



Early Detection of Microvascular Ischemia Through Cardiopulmonary Exercise Testing in a Cardiac Rehabilitation Program

María Vega Bayón^{1*}, Ernesto Torres Toledo², David Morcillo Corominas³, Ana Vallejo Yuste⁴, Paz Sanz Ayán⁵

Abstract

Introduction: Cardiopulmonary exercise testing (CPET) is an exercise test that integrally evaluates cardiovascular, respiratory, and metabolic responses to physical effort, allowing an accurate assessment of functional capacity and ventilatory efficiency. It is characterized by high sensitivity and specificity, as well as the ability to detect myocardial ischemic alterations at an early stage, even before they become evident through conventional imaging techniques. In this context, its application during cardiac rehabilitation programs may provide relevant information for the diagnosis and safe management of patients with suspected coronary microvascular disease. The aim of this clinical case is to highlight the usefulness and feasibility of CPET for the early detection of microvascular ischemia in the setting of cardiac rehabilitation.

Clinical observation: We present the case of a 54-year-old woman referred to cardiac rehabilitation with a diagnosis of non-obstructive apical hypertrophic cardiomyopathy and recurrent atrial fibrillation. The patient reported dyspnea with mild exertion, corresponding to New York Heart Association (NYHA) functional class III, as well as occasional chest pain. An initial evaluation using CPET revealed severe functional limitation, classified as Weber class C, together with significant ventilatory impairment (Arena class 4), which justified the indication for a structured cardiac rehabilitation program. After completion of the program, a repeat CPET demonstrated objective criteria of myocardial ischemia according to Belardinelli.

Conclusions: This case highlights the usefulness of CPET for the early detection of microvascular myocardial ischemia in patients without a prior diagnosis based on conventional testing. Moreover, CPET is reinforced as a fundamental tool for designing individualized training programs, optimizing functional capacity, and ensuring patient safety during cardiac rehabilitation.

Keywords: Cardiopulmonary Exercise Testing; Coronary Microvascular Dysfunction; Myocardial Ischemia; Cardiac Rehabilitation; Hypertrophic Cardiomyopathy

Introduction

Cardiopulmonary exercise testing (CPET) is an exercise stress test that simultaneously evaluates the cardiovascular, respiratory, and metabolic responses to exercise. It allows assessment of functional capacity, ventilatory efficiency, and the detection of different exercise-induced pathologies, making it useful for diagnosis, prognosis, and the planning of cardiac rehabilitation programs. This technique is distinguished by its ability to identify myocardial

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ischemia at an early stage, among other pathological entities [1,2]. When analyzing the pathophysiological sequence of the so-called ischemic cascade, the earliest alterations correspond to disturbances in myocardial contractility. Subsequently, abnormalities appear in oxygen consumption kinetics, leading to the development of abnormal oxygen pulse curves. In later phases, alterations in myocardial perfusion develop, which can be demonstrated using imaging techniques such as SPECT. This is followed by changes in intracardiac pressures, assessable through hemodynamic studies, and then by electrocardiographic abnormalities. Finally, as the process progresses, anginal symptoms emerge. Thus, CPET is positioned as a tool capable of detecting myocardial ischemia at earlier stages than most conventional diagnostic techniques [3]. In CPET, these abnormalities in oxygen consumption kinetics related to the presence of myocardial ischemia are reflected, according to the criteria proposed by Belardinelli, as an oxygen pulse morphology characterized by an early rise followed by a sustained plateau, associated with a VO_2 curve showing a double ascending slope—particularly when peak VO_2 does not exceed 90% of the predicted value [1]. Moreover, CPET demonstrates high sensitivity and specificity compared with conventional exercise testing [1]. Specifically, it shows a sensitivity of 88% and a specificity of 98% for the detection of exercise-induced myocardial ischemia, compared with conventional exercise testing, which shows a sensitivity of only 45% and a specificity of 85% [2]. Therefore, CPET provides a differential approach for the evaluation of exercise-induced myocardial ischemia in the presence of coronary stenoses, whether fixed or dynamic. In this article, we examine the case of a 54-year-old woman with hypertrophic cardiomyopathy and paroxysmal atrial fibrillation. She presented with dyspnea and chest pain, and conventional tests for ischemia detection were negative. After completing a cardiac rehabilitation program, CPET was performed, revealing criteria of myocardial ischemia. This case highlights the role of exercise as a trigger of ischemia in specific clinical situations, as well as the fundamental relevance of CPET as a diagnostic tool in this context.

Materials and Methods

We present the case of a 54-year-old woman referred to Cardiac Rehabilitation due to progressive functional limitation secondary to exertional dyspnea in the context of non-obstructive apical hypertrophic cardiomyopathy and recurrent atrial fibrillation. She reported dyspnea during light exertion (NYHA functional class III), episodes of oppressive precordial chest pain, and occasional postprandial epigastric pain. Physical examination revealed a regular sinus rhythm, no audible murmurs, no pulmonary crackles, and mild peripheral edema. She had no musculoskeletal limitations affecting exercise capacity. As complementary studies, blood tests and an electrocardiogram were performed, both

without relevant abnormalities. In addition, transthoracic echocardiography and cardiac magnetic resonance imaging showed concentric hypertrophy of the apical segments of the left ventricle, along with severe left atrial dilation (43 ml/m²).

Results

To assess functional capacity, a cardiopulmonary exercise test (CPET) was performed on a treadmill. The results showed a severely reduced functional capacity, with a peak VO_2 of 13.8 ml/kg/min, corresponding to 48% of the predicted value. Severe ventilatory inefficiency was also observed, consistent with significant cardiocirculatory limitation. Based on these findings, the patient was classified as Weber Class C and Arena Ventilatory Class IV.⁴ These results confirmed severe functional limitation with marked ventilatory impairment, in agreement with the patient's reported symptoms and cardiac phenotype, thereby supporting the indication for cardiac rehabilitation. After completing a structured and supervised cardiac rehabilitation program lasting two months, with a frequency of three sessions per week, which combined moderate-intensity interval aerobic exercise and circuit-based strength training, conducted in a group setting with individualized intensity according to prior functional test results, a functional reassessment was performed. A new submaximal CPET was conducted using a cycle ergometer. Given the submaximal nature of the test, functional capacity was assessed using the Oxygen Uptake Efficiency Slope (OUES), which reached 60.39% of the predicted value, corresponding to a moderately reduced functional capacity. Mild ventilatory inefficiency was observed, with a notable improvement compared with the pre-rehabilitation evaluation. Mild signs of deconditioning persisted, reflected by a significant oxygen debt and an early transition to anaerobic metabolism, although with improvement compared with the previous test. During the exercise test, a transient decrease in oxygen pulse and VO_2 was observed at 5 minutes and 30 seconds of exercise, corresponding to a workload of 51 W and a heart rate of 111 bpm, followed by subsequent recovery. These findings meet the Belardinelli criteria and are suggestive of myocardial ischemia (Figure 1). It is noteworthy that these alterations occurred during maximal exercise and outside the patient's usual training threshold, with no evidence of ST-segment depression.

After completion of the test, the findings compatible with ischemia were formally communicated to the Cardiology Department, and individualized training recommendations were established. These recommendations included the definition of specific heart rate and workload ranges, with the aim of optimizing physical conditioning and preventing the exceedance of the identified ischemic thresholds. According to the Wasserman threshold table, the patient will continue her exercise program within a workload range between 35 and

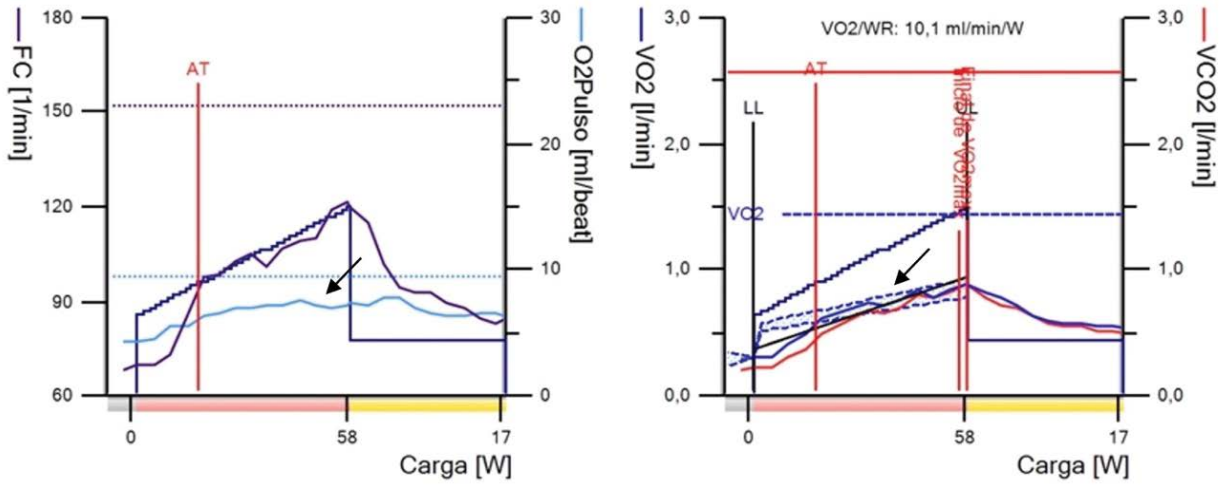


Figure 1: Wasserman plots 2 and 3.

4 curvas de umbral.												
	Unidad	Pred.	Reposo	AT	AT / %Máx	AT / %Pred.	RCP	Max. VO2	Max. VO2 / %Pred.	Carga Max.	Recovery (1min)	Recovery (2min)
Tiempo	min:sec		0:04 - 0:54	1:52	38	-	4:26	6:20 - 6:35	-	6:35	1:02	2:01
Carga	W ⁽⁹⁹⁾	118	0	35	60	30	47	58	49	58	17	17
VO2	l/min ⁽⁹⁾	1,44	0,30	0,65	74	45	0,81	0,88	61	0,86	0,75	0,63
VO2/kg	ml/min/kg ⁽⁹⁾	19,2	4,0	8,7	74	45	10,8	11,7	61	11,5	10,0	8,4
VCO2	l/min ⁽¹¹⁾	2,57	0,21	0,54	61	21	0,75	0,88	34	0,87	0,71	0,63
RER	⁽⁹⁾	1,21	0,71	0,83	82	68	0,92	1,01	83	1,00	0,94	0,98
FC	1/min ⁽⁹⁹⁾	152	69	103	86	68	105	119	78	120	92	94
%HR	%		43	63	86	-	65	74	-	74	57	58
O2Pulso	ml/beat ⁽³⁰⁾	9,5	4,3	6,3	86	66	7,6	7,3	77	7,3	7,7	6,7
VE	l/min ⁽¹¹⁾	71	8	18	57	25	26	32	45	31	24	22
Bf	1/min ⁽⁹⁾	55	14	20	70	36	26	28	51	28	24	22
Vt	l ⁽⁹⁾	2,19	0,55	0,90	83	41	0,98	1,07	49	1,07	0,96	0,93
BR	% ⁽¹³⁾	20	90	78	-	-	68	61	-	62	70	73
VE/VO2	⁽³⁰⁾	35,0	19,5	23,9	74	68	27,9	32,1	92	31,6	27,8	29,8
VE/VCO2			27,4	28,7	90	-	30,5	31,9	-	31,7	29,5	30,4
PETO2	mmHg ⁽⁹⁾	90	90	92	93	102	95	100	111	99	96	98
PETCO2	mmHg		36	37	102	-	37	36	-	36	38	37
Vd(g)/Vt	% ⁽⁹⁾	19,0	9,9	15,3	78	81	19,4	19,7	104	19,3	19,1	18,1
SPA	mmHg ⁽⁹⁾	207	115	123	88	59	121	139	67	139	-	172
DPA	mmHg ⁽⁹⁾	99	85	87	116	88	81	75	76	75	-	85

Figure 2: AT: Anaerobic Threshold, RCP: Respiratory Compensation Point, VO2: Oxygen consumption, VCO2: Carbon dioxide consumption, RER: Respiratory Exchange Ratio, HR: Heart rate, %HR: Percentage of maximum heart rate, VE: Minute ventilation, Bf: Breathing frequency, Vt: Tidal volume, BR: Breathing reserve, PETO2: End-tidal oxygen pressure, PETCO2: End-tidal carbon dioxide pressure, SPA: Systolic arterial pressure, DPA: Diastolic arterial pressure.

47 W. Exercise intensity was prescribed primarily based on workload (W), as adjustment according to heart rate was not considered appropriate due to the history of atrial fibrillation.

Discussion

This clinical case illustrates the usefulness of functional assessment by means of cardiopulmonary exercise testing in a patient with negative conventional tests for ischemia detection. Structured and supervised cardiac rehabilitation led to a clinically relevant improvement in both ventilatory efficiency and functional capacity. These findings are consistent with those reported by Mazzucco et al., who analyzed a sample of 22 patients with myocardial ischemia after completing a cardiac rehabilitation program and observed a statistically significant reduction in exercise-induced ischemia, as well as significant improvements in exercise capacity [5]. Furthermore, post-rehabilitation reassessment using CPET enabled the early identification of criteria suggestive of myocardial ischemia during high-intensity exercise [6,7]. The findings observed are in line with those described by Belardinelli et al., who conducted a prospective study in 1,265 subjects with chest pain and no documented coronary artery disease, evaluated by cardiopulmonary exercise testing. Of these, 73 had a positive CPET. In addition, patients with a peak VO_2 greater than 91% of the predicted value and absence of CPET parameters suggestive of myocardial ischemia showed no evidence of obstructive coronary artery disease in 100% of cases. Moreover, during follow-up, cardiac events were recorded in 32 patients with a positive CPET and in 8 patients with a negative CPET [7]. These findings reinforce the role of cardiopulmonary exercise testing in the evaluation of myocardial ischemia, highlighting its value not only as a prognostic and follow-up tool, but also as a safety instrument for individualized exercise prescription [8]. They also underscore the importance of personalized cardiac rehabilitation programs aimed at optimizing both functional capacity and risk stratification during physical training [9,10].

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