



Original Article

Factors Affecting the Response to Exercise in Patients with Severe Pulmonary Arterial Hypertension

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ARTICLE INFO

Article history:

Received May 28, 2010

Accepted July 31, 2010

Keywords:

Pulmonary arterial hypertension
Ergospirometry
Echocardiography
Natriuretic peptides

ABSTRACT

Introduction: Ergospirometry objectively quantifies exercise capacity. Up until now, the response to exercise evaluated by ergospirometry in patients with pulmonary arterial hypertension has only been described in recently-diagnosed patients.

We aimed to describe the response to exercise of patients with severe pulmonary arterial hypertension under specific treatment and define which parameters determine their exercise capacity.

Patients and method: Ours was a cross-sectional study including 80 patients, of whom 57 were women, with a mean age of 44 (13), with severe pulmonary arterial hypertension (48 idiopathic, 14 rapeseed oil poisoning, 13 collagenosis, 5 human immunodeficiency virus). Mean pulmonary pressure at diagnosis was 61(15) mmHg and patients had received 49(33) months of treatment since diagnosis. NTproBNP was determined and echocardiography and ergospirometry were performed.

Results: Our patients, who were receiving specific treatment, presented typical behavior of patients with pulmonary arterial hypertension on ergospirometry, although with less limitation in aerobic capacity and ventilatory efficiency. Being male ($p=0.004$), presenting high ventilatory equivalent for carbon dioxide at the anaerobic threshold ($p<0.001$) and NTproBNP ($p=0.006$) were all associated in the multivariate analysis with poorer peak oxygen uptake. Meanwhile, less time under treatment ($p=0.01$), right ventricle dilatation ($p<0.001$) and high ventilatory equivalent for carbon dioxide at the anaerobic threshold ($p<0.001$) were associated with poorer percentage of predicted values.

Conclusions: In pulmonary arterial hypertension, right ventricle dysfunction (RV dilatation and high NTproBNP), ventilatory inefficiency, being male and recent diagnosis (implying less time receiving treatment) can be considered predictors for impaired functional capacity.

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Factores determinantes de la capacidad de ejercicio en pacientes con hipertensión arterial pulmonar severa

RESUMEN

Palabras clave:

Hipertensión arterial pulmonar
Ergoespirometría
Ecocardiografía
Péptidos natriuréticos

Introducción: La ergoespirometría cuantifica objetivamente la capacidad de ejercicio. Hasta ahora, solo se ha descrito el comportamiento al ejercicio mediante ergoespirometría en la hipertensión arterial pulmonar en pacientes recién diagnosticados.

El objetivo fue describir el comportamiento al ejercicio de pacientes con hipertensión arterial pulmonar severa bajo tratamiento y definir que parámetros lo determinan.

Pacientes y método: Estudio transversal realizado en 80 pacientes, 57 mujeres, 44 (13) años, con hipertensión arterial pulmonar severa (48 idiopática, 14 aceite colza, 13 colagenosis, 5 virus del sida), presión pul-

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monar media al diagnóstico 61 (15) mmHg y 49 (33) meses bajo tratamiento, en los que se determinó NTproBNP y realizó ecocardiograma y ergoespirometría.

Resultados: Nuestros pacientes, bajo tratamiento específico, presentaron el comportamiento típico de los pacientes con hipertensión arterial pulmonar en la ergoespirometría, aunque con menor limitación de capacidad aeróbica y de eficiencia ventilatoria. Ser varón ($p = 0,004$), presentar elevados equivalente ventilatorio de dióxido de carbono en el umbral anaeróbico ($p < 0,001$) y NTproBNP ($p = 0,006$) se asociaron al análisis multivariado con peor consumo de oxígeno en el máximo esfuerzo mientras que con peores cifras del valor porcentual respecto al predicho lo hicieron: menos tiempo de tratamiento ($p = 0,01$), la dilatación del ventrículo derecho ($p < 0,001$) y un elevado equivalente ventilatorio de dióxido de carbono en el umbral anaeróbico ($p < 0,001$).

Conclusiones: En la hipertensión arterial pulmonar, se pueden considerar predictores de peor capacidad funcional la disfunción ventricular derecha (dilatación del VD y elevación de NTproBNP), la ineficiencia ventilatoria, el sexo masculino y el reciente diagnóstico, que implica menor tiempo bajo tratamiento.

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Introduction

Evaluating functional capacity is key in the study of patients with pulmonary arterial hypertension (PAH) as it defines their stability and has prognostic implications.¹ This evaluation includes the estimation of functional class, the six-minute walk test and ergospirometry.² The functional class, according to the modified version by the World Health Organization (WHO Classification), depends on the subjectivity of the patient and physician and is not very reproducible, especially when classifying patients in classes II-III.³ The six-minute walk test is the only method approved for evaluating functional capacity in PAH. It does, however, have several limitations^{2,4,5} and it has not been validated in patients in functional classes I-II or in younger patients, where it does not detect right ventricular (RV) failure.¹

Ergospirometry provides a non-invasive, objective and reproducible evaluation of functional capacity, analyzing the limiting physiopathological mechanisms. Nevertheless, performing and interpreting ergospirometry are both complex and require experience.^{6,7} Thoroughly validated in left ventricular systolic dysfunction, its complexity has delayed its use in multicenter PAH assays, although its clinical applicability and prognostic implications have been clearly demonstrated⁸⁻¹² (fig. 1). In fact, in the recent guidelines of the European Society of Cardiology¹, it is considered an indispensable tool. It evaluates two types of parameters: aerobic capacity and ventilatory efficiency. Among the former, which quantify functional capacity, are peak oxygen uptake (VO_2) and its predicted percentage ($\%VO_{2,pred}$) according to age, sex, weight and height.⁶ The loss of ventilatory efficiency (fig. 1), typical of this pathology and responsible for its main symptom - dyspnea, is evaluated by means of ventilatory equivalent ($EqCO_{2,UA}$ or coefficient between ventilation and the production of carbon dioxide) and the partial pressure at the end of expiration for carbon dioxide at the anaerobic threshold.²

For the diagnosis and follow-up of PAH patients, echocardiography and biomarker studies are also essential, such as the N-terminal fragment of the brain natriuretic peptide, or BNP (NTproBNP).¹ Echocardiography estimates hemodynamic variables and studies the anatomy and function of the RV.¹³⁻¹⁵ NTproBNP, released in response to the parietal stress that the RV undergoes and correlates with its function,¹⁶ is an independent prognostic marker and has also been shown to be related with functional capacity.^{17,18} The main studies that have analyzed response to exercise by ergospirometry in patients with PAH have done so in recently-diagnosed populations (incident cases)^{5,8,18} and, to date, there is no data on this behavior in patients already undergoing treatment. Based on this fact, our aim is to describe the response to exercise in PAH patients receiving specific treatment (prevalent cases) and to try to discover its determinants, given on one hand its great clinical relevance for prognosis and as a

guideline for choosing treatment as well as the moment for transplantation, and, on the other hand, the complexity that is involved in its exact estimation using ergospirometry.

Patients and Method

Study Design

Ours is a cross-sectional study, and the population was made up of a group of patients from the PAH Unit of our hospital. The sampling was consecutive, and all those patients who came to our consultation between December 2006 and December 2007 were invited to participate if they met the inclusion criteria: severe PAH (idiopathic or associated with collagenosis, human immunodeficiency virus or rapeseed oil poisoning) in functional classes I-III and a signed informed consent. At the time of this study, the Unit was treating 222 patients.

After the clinical evaluation, blood samples were taken for analysis to determine NTproBNP (Elecsys proBNP^{II}® test, Elecsys Modular Analytics E170® module) and echocardiograms were performed (Vingmed Vivid-7® echocardiograph, storage in cine loop format with three consecutive beats and offline analysis using EchoPAC® commercialized software). Afterwards, ergospirometry was carried out with a cycle ergometer (Ergometrics, Ergoselect 100P® model) and protocol with an initial load of 0 watts and increments of 5 watts/45 seconds (pedaling rate of 40-60 revolutions/minute). The analysis of gases (Oxycom® model) was done "breath by breath", averaged every 15 seconds. The test ended when the patient was not able to maintain the pedaling frequency or with the appearance of signs or symptoms indicative of ergometry interruption. The load was then lowered to 0 watts and the patient continued pedaling one minute more.

Variables Collected

For our study, we collected clinical variables (sex, age, evolution time under treatment, need for combined treatment, long-term response to calcium antagonists), biomarkers (concentration of NTproBNP), variables derived from ergospirometry that quantify ventilatory efficiency ($EqCO_{2,UA}$ and partial pressure of carbon dioxide at the end of expiration at the anaerobic threshold) and different echocardiographic parameters (morphology and function of RV, ventricular interdependence and hemodynamics).

Objectives

The objectives of our study were, first of all, to describe the response to exercise, evaluated by means of ergospirometry, of

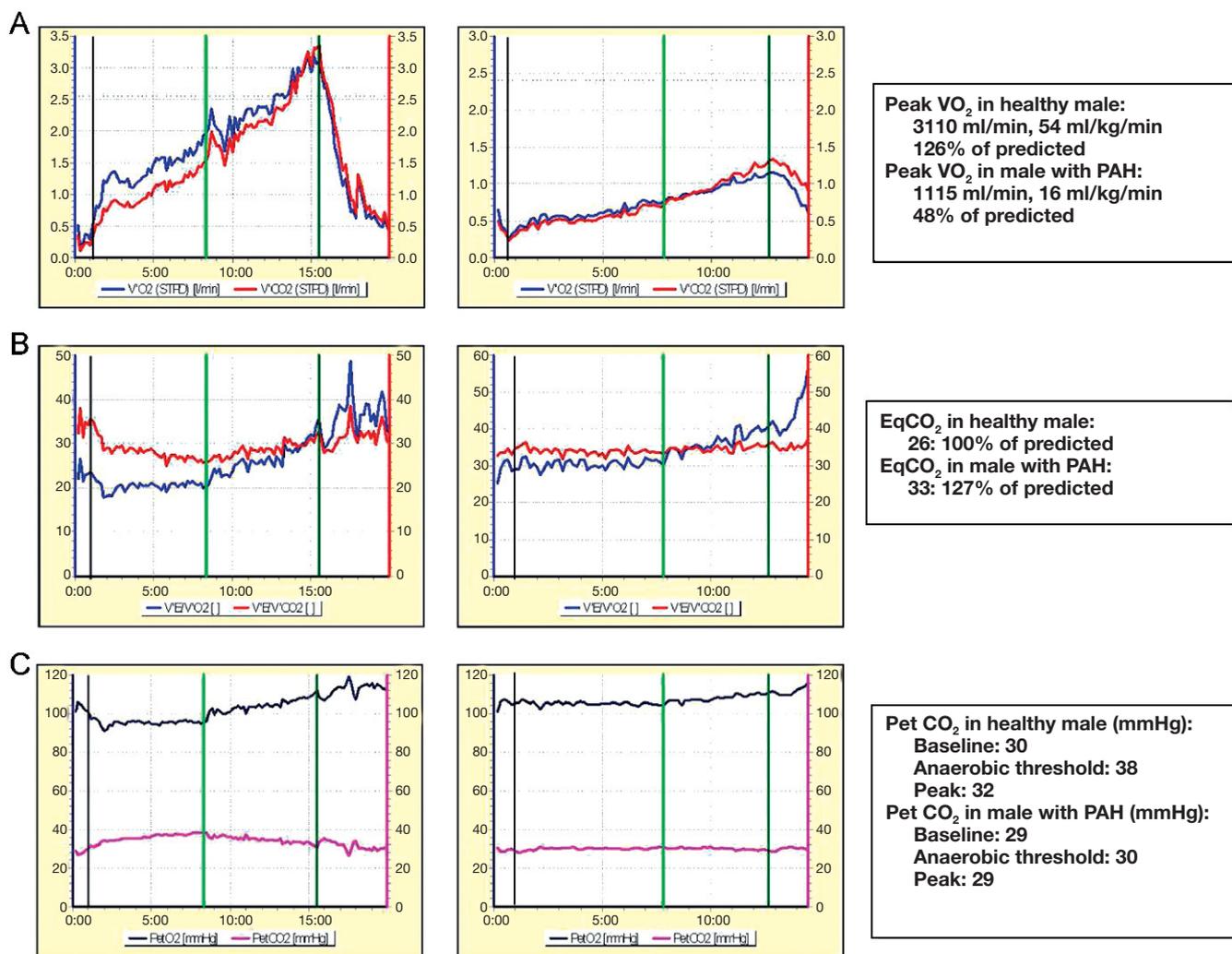


Figure 1. Ergospirometric parameters in a healthy 45-year-old male and in another of the same age with functional class III idiopathic PAH. A) Aerobic capacity: oxygen consumption (VO_2). The vertical green line indicates the anaerobic threshold. B) and C) Ventilatory efficiency. B) $EqO_2/EqCO_2$: ventilatory equivalent for oxygen/carbon dioxide. C) $PetO_2/CO_2$: partial pressure and the end of expiration of oxygen/carbon dioxide.

patients with PAH receiving specific treatment. The second aim was to define which echocardiographic and clinical parameters, including concentration of NTproBNP, can be taken as predictors of exercise capacity (quantified by VO_2 at maximum effort and $\%VO_{2,pred}$, objective variables) in these patients.

Statistical Analysis

The quantitative variables were summarized by means and standard deviation and in all cases the variables were checked for normality. To compare those of normal distribution, the t-Student's test was applied in two groups. In the case of non-normal distributions, the non-parametric equivalent Mann-Whitney U was used. The correlation between two quantitative variables was studied using Pearson's correlation coefficient. Given that the dependent variables are quantitative (VO_2 at maximum effort and $\%VO_{2,pred}$), a multiple linear regression was used. Due to the limited sample size, we opted for various models, with a maximum of 8 variables in each in order to avoid saturation. The variables included in the maximum model were all those that showed statistical significance in the univariate analysis (result of the analysis of individual correlations with each).

We selected those with clinical relevance according to current theoretical knowledge regarding the influence of each predictive variable on the dependent variables (VO_2 at maximum effort and $\%VO_{2,pred}$). Last of all, the Parsimony principle was applied, opting for the simplest model that was clinically compatible with current knowledge. The residuals were evaluated graphically to check the assumptions of the model and the analysis was compatible with normality and homoscedasticity. At the same time, we checked for possible collinearities in case it were necessary to correct for these, but none were detected. The level of significance in all the hypothesis contrasts was 0.05. The statistical treatment was carried out with the SPSS 14.00® program.

Results

Description of the Sample

The sample was comprised of 85 patients (62 women), diagnosed between January 1990 and September 2007 (69% before 2005 and 14% the same year of the study), with a mean pulmonary pressure at diagnosis of 61 (15) mm Hg. In 51 (60%) cases, PAH was idiopathic,

while it was associated in 15 (17.6%) with collagenosis, in 14 (16.5%) with rapeseed oil poisoning and in 5 (5.9%) with HIV. The time of evolution under treatment before ergospirometry was 49 (33) months. At the time, 44 (51.8%) cases were receiving combined treatment and the WHO functional class was 1.88 (0.71).

Test Descriptions

The distance walked in the six-minute walk test (6MWT) was 469 (89) m. As for ergospirometry, five women were unable to pedal due to mechanical problems. Of the remaining 80 patients, none presented complications during the test (Table 1). In 77 (96%) cases, it was possible to determine the anaerobic threshold and 57 (72%) reached a respiratory coefficient or RER > 1.1, indicative of a good level of effort reached. The correlations between VO₂ at maximum effort and the main variables of ventilatory inefficiency (EqCO₂UA and Pet CO₂ partial pressure of CO₂ at the end of expiration at the anaerobic threshold) are shown in Figure 2. Regarding VO₂ at maximum effort and the 6MWT, the correlation coefficient was 0.66 (p < 0.001).

The concentration of NTproBNP in the 80 patients who performed ergospirometry was 697 (808) pg/ml, (range 10 - 3,648). Table 2 reports the echocardiographic findings in these patients.

Uni- and Multivariate Analyses

In the univariate analysis, the main variables that were associated with a significant increase in VO₂ at maximum effort were: younger

age (p 0.029), lower concentration of NTproBNP (p<0.001), receiving monotherapy (p 0.046), presenting less ventilatory inefficiency (less EqCO₂UA, p<0.001) or better echocardiographic parameters ([Table 3] and [Table 4]). The main variables that were associated with a significant increase in %VO₂pred were: older age (p 0.006), more time being treated (p 0.018), presenting lower concentration of

Table 1
Results of the ergospirometry

	Mean (SD)	Interval
Load reached (watts)	55 (19)	25-105
VO ₂ (ml/kg/min) at maximum effort	17.8 (4.1)	8.8-27.4
%VO ₂ pred (%) at maximum effort	65 (17)	29-105
VO ₂ at AT (ml/kg/min)	12.1 (2.5)	6.5-17.9
%VO ₂ pred at AT (%)	74 (19)	35-130
EqCO ₂ at AT	33 (9)	19-62
% EqCO ₂ predicted at AT (%)	122 (32)	73-220
PetCO ₂ at AT (mmHg)	35 (8)	17-59
RER	1.13 (0.1)	0.9-1.66

Values are expressed as means (standard deviation); %VO₂pred: percent predicted peak VO₂; AT: anaerobic threshold; EqCO₂: ventilatory equivalent of carbon dioxide; PetCO₂: partial pressure of end-tidal carbon dioxide; SD: standard deviation; VO₂: oxygen consumption.

Table 2
Results of echocardiography

	Mean (SD)	Interval
Diastolic diameter of RV (mm)	43 (5)	26-64
Diastolic area of RV (cm ²)	24 (7)	11-41
Systolic area of RV (cm ²)	17 (6)	7-33
RV area (cm ²)	21 (8)	9-47
RV Shortening fraction (%)	29 (9)	7-55
TAPSE (mm)	17 (5)	9-31
RV Tei index	0.62 (0.27)	0.14-1.37
LV diastolic eccentricity index	1.47 (0.32)	1-2.5
LV systolic eccentricity index	1.96 (0.74)	1.01-4.8
RV area/LV area	1.4 (0.6)	0.6-3.3
Cardiac output (l/min)	4.08 (1.06)	1.86-6.67
RV-RA gradient (mm Hg)	77 (19)	35-124
Mean pressure in RV (mm Hg)	7 (3.5)	1-15

Values are expressed as means (standard deviation); LV: left ventricle; RA: right auricle; RV: right ventricle; SD: standar deviation; TAPSE: tricuspid annular plane systolic excursion.

Table 3
Parameters associated with VO₂ at maximal effort (ml/kg/min) in the univariate analysis

	β	CI 95%	P
Age	-0.075	-0.14 to -0.008	0.029
NTproBNP	-0.002	-0.003 to -0.001	<0.001
EqCO ₂ UA	-0.211	-0.307 to -0.115	<0.001
EqCO ₂ at maximal effort	-0.122	-0.191 to -0.053	0.001
PetCO ₂ UA	0.207	0.104 to -0.31	<0.001
RV diastolic area	-0.134	-0.265 to -0.003	0.04
LV diastolic eccentricity index	-3.683	-6.55 to -0.816	0.013
RV-RA gradient	-0.109	-0.156 to -0.062	<0.001
RA area	-0.156	-0.275 to -0.036	0.011
Diastolic diameter of RV	-0.154	-0.263 to -0.046	0.006
RV Tei index	-4.418	-7.941 to -0.895	0.015
RV area/LV area	-2.611	-4.045 to -1.177	0.001

Abbreviations defined previously.

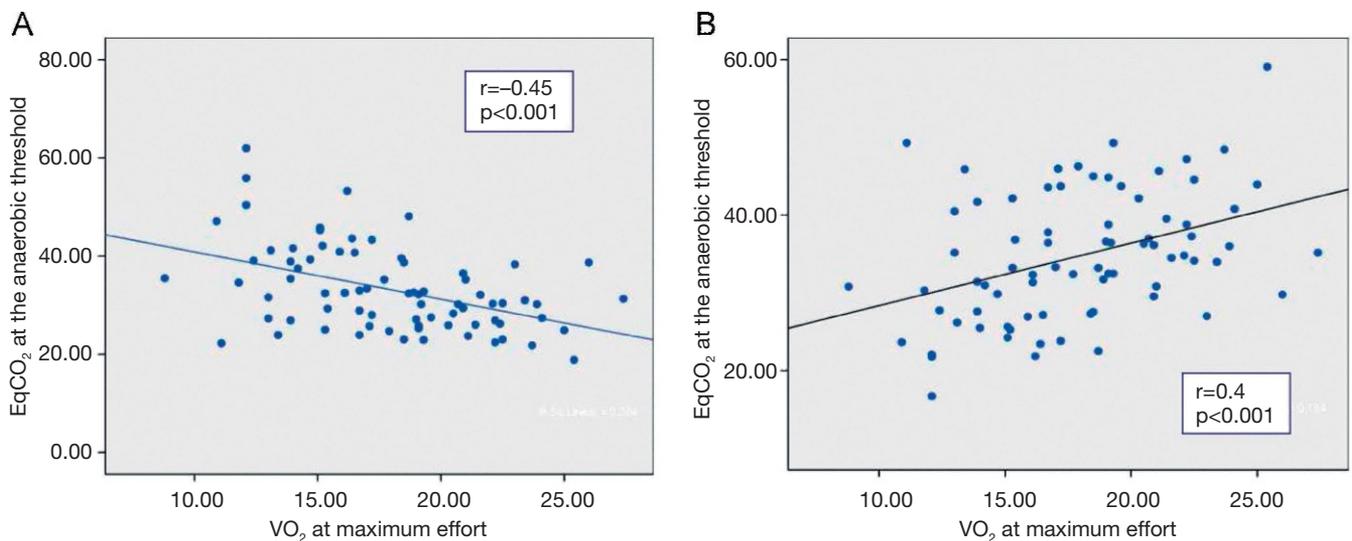


Figure 2. Regression lines between VO₂ max and EqCO₂ and PetCO₂ at the AT.

Table 4
Parameters associated with VO₂ at maximal effort %VO₂pred in the univariate analysis

		Mean	SD	Mean difference	CI 95%	p
VO ₂ (ml/kg/min) at maximal effort	Yes	18.8	4.5	1.87	0.37-3.71	0.046
	No	16.9	3.5			
%VO ₂ pred						
Sex	Women	69.0	16.6	12.5	4.4-20.6	0.003
	Men	58.4	16.0			
Combined treatment	Yes	61.5	16.5	7.9	0.41-15.5	0.03
	No	69.5	17.5			

Abbreviations have been previously defined.

Table 5
Parameters associated with %VO₂pred in the univariate analysis

	β	CI 95%	p
Age	0.39	0.11 to 0.66	0.006
Months of treatment	0.13	0.02 to 0.24	0.018
NTproBNP	-0.009	-0.13 to -0.004	<0.001
EqCO ₂ UA	-1.2	-1.5 to -0.82	<0.001
PetCO ₂ UA	1.24	0.83 to 1.65	<0.001
RV diastolic area	-1.24	-1.7 to -0.76	<0.001
LV diastolic eccentricity index	-24.0	-35.2 to -13.3	<0.001
Cardiac output	4.31	0.84 to 7.78	0.01
RV-RA gradient	-0.38	-0.58 to -0.18	<0.001
RA area	-0.83	-1.3 to -0.37	0.001
RV diastolic diameter	-1.35	-1.7 to -0.99	<0.001
RV Tei index	-32.3	-45.4 to -19.2	<0.001
TAPSE	1.17	0.37 to 1.97	0.005
RV area/LV area	-16.15	-21.5 to -10.7	<0.001

Abbreviations have been previously defined.

Table 6
Equations of the straight line for VO₂ at maximal effort and %VO₂pred

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VO ₂ (ml/kg/min)=28.505–2.592×sex–0.224×EqCO ₂ UA–0.001×NTproBNP (pg/ml)
%VO ₂ pred=125.362–1.014×VDd (mm)–0.63×EqCO ₂ UA+0.095×months of treatment

"Sex" corresponds to a value of 0 if the patient is male, and 1 if female. For VO₂ at maximal effort: sex, p=0.004; EqCO₂UA, p<0.001; NTproBNP, p=0.006. For %VO₂pred: VDd, p<0.001; EqCO₂UA, p<0.001; months of treatment, p 0.01.

NTproBNP (p<0.001), being female (p 0.003), receiving monotherapy (p 0.03), having less ventilatory inefficiency (less EqCO₂UA, p<0.001) or better echocardiographic parameters (Tables 4 and 5).

As for the multivariate analysis, the variables finally included for the VO₂ at maximum effort model were: age, sex, pressure gradient between the right ventricle and auricle, the diastolic diameter of the RV, NTproBNP, EqCO₂UA and maximum effort and partial pressure at the end of expiration of carbon dioxide at the anaerobic threshold. For the %VO₂pred, the variables were: age, sex, months of treatment, NTproBNP, EqCO₂UA, partial pressure at the end of expiration of carbon dioxide, diastolic diameter of the RV and the gradient of pressure between the right ventricle and auricle. In the end, the only variables that were independently and significantly associated with poorer levels of VO₂ at maximum effort (ml/kg/min) were being male (p 0.004) and presenting a poorer degree of ventilatory efficiency (high value of EqCO₂UA) (p<0.001) or increased NTproBNP (p=0.006). Meanwhile, the only variables associated with a low %VO₂pred were the degree of RV dilation (estimated by its diastolic diameter) (p<0.001), having less months receiving specific treatment (p 0.01) and, once again, presenting a poorer degree of ventilatory efficiency (EqCO₂UA, p<0.001). The equations of the straight line of the resulting models are shown in Table 6.

Discussion

Although the 6MWT is to date the only method validated by the FDA and the EMEA for quantifying exercise capacity when evaluating the effects of treatment in PAH, ergospirometry is gaining in interest. Although the correlation between the 6MWT and VO₂ at maximum effort is strong (as demonstrated by the results of our study and that of other previously-published series, in patients with PAH, r 0.7 p <0.0015, as well as in chronic obstructive pulmonary disease, r 0.78, p<0.0001¹⁹), ergospirometry provides much more information about the physiopathology of the disease, and more objectively, than the 6MWT. In fact, recent guidelines about the diagnosis, follow-up and therapeutic management of these patients consider it essential.¹

The exercise response of our patients, which to date constitute the longest series published about PAH patients who underwent subjected to ergospirometry, echocardiography and NTproBNP determination, was characterized by a mild-moderate reduction in the parameters of aerobic capacity associated with a more notable deterioration in ventilatory efficiency. The behavior is typical of patients with PAH.² However, when we compare our results with those of the longest published series,^{5,8,18} we observe that our case mix presents less limitation of exercise capacity. On one hand, this phenomenon may be due to the long evolution time of our patients and, on the other, to the beneficial effect of treatment. While other series dealt with recently-diagnosed cases (incident cases), ours was made up of diagnosed cases that had been treated over a long period of time (prevalent cases), or in other words, a group of long-term survivors (in fact, 69% had been diagnosed and had started treatment before 2005). This implies the loss, either by death or transplantation, of the cases with poor evolution and modest response to drug therapy, and therefore poorer functional capacity. In fact, according to the recently-published data of the preliminary analysis by the Spanish Registry of Pulmonary Hypertension (REHAP),²⁰ prevalent patients present better survival in the first year than do incident patients (99 vs. 88%, p<0.05). This is possibly related to a less malignant disease form, with better response to medication, and therefore better exercise capacity. We may thus consider that length of treatment time acts as a determining factor for exercise capacity (%VO₂pred) and that its positive influence on functional capacity is able to counteract the negative effect of aging.

Both age and sex are very important determinants of exercise capacity in healthy subjects. Logically, this decreases with age and is lower in females.⁶ In our series, the exercise capacity (estimated with %VO₂pred) of women was superior to that of men. Although this fact should be interpreted cautiously due to the limited number of males in the sample, it should also be considered that two recently-published registers (French²¹ and American²²) have demonstrated that males present greater mortality and less exercise capacity, evaluated by means of the 6MWT and the WHO functional class.

In our unit, as recommended by the latest guidelines on PAH of the European Society of Cardiology,¹ our follow-up of the patients

was guided by objectives. If these are not met, treatment must be increased by associating drug therapies. At the moment this study was done, however, ergospirometry was still not considered a prognostic factor for therapeutic modifications. Therefore, when patients that were already receiving combined treatment (a reflection of poorer clinical and echocardiographic parameters and a greater concentration of NTproBNP) did the test, they presented poorer exercise capacity.

NTproBNP and echocardiogram represent right ventricular function parameters: the former, biochemical,¹⁶ and the latter, morphological and hemodynamic. Progressive RV dysfunction, produced in the advanced stages of the disease and which is expressed through the deterioration of both types of variables,¹⁸ is also reflected by a deterioration in work capacity.

EqCO₂UA together with the partial pressure of CO₂ at the end of expiration are the parameters that best describe the deterioration of the ventilatory efficiency, distinctive of PAH (fig. 1)²³: the higher the EqCO₂UA and lower the CO₂ partial pressure, both baseline and at the anaerobic threshold, the greater the ventilatory inefficiency, meaning that greater ventilation is needed to achieve efficient gas exchange. Ventilatory inefficiency plays a very important role in the symptomatology of PAH as it is mainly responsible for dyspnea upon exertion, the key limiting symptom of these patients₂, that influences in their exercise capacity: the greater the ventilatory inefficiency, the poorer the aerobic capacity, meaning poorer VO₂ at maximal effort (fig. 2).

Finally, in the multivariate analysis, in which we synthesize the relationships between the variables studied in the univariate, we observed that the main determinants for exercise capacity are: 1) the degree of ventilatory inefficiency, expressed by EqCO₂UA; 2) increased NTproBNP and dilatation of the RV, variables that express differently the deformation and dysfunction of the right ventricle; and 3) being male, and the months having received treatment, meaning the time of evolution after diagnosis. Data regarding these variables and their evolution give the specialist the ability to anticipate possible changes in functional capacity, which is a very important prognostic determinant and indispensable tool in the follow-up guided by objectives of the PAH patient, without having to perform ergospirometry, in the case that this technique is not available, and without having to perform up to maximum tolerance (calculating EqCO₂ at the anaerobic threshold) in the more limited cases.

One of the obstacles of this study was the limited number of cases, although this problem is common to all series studied in one single center given the low incidence (3 cases/million/year) and prevalence (16 cases/million) of PAH in Spain,²⁰ This has kept us from being able to carry out the statistical analysis in different subgroups (etiological, although the four belong to group I of the PAH classification, age, functional class, type of treatment). It also limits the value of the multivariate analysis which was carried out with a great number of variables (clinical, biochemical, echocardiographic and ergospirometry) for a sample of 80 patients, selecting those with greater clinical relevance. Another of the limitations was the absence of a hemodynamic study at the completion of the ergospirometry, although the echocardiogram provided information that can be analyzed as indirect hemodynamic data.

Conclusions

The results of our study reflect that PAH patients receiving specific treatment present a response to exercise (estimated by ergospirometry) that is typical of this pathology, although with a more benign behavior of the aerobic capacity and ventilatory efficiency than previously described.

The factors associated with impaired exercise capacity are: being male, RV dilatation, high NTproBNP, degree of ventilatory inefficiency and less evolution time under treatment. Monitoring these data in

the patient follow-up allow us to occasionally anticipate clinically-relevant deterioration in functional capacity and can be of use in optimizing the management of patients with PAH.

Abbreviations

- VO₂: oxygen uptake
- %VO₂pred: percentage of oxygen uptake with regards to the predicted value according to age, sex, weight and height
- EqCO₂UA: ventilatory equivalent of carbon dioxide at the anaerobic threshold
- PAH: pulmonary arterial hypertension
- RV: right ventricle

Funding

This study was made possible thanks to a research contract with Glaxo SmithKline®.

Acknowledgements

To Tina, Asun and Fernando. Without you, this paper would not have been possible.

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