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MESTRADO INTEGRADO EM MEDICINA

Comparison of different physiological parameters in exercise intensity prescription in heart failure patients

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Resumo

Introdução: A reabilitação cardíaca (RC) tem recomendação classe IA para pacientes com insuficiência cardíaca (IC). A prescrição individualizada da intensidade de exercício é fundamental para potencializar os efeitos benéficos do treino aeróbico, bem como para garantir a sua segurança. Vários domínios de intensidade podem ser descritos de acordo com os parâmetros fisiológicos recomendados, como o primeiro limiar ventilatório (LV1), percentagem do pico de consumo de oxigénio (VO2), percentagem do pico da frequência cardíaca (FC) e percentagem da frequência cardíaca de reserva (FCR). A sua consistência em orientar a prescrição de exercício em populações com IC ainda não foi abordada adequadamente.

Objetivo: Comparar a consistência entre os parâmetros fisiológicos comummente usados na classificação do domínio da intensidade de exercício em pacientes com IC.

Métodos: Esta é uma análise retrospetiva de 163 pacientes com IC, independentemente da fração de ejeção do ventrículo esquerdo (FEVE), submetidos a um teste de exercício cardiopulmonar máximo (TECP). As percentagens do pico VO2, frequência cardíaca (FC) máxima e cardíaca de reserva (FCR) foram obtidas no LV1 e em 40, 75 e 85% do pico de VO2. Foram comparadas as classificações nos diferentes domínios de intensidade de exercício, definidos pelas diretrizes atuais da Sociedade Europeia de Cardiologia (SEC), de acordo com cada parâmetro utilizado.

Resultados: O LV1 foi observado em 82 ± 10% da FC máxima, 54 ± 25% da FCR e 54 ± 17% do pico de VO2, correspondendo à zona de treino de alta intensidade da SEC para a FC máxima e intensidade moderada para % FCR e % de pico VO2. Usando % pico de VO2 e % pico de FC, 78% dos pacientes foram classificados no domínio de intensidade correta do exercício (moderada-alta) no LV1, mas caíram para cerca de 58% quando usaram % FCR. A concordância dos índices recomendados de intensidade de exercício no LV1 foi superior para pacientes com FEVE reduzida e pacientes com maior capacidade de exercício.

Conclusão: Os dados do nosso estudo informam sobre os perigos de prescrever exercícios usando outros índices para além do limiar ventilatório e enfatizam a necessidade de um TECP máximo para uma prescrição adequada de exercícios para pacientes com IC.

Palavras-chave: insuficiência cardíaca, reabilitação cardíaca, prescrição de exercícios, teste de exercício cardiopulmonar.

Abstract

Introduction: Cardiac rehabilitation (CR) has a class IA recommendation for heart failure (HF) patients. The individualized exercise intensity prescription is crucial to enhance the beneficial effects of aerobic training as well as to guarantee its safety. Several intensity domains can be described according to the recommended physiologic parameters such as first ventilatory threshold (VT1), percentage of peak oxygen uptake (VO_2), percentage of peak heart rate (HR) and percentage of heart rate reserve (HRR). Their consistency in guiding exercise prescription in HF populations has not been adequately addressed.

Purpose: To compare the consistency between commonly used physiologic parameters in exercise intensity domain classification of HF patients.

Methods: This is a retrospective analysis of 163 HF patients irrespective of left ventricle ejection fraction (LVEF) that underwent a maximal cardiopulmonary exercise test (CPET). The percentages of peak VO_2, peak heart rate (HR) and heart rate reserve (HRR) were obtained at VT1 and at 40, 75 and 85% of peak VO_2. Classifications across the different exercise intensity domains, defined by the current European Society of Cardiology (ESC) guidelines, according to each parameter used were compared.

Results: VT1 was observed at 82 ± 10% of Peak HR, 54 ± 25% of HRR and 54 ± 17% of Peak VO2, corresponding to the ESC high intensity training zone for peak HR, and moderate intensity for % HRR and % Peak VO_2. Using % Peak VO2 and % Peak HR, 78% of the patients were classified in the correct exercise intensity domain (moderate-high) at VT1 but dropped to about 58% when using % HRR. Concordance of the recommended indices of exercise intensity at VT1 was superior for patients with reduced LVEF and patients with higher exercise capacity.

Conclusion: Our study data inform us about the hazards of prescribing exercise using indices other than ventilatory threshold and emphasizes the need for a maximal CPET to an adequate prescription of exercise to HF patients.

Key words: heart failure, cardiac rehabilitation, exercise prescription, cardiopulmonary exercise test.

List of abbreviations and acronyms

ACEi - angiotensin-converting-enzyme inhibitors
AF - atrial fibrillation
ARA - angiotensin-II-receptor antagonists
βb - beta-blockers
CPET - cardiopulmonary exercise test
CR - cardiac rehabilitation
EI - exercise intensity
ESC - European Society of Cardiology
ET - exercise training
FC - functional class
HF - heart failure
HFpEF - heart failure with preserved ejection fraction
HR - heart rate
HRR - heart rate reserve
IQR - interquartile range
LVEF - left ventricle ejection fraction
NT-pro-BNP - N-terminal prohormone of brain natriuretic peptide
NYHA - New York Heart Association
PA - physical activity
RER - respiratory exchange ratio
SD - standard deviation
VCO_2 – carbon dioxide production
VE – minute ventilation
VO_2 - oxygen uptake
VTs - ventilatory thresholds
VT1 - first ventilatory threshold
VT2 - second ventilatory threshold
W - work rate

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Introduction

Exercise training (ET) is an important component of the treatment of patients with heart failure (HF) because it improves quality of life and reduces hospitalizations[1-4]. Like any drug dosage, the prescription of ET intensity is critical to guarantee the safety of this nonpharmacological intervention and to ensure its efficacy[5, 6]. Strenuous exercise is associated with higher risk of ventricular arrhythmias and sudden death[5, 7-9], as well as with a prothrombotic status mediated by platelet and thrombin activation[10]. Therefore, supervised exercise at lower intensity training is recommended to those patients stratified as high-risk. On the other hand, patients need to reach a certain intensity threshold for improving their cardiovascular health[11, 12].

The way we currently define exercise intensity (EI) is quite variable: several indices are recommended that demarcate the different training zones (low, moderate, high, and very-high)[13, 14]. Usually, percentages of maximal physiological parameters are used to categorize exercise intensity domains, such as % peak oxygen uptake (VO2) and % peak heart rate (HR). Another commonly used parameter is the heart rate reserve (HRR) and its percentage[5, 6, 14]. The different cut-offs of these variables are presented as interchangeable in defining the intensity domains[13]. For instance, it is assumed that a patient will be exercising at a moderate intensity if he reaches 40-69% of his HRR or Peak VO_2 or 55-74% of his Peak HR[5]. However, little data exists on the internal consistency between these indices in HF patients. In addition, the agreement of these indices with the ventilatory thresholds (VT) assessed by a maximal cardiopulmonary exercise test (CPET) is also unclear in HF patients[12]. VTs identification are based on a strong physiological rationale of the metabolic response to exercise and empirical data[11], as they allow to characterize the individual patient response to exercise[15]. This issue is particularly relevant in HF populations because they include high-risk patients to whom safety during ET is a sensible concern. In addition, HF patients are very heterogeneous in their exercise capacity and chronotropic response[6, 13], which can potentially impact on the precision of the currently recommended indices to prescribe ET.

We aimed to study the internal consistency between the commonly used exercise intensity measures (% Peak VO_2, % Peak HR and % HRR) in the classification of the different exercise intensity domains, and the concordance of these indices with ventilatory thresholds in patients with HF.

Methods

Population and design

This retrospective observational study included patients with HF referred to the Cardiac Rehabilitation Unit of Centro Hospitalar Universitário de Santo António (Porto, Portugal) between January 2019 and June 2022. We included all patients with HF according to the criteria of the European Society of Cardiology (ESC) irrespective of left ventricle ejection fraction (LVEF)[2]. We excluded those with paced rhythm at the time of exercise testing. Electronic health records were reviewed for clinical characteristics (including comorbidities, medications, and echocardiographic data) and CPET report data. Our hospital Human Research Committee approved this retrospective chart review and waived the requirement for informed consent (2021.187(154-DEFI/160-CE).

Exercise assessments

Exercise capacity was evaluated through a maximal CPET testing on a treadmill (Medisoft, Model 870C). The testing protocol was chosen according to the patient´s physical activity (PA) level (modified Naughton, Bruce, or Gardner-Skinner). The CPET was conducted under medical supervision, with electrocardiography continually monitored throughout the protocol. Using a stationary metabolic cart system (Geratherm® Respiratory Ergostik, under BLUE CHERRY®), respiratory gas exchange measurements were obtained breath-by-breath and recorded every 30 seconds. Heart rate and blood pressure were recorded at regular intervals throughout the test. During CPET testing, patients were strongly encouraged to achieve a 16 in the Borg rating of perceived exertion (6 to 20 scale), and a respiratory exchange ratio >1.10. Peak VO_2 was determined as the highest VO_2 achieved during exercise. The first ventilatory threshold (VT1) was determined using the nadir of the VE/VO_2 versus work rate (W) relationship. The second ventilatory threshold (VT2) was determined, using the VE versus VCO_2 plot, on the point where VE increases out of proportion to VCO_2, and the nadir of the VE/VCO_2 versus W relationship. However, VT2 was only reported in two patients and was therefore not considered for the analysis. VO_2 and HR were determined at VT1 and VT2 as well as at 40%, 70% and 85% of Peak VO_2 (according to the training zones identified in the ESC guidelines)[5]. HRR was calculated as the difference between the peak and resting HR and expressed as % HRR at those exercise periods. We used the EI domains depicted in the ESC guidelines[5, 14, 16] for comparison of the different EI indices. VT1 was considered to be the physiological transition to moderate-high intensity domain[14].

Statistical analysis

Statistical analysis was preformed using IBM SPSS version 27.0 (IBM SPSS Statistics, Chicago, IL, USA). In the descriptive analysis, normally distributed continuous variables were described using mean and standard deviation (SD), whereas for non-normally distributed variables, median and interquartile range (IQR) were used. For group comparison, Chi-square test was used for categorical variables, and t-student or Mann-Whitney U tests were used for continuous variables depending on distribution normality. For the whole study population, we compared the concordance rates between the different EI measures at VT1 and the ESC EI domains and assessed the agreement percentage. Agreement between % Peak HR and % HRR, and % Peak VO_2 at 40%, 70% and 85% was also assessed.

Two subgroup analyses were done. We stratified the patients according to their LVEF in two groups: preserved (LVEF ≥ 50%) and reduced (LVEF < 50%). The concordance rates between the different EI measures at VT1 and the ESC exercise intensity domains were compared between these groups. A similar analysis was done by dividing patients according to their physical fitness and overall exercise capacity in two groups defined by the median Peak VO_2. Two sensitivity analysis were performed excluding patients on atrial fibrillation at the time of CPET and patients that were not on beta-blockers. The significance level was set at < 0.05 (two-tailed).

Results

Demographic and clinical characteristics

Of a total of 259 CPETs performed during the study period to HF patients, 88 were excluded as they were repeated tests on the same patients; 8 other cases were excluded because the patients were on paced rhythm at the time of the CPET (Figure 1). Therefore, 163 patients were included in the analysis. 105 (64%) were male and the overall mean age was 61 ± 11 years. Regarding the HF phenotype, most of the patients, 107 (66%), had reduced LVEF, 28 (17%) had mildly reduced LVEF and 28 (17%) had preserved LVEF. Ischemic cardiomyopathy was the cause of HF in 62 (38%) patients. The mean LVEF was 36 ± 12% and 71% of patients were in New York Heart Association (NYHA) Functional Class (FC) II. The main comorbidities of this population were dyslipidemia (66%) and hypertension (64%), and almost half of the population was diabetic (45%). History of atrial fibrillation was present in 39 (24%) individuals, but only 10 (6.1%) had this rhythm at the time of CPET. Most patients were on beta-blockers (93%) and on angiotensin-converting-enzyme inhibitors (ACEi) or angiotensin-II-receptor antagonists (ARA) (84%). 41 (25%) patients had implanted cardiac devices (pacemakers, cardiac-resynchronization therapy devices and implantable cardioverter-defibrillators). A detailed demographic and clinical characterization of the study population can be found on Table I.

CPET data

In the 163 CPETs included in the analysis, the most common protocol was Modified Naughton in 116 (71%) patients, followed by Modified Bruce in 25 (15%) patients. Most of the patients were in sinus rhythm during the test (94%). Mean exercise duration was 09min25sec ± 03min32sec and mean peak respiratory exchange ratio (RER) was 1.06 ± 0.12. Although perception of maximal exertion was documented for all patients, peak RER ≥ 1.05 was attained in 91 (56%) cases. Mean Peak HR was 121 ± 21 beats per minute (bpm) and mean Peak VO_2 was 18.3 ± 5.4 mL/Kg/min. Mean HRR was 47 ± 18 bpm. At VT1 mean HR was 96 ± 21 bpm and mean VO_2 was 10.0 ± 4.4 mL/Kg/min (41.6 ± 20.1% of predicted Peak VO_2). Detailed CPET data can be found on Tables II and III.

Consistency between VT1 and the guideline-based exercise intensity indices

VT1 was observed at 82 ± 10% of Peak HR, corresponding to the ESC high intensity training zone. However, the same threshold was found at 54 ± 25% of HRR and 54 ± 17% of Peak VO_2, corresponding to the moderate intensity training zone.

Considering VT1 as the physiological transition to a moderate to high intensity training zone, and using % Peak VO2, 78% of the patients were classified in the correct EI domain (moderate-high) at VT1. % HRR was the parameter with the worst concordance (58%) because it tended to underestimate the EI, placing 27% of patients at an inferior training zone at VT1. % Peak HR showed a similar concordance to % Peak VO2 (78% of patients appropriately classified) but overestimated intensity in a higher proportion of patients (22%) - Table IV and Figure 2.

Considering the % Peak VO_2 cut-offs elicited in the ESC guidelines (40% as the transition point to moderate intensity, 70% to high intensity, and 85% to very high intensity) as the baseline measure of EI, its internal consistency with the other recommended indices is presented at Table V. At 40% of Peak VO_2, consistency is high when using % Peak HR (74% of patients classified in moderate intensity exercise domain) but drops to 3.2% when using % HRR. Similar results are found at 70% of Peak VO_2, where 81% of patient are correctly classified in the high intensity domain according to % Peak HR but only 5.7% are assigned to this category according to the % HRR. On the contrary, at 85% of Peak VO_2, consistency drops for % Peak HR (only 47% of patients adequately classified in the very high intensity domain), and % HRR consistency remains low (13%).

Subgroup and sensitivity analyses

We divided our study population according to LVEF: 135 patients with reduced LVEF and 28 patients with preserved LVEF. Patients with preserved LVEF were older (65.0 ± 13.3 vs 60.3 ± 10.4 years; $p = 0.043$), had lower prevalence of males (43% vs 69%; $p = 0.009$) and had higher prevalence of atrial fibrillation history (50% vs 19%; $p < 0.001$) - Supplementary Table VI. Exercise capacity was superior in the reduced LVEF group when measured by Peak VO_2 (18.7 ± 5.5 vs 15.1 ± 4.8 mL/Kg/min; $p = 0.017$) but showed no differences when the % Predicted Peak VO_2 (73.5 ± 19.4 vs 77.3 ± 19.9; $p = 0.351$) were compared. Concordance of the recommended indices of EI at VT1 was superior for patients with reduced LVEF. Classification of patients according to % Peak VO_2 had a 79% correspondence to the moderate to high intensity domain in reduced LVEF patients compared to 73% in preserved LVEF patients. The differences are more evident for the other indices, such as % Peak HR: 80% concordance in reduced LVEF group vs 68% in the preserved LVEF group and regarding % HRR: 62% in reduced LVEF group vs 50% in the preserved LVEF group (Supplementary Table VII).

Another subgroup analysis was done in respect to the exercise capacity and overall physical fitness of patients. They were stratified in two groups according to median Peak VO_2, (17.4 mL/Kg/min). In general, patients with higher exercise capacity (Peak VO_2 above the median) were younger (57.9 ± 11.0 vs 64.4 ± 10.2 years; $p < 0.001$), more likely to be male (73% vs 56%; $p = 0.019$), had higher prevalence of reduced LVEF (92% had LVEF < 50% vs 74% with LVEF ≥ 50%; $p = 0.019$), had a lower baseline NT-pro-BNP (286 ± 634 vs 726 ± 1721 pg/mL; $p < 0.001$); history of atrial fibrillation (15% vs 34%; $p = 0.004$) and chronic kidney disease (6% vs 24%; $p = 0.002$) were less prevalent and hemoglobin concentration was higher (14.7 ± 1.4 vs 13.6 ± 1.8 g/dL; $p < 0.001$) - Supplementary Table VIII. The concordance of the recommended indices of EI at VT1 was superior for patients with higher exercise capacity. Classification of patients according to % Peak VO_2 had 86% correspondence to the moderate to high intensity domain in patients with higher exercise capacity compared to 69% in the other group. The differences persisted for the other indices, such as % Peak HR: 91% concordance in higher exercise capacity group vs 64% in the other group. Regarding % HRR, 62% in higher exercise capacity group vs 57% in the other group (Supplementary Table IX).

Two sensitivity analyses were performed: one excluding patients on atrial fibrillation at the time of the CPET (10 patients), and the other excluding patients not on beta-blockers (12 patients). Concordance of the recommended indices of EI at VT1 with the ESC guidelines training zones was not significantly different after excluding these subsets of patients (Supplementary Tables X and XI).

Discussion

The main findings of our study are the following. First, in one out of five HF patients the EI domain will be misclassified by current recommended indices when compared to the gold standard VT1. Second, the % HRR was the parameter with the worst performance; % Peak VO_2 and % Peak HR were similar but tended to under- and overestimate the EI, respectively. Third, the performance of exercise indices was worse in patients with HFpEF and in those with worse physical fitness.

At least, 20% of HF patients enrolled to a cardiac rehabilitation program will have an inadequate exercise prescription if we do not use ventilatory thresholds to guide our decision. If we use % Peak HR we will risk prescribing low-intensity exercise to 1 out of 5 HF patients and waste the potential benefits of the exercise sessions. On the contrary, using % Peak VO_2 might lead us to prescribe very high-intensity exercise and possibly deal with the associated risks and discomfort caused to the overexercising patient.

In 2019 Hansen et al.[13] studied a group of patients with cardiovascular disease who performed a maximal cardiopulmonary exercise test on a cycloergometer. At the same level of effort (both VT1 and VT2), different physiologic parameters corresponded to different recommendation-based EI domains, prompting the authors to suggest the adjustment of the recommendations in place at the time. Furthermore, they also observed that in physically deconditioned patients (with lower absolute Peak VO_2) there was a greater discordance of the EI domains. Also, in another study[15], following the 2020 ESC guidelines, it was shown that when considering % Peak VO_2, a better concordance between the first threshold and the moderate intensity domain was elicited. On the contrary, when the HR parameters (% peak HR and %HRR) were used, a greater incongruity was noticed between VTs and EI domains. The results of our study were in line with these. However, in these studies, the populations selected were heterogenous, including patients with different cardiovascular diseases. From coronary artery disease to hypertrophic cardiomyopathy, only a proportion of them had HF. There is still very little data specifically for exercise intensity prescription in HF patients. As such, we provide further insight, in a selected HF population, and especially about two subgroups of patients, reduced LVEF vs. preserved LVEF, and its correspondence to the most recent guidelines.

In our study, when applying the 2020 ESC guidelines[5], the %HRR demonstrated a low matching between VT1 and its respective EI domain (58% were classified in the correct EI domain). Also, 27% were placed at an inferior training zone at VT1, which means these results were below the expected level of EI (ie, less than moderate), likely leading to safety concerns in cardiac rehabilitation of HF patients. This was observed in previous studies, where using %HRR turned out to be an underestimation of the EI domain[12, 13, 15]. Moreover, in those same studies, like ours, there is a greater consistency at VT1 with the expected EI domains using % Peak VO_2.

To explain why there is such discrepancy and underestimation when using % HRR as an EI index, we need analyze our population's characteristics. First, chronotropic incompetence is one of the hallmarks of the HF patient, which by definition limits HRR. This way, patients with chronotropic incompetence will be expected to reach a higher % HRR earlier than healthy ones. Second, it is also known that adequate increment of HR during exercise is essential for the ability to perform sustained aerobic exercise[17]. This seems a plausible cause to the fact that, when measuring the % HRR, the corresponding EI domain will come below what would be expected. On the other hand, in a previous study[18], comparing HF patients on beta-blockers (βb) with HF patients off βb and normal individuals, it was observed that HF patients off βb had a superior HR at rest and a subsequent lower HR at peak (when compared to normal individuals), resulting in a lower HRR. Moreover, the HF patients on βb had an even lower HR at rest and peak, meaning an even lower HRR, when compared to both HF patients off βb and normal individuals. On the contrary, both rest and Peak VO_2 values had no correlation whatsoever with the usage or not of this type of medication. Considering this relationship and the fact that 93% of the patients in our population were on βb, we conclude that these factors probably influenced the results, as HF patients, especially on beta blockers, will demonstrate lower EI domains at VT1 when classified according to %HRR, resulting in an underestimation of EI.

Furthermore, our subgroup analysis, comparing patients with preserved vs reduced LVEF, demonstrated that there was a higher discordance of the recommended indices of exercise intensity at VT1 in patients with preserved LVEF. It is known that this subgroup of patients is usually older, more likely female and have a higher prevalence of non-CV comorbidities[2]. Also, another known characteristic of these patients is their reduced aerobic capacity, as elicited by lower Peak VO_2, resulting in a more deconditioned life[19]. To our knowledge this is the first study to demonstrate these differences between these two subgroups of patients in a highly selected HF-only cohort.

Our study also demonstrated that patients with HF with preserved LVEF have lower mean Peak VO_2, but when comparing the % of predicted peak VO_2 across the two phenotypes, we found no significant differences. This might be due to the higher burden of comorbidities and the older age of this population.

Similarly, and concordant to what was previously described by Hansen et al.[13], patients with lower aerobic capacity also showed lower concordance rates between the intensity indices and the EI domains at VT1.

Regarding atrial fibrillation (AF), these patients frequently have impaired exercise capacity due to loss of atrial contraction and thus lower cardiac output. This usually leads to lower absolute Peak VO_2 and VO_2 at VT1 compared to patients in sinus rhythm[14]. Although, our study had 39 (24%) individuals with history of AF, only 10 (6.1%) presented with this rhythm at the time of CPET. A sensitivity analysis was performed excluding this last subgroup of patients, that showed that the concordance of the recommended indices of exercise intensity at VT1 with the ESC guidelines training zones was not significantly different from the general cohort.

A recent scientific statement by the American Heart Association / American College of Cardiology[20] revealed a comprehensive review of the available literature on exercise training prescription in HF with preserved LVEF. While some of the studies that generated evidence for ET prescription used HR based parameters for exercise prescription, despite having submitted the patients to a CPET[21-23], others used % Peak VO_2 related indexes[24, 25]. Apparently, none used a VT1 based approach.

Finally, our study demonstrated that when we used the % Peak VO_2 and % Peak HR, to prescribe moderate EI in HF patients under β-blocker therapy, most patients were classified in the correct training zone (78% and 77,9%, respectively). However, the parameter of % Peak HR overestimated intensity in a higher proportion of patients (22%), leading to a wrong prescription in these patients with a lower than recommended EI. On the other hand, when using the percentage of HRR, in a HF β-blocked patient, EI prescription above the recommended threshold may occur in approximately 27% of cases, leading to possible safety concerns. Therefore, this paper emphasizes the importance of using a threshold-based approach to EI prescription especially in HF patients under βb therapy.

Limitations

Our study has several limitations that need to be acknowledged. First, the retrospective nature of the study and the fact that it comprises a highly selected HF cohort referred to a cardiac rehabilitation center lead limit the generalizability of these results to other patient groups. Second, VT2 was only reported in two patients and was therefore not considered for the analysis, which limits ET discrimination and comparison with the available literature. Third, the low percentage of patients (17%) who had preserved LVEF in our cohort limit the extrapolation of our conclusion to HFpEF.

Conclusion

Along with drugs and devices, exercise training is an important pillar of modern HF treatment. Most cardiovascular studies on exercise prescription involved patients with coronary artery disease that significantly differ from HF ones. Our study data inform us about the hazards of prescribing exercise using indices other than ventilatory indices and emphasizes the need for a maximal CPET to an adequate prescription of exercise to HF patients.

Appendix

Tables

Table I - Clinical characteristics of the studied population (n = 163) **

General features	Mean (SD) or n (%)
Age (years)	61.1 (11.0)
Gender (males)	105 (64.4)
BMI (Kg/m^2)	27.3 (5.29)
Educational level	
No education	3 (1.80)
1 – 4 years	47 (28.8)
5 – 9 years	52 (31.9)
10 – 12 years	19 (11.7)
Superior (university)	10 (6.10)
Ejection fraction (%)	36.2 (12.4)
Heart failure classification according to LVEF	
HF preserved EF (≥ 50%)	22 (13.5)
HF mildly reduced EF (41-49%)	28 (17.2)
HF reduced EF (≤ 40%)	107 (65.6)
HF recovered EF	6 (3.70)
Heart failure etiology	
Ischemic	62 (38.0)
NYHA functional class	
I	34 (20.9)
II	116 (71.2)
III	12 (7.40)
Pro-BNP (pg/mL) *	415 (993)
Comorbidities	
Hypertension	105 (64.4)
Diabetes mellitus	73 (44.8)
Dyslipidemia	108 (66.3)
Obesity	46 (28.2)
Tobacco use	
Active smoker	31 (19.0)
Previous smoker	54 (33.1)
Pack-years (units)	46.6 (35.3)
Previous MI	44 (27.0)
Atrial fibrillation history	39 (23.9)
Peripheral artery disease	19 (11.7)
Previous stroke	8 (4.90)
Chronic kidney disease	24 (14.7)

COPD	14 (8.60)
OSA	14 (8.60)
Cancer history	20 (12.3)
Musculoskeletal disease	32 (19.6)
Chronic medication	
ASA	66 (40.5)
Clopidogrel	28 (17.2)
Ticagrelor	7 (4.30)
VKA	15 (9.20)
DOAC	39 (23.9)
Beta-blocker	151 (92.6)
ACEi/ARA	137 (84.0)
Sacubitril/Valsartan	61 (37.4)
MRA	118 (72.4)
Diuretics	98 (60.1)
Statin	125 (76.7)
Ezetimibe	13 (8.00)
Amiodarone	26 (16.0)
Digoxin	9 (5.50)
SGLT2i	96 (58.9)
OAD agents	105 (64.4)
Insulin	13 (8.00)
NIV therapy	5 (3.10)
Implanted devices – total	41 (25.2)
Pacemaker	1 (0.60)
CRT	18 (11.0)
ICD	22 (13.5)
Hemoglobin (g/dL)	14.2 (1.67)
HbA1c (%) *	5.90 (0.90)
Total cholesterol (mg/dL) *	156 (64.0)
LDL cholesterol (mg/dL)	87.7 (33.9)

ACEi = angiotensin converting enzyme inhibitor; ARA = angiotensin II receptor antagonist; ASA = acetylsalicylic acid; BMI = body mass index; COPD = chronic obstructive pulmonary disease; CRT = cardiac resynchronization therapy; DOAC = direct oral anticoagulant; EF = ejection fraction; HbA1c = hemoglobin A1c; HF = heart failure; ICD = implantable cardioverter-defibrillator; LDL = low-density lipoprotein; LVEF = left ventricle ejection fraction; MI = myocardial infarction; MRA = mineralocorticoid receptor antagonist; NIV = non-invasive ventilation; NYHA = New York Heart Association; OAD = oral anti-diabetic; OSA = obstructive sleep apnea; Pro-BNP = pro-brain natriuretic peptide; SD = standard deviation; SGLT2i = sodium-glucose co-transporter 2 inhibitor; VKA = vitamin K antagonist.

** Variable with a non-normal distribution. Values correspond to median (interquartile range).*

*** Some totals do not add up to 163 due to missing data.*

Table II - CPET characteristics in the studied population (n = 163) *

Feature	Mean (SD) or n (%)
Protocol	
Bruce	19 (11.7)
Modified Bruce	25 (15.3)
Gardner-Skinner	2 (1.20)
Modified Naughton	116 (71.2)
Rhythm during CPET	
Sinus	153 (93.9)
Atrial fibrillation	10 (6.10)
Exercise duration (min:sec)	09:25 (03:32)
Reason for exercise interruption	
Fatigue	130 (79.8)
Dyspnea	15 (9.20)
Chest pain	2 (1.20)
Claudication	7 (4.30)
Other	5 (3.10)
ST-segment changes suggesting ischemia	15 (9.20)

CPET = cardiopulmonary exercise test; SD = standard deviation.
** Some totals do not add up to 163 due to missing data.*

Table III - CPET data of the studied population (n = 163)

Parameter – mean (SD)*	**Basal**	**Peak**	**% Predicted peak**	**VT1**
HR (bpm)	74.1 (12.3)	121 (21.0)	76.3 (12.6)	96.0 (21.0)
HRR (bpm)	46.9 (17.9)		-	-
SBP (mmHg)	123 (29.0)	166 (30.1)	-	-
DBP (mmHg)	76.7 (13.6)	77.0 (18.0)	-	-
BF (cpm)	18.3 (4.49)	33.7 (6.25)	-	-
SaO_2 (%)	96.0 (2.00)	95.0 (3.00)	-	-
FEV_1 (L)	2.35 (0.71)	-	-	-
VO_2 (L/min)	0.29 (0.11)	1.38 (0.48)	74.1 (19.5)	0.76 (0.36)
VO_2 (mL/Kg/min)	3.80 (1.20)	18.3 (5.38)		10.0 (4.39)
VCO_2 (L/min)	0.24 (0.06)	1.47 (0.58)	-	-
VE (L/min)	11.0 (3.00)	55.4 (18.2)	68.1 (17.0)	-
VE/VO_2	32.4 (6.86)	37.0 (8.13)	-	25.6 (6.25)
VE/VCO_2	38.9 (6.61)	35.0 (6.82)	-	32.0 (6.55)
O_2 pulse (mL/beat)	3.80 (1.33)	11.4 (3.36)	-	-
$PETCO_2$ (mmHg)	30.0 (5.00)	34.0 (6.00)	-	30.0 (6.00)
RER	-	1.06 (0.12) **	-	-

BF = Breathing frequency; bpm = beats per minute; CPET = cardiopulmonary stress test; cpm = cycles per minute; DBP = diastolic blood pressure; FEV1 = forced expiratory volume in 1 second; HR = heart rate; HRR = heart rate reserve; PETCO2 = end-tidal CO2; RER = respiratory exchange ratio; SaO2 = arterial blood oxygen saturation; SBP = systolic blood pressure; SD = standard deviation; VE = minute ventilation; VCO2 = carbon dioxide production; VO2 = oxygen uptake; VT1 = first ventilatory threshold.

** In variables with a non-normal distribution, values correspond to median and (interquartile range).*

Table IV - Concordance of recommended indices of exercise intensity (%VO2max, %HRmax, %HRR) at VT1 with the ESC guidelines training zones (in grey).

Patients' response to exercise (n = 163)	**At VT1**		
	% Peak VO_2	**% Peak HR**	**%HRR**
Mean (SD) or median (IQR)	53.7 (17.0)	82.1 (10.4)	53.5 (25.1)
Guidelines exercise intensity (% prevalence)			
Low	19.5	0.00	27.2
Moderate to high	**78.0**	**77.9**	**58.3**
Very high	2.50	22.1	12.3

ESC = European Society of Cardiology; HR = heart rate; HRR = heart rate reserve; IQR = interquartile range; SD = standard deviation; VO_2 = oxygen uptake; VT1 = first ventilatory threshold.

Table V - Internal consistency of recommended indices of exercise intensity according to the ESC guidelines training zones (in grey).

Patients' response to exercise (n = 163)	At 40% Peak VO_2		At 70% Peak VO_2		At 85% Peak VO_2	
	% Peak HR	**%HRR**	**% Peak HR**	**%HRR**	**% Peak HR**	**%HRR**
Mean (SD) or median (IQR)	68.5 (10.0)	18.8 (17.0)	81.3 (6.40)	50.4 (12.8)	89.8 (5.49)	73.9 (14.0)
Guidelines exercise intensity (% prevalence)						
Low	3.20	**96.8**	0.00	16.4	0.00	1.30
Moderate	**74.4**	3.20	11.9	**78.0**	0.00	20.9
High	22.4	0.00	**80.5**	5.70	**52.7**	**54.6**
Very high	0.00	0.00	7.50	0.00	47.3	13.2

ESC = European Society of Cardiology; HR = heart rate; HRR = heart rate reserve; IQR = interquartile range; SD = standard deviation; VO_2 = oxygen uptake

Figures

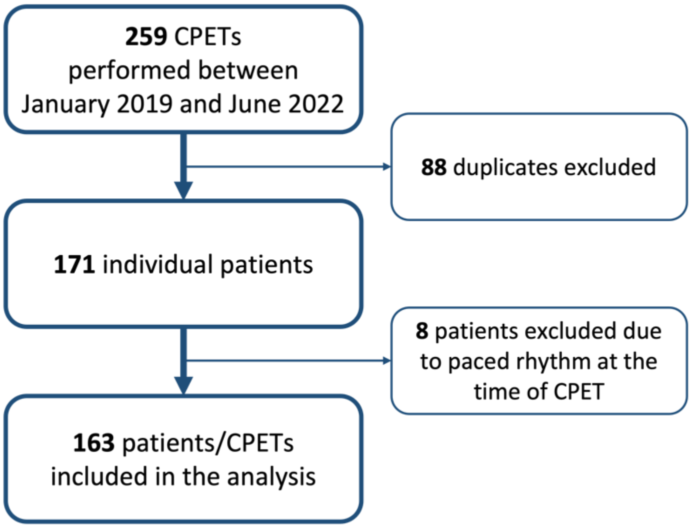

Figure 1 - Study population flowchart.

CPET = Cardiopulmonary exercise test.

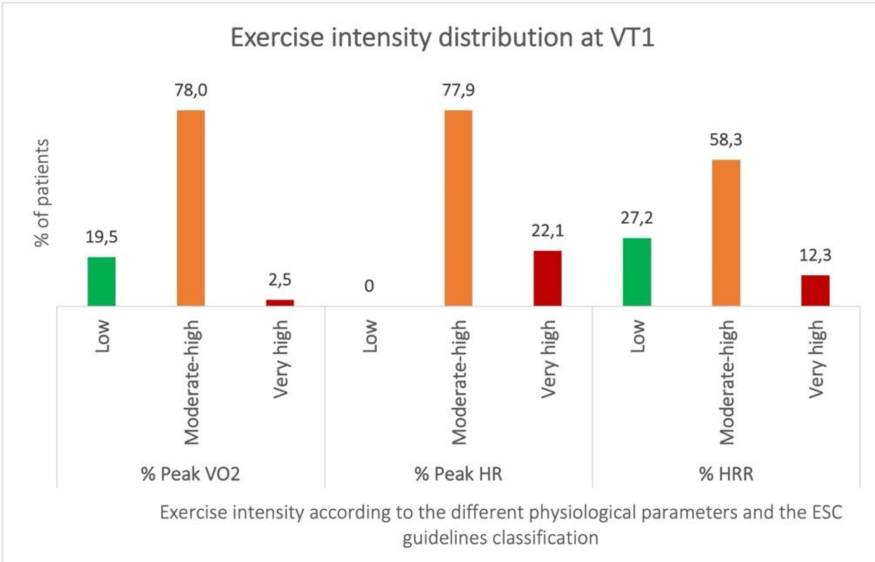

Figure 2 - Exercise intensity distribution at VT1 according to the different studied physiological parameters (% Peak VO2, % Peak HR, % HRR) and the ESC guidelines classification.

Supplements

Table VI - Clinical characteristics of the studied population according to HF phenotype (reduced EF, LVEF<50%; preserved EF, LVEF ≥ 50%).

General features [mean (SD) or n (%)]	**HF reduced EF (n = 135)**	**HF preserved EF (n = 28)**	**Total (n = 163) ****	**p value**
Age (years)	60.3 (10.4)	65.0 (13.3)	61.1 (11.0)	0.043
Gender (male)	93 (68.9)	12 (42.9)	105 (64.4)	0.009
BMI (Kg/m^2)	27.0 (5.00)	28.8 (6.41)	27.3 (5.29)	0.166
Educational level				
No education	3 (2.80)	0 (0.00)	3 (1.80)	
1 – 4 years	36 (33.6)	11 (45.8)	47 (28.8)	
5 – 9 years	45 (42.1)	7 (29.2)	52 (31.9)	0.184
10 – 12 years	17 (15.9)	2 (8.30)	19 (11.7)	
Superior (university)	6 (5.60)	4 (16.7)	10 (6.10)	
Ejection fraction (%)	32.3 (9.53)	55.9 (4.77)	36.2 (12.4)	< 0.001
Ischemic etiology	55 (40.7)	7 (25.9)	62 (38.0)	0.148
NYHA functional class				
I	30 (22.2)	4 (14.8)	34 (20.9)	
II	95 (70.4)	21 (77.8)	116 (71.2)	0.684
III	10 (7.40)	2 (7.40)	12 (7.40)	
Pro-BNP (pg/mL) *	374 (998)	652 (988)	415 (993)	0.644
Comorbidities				
Hypertension	85 (63.4)	20 (71.4)	105 (64.4)	0.420
Diabetes mellitus	59 (44.0)	14 (50.0)	73 (44.8)	0.564
Dyslipidemia	86 (65.2)	22 (78.6)	108 (66.3)	0.168
Obesity	35 (26.1)	11 (39.3)	46 (28.2)	0.372
Tobacco use				
Active smoker	28 (21.1)	3 (10.7)	31 (19.0)	0.005
Previous smoker	50 (37.6)	4 (14.3)	54 (33.1)	
Previous MI	39 (29.1)	5 (17.9)	44 (27.0)	0.224
Atrial fibrillation history	25 (18.7)	14 (50.0)	39 (23.9)	< 0.001
Peripheral artery disease	15 (11.2)	4 (14.3)	19 (11.7)	0.644
Previous stroke	7 (5.20)	1 (3.60)	8 (4.90)	0.714
Chronic kidney disease	18 (13.4)	6 (21.4)	24 (14.7)	0.279
COPD	11 (8.20)	3 (10.7)	14 (8.60)	0.668
OSA	9 (6.70)	5 (17.9)	14 (8.60)	0.056
Cancer history	17 (12.7)	3 (10.7)	20 (12.3)	0.773
Musculoskeletal disease	26 (19.4)	6 (21.4)	32 (19.6)	0.807
Chronic medication				
ASA	54 (40.3)	12 (42.9)	66 (40.5)	0.802

Clopidogrel	23 (17.2)	5 (17.9)	28 (17.2)	0.930
Ticagrelor	7 (5.20)	0 (0.00)	7 (4.30)	0.216
VKA	13 (9.70)	2 (7.10)	15 (9.20)	0.671
DOAC	24 (17.9)	15 (53.6)	39 (23.9)	< 0.001
Beta-blocker	128 (95.5)	23 (82.1)	151 (92.6)	0.010
ACEi/ARA	117 (87.3)	20 (71.4)	137 (84.0)	0.034
Sacubitril/Valsartan	54 (40.3)	7 (25.0)	61 (37.4)	0.129
MRA	107 (79.9)	11 (39.3)	118 (72.4)	< 0.001
Diuretics	81 (60.4)	17 (60.7)	98 (60.1)	0.979
Statin	106 (79.1)	19 (67.9)	125 (76.7)	0.197
Ezetimibe	12 (9.00)	1 (3.60)	13 (8.00)	0.340
Amiodarone	15 (11.2)	11 (39.3)	26 (16.0)	< 0.001
Digoxin	6 (4.50)	3 (10.7)	9 (5.50)	0.190
SGLT2i	81 (60.4)	15 (53.6)	96 (58.9)	0.501
OAD agents	87 (64.9)	18 (64.3)	105 (64.4)	0.949
Insulin	10 (7.50)	3 (10.7)	13 (8.00)	0.565
NIV therapy	3 (2.20)	2 (7.10)	5 (3.10)	0.172
Implanted devices – total	38 (28.2)	3 (10.8)	41 (25.2)	
Pacemaker	0 (0.00)	1 (3.6)	1 (0.60)	0.019
CRT	17 (12.6)	1 (3.6)	18 (11.0)	
ICD	21 (15.6)	1 (3.6)	22 (13.5)	
Hemoglobin (g/dL) *	14.4 (2.10)	13.7 (2.30)	14.2 (1.67)	0.033
HbA1c (%) *	5.90 (0.80)	6.25 (1.30)	5.90 (0.90)	0.237
Total cholesterol (mg/dL) *	155 (59.0)	156 (67.0)	156 (64.0)	0.609
LDL cholesterol (mg/dL) *	86.0 (43.0)	79.5 (59.0)	87.7 (33.9)	0.755

ACEi = angiotensin converting enzyme inhibitor; ARA = angiotensin II receptor antagonist; ASA = acetylsalicylic acid; BMI = body mass index; COPD = chronic obstructive pulmonary disease; CRT = cardiac resynchronization therapy; DOAC = direct oral anticoagulant; EF = ejection fraction; HbA1c = hemoglobin A1c; HF = heart failure; ICD = implantable cardioverter-defibrillator; LDL = low-density lipoprotein; LVEF = left ventricle ejection fraction; MI = myocardial infarction; MRA = mineralocorticoid receptor antagonist; NIV = non-invasive ventilation; NYHA = New York Heart Association; OAD = oral anti-diabetic; OSA = obstructive sleep apnea; Pro-BNP = pro-brain natriuretic peptide; SD = standard deviation; SGLT2i = sodium-glucose co-transporter 2 inhibitor; VKA = vitamin K antagonist.

** Variable with a non-normal distribution. Values correspond to median (interquartile range).*

*** Some totals do not add up to 163 due to missing data.*

Table VII - Concordance of recommended indices of exercise intensity (% Peak VO2, % Peak HR, %HRR) at VT1 with the ESC guidelines training zones (in grey) stratified by HF phenotype (reduced EF, LVEF < 50%; preserved EF, LVEF ≥ 50%).

Patients' response to exercise (n = 163)	**Peak VO_2** (ml/kg/min)	**At VT1** % Peak VO_2	% Peak HR	%HRR
Reduced LVEF (n = 135)				
Mean (SD) or median (IQR) *	18.7 (5.51)	52.6 (16.3)	81.6 (10.4)	53.2 (24.6)
Guidelines exercise intensity (% prevalence)				
Low		19.5	0.00	25.6
Moderate to high		**77.8**	**79.8**	**61.7**
Very high		1.50	20.2	12.8
Preserved LVEF (n = 28)				
Mean (SD) or median (IQR) *	15.1 (4.83)	58.9 (19.9)	84.3 (10.5)	60.1 (51.0)
Guidelines exercise intensity (% prevalence)				
Low		19.2	0.00	38.5
Moderate to high		**73.1**	**68.0**	**50.0**
Very high		7.70	32.0	11.5
p value between groups	0.017	0.086	0.239	0.762

EF = ejection fraction; ESC = European Society of Cardiology; HF = heart failure; HR = heart rate; HRR = heart rate reserve; IQR = interquartile range; LVEF = left ventricle ejection fraction; SD = standard deviation; VO_2 = oxygen uptake; VT1 = first ventilatory threshold.

** In variables with a non-normal distribution, values correspond to median and (interquartile range).*

Table VIII - Clinical characteristics of the studied population according to according to exercise fitness (Peak VO2 above median: ≥ 17.4 mL/Kg/min vs Peak VO2 below median: < 17.4 mL/Kg/min).

General features [mean (SD) or n (%)]	**Below median (n = 81)**	**Above median (n = 82)**	**Total (n = 163) ****	**p value**
Age (years)	64.4 (10.2)	57.9 (11.0)	61.1 (11.0)	< 0.001
Gender (males)	45 (55.6)	60 (73.2)	105 (64.4)	0.019
BMI (Kg/m^2)	28.1 (5.52)	26.6 (4.98)	27.3 (5.29)	0.066
Educational level				
No education	2 (3.00)	1 (1.60)	3 (1.80)	
1 – 4 years	27 (40.3)	20 (31.3)	47 (28.8)	
5 – 9 years	21 (31.3)	31 (48.4)	52 (31.9)	0.392
10 – 12 years	11 (16.4)	8 (12.5)	19 (11.7)	
Superior (university)	6 (9.00)	4 (6.30)	10 (6.10)	
Ejection fraction (%)	37.8 (14.0)	34.6 (10.6)	36.2 (12.4)	0.104
Heart failure classification according to LVEF				
HF preserved EF	16 (19.8)	6 (7.30)	22 (13.5)	
HF mildly reduced EF	10 (12.3)	18 (22.0)	28 (17.2)	0.019
HF reduced EF	50 (61.7)	57 (69.5)	107 (65.6)	
HF recovered EF	5 (6.20)	1 (1.20)	6 (3.70)	
Ischemic etiology	37 (45.7)	25 (30.9)	62 (38.0)	0.052
NYHA functional class				
I	12 (14.8)	22 (27.2)	34 (20.9)	
II	62 (76.5)	54 (66.7)	116 (71.2)	0.148
III	7 (8.60)	5 (6.20)	12 (7.40)	
Pro-BNP (pg/mL) *	726 (1721)	286 (634)	415 (993)	< 0.001
Comorbidities				
Hypertension	56 (70.0)	49 (59.8)	105 (64.4)	0.172
Diabetes mellitus	42 (52.5)	31 (37.8)	73 (44.8)	0.060
Dyslipidemia	54 (68.4)	54 (66.7)	108 (66.3)	0.820
Obesity	26 (32.5)	20 (24.4)	46 (28.2)	0.492
Tobacco use				
Active smoker	7 (8.90)	24 (29.3)	31 (19.0)	0.005
Previous smoker	30 (38.0)	24 (29.3)	54 (33.1)	
Previous MI	27 (33.8)	17 (20.7)	44 (27.0)	0.063
Atrial fibrillation history	27 (33.8)	12 (14.6)	39 (23.9)	0.004
Peripheral artery disease	11 (13.8)	8 (9.80)	19 (11.7)	0.430
Previous stroke	4 (5.00)	4 (4.90)	8 (4.90)	0.971
Chronic kidney disease	19 (23.8)	5 (6.10)	24 (14.7)	0.002
COPD	7 (8.80)	7 (8.50)	14 (8.60)	0.961
OSA	8 (10.0)	6 (7.30)	14 (8.60)	0.543
Cancer history	13 (16.3)	7 (8.50)	20 (12.3)	0.136

Musculoskeletal disease	15 (18.8)	17 (20.7)	32 (19.6)	0.751
Chronic medication				
ASA	38 (47.5)	28 (34.1)	66 (40.5)	0.084
Clopidogrel	16 (20.0)	12 (14.6)	28 (17.2)	0.366
Ticagrelor	6 (7.50)	1 (1.20)	7 (4.30)	0.049
VKA	9 (11.3)	6 (7.30)	15 (9.20)	0.388
DOAC	26 (32.5)	13 (15.9)	39 (23.9)	0.013
Beta-blocker	74 (92.5)	77 (93.9)	151 (92.6)	0.723
ACEi/ARA	63 (78.8)	74 (90.2)	137 (84.0)	0.043
Sacubitril/Valsartan	29 (36.3)	32 (39.0)	61 (37.4)	0.716
MRA	54 (67.5)	64 (78.0)	118 (72.4)	0.131
Diuretics	54 (67.5)	44 (53.7)	98 (60.1)	0.072
Statin	67 (83.8)	58 (70.7)	125 (76.7)	0.048
Ezetimibe	5 (6.30)	8 (9.80)	13 (8.00)	0.412
Amiodarone	15 (18.8)	11 (13.4)	26 (16.0)	0.355
Digoxin	6 (7.50)	3 (3.70)	9 (5.50)	0.286
SGLT2i	46 (57.5)	50 (61.0)	96 (58.9)	0.653
OAD agents	53 (66.3)	52 (63.4)	105 (64.4)	0.706
Insulin	9 (11.3)	4 (4.90)	13 (8.00)	0.136
NIV therapy	4 (5.00)	1 (1.20)	5 (3.10)	0.164
Implanted devices – total	24 (29.5)	17 (20.8)	41 (25.2)	
Pacemaker	1 (1.20)	0 (0.00)	1 (0.60)	0.481
CRT	10 (12.3)	8 (9.80)	18 (11.0)	
ICD	13 (16.0)	9 (11.0)	22 (13.5)	
Hemoglobin (g/dL)	13.6 (1.78)	14.7 (1.37)	14.2 (1.67)	< 0.001
HbA1c (%) *	6.00 (1.10)	5.80 (0.80)	5.90 (0.90)	0.023
Total cholesterol (mg/dL) *	155 (66.0)	157 (59.0)	156 (64.0)	0.586
LDL cholesterol (mg/dL) *	74.0 (47.0)	88.0 (51.0)	87.7 (33.9)	0.231

ACEi = angiotensin converting enzyme inhibitor; ARA = angiotensin II receptor antagonist; ASA = acetylsalicylic acid; BMI = body mass index; COPD = chronic obstructive pulmonary disease; CRT = cardiac resynchronization therapy; DOAC = direct oral anticoagulant; EF = ejection fraction; HbA1c = hemoglobin A1c; HF = heart failure; ICD = implantable cardioverter-defibrillator; LDL = low-density lipoprotein; LVEF = left ventricle ejection fraction; MI = myocardial infarction; MRA = mineralocorticoid receptor antagonist; NIV = non-invasive ventilation; NYHA = New York Heart Association; OAD = oral anti-diabetic; OSA = obstructive sleep apnea; Pro-BNP = pro-brain natriuretic peptide; SD = standard deviation; SGLT2i = sodium-glucose co-transporter 2 inhibitor; VKA = vitamin K antagonist; VO_2 *= oxygen uptake.*

** Variable with a non-normal distribution. Values correspond to median (interquartile range).*

*** Some totals do not add up to 163 due to missing data.*

Table IX - Concordance of recommended indices of exercise intensity (% Peak VO2, % Peak HR, %HRR) at VT1 with the ESC guidelines training zones (in grey) stratified by exercise capacity (Peak VO2 above median: ≥ 17.4 mL/Kg/min vs Peak VO2 below median: < 17.4 mL

Patients' response to exercise (n = 163)	**Peak VO_2** (ml/kg/min)	**At VT1**		
		% Peak VO_2	**% Peak HR**	**%HRR**
Peak VO_2 < 17.4 mL/Kg/min (n = 81)				
Mean (SD) or median (IQR) *	14.4 (2.95)	51.9 (18.6)	87.0 (8.52)	60.3 (26.1)
Guidelines exercise intensity (% prevalence)				
Low		26.9	0.00	24.7
Moderate to high		**69.2**	**64.0**	**57.1**
Very high		3.80	36.0	18.2
Peak VO_2 ≥ 17.4 mL/Kg/min (n = 82)				
Mean (SD) or median (IQR) *	21.8 (6.15)	55.0 (19.5)	77.4 (9.91)	47.0 (22.3)
Guidelines exercise intensity (% prevalence)				
Low		12.3	0.00	30.5
Moderate to high		**86.4**	**91.1**	**62.2**
Very high		1.20	8.90	7.30
p value between groups	< 0.001	0.180	< 0.001	< 0.001

ESC = European Society of Cardiology; HR = heart rate; HRR = heart rate reserve; IQR = interquartile range; LVEF = left ventricle ejection fraction; SD = standard deviation; VO_2 = oxygen uptake; VT1 = first ventilatory threshold.

** In variables with a non-normal distribution, values correspond to median and (interquartile range).*

Table X - Concordance of recommended indices of exercise intensity (%VO2max, %HRmax, %HRR) at VT1 with the ESC guidelines training zones (in grey), excluding patients in atrial fibrillation at the time of CPET.

Patients' response to exercise (n = 153)	**At VT1**		
	% Peak VO_2	**% Peak HR**	**%HRR**
Mean (SD) or median (IQR)	53.2 (17.1)	81.9 (10.5)	52.9 (25.2)
Guidelines exercise intensity (% prevalence)			
Low	20.7	0.00	28.7
Moderate to high	**76.7**	**78.8**	**58.7**
Very high	2.70	21.2	12.7

CPET = cardiopulmonary exercise test; ESC = European Society of Cardiology; HR = heart rate; HRR = heart rate reserve; IQR = interquartile range; SD = standard deviation; VO_2 *= oxygen uptake; VT1 = first ventilatory threshold.*

Table XI - Concordance of recommended indices of exercise intensity (%VO2max, %HRmax, %HRR) at VT1 with the ESC guidelines training zones (in grey), excluding patients not on beta-blockers at the time of CPET.

Patients' response to exercise (n = 151)	**At VT1**		
	% Peak VO_2	**% Peak HR**	**%HRR**
Mean (SD) or median (IQR)	53.1 (16.3)	82.0 (10.5)	54.1 (25.1)
Guidelines exercise intensity (% prevalence)			
Low	19.0	0.00	25.9
Moderate to high	**78.9**	**77.5**	**61.9**
Very high	2.00	22.5	12.2

CPET = cardiopulmonary exercise test; ESC = European Society of Cardiology; HR = heart rate; HRR = heart rate reserve; IQR = interquartile range; SD = standard deviation; VO_2 = oxygen uptake; VT1 = first ventilatory threshold.

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