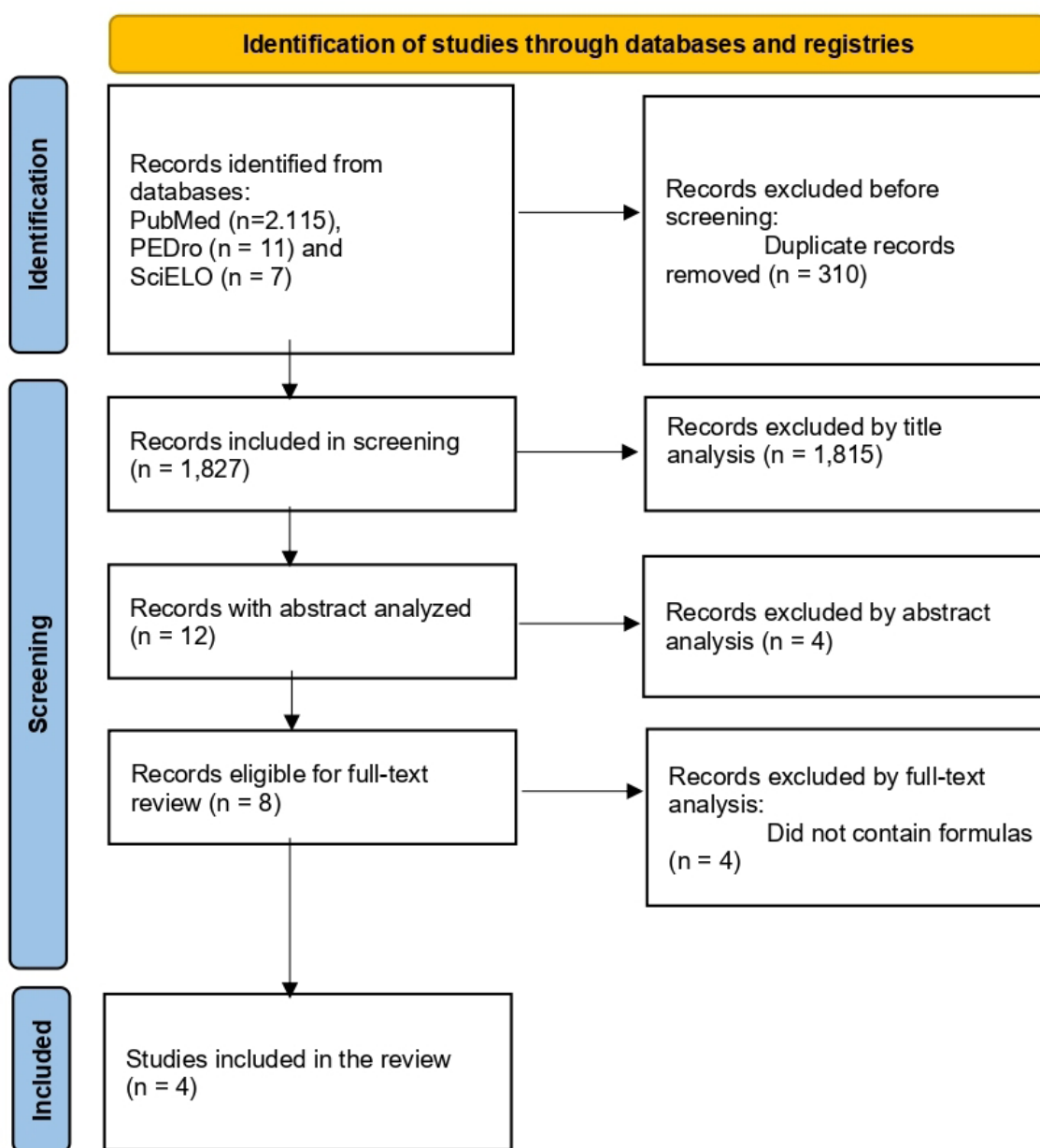


Figure 1 - Identification of studies through databases and registries.

Table 1 - Authors, year of publication, objectives, methods, and results of the 4 final articles included in this study.

Author/Year of Publication	Population/Sample	Objectives	Proposed Equation and Main Findings
Clinton A. Brawner <i>et al.</i> ^{14/2004}	Congenital Heart Disease	To develop and validate an age-specific equation to predict HR _{max} in patients receiving beta-blocker therapy.	The methodology of this study was based on data from specific patients using exercise tests and statistical analyses to construct a HR _{max} prediction equation. Data were retrieved from the Henry Ford Preventive Cardiology Outcomes (PRECO) database. It was concluded, through the use of exercise test data, that the equation $HR_{max} = 164 - 0.7 \times \text{age}$ provides a more reliable estimate of HR _{max} than previously established equations, thereby supporting the assessment of maximal effort during exercise testing.
Damiano Magri <i>et al.</i> ^{15/2022}	Patients with heart failure with reduced ejection fraction 3,487 patients	To improve HR _{max} prediction in patients undergoing beta-blocker treatment.	A new equation was developed and the Keteyian equation was externally validated in comparison with historical formulas, using data from maximal cardiopulmonary exercise testing. The new equation $(109 + (0.5 \times HR_{rest}) - (0.5 \times \text{age}) + (0.2 \times \text{left ventricular ejection fraction}) - 5 \text{ (if Hemoglobin} < 11 \text{ g/dL)})$ demonstrated a significantly lower Mean Absolute Percentage Error compared to the Fox and Tanaka equations, and a slightly lower Mean Absolute Percentage Error than the Keteyian formula $(114 + 0.5 \times HR_{rest} - 0.5 \times \text{age})$.
Jean-Yves Tabet <i>et al.</i> ^{16/2006}	Post-myocardial infarction patients 115 patients	To assess whether the training HR (THR) calculated using the Karvonen formula is comparable to the HR at VT2 in beta-blocker-treated patients and, if not, to propose a new formula.	A cardiopulmonary exercise test was performed to determine VT2. The THR calculated using the Karvonen formula was compared with the HR at VT2 in a derivation sample (n = 58) and a validation sample (n = 57). The Karvonen training HR was significantly lower than the HR at the anaerobic threshold in the first patient sample. Accordingly, a “modified Karvonen training heart rate”: $0.8 \times (HR_{max} - HR_{rest}) + HR_{rest}$ was derived by linear regression in the derivation sample and prospectively evaluated in the validation sample. The modified Karvonen training HR was closer to the HR at the anaerobic threshold than the standard Karvonen training HR.
Isabel Díaz-Buschmann, <i>et al.</i> ^{17/2014}	Patients with Cardiovascular Disease 102 patients on beta-blocker therapy and 39 not treated with beta-blockers	To verify the utility of currently recommended exercise training HR (THR) levels and to demonstrate the limitations of different HR-based methods for calculating exercise intensity in patients treated with and without beta-blockers.	HR was calculated at the first ventilatory threshold (VT1) and the second ventilatory threshold (VT2). It is recommended that patients not treated with beta-blockers exercise using the Karvonen formula applying 70% of heart rate reserve or 85% of HR _{max} , while those using beta-blockers should do so using the Karvonen formula applying 60% of heart rate reserve or 80% of HR _{max} .

Abbreviations: HR (heart rate); THR (training heart rate); VT1 (first ventilatory threshold); VT2 (second ventilatory threshold); HR_{max} (maximum heart rate); HR_{rest} (resting heart rate).

DISCUSSION

The estimation of maximum heart rate (HR_{max}) and the prescription of exercise intensity in patients on beta-blocker therapy must be understood from two main perspectives: methods based on predictive equations, and methods based on individual physiological responses, such as ventilatory thresholds^{1,3}.

Traditional HR_{max} prediction equations, widely used in healthy populations, present important limitations when applied to patients on beta-blocker therapy, as these agents reduce the chronotropic response to exercise^{4,7}. In this context, classical equations may overestimate HR_{max} in this population^{8,9}. Consequently, specific equations have been developed with the aim of improving the accuracy of HR_{max} estimation, demonstrating superior perfor-

mance compared to traditional models, particularly by accounting for the physiological particularities of these patients^{10,11}.

Brawner *et al.*¹⁴ developed a specific equation to estimate HR_{max} in patients with cardiac disease on beta-blocker therapy. The methodology of this study was based on data from specific patients using exercise tests and statistical analyses to construct a HR_{max} prediction equation, with data retrieved from the Henry Ford Preventive Cardiology Outcomes (PRECO) database. It was concluded, through the use of exercise test data, that the equation $HR_{max} = 164 - 0.7 \times \text{age}$ provides a more reliable estimate of HR_{max} than the previously established “220 – age” equation, thereby supporting the assessment of maximal effort during exercise testing. Thus, the

new formula is more appropriate for these patients, who present an altered chronotropic response due to beta-blocker use, contributing to more precise exercise prescription.

Furthermore, more recent approaches propose the incorporation of clinical variables, such as left ventricular ejection fraction and laboratory parameters, with the aim of increasing estimation accuracy¹¹. Although this strategy represents an important conceptual advance, its clinical applicability may be limited, since such variables are not always available across all care settings, particularly outside hospital environments or specialized centers^{2,3}.

Magrì *et al.*¹⁵ assessed HR_{max} estimation in patients with heart failure on beta-blocker therapy. The study included outpatients with heart failure with reduced ejection fraction receiving optimized beta-blocker therapy, in order to develop a new equation and externally validate the Keteyian equation in comparison with historical formulas, using data from maximal cardiopulmonary exercise testing. The new equation ($109 + (0.5 \times \text{HR}_{\text{rest}}) - (0.5 \times \text{age}) + (0.2 \times \text{left ventricular ejection fraction}) - 5$ (if Hemoglobin < 11 g/dL)) demonstrated a significantly lower Mean Absolute Percentage Error compared to the Fox and Tanaka equations, and a slightly lower Mean Absolute Percentage Error than the Keteyian formula ($114 + 0.5 \times \text{HR}_{\text{rest}} - 0.5 \times \text{age}$).

Brawner *et al.*¹⁴ and Magrì *et al.*¹⁵ demonstrated that traditional formulas such as “220 – age” are inaccurate in patients on beta-blocker therapy. Brawner *et al.*¹⁵ propose a simple age-based equation with better clinical applicability, whereas Magrì *et al.*¹⁶ present a more comprehensive and accurate equation by incorporating clinical variables.

With respect to exercise intensity prescription, indirect methods based on heart rate – such as those utilizing heart rate reserve – remain widely used due to their practicality^{6,12}. However, evidence indicates that these methods may not accurately reflect physiological thresholds in patients on beta-blocker therapy, potentially resulting in prescription of intensity below or above the optimal range^{13,14}.

Tabet *et al.*¹⁶ assessed the accuracy of the Karvonen formula for prescribing training heart rate in post-infarction patients on beta-blockers. A total of 115 beta-blocked patients recovering from myocardial infarction underwent cardiopulmonary exercise testing to determine VT2. The training HR determined by the Karvonen formula was compared with the HR at the anaerobic threshold in a derivation sample (n = 58) and a validation sample (n = 57). The Karvonen training HR was significantly lower than the HR at the anaerobic threshold

in the first patient sample. A “modified Karvonen training heart rate”: $0.8 \times (\text{maximum heart rate} - \text{resting heart rate}) + \text{resting heart rate}$, was then calculated by linear regression in the derivation sample and prospectively evaluated in the validation sample. The modified Karvonen training HR was closer to the HR at the anaerobic threshold than the standard Karvonen training HR, and the difference between the modified Karvonen training HR and the HR at the anaerobic threshold was clinically relevant in only 5% of patients.

In contrast, prescription based on ventilatory thresholds (VT1 and VT2) is considered the gold standard, as it enables more precise individualization of exercise intensity based on the patient’s metabolic responses^{1,12}. However, the requirement for cardiopulmonary testing with gas analysis limits its routine use, which sustains the relevance of indirect methods in clinical practice³.

Díaz-Buschmann *et al.*¹⁷ investigated the recommended HR level for exercise and the different methods for calculating target HR in patients with and without beta-blocker use. Patients underwent maximal exercise testing with gas analysis, and the following parameters were calculated: first ventilatory threshold (VT1), second ventilatory threshold (VT2), exercise time, maximum workload, metabolic parameters, resting HR (HR_{rest}), peak HR (HR_{peak}), HR at VT1 and VT2, and 75%, 80%, and 85% of HR_{max} (HR75%, HR80%, HR85%). Exercise HR was also determined using the Karvonen formula, applying 60%, 70%, and 80% of heart rate reserve (HRKarv0.6, HRKarv0.7, and HRKarv0.8). This study included 102 patients on beta-blocker therapy and 39 not treated with beta-blockers, and recommended that patients not treated with beta-blockers exercise at HRKarv0.7 or HR85%, while those on beta-blockers do so at a target HR of HRKarv0.6 or HR80%. Results showed that patients on beta-blocker therapy presented significantly lower HR values during exercise, which was expected given the pharmacological effect of the medication. Furthermore, when exercise intensity is prescribed based on percentages of peak HR or by the Karvonen formula, greater efficacy is observed at higher HR values within safe limits. The authors highlight that recommendations should differ between individuals who use and those who do not use beta-blockers. To ensure safety and effectiveness, exercise intensity should lie between the first and second ventilatory thresholds (VT1 and VT2). However, methods based solely on HR may lead some patients to train outside this optimal zone. Finally, the authors recommend that patients on beta-blocker therapy use approximately 60% of heart rate reserve (Karvonen) or approximately 80% of

maximum or peak HR as reference values for exercise prescription.

The comparison among different approaches reveals that no single ideal method exists that is universally applicable to all contexts. Specific equations and adjusted methods may improve estimation of exercise intensity, but their selection must consider resource availability, the patient's clinical profile, and the setting of application^{1,12,13}.

Díaz-Buschmann *et al.*¹⁷ and Tabet *et al.*¹⁶ analyzed exercise intensity prescription in patients on beta-blocker therapy using ventilatory thresholds, particularly VT2, as a reference. Both agree that methods based solely on heart rate may not accurately reflect the anaerobic threshold. However, they present divergent results regarding the optimal intensity derived from the Karvonen formula: while Díaz-Buschmann *et al.*¹⁷ recommend approximately 60% of heart rate reserve (HRKarv 0.6), Tabet *et al.*¹⁶ demonstrate that values below 0.8 underestimate the HR at the anaerobic threshold, proposing a modified formula equivalent to approximately 80% of heart rate reserve. This discrepancy suggests that prescription based on fixed percentages of HR may vary according to the population studied. In the study by Tabet *et al.*¹⁶, composed of patients in the early post-infarction phase, the traditional formula proved insufficient, indicating the need for higher intensity to reach VT2. Díaz-Buschmann *et al.*¹⁷, in turn, adopted a more conservative approach, prioritizing safety within the VT1–VT2 range. Thus, although both studies use VT2 as the physiological reference, the findings reinforce that optimal prescription must be individualized, with cardiopulmonary exercise testing as the gold standard, while generalized formulas may lead to either underestimation or overestimation of exercise intensity^{16,17}.

CONCLUSION

The review of these articles demonstrated the importance of correct exercise prescription when intensity is maintained between the aerobic (VT1) and anaerobic (VT2) thresholds, ensuring safety and efficacy in cardiac rehabilitation programs. The articles provided insight into how to predict maximum heart rate and more precisely prescribe exercise intensity in patients with cardiac disease on beta-blocker therapy – even without direct gas analysis – supplying healthcare professionals with more effective and safer tools for planning physical training in complex clinical contexts. Different

Another relevant aspect concerns differences among the populations studied. The analyzed studies include patients ranging from those with coronary artery disease to individuals in post-infarction rehabilitation and patients with heart failure with reduced ejection fraction^{6,11,12}. These conditions present distinct physiological responses to exercise, which may directly influence the applicability and accuracy of the proposed equations. Accordingly, generalization of results should be performed with caution.

This review presents limitations that should be considered when interpreting the findings. First, the small number of included studies may limit the robustness of the conclusions. Furthermore, significant heterogeneity was observed among the populations analyzed, including different clinical conditions, levels of cardiovascular impairment, and rehabilitation contexts, which makes direct comparisons among studies difficult.

Another important point concerns the differences in assessment protocols and methods used for determining exercise intensity, which may influence the results and their interpretation. Additionally, the search strategy may have limited the inclusion of relevant studies, particularly those published in databases not covered or in languages other than those searched.

The limitation related to the clinical applicability of the proposed equations should also be considered, since some depend on variables not widely available in clinical practice, restricting their use to specific settings.

Finally, there is a need for further studies to validate these equations in different populations, including patients with multiple comorbidities, different beta-blocker regimens, and varying levels of physical conditioning, in order to expand the applicability of the findings.

methods for estimating maximum heart rate and their application in specific situations involving stable patients with heart failure with reduced ejection fraction were identified. For exercise prescription, methods based on heart rate reserve as well as the use of percentages of maximum heart rate were highlighted.

For patients on beta-blocker therapy following acute myocardial infarction, adaptations to these methods were described, reinforcing the importance of individualized adjustments for safe and effective physical training prescription.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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