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The limit of physiological adaptation of the right ventricle to endurance training

M. I. Barriopedro^a, J. J. Ramos Álvarez^b, J. F. Forteza-Alberti^{c,d}, F. J. Calderón-Montero^a

^a Facultad de Ciencias de la Actividad Física y el Deporte, INEF, Universidad Politécnica de Madrid, Madrid, España.

^b Escuela de Medicina de la Educación Física y del Deporte, Facultad de Medicina, Universidad Complutense de Madrid, Madrid, España.

^c Instituto Internacional de Cardiología, Universidad Católica de Murcia, Murcia, España.

^d Departamento de Cardiología, Hospital Universitario Son Espases, Palma de Mallorca, España.

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ABSTRACT

Revision

The study aims to conduct a review of right ventricle, measured by echocardiography or magnetic resonance imaging, in athletes with high dynamic component and moderate static, the limit of the physiological adaptation. A search was carried out in the Medline database up to the end of 2017. This study showed that the mean values for the different measurements of the right ventricle in athletes are significantly greater than that of sedentary controls. In two of the 12 studies that analyzed mean diameter of the right ventricle in apical 4C, including 1477 endurance athletes and 498 controls, with high heterogeneity. Endurance athletes presented significantly higher longitudinal diameter of the RV in apical absolutes scores compared to control. The end diastolic volume and end systolic volume measured by magnetic resonance imaging, showed a significant standardized mean difference favoring athletes with a moderate heterogeneity.

Keywords: Physiological adaptation; Right ventricle; Meta-analysis; Endurance athletes; High dynamic component.

El límite de la adaptación fisiológica del ventrículo derecho al entrenamiento de resistencia

RESUMEN

El estudio tiene como objetivo realizar una revisión del ventrículo derecho, medido por ecocardiografía o resonancia magnética, en deportistas con alto componente dinámico y estático moderado, el límite de la adaptación fisiológica. Se realizó una búsqueda en la base de datos Medline hasta finales de 2017. Este estudio mostró que los valores medios de las diferentes mediciones del ventrículo derecho en los deportistas son significativamente mayores que los de los controles sedentarios. En dos de los 12 estudios que analizaron el diámetro medio del ventrículo derecho en apical 4C, incluyendo 1477 atletas de resistencia y 498 controles, con alta heterogeneidad. Los atletas de resistencia presentaron un diámetro longitudinal del VD en absolutas apicales significativamente mayor en comparación con los controles. El volumen diastólico final y el volumen sistólico final medidos por resonancia magnética, mostraron una diferencia media estandarizada significativa a favor de los atletas con una heterogeneidad moderada. *Palabras clave:* Adaptación fisiológica; Ventrículo derecho; Meta-análisis; Atletas de resistencia; Alto componente dinámico.

O limite da adaptação fisiológica do ventrículo direito ao treino de resistência

RESUMO

O estudo visa conduzir uma revisão do ventrículo direito, medido por ecocardiografia ou ressonância magnética, em atletas com elevada componente dinâmica e estática moderada, o limite da adaptação fisiológica. Foi realizada uma pesquisa na base de dados Medline até ao final de 2017. Este estudo mostrou que os valores médios das diferentes medidas do ventrículo direito em atletas são significativamente superiores aos dos controlos sedentários. Em dois dos 12 estudos que analisaram o diâmetro médio do ventrículo direito em 4C apical, incluindo 1477 atletas de endurance e 498 controlos, com elevada heterogeneidade. Os atletas de resistência apresentaram um diâmetro longitudinal do VD significativamente mais elevado nas pontuações absolutas apicais, em comparação com os controlos. O volume diastólico final e o volume sistólico final medido por ressonância magnética, mostraram um adiferença média padronizada significativa, favorecendo os atletas com uma heterogeneidade moderada.

Palavras chave: Adaptação fisiológica; Ventrículo direito; Meta-análise; Atletas de resistência; Componente altamente dinâmica.

* Corresponding author.

E-mail-address: franciscojavier.calderon@upm.es (F. J. Calderón-Montero).

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Introduction

Although the right ventricle is situated anatomically parallel to the left ventricle, functionally it is "connected" in series, as both ventricles have the same cardiac output (CO) in average values.¹ The equality in cardiac output means that the systolic volume of the right ventricle is the same as that of the left ventricle in spite of considerable anatomical and physiological differences.^{2,3} However, both pumps exert a different pressure on their respective vascular tree. The right ventricle exerts about 4 times less pressure, so that the resistance of the respiratory vascular tree is about 10 times lower than the systemic vascular tree. During dynamic exercise of moderate to high intensity there is an increase in CO and central venous pressure (CVP).⁴ A sustained increase in CVP as occurs in sports with high dynamic and moderate static components could condition the maximum physiological limit of cardiac adaptation to training.

The described conditions mean that the phenomena of physiological adaptation to training are exerted in a similar fashion on both sides of the heart. Thus, the right ventricle should experience similar modifications to the left ventricle in order to satisfy the same demand produced during exercise, as Henschen⁵ proposed intuitively. However, in spite of the development of echocardiography since 1970, interest in the adaptation of the right ventricle to training has been practically non-existent. In fact, in a review study published in 1986 on athlete's heart, of the 29 articles reviewed, only 8 had taken measurements of the right ventricle using one-dimensional echocardiography.⁶ As Vitarelli affirms the right ventricle has been the "forgotten ventricle" and it is only since the last two decades that interest in the field of cardiology has also focused on evaluating the function of the right ventricle.³ As a consequence, there has been a considerable increase in studies devoted to understanding the adaptation of the right ventricle to training.

The objective of this study was to perform a meta-analysis on articles dealing with the dimensions of the right ventricle in athletes who develop a high dynamic and moderate static component. The review considered articles where the measurement of the right ventricle (RV) were made either by echocardiography or by nuclear magnetic resonance considered the gold standard for evaluating cardiac dimensions.⁷

Methods

This paper reviews the adaptation of the right ventricle to endurance training from a strictly physiological perspective. A search was carried out in the Medline database up to the end of 2017, including printed articles. The initial search term was: "right ventricle and athletes OR sport and echocardiography OR magnetic resonance" only of human subjects and in English. In addition, knowing the existence of a doctoral thesis published in Spain on the right ventricle in athletes, it was considered appropriate to include the results in the meta-analysis, because it meets the search requirements. The following criteria were taken into account for the selection of the studies to be reviewed:

1°) First criterion: Athletes who practiced disciplines belonging to Categories II and/or III of the classification by Mitchell,⁸ independently of the level of the static component.

2º) Second criterion: Measurements recorded by:

- Echocardiography. At least 3 measurements of the right ventricle at rest or before participating in a determined event, according to the guidelines for standardizing echocardiographic measurements of the right ventricle.³⁻⁶
- Nuclear magnetic resonance. Measurements of the volume of the right ventricle in diastole and systole and the myocardial mass.

 3°) Third criterion: The studies had to present the following data and comply with the following criteria:

• Age (mean and SD)

 \bullet Anthropometric data: weight, height and body surface area (mean and SD)

- Years of training (mean and SD)
- Absence of pathologies
- Presence of sedentary controls

• Male sex. Given that it has been shown that there are differences in cardiac measurements between the two sexes, this study only considered data on men.

• Age range. Studies were eliminated that focused on populations at the growing stage or ages when the heart begins to deteriorate.

Data collection

The articles were selected by two of the authors (FJC and MB) according to the established criteria. All the data were entered onto a spreadsheet (FJC) and the units of the echocardiographic and nuclear magnetic resonance measurements were reviewed (FJC and MB). In those articles that studied the variations experienced during the competition or the recovery, the values of the analyzed variables were those corresponding to the initial state (Figure 1).



Figure 1. Results of the bibliographic search on the different studies using echocardiography or nuclear magnetic resonance for inclusion in the meta-analysis.

Data synthesis and statistical analysis

Data were analyzed using the Review Manager 5.3 statistical package.⁹ A standardized mean difference (SMD); and its corresponding 95% confidence intervals (CIs) were estimated as a measure of effect size. Their interpretation was based on the following criteria: small: ≤ 0.49 ; moderate: 0.50 – 0.79 and large: ≥ 0.80 .⁹ Heterogeneity between studies was tested using Chi-square and I² statistical tests. A P-value of less than 0.1 indicated a statistically significant heterogeneity for the Chi-square test.¹ The percentage of I² represented the degree of heterogeneity: percentages of 25, 50, and 75% indicated a low, moderate, and high degree of heterogeneity, respectively.¹⁰ When significant heterogeneity was found a random-effects model was used to pool the study results; otherwise, a fixed-effects model was adopted. For all analyses, a forest plot was generated to display results.

Although some articles used Foale abbreviations, for a clearer understanding of the text we have used those of Rudski et al.¹¹. The variables that were taken into account for the meta-analysis and their nomenclature were as follows:

1º) Dimensions of the right ventricle

- Diameter of the RVOT by parasternal long axis (RVOT-Prox long axis)
- Diameter of the proximal RVOT by parasternal short axis (RVOT-Prox short axis)
- Diameter of the distal RVOT by parasternal short axis (RVOT-Distal short axis)
- Basal diameter of the RV in apical 4 (RVD1)
- Mean diameter of the RV in apical 4C (RVD2)
- Longitudinal diameter of the RV in apical (RVD3)
- Diastolic area of the RV in apical 4C
- Systolic area of the RV in apical 4C

 2°) Thickness of the RV in M-mode or 2D, parasternal and subcostal projections

Results

Echocardiographic measures

The characteristics of the included studies, published between 2002 and 2017 are shown in <u>Table 1</u>. Since not all of them included all the measures, we selected those measures that appeared in at least 5 studies.

The forest plots for the 5 studies in which RVD1 was measured in relation to body surface area (Figure 2). One of the studies⁸ included 2 samples from endurance athletes and 2 samples from controls. The sample for the meta-analysis involved a total of 939 endurance athletes and 316 controls. The endurance athletes presented significantly higher RVD1 relative scores compared to controls (SMD = 0.98, 95% CI: 0.62-1.35, Z = 5.29, *P* < 0.001) with significant heterogeneity in these estimates (I² = 82%, P < 0.001).

Table 1. Studies, published between 2002 and 2017

RVD2 abs (Figure 2) appeared in 12 studies, one of them with 2 samples from endurance athletes and one from controls.¹² These studies included 1477 endurance athletes and 498 controls. Analysis of combined results showed a significant SMD favoring athletes with high heterogeneity in these estimates (SMD = 1.12, 95% CI: 0.78-1.47, Z = 6.32, P < 0.001, $I^2 = 88\%$, P < 0.001).

Eight studies included RVD3 (<u>Figure 2</u>) or RV LAX abs measurements, involving 1357 endurance athletes and 415 controls. Endurance athletes presented significantly higher RVD3 absolutes scores compared to controls (SMD = 0.64, 95% CI: 0.52-0.76, Z = 10.5, P < 0.001, $I^2 = 6\%$, P = 0.38)

RVOTprox absolute (Figure 3) was measured in 8 studies involving 859 endurance athletes and 365 controls and the thickness of the right ventricle wall (RVWT) abs (Figure 3) in 7 studies (1232 endurance athletes and 372 controls). Endurance athletes presented significantly higher RVOTprox abs scores (SMD = 0.47, 95% CI: 0.24-0.70, Z = 3.96, P < 0.001) and RVWT abs scores (SMD = 0.70, 95% CI: 0.22-1.18, Z = 2.83, P = 0.005) compared to controls, with significant heterogeneity in these estimates (I² = 61%, P < 0.01 for RVOTprox abs and I² = 92%, P < 0.001 for RVWT abs scores).

Finally, RVFAC abs (%) (Figure 3) was measured in 6 studies (594 endurance athletes and 235 controls). No differences were found between endurance athletes and controls (SMD = 0.31, 95% CI: -0.20-0.83, Z = 1.18, P = 0.240) although a high variability was found in these studies (I² = 89%, P < 0.001).

Resonance measures

<u>Table 2</u> shows the baseline characteristics of the twelve studies included in this review, published between 2010 and 2017. We select those measures that at least appeared in 5 studies.

Author	Echocardiographic parameters	Number of athletes and	Sports from category C	Foale or Rutsky measurement criteria
Baucem et al., 2008	RVD2; RVD3 ; RVOTProx RVFAC abs	40 athletes 40 sedentary	Soccer (28.7 %) Volleyball (10.25) Running (2.5 %)	Foale
Baggish et al., 2010	RVD2; RVFAC abs	20 athletes 20 sedentary	Rowing	Lang
De Luca et al., 2013	RVOTProx	25 athletes 20 sedentary	20 Soccer, 5 Basketball	Rudski
Erol et al., 2002	RVD2	36 athletes 16 sedentary	14 Running	Not mentioned
Esposito et al., 2014	RVD2; RVD3; RVWT abs	40 athletes 43 sedentary	Rowing	Italian Society of cardiology
Gjerdalen et al., 2014	RVD1, RVD2, RVD3, RVWT abs	504 athletes 47 sedentary	Soccer	Lang; Horton, Ruski
Henriksen et al., 1998	RVD2; RVD3; RVOTProx	82 athletes 29 sedentary	Orienteering	Foale
King et al., 2013	RVD2; RVWT abs	42 athletes 17 sedentary	18 Rowing and 24 Soccer	Lang
Pagourelias et al., 2013	RVD2; RVD3; RVOTProx RVFAC abs	80 athletes 26 sedentary	Cycling, Running and Triathlon	Lang
Popovic et al., 2011	RVOTProx	21 athletes 20 sedentary	Waterpolo	Foale
Simsek et al., 2013	RVD2; RVFAC abs	44 athletes 30 sedentary	Long distance running	Rudski
Teske et al., 2009	RVD1	117 athletes 94 sedentary	Long distance running	American Society of Echocardiography
Utomi et al., 2015	RVD1; RVD2; RVD3; RVOTProx; RVWT abs	19 athletes 21 sedentary	Long distance running	Lang
Vitarelli et al., 2013	RVFAC abs; RVWT abs	35 athletes 35 sedentary	Endurance	Lang
Zaidi et al., 2013	RVFAC abs; RVWT abs	375 athletes 84 sedentary	Endurance. Badminton, Basketball, Boxing, Canoeing, Cycling, Hockey, Middle and long distance running, Rowing, Soccer, Skating, Squash, Swimming, Tennis and Triathlon	Lang and Ruski
Heras E., 2016	RVOT-Prox long axis RVOT-Prox short axis RVOT-Distal short axis; RVD1; RVD2; RVD3; VD Thickness	217 athletes 125 athletes CI	Middle and long distance running, Badminton, Orienteering, Soccer, Field hockey, Padel, Basketball, Swimming, Handball	Lang and Ruski

RVD2: Mean diameter of the RV in apical 4C; RVD3: Longitudinal diameter of the RV in apical; RVOT: Right ventricular outflow tract; RVWT: Thickness of the right ventricle wall; RVD1rel: Basal diameter of the RV in apical 4

Study (B)(D1 col)	Std.	Mean Difference	Std. Mean Difference
Study (KVD11el)	weight iv	, Randoni, 95% Ci	IV, Railuolli, 95% Cl
Gjerdalen et al., 2014	18.7%	0.84 [0.94, 1.14]	
Hennksen et al., 1998	10.9%	1.44 [0.97, 1.90]	
Heras et al., 2016	19.9%	0.38 [0.16, 0.60]	and the second se
Teske et al., 2009 (a)	17.4%	1.16[0.78, 1.54]	
Teske et al., 2009 (b)	15.8%	1.16[0.69, 1.64]	
Utomi et al., 2015	12.4%	1.12 [0.45, 1.79]	10 million (10 mil
Total (95% CI)	100.0%	0.98 [0.62, 1.35]	•
Heterogeneity: Tau ² = 0.1	6; Chi ² = 27.7	2, df = 5 (P < 0.0001); l ² = 82%	
Test for overall effect Z =	5.29 (P < 0.0	0001)	Favors [controls] Favors [Athletes]
er t (DVD2 abc)	S	td. Mean Difference	Std. Mean Difference
Study (RVD2 abs)	weight	IV, Random, 95% CI	IV, Random, 95% CI
Baggish et al., 2010	5.2%	3.68 [2.63, 4.73]	
Bauce et al., 2008	8.4%	0.28 [-0.16, 0.72]	
Erol & Karakelleoglu, 2002	0.2%	2.82[1.77, 3.87]	
Circulation at al., 2014	8.2%	1.44 [0.96, 1.93]	
Gjerdalen et al., 2014	9.0%	0.35 [0.05, 0.65]	
Herne et el 2016	0.270	0.00 (0.47, 0.60)	-
Heras et al., 2010	9.3%	1.64 (0.06.0.42)	
King et al., 2013 (a)	0.3%	1.04 [0.00, 2.42]	
Ring et al., 2013 (b) Regeneration at al. 2012	0.9%	0.00.00.60.1.461	
Pirecele et al., 2013	0.310	0.03 [0.03, 1.40]	
Litomi et al., 2015	7 4 96	0.32 [0.43, 1.41]	
Zaidi et al. 2013	9.3%	0.69 [0.45 0.93]	+
	0.010	0.00 [0.10, 0.00]	
Total (95% CI)	100.0%	1.12 [0.78, 1.47]	· · · · · · · · · · · · · · · · · · ·
Heterogeneity: Tau ² = 0.33	3; Chi² = 96.90), df = 12 (P < 0.00001); I ² = 88%	-4 -2 0 2 4
Test for overall effect: Z = 6	6.32 (P < 0.00	001)	Favors [Controls] Favors [Athletes]
		Std. Mean Difference	Std. Mean Difference
Study (RVD3 abs)	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Bauce et al., 2008	7.1%	0.55 [0.10, 0.99]	
Esposito et al., 2014	7.0%	0.83 [0.38, 1.28]	
Gierdalen et al., 2014	15,5%	0.73 [0.43, 1.03]	
Henriksen et al. 1998	7.6%	0.63 (0.20, 1.06)	
Herec et al. 2016	28.1%	0.56 [0.33, 0.78]	
Panouraliae at al 201	2 7 2 96	0.16 [.0.29 0.60]	
Litemi et al. 2016	3 7.2%	0.72 [0.09 4 26]	
Zaidi et al., 2013	3.4%	0.72 [0.06, 1.36]	
Z SHITL MESH 2011 S	74 1 %	0.77.0(53.1)7	

Total (95% CI)	100.0%	0.64 [0.52, 0.76]				•	
Heterogeneity: Chi ² = 3	7.45, df = 7 (P = 1	0.38); I ² = 6%	H	<u> </u>			
Test for overall effect: Z = 10.50 (P < 0.00001)		00001)	Favors [Controls] Favors [Athletes]] 2

Figure 2. Forest plots corresponding to the following echocardiographic parameters considered in this work: RVD1, RVD2 and RVD3. RVD1rel: Basal diameter of the RV in apical 4 (relative); RVD2abs: Mean diameter of the RV in apical 4C (absolute); RVD3: Longitudinal diameter of the RV in apical (absolute)

	5	Std. Mean Difference	Std. Mean Difference
Study (RVOTprox abs)	Weight	IV, Random, 95% Cl	IV, Random, 95% CI
Bauce et al., 2008	12.5%	0.06 [-0.38, 0.49]	
De Luca et al., 2013	9.1%	0.24 [-0.35, 0.83]	
Henriksen et al., 1998	12.7%	0.60 [0.17, 1.03]	
Heras et al., 2016	18.8%	0.20 [-0.02, 0.42]	
Pagourelias et al., 2013	11.9%	0.91 [0.45, 1.37]	
Popovic et al., 2011	8.2%	0.91 [0.27, 1.56]	
Utomi et al., 2015	8.6%	0.25 [-0.38, 0.87]	
Zaidi et al., 2013	18.2%	0.66 [0.41, 0.90]	
Total (95% CI)	100.0%	0.47 [0.24, 0.70]	•
Heterogeneity: Tau ² = 0.0	8; Chi ² = 18	.15, df = 7 (P = 0.01); I ² = 619	
Test for overall effect: Z =	3.96 (P < 0	0001)	-2 -1 U 1 2 Favors [Controls] Favors [Athletes]

	Std. Mean Difference		Std. Mean Difference IV, Random, 95% Cl	
Study (RVWT abs)	VWT abs) Weight IV, Random, 95% CI			
Esposito et al., 2014	11.8%	2.72 [2.12, 3.32]		
Gjerdalen et al., 2014	13.7%	0.61 [0.31, 0.91]	-	
Heras et al., 2016	14.0%	0.62 [0.39, 0.84]		
King et al., 2013 (a)	11.3%	0.43 [-0.24, 1.10]		
King et al., 2013 (b)	11.7%	0.00 [-0.62, 0.62]		
Utomi et al., 2015	10.9%	1.63 [0.91, 2.36]		
Vitarelli et al., 2013	12.7%	-0.25 [-0.72, 0.23]		
Zaidi et al., 2013	14.0%	0.10 [-0.14, 0.34]		
Total (95% CI)	100.0%	0.70 [0.22, 1.18]	+	
Heterogeneity: Tau ² = 0	.42; Chi=	85.92, df = 7 (P < 0.00001); P = 92%		
Test for overall effect: Z	= 2.83 (P =	0.005)	-2 -1 U 1 2 Favors (Controls) Favors (Athletes)	

	5	Std. Mean Difference	Std. Mean Difference
Study (RVFAC abs)	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Baggish et al., 2010	14.2%	1.50 [0.79, 2.21]	
Bauce et al., 2008	17.0%	-0.24 [-0.68, 0.20]	
Pagourelias et al., 2013	16.7%	1.08 [0.62, 1.55]	
Simsek et al., 2013	16.8%	0.17 [-0.30, 0.63]	
Vitarelli et al., 2013	16.7%	-0.14 [-0.61, 0.33]	
Zaidi et al., 2013	18.6%	-0.25 [-0.49, -0.01]	
Total (95% CI)	100.0%	0.31 [-0.20, 0.83]	-
Heterogeneity: Tau ² = 0.3	6: Chi ² = 43	.66. df = 5 (P < 0.00001); P = 89%	
Test for overall effect: Z =	1.18 (P = 0	24)	-2 -1 0 1 2 Favors [Controls] Favors [Athletes]

Figure 3. Forest plots corresponding to the following echocardiographic parameters considered in this work: RVOT absolute, RVWT and RVFAC. RVOT: Right ventricular outflow tract; RVWT: Thickness of the right ventricle wall; RVFAC: Right ventricular fractional area



		1	
Author	Nuclear magnetic	Number of athletes and sedentary	Sports from Category C
	resonance parameters	subjects	
Dupont et al., 2017	EDV rel	12 athletes	Triathlon
	CI rel	12 sedentary	
Esch et al., 2010	EDV abs; ESV abs	8 athletes	2 Cycling, 5 Triathlon, 1 Biathlon
		8 sedentary	
La Gerche et al., 2011	EDV abs; ESV abs	39 athletes	7 Marathon, 9 Cross country skiing, 10 Long-distance runners,
		14 sedentary	13 Ultra-triathlon
La Gerche et al., 2015	EDV abs; ESV abs	10 athletes	Triathlon and Cycling
		7 sedentary	
Luijkx et al., 2013	EDV rel; ESV abs; Mass rel	52 athletes	
-		52 sedentary	
Luijkx et al., 2012	EDV rel; ESV abs; Mass rel	93 athletes	54 III C and 93 III A Mitchell)
•		56 sedentary	
Perseghin et al., 2007	EDV abs; EDV rel	9 athletes	Marathon
C A		10 sedentary	
Petersen et al., 2006	EDV rel; ESV abs; CI rel	23 athletes	15 Rowing, 2 Swimming, 6 Triathlon
		21 sedentary	Ŭ Ŭ
Prakken et al., 2010	EDV abs; EDV rel; ESV abs;	46 athletes	Rowing, Biathlon, Triathlon, Water polo
	Mass rel	56 sedentary	
Scharf et al., 2010	EDV rel; Mass rel; CI rel	29 athletes	Soccer
		29 sedentary	
Scharf et al., 2010	EDV rel; Masa rel; CI rel	26 athletes	Triathlon
		27 sedentary	
Steding-Ehrenborg et al., 2015	EDV abs; ESV abs; CI rel	6 athletes	Endurance
		8 sedentary	

EDV = End Diastolic volume (absolute and relative); ESV = End systolic volume (absolute); Mass = myocardial mass (absolute and relative); CI = cardiac index



Figure 4. Forest plots corresponding to the following magnetic resonance parameters considered in this work: absolute End Diastolic Volume (EDV abs), relative End Diastolic Volume (EDV rel), absolute End Systolic volume (ESVabs) and myocardial mass (Mass).

The EDV abs (Figure 4) was measured in 6 studies; one of them¹³ included 2 samples from endurance athletes and 2 samples from controls. These studies involved 134 endurance athletes and 119 controls. EDV rel (Figure 4) was measured in 7 studies (347 endurance athletes and 263 controls), one of them (8) including 2 samples from endurance athletes and 1 sample from controls. Endurance athletes presented significantly higher EDV abs scores

(SMD = 1.41, 95% CI: 1.12-1.69, Z = 9.62, P < 0.001, I^2 = 20%, P = 0.28) and EDV rel scores (SMD = 1.63, 95% CI: 1.36-1.90, Z = 11.88, P < 0.001) compared to controls. In SMD estimates for EDV rel scores moderate heterogeneity was found (I^2 = 50%, P = 0.04).

ESVabs (Figure 4) was measured in 8 studies, one of them with 2 samples from endurance athletes and one from controls¹⁴ and another one¹³ included 2 samples from endurance athletes and 2

samples from controls. These studies included 350 endurance athletes and 294 controls. The analysis of combined results showed a significant SMD favoring athletes with a moderate heterogeneity in these estimations (SMD = 1.30, 95% CI: 1.03-1.58, Z = 9.24, P < 0.001, I2 = 52%, P = 0.03).

Five studies included Mass rel measures (Figure 4), one of them with 2 samples from endurance athletes and one from controls.¹⁴ These studies included 330 endurance athletes and 220 controls. Endurance athletes presented significantly higher Mass rel scores compared to controls with a high heterogeneity in these estimations (SMD = 1.35, 95% CI: 0.81-1.89, Z = 4.86, P < 0.001, I² = 88%, P < 0.001). Finally, five studies included IC rel measures, one of them¹⁵ included 2 samples from endurance athletes and 113 controls. Endurance athletes presented significantly higher IC rel scores compared to controls with a moderate heterogeneity in these estimations (SMD = 0.47, 95% CI: 0.20-0.74, Z = 3.42, P < 0.001, I² = 46%, P = 0.10).

Discussion

The aim of this review was to characterize the limit of physiological adaptation of the right ventricle in endurance athletes by means of echocardiography and magnetic resonance imaging. As Morganroth¹⁶ rightly surmised more than a century ago, the adaptation of the right ventricle had to "symmetrically match" that of the left ventricle. In fact, the balance of the right/left adaptation was demonstrated later by,^{14,17,18} although La Gerche¹⁹ obtained higher values in the left ventricle/right ventricle ratio suggesting a different physiological adaptation mechanism to training, as the right ventricle is more sensitive to the volume overload resulting from greater venous return during exercise.

1) Discussion of the echocardiographic results. This study showed that the mean values for the different measurements of the right ventricle in athletes are significantly greater than that of sedentary controls. However, the differences found in some studies may be due to 1) problems arising from the echocardiographic technique and 2) the way the different authors defined endurance athletes and sedentary controls.

The technical echocardiographic problems include: 1) the placement of the transducer to obtain the best image, 2) the unequivocal delimitation of the axes of the right ventricle (short and long axis), 3) the inclusion or not of certain structures in the different measurements of the right ventricle, which has made it difficult in many cases to standardize them, and 4) the delimitation of the endocardial borders, given the considerable trabeculation of this chamber.

Regarding the selection of the population of athletes and controls, it is necessary to bear in mind the characteristics of endurance athletes. For example, the population studied by Gjerdalen et al.²⁰ includes soccer players whose static component is notably lower than rowers, cyclists and long-distance runners. Soccer is characterized by high-intensity intermittent activity and although aerobic energy contributes significantly to performance in this sport, a high anaerobic capacity is also required.^{11,21-24} The maximum oxygen consumption reached by soccer players on average is lower than that obtained by endurance athletes.²⁵

Oxygen consumption ($\dot{V}\,O_2$) is a parameter that integrates the functions of uptake (respiratory system), pumping, transport and distribution (cardiorespiratory system) and use (mainly muscle tissue). Therefore, the athletes with a greater $\dot{V}\,O_2$ develop a greater ventricular function which translates into a higher degree of adaptation. Moreover, the selection of the controls is also of utmost importance.

The study by Heras²⁶ did not include a sedentary population, but it was decided to use the "opposite extreme" IA of Mitchell's classification (golf, Olympic shooting) that is, sports with low dynamic and static components. Although it may in fact be questionable to choose these athletes as controls, the values of the different echocardiographic measurements are within normal limits for the sedentary population.³⁻⁶ It is also exceptional for the different studies included in this review to adequately describe the characteristics of the control population. In our understanding it is not enough to indicate that the control population did not suffer from any cardiac pathology and that it was physically inactive. To really understand the possibilities of physiological adaptation the control population should have revealed conditions of "cardiac atrophy" as happens to people on bed-rest or those who have been in space for a long time. In this type of study, the mean loss of heart muscle mass measured by resonance is 14%.¹⁴

RVD1. In several studies ^{8,15,18,19,27} which measured this variable the endurance athletes had higher values than the sedentary controls. In this echocardiographic measurement Heras showed a difference of means of 0.38. As indicated above this value may be due to the consideration of athletes from category IA as the control population. Mitchell's classification⁸ may have a clear cardiological indication but not from the viewpoint of the athletes' cardiac overload. Currently, golfers, for example, have very comprehensive training including dynamic and static overload, so that they may experience a certain degree of adaptation.

<u>RVD2</u>. This echocardiographic measurement also shows a great amount of heterogeneity among the different studies^{12,15,18-20,23,24,26-³⁰ due both to the small differences found between athletes and sedentary controls^{15,19,27,30} and also to the higher values of the athletes compared to sedentary controls.^{20,23} Bauce and Gjerdalen^{20,31} include in the athlete population soccer players and volleyball players who are clearly not classified at the maximum limit of adaptation (Mitchell's category IIIC).²}

<u>RVD3</u>. In contrast to the previous measurements, the degree of homogeneity in this variable was very high in all the studies that analyzed it.^{15,18,19,24,27-30} Only Pagourelias et al.³² observed similar values in the studied athlete population and the sedentary controls. This homogeneity probably suggests that this measurement was not affected by the echocardiographic technique or the choice of the athletes. The results of this author attract attention as the athlete population is clearly made up of endurance athletes and also a consensus method was used.⁶

<u>RVOTProx</u>. Although moderately heterogeneous, the values found by Bauce et al., De Luca et al., Heras and Popovic et al.^{26,31,33,34} are similar between the athlete population and the sedentary controls. With regard to the results of Heras,²⁶ it seems reasonable to think that the population chosen to compare with the endurance athletes was not suitable, as indicated above.

<u>RVFAC abs (%).</u> The high degree of heterogeneity in this echocardiographic measurement observed in the studies that analyzed it^{20,26,28-30,35} is due, in our opinion, to the echocardiographic methodology used. As the measurement is taken during the two phases of the cardiac cycle (systole and diastole) it is highly conditioned. The phases of the cardiac cycle considered for the left ventricle cannot be extrapolated. The pressure/volume ratio in the right ventricle has been defined as a trapezium or triangle, with a poor definition of the periods of isovolumetric contraction and relaxation that are observed in the left ventricle.

<u>RVWT abs</u>. Again, the high degree of heterogeneity in this measurement is due to the inherent errors that can be made when measuring the thickness of the myocardium of the right ventricle. Thus, while Espósito et al. and Utomi et al.^{37,38} found considerable differences for this measurement between endurance athletes and sedentary controls, other authors that measured this variable^{12,15,27,29,35} did not observe significant differences.

2) Discussion of the results of the magnetic resonance. In contrast to the echocardiographic measurements, the homogeneity found between the different volumetric values

presented in the different studies that measured them using magnetic resonance is worthy of note. The differences in effect size between the resonance and the echocardiograph are due to the greater accuracy of the former in quantification, as the structural limits are determined more precisely. In fact, magnetic resonance constitutes the gold standard for determining volumes, for this reason we think that the differences observed in the volumetric measurements taken by magnetic resonance may be due more to the selection of the sample of athletes and sedentary controls than the technique itself. However, other parameters measured using magnetic resonance, the relative myocardial mass (Mass rel) and the relative cardiac index (CI rel) showed a great deal of heterogeneity. In these two measurements the differences are due both to the technique itself and to the selection of the study subjects.

<u>EDV</u> abs. Only the study by Perseghin et al.³⁹ failed to demonstrate differences in this measurement, while in the rest of the studies^{7,8,13,32,40} the ventricular volume was greater in the endurance athlete population studied. It is curious that although the athlete population studied by Perseghin et al.³⁹ was clearly made up of endurance athletes, no differences were found compared to the control group.

<u>EDV rel.</u> The evaluation of the right ventricular volume relative to body surface area showed significant differences between the two populations. Of note are the extreme values: no differences in the study by Perseghin et al.³⁹ and considerable differences in that by Dupont et al.⁴¹.

<u>Mass rel</u>. The heterogeneity in this measurement is due both to the selection of the endurance athletes as to the errors that can be made in the valuation of the right myocardial mass. With regard to the former problem, all the resonance studies consulted were carried out with endurance athletes that could be included in Mitchell's group IIIC,⁸ with the exception of the study by Scharf,⁴² who carried it out with soccer players.

<u>CI rel</u>. The heterogeneity of this variable seems coherent as the heart output depends on the size of the body and although it is relativized by body surface area, the values are very similar among individuals from the same type.

In conclusion, this review study shows that the right ventricle experiences an adaptation to endurance training, but without reaching values that are considered pathological. This adaptation is a consequence of the high heart output that the athletes develop during training and competition. In spite of the statistical differences found in this meta-analysis, it can be stated that the effect size measures in this review are within the moderate to high range.⁹ This means that the percentage of control subjects with values lower than those of the endurance athletes in some measurements of the right ventricle reached more than 70%. Finally, the differences found between the two techniques used (echocardiography and resonance) should be underlined.

Limitations of the study. We consider that to be able to compare the degree of adaptation of the two cardiac pumps it would have been advisable to analyze the structural variables using echocardiography and magnetic resonance. Because in spite of the studies that present a similar degree of adaptation of the two ventricles, there are also others that indicate the opposite.

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