ORIGINAL ARTICLE

New Method for Estimating Left Atrial Volume Based on an Irregular Base Cylinder Model using Magnetic Resonance Imaging: Comparison with the Area-Length Method

Nuevo método para la estimación del volumen de la aurícula izquierda por resonancia magnética basado en un modelo cilíndrico de base irregular: comparación con el método de área-longitud

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ABSTRACT

Background: Left atrial volume quantification is of great importance in various pathologies. For this purpose, models derived from echocardiography have been applied in magnetic resonance imaging, although they may not be completely accurate.
Objective: To validate a new method for estimating left atrial volume that is practical and more accurate than the method most commonly used at present.
Methods: Images of patients included in a cardiac magnetic resonance imaging database were used. Direct volumetric quantification and volumetric estimates using the area-length (AL) method and the irregular base cylinder (*cilindro de base irregular*, CBI) method were performed to measure correlation.
Results: Studies from 25 patients were analyzed. The mean age was 44 ± 15 years; 52% were male and 84% were studied on an outpatient basis. Pearson's correlation coefficient was higher for the CBI method (r=0.93; p <0.001) than for the AL method (r=0.83; p <0.001). The Bland-Altman analysis showed lower dispersion for the CBI method [-5.73 mL (18.6 to -30.11)] than for the AL method [-1.18 mL (43.82 to -46.17)]. Interobserver variability was lower for the CBI method [4.94 mL (44.76 to -34.88)] than for the LA method [19.7 mL (65.91 to -26.51)].
Conclusions: The CBI model showed better correlation than the AL model. We consider it a valid alternative that is equally simple and more accurate than the AL method for estimating left atrial volume by magnetic resonance imaging.

Key words: Cardiac magnetic resonance - Left atrium - Volume - Irregular base cylinder

RESUMEN

Introducción: La cuantificación volumétrica de la aurícula izquierda es de suma importancia en diversas patologías. Para ello se han aplicado en resonancia magnética modelos derivados de la ecocardiografía que pueden no ser completamente exactos.
Objetivo: Validar un nuevo método para estimación del volumen de la aurícula izquierda que sea práctico y más preciso que el más utilizado en la actualidad.
Material y métodos: Se utilizaron las imágenes de pacientes de una base de datos de resonancia magnética cardíaca (RMC). Se realizaron la cuantificación volumétrica directa, y las estimaciónes volumétricas por método de área-longitud (AL) y cilindro de base irregular (CBI) para medir correlación.
Resultados: Se analizaron los estudios de 25 pacientes. La edad media fue de 44±15 años; el 52% era de sexo masculino y el 84% pacientes estudiados en forma ambulatoria. El coeficiente de correlación de Pearson fue mayor para el método CBI (r = 0,93; p < 0,001) que para el de AL (r = 0,83; p < 0,001). El análisis de Bland-Altman mostró menor dispersión para el método CBI [- 5,73 mL (18,6 a -30,11)] que para el método AL [-1,18 mL (43,82 a -46,17)]. La variabilidad interobservador fue menor para el método CBI [4,94 mL (44,76 a -34,88)] que para el método AL {19,7 mL (65,91 a -26,51)].
Conclusión: El modelo CBI mostró mejor correlación que el de AL. Consideramos que representa una alternativa válida, igualmente simple y más precisa que el método de AL para la estimación del volumen de la aurícula izquierda por RMC.

Palabras clave: Resonancia magnética cardíaca - Aurícula izquierda - Volumen - Cilindro de base irregular

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INTRODUCTION

The left atrium (LA) plays an important role in cardiac physiology, and its volume has been associated with various clinical conditions such as atrial fibrillation, heart failure, and increased cardiovascular risk. (1-3) Therefore, its volumetric measurement is an essential parameter in imaging studies in clinical practice.

The most commonly used echocardiographic methods for estimating LA volume are area-length (AL) and Simpson methods. (4,5) Cardiac magnetic resonance (CMR) imaging allows global and multiplanar assessment of the LA, and indirect estimates or direct quantification can be performed, the latter being the most accurate but also the most labor-intensive. The AL method has been the most widely used in CMR imaging from the beginning and remains the method of choice in our setting. (6-10) Despite its greater simplicity, it may not accurately reflect LA volume. Direct quantification of LA volume requires a greater number of slices for CMR imaging acquisition, resulting in a longer study and its subsequent analysis. (10-12)

Objectives

To propose and validate an alternative method for estimating LA volume using CMR. To compare accuracy and agreement of this new method with the AL method, using direct quantification by complete volumetric tracing of the LA in CMR imaging studies as the gold standard.

METHODS

Study population

Twenty-five patients aged over 18 years were randomly selected from a database of CMR imaging at our center. Patients were excluded if they had complex atrial anatomy, such as congenital heart disease with Fontan-Kreutzer circulation, poor image quality due to technical artifacts, or if, for any reason, they had not completed acquisition of the basic images required for analysis.

CMR imaging protocol

The images were acquired using a Siemmens Magneton Aera 1.5 T scanner. Image acquisition was performed in the supine position, with retrospective electrocardiography gating. The center basic CMR imaging acquisition protocol includes cine images obtained using steady-state free precession (SSFP) sequences in 2-chamber (2C), 3-chamber (3C), 4-chamber (4C), and complete short-axis (SA) views. During acquisition of the complete ventricular short-axis stack, the center protocol routinely includes the atria.

Image analysis

All images were analyzed using the free software Segment v4.0 (Medviso, Lund, Sweden). Two independent analyses were performed by two researchers experienced in the method. All measurements were performed at end-systole. The LA volume was directly quantified by manual tracing, excluding the left atrial appendage and pulmonary veins on all slices, and this was assumed to be the reference value. The estimation was performed using the usual biplane area-length (AL) method and the newly proposed irregular base cylinder (CBI) method.

When estimating the volume using the AL method, the area and height (length) of the LA were measured in the 2C and 4C cine views. The following formula was used: 8/3 Π (2C area x 4C area) / length.

When estimating the volume using the CBI method, the base of the cylinder was measured. The atrial area was traced in a perpendicular slice to its major axis, obtained from the complete short-axis acquisition between the orifice of the left atrial appendage and the orifices of the pulmonary veins; the atrial height was measured from the mitral annulus to the atrial roof in the 4C view. The volume was calculated using the area x height formula.

Statistical analysis

Continuous variables are presented as mean ± standard deviation (SD) or median and interquartile range (IQR) according to their distribution. Categorical variables are presented as frequencies and percentages. Both estimates were compared with the gold standard (direct volumetry) using Pearson's correlation coefficient (r). A Bland-Altman analysis was performed to assess mean differences and dispersion between both methods and the gold standard.

RESULTS

Baseline characteristics

From our center imaging database, we analyzed previously acquired images from 25 patients with a mean age of 44 ± 15 years. Fifty-two percent were male, and 84% had been studied on an outpatient basis. The most frequent diagnoses included hypertrophic cardiomyopathy (20%), ventricular arrhythmia (16%), ischemic heart disease (16%), and dilated cardiomyopathy (12%). The mean left ventricular ejection fraction (LVEF) was 59 ± 8% and the mean left atrial volume was 97 ± 38 mL. The remaining baseline characteristics are presented in Table 1.

Quantification methods

Figure 1 shows images of direct LA volume measurement using the AL and CBI methods.

The correlation measured against direct volumetric quantification was very high for both methods (Figure 2). Pearson's correlation coefficient was higher for the CBI method ($r=0.93$; $p<0.001$) than for the AL method ($r=0.83$; $p<0.001$). The Bland-Altman analysis showed low bias for both methods, with less dispersion for the CBI method [-5.73 mL (18.6 to -30.11)] than for the AL method [-1.18 mL (43.82 to -46.17)]. Interobserver variability was lower for the CBI method [4.94 mL (44.76 to -34.88)] than for the AL method [19.7 mL (65.91 to -26.51)] (Figure 3).

DISCUSSION

Our results show an excellent correlation between both methods and direct volumetric quantification, with a higher correlation for the newly proposed method (CBI). In addition, dispersion with the new method is lower than with the AL method, and its interobserver reproducibility is higher.

It should be noted that acquiring the entire atrial volume is not necessary, since the base of the cylinder can be obtained with a slice beyond the mitral annulus plane. This makes the method practical and does not

Table 1. Population characteristics

Variables	Value
Age, years, mean (SD)	45 (15)
Male sex, n (%)	13 (52)
Weight, kg, mean (SD)	80 (19)
Height, cm - mean (SD)	169 (24)
Body surface area, m², mean (SD)	1.94 (0.29)
LV EDV, mL, median (IQR)	161 (134-187)
LV ESV, mL, median (IQR)	63 (42-85)
LVEF, %, mean (SD)	59 (8)
LV mass, g, mean (SD)	115 (43)
LA volume, mL, mean (SD)	97 (38)
Main pathology	
Hypertrophic cardiomyopathy, n (%)	5 (20)
Ventricular arrhythmia, n (%)	4 (16)
Ischemic heart disease, n (%)	4 (16)
Dilated cardiomyopathy, n (%)	3 (12)
Other, n (%)	9 (36)

EDV: end-diastolic volume; ESV: end-systolic volume; IQR: interquartile range; LA: left atrium; LV: left ventricle; LVEF: left ventricular ejection fraction; SD: standard deviation

require additional time for image acquisition.

The AL method is excellent, and its use in two-dimensional echocardiography has probably been the best option for approximating the actual volume, given the impossibility of direct quantification or the interposition of strictly orthogonal short-axis planes. For years, this method, derived from echocardiography, was adopted in CMR imaging because of its good correlation with direct quantification and the ease of image acquisition and processing.

From a clinical perspective, accurate estimation of LA volume is particularly important. In the context of remodeling, LA dilation is a marker of what is occurring in a patient's chronic hemodynamics. Volumetric measurement can provide a parameter for longitudinal assessment and is an independent predictor for major cardiovascular events, atrial fibrillation, heart failure, and embolic events. (13-20) In some cases, small differences in LA volumetric estimation may lead to a different diagnostic interpretation when values are close to the cutoff point defined by clinical guidelines or consensus statements. Therefore, greater precision in estimation would be expected to improve diagnostic accuracy and consequently benefit clinical practice.

Furthermore, according to our observations, the lower interobserver variability makes CBI a more

Fig. 1. Left atrial measurements performed in the complete short-axis, 4C, and 2C views with manual endocardial tracing at end-systole. Direct volumetry (A-B-C-D). AL method (E-F). CBI method (G-H)

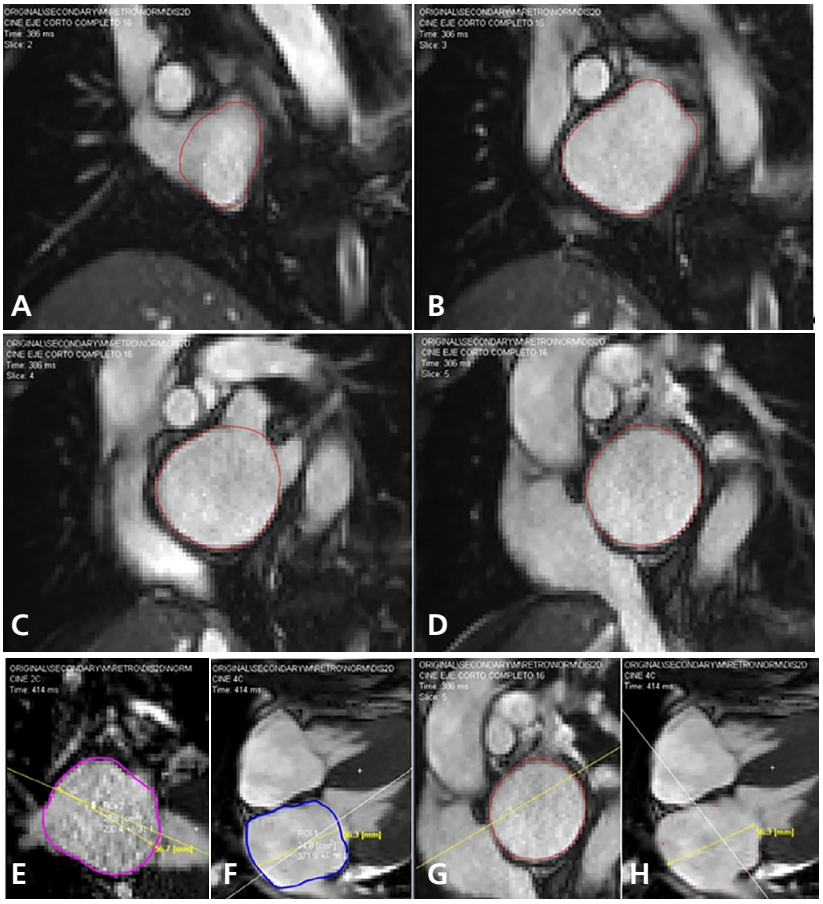


Fig. 2. Correlation between measurements by direct volumetry and area-length method (blue) and CBI method (red).

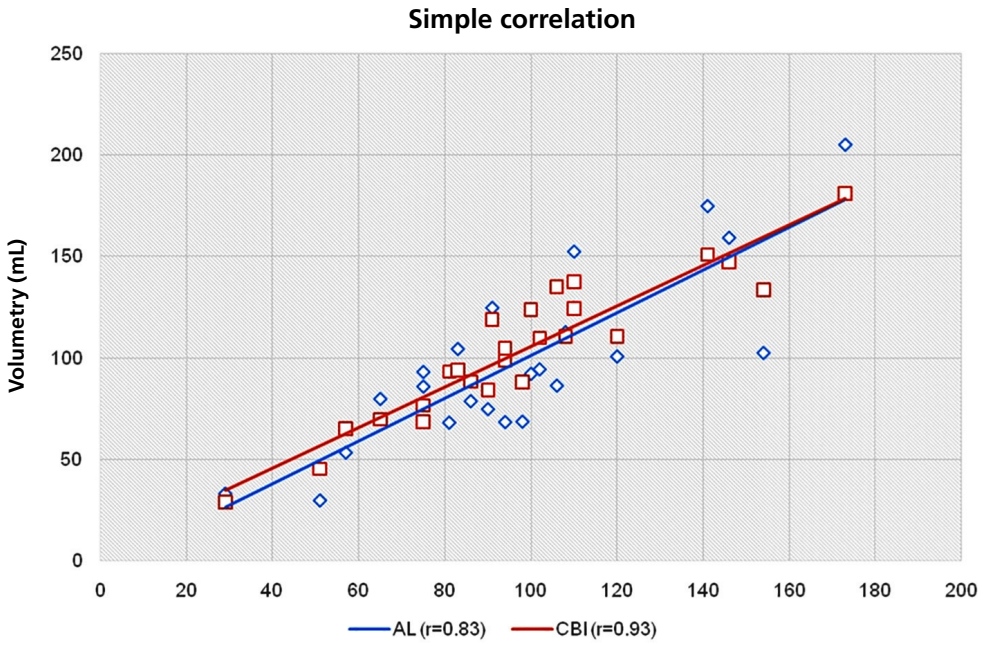
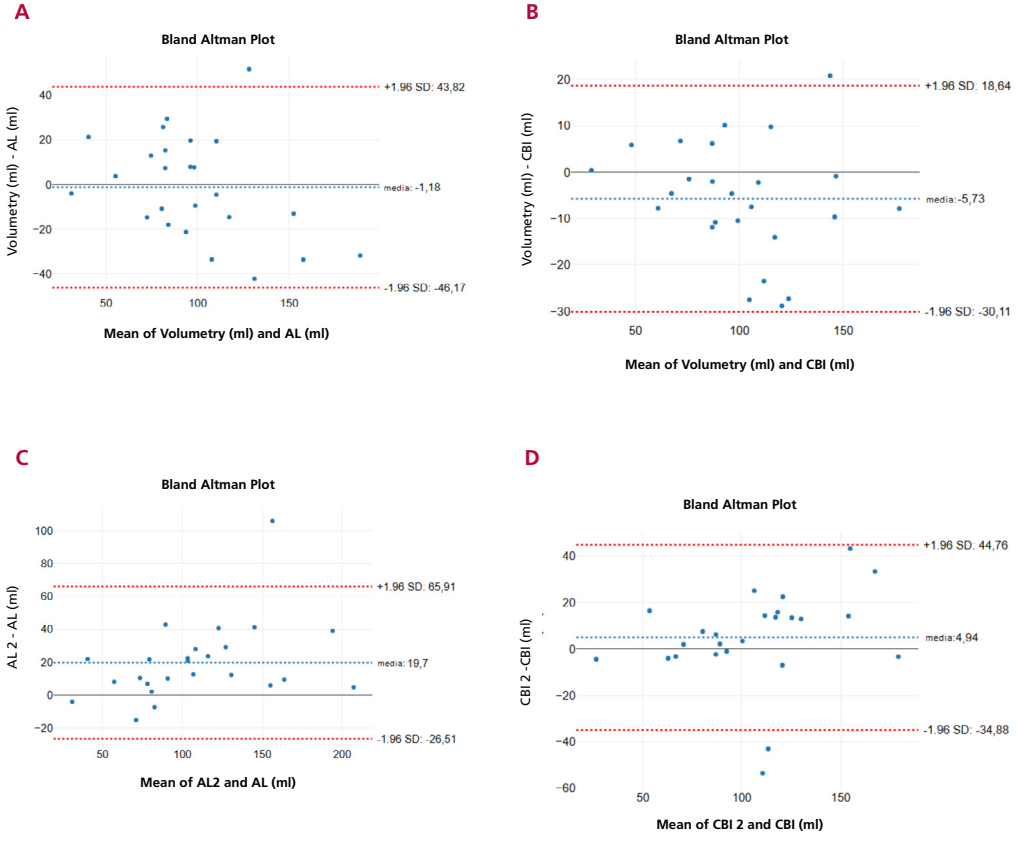


Fig. 3. Mean differences and dispersion in the measurement of left atrial volume: (**A**) Direct volumetry and area-length method. (**B**) Direct volumetry and irregular base cylinder method. Interobserver variability: (**C**) area-length method, (**D**) irregular base cylinder method.



AL: area-lenght; CBI: irregular base cylinder

robust method that may be particularly valuable in multicenter studies or serial evaluations, where methodological stability is essential to detect real changes in atrial remodeling.

In summary, CMR has the advantage over two-dimensional echocardiography of allowing image slices at any desired orientation and facilitates the use of geometric figures and shapes that better fit volumetric estimation. We believe that the CBI method, with its slightly more accurate approximation than the method commonly used, without compromising its practicality, may improve the interpretation of the study.

Limitations

A small number of cases were used assuming a coefficient r >0.8, and although the selection in the database was random, this geometric model and the AL method may not be extrapolated to all atrial morphologies.

CONCLUSIONS

The CBI method showed a better correlation with the direct measurement standard than that the AL method. It therefore represents a valid alternative that is equally simple and more accurate than the method commonly used to estimate LA volume by CMR.

Conflicts of interest

None declared.

(See authors' conflict of interests forms on the web).

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ORIGINAL ARTICLE

Clinical and Imaging Factors Associated with Lower Peak Oxygen Consumption in Patients with Hypertrophic Cardiomyopathy: the Value of Ventricular Strain by Magnetic Resonance Imaging

Factores clínicos e imagenológicos asociados a un menor consumo máximo de oxígeno en pacientes con miocardiopatía hipertrófica: el valor del strain ventricular por resonancia magnética

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ABSTRACT

Background: Peak oxygen consumption (peak VO_2) is a key marker for assessing functional capacity and prognosis in patients with hypertrophic cardiomyopathy (HCM). Although multiple factors can influence this parameter, its relative impact and predictive value are not fully established.
Objective: The aim of this study was to analyze the association between clinical, echocardiographic, and cardiac magnetic resonance imaging (CMR) variables with peak VO_2 in patients diagnosed with HCM.
Methods: A retrospective, observational, single-center cohort study was conducted in patients diagnosed with sarcomeric HCM belonging to an institutional HCM registry between January 2017 and March 2025, who had echocardiography, CMR, and oxygen consumption tests performed within less than a year of each other. Clinical, imaging, and functional data were collected from electronic medical records. Cardiac magnetic resonance scans were done with a 1.5-T magnet (Avanto, Siemens Medical Solutions®, Erlangen, Germany). Late gadolinium enhancement (LGE) quantification and global longitudinal strain by CMR (GLS-CMR) were obtained using Circle Cardiovascular Imaging software (Tissue Tracking, cvi42). Univariate and multivariate linear regression models were used to evaluate associations with peak VO_2.
Results: Fifty-four patients with mean age of 53 ± 18 years (59% men) were included in the study. Mean peak VO_2 was 23.5±9.6 mL/kg/min. In the univariate analysis, male sex ($p=0.001$), indexed right ventricular end-diastolic volume ($p<0.001$), and GLS-CMR ($p=0.030$) were significantly associated with higher peak VO_2. Age was inversely associated with peak VO_2 ($p<0.001$). No significant associations were found with left ventricular ejection fraction, intraventricular obstructive gradient, left ventricular mass index, or LGE. In the multivariate analysis, the variables that showed an independent association with lower peak VO_2 were female sex ($p=0.007$), older age at diagnosis ($p<0.001$), and lower GLS-CMR value ($p=0.033$).
Conclusions: In patients with HCM, female sex, older age, and lower left ventricular global longitudinal strain by CMR were independently associated with lower peak VO_2. These findings highlight the usefulness of myocardial strain as a complementary functional marker that could contribute to improve prognostic stratification in this population.

Key words: Hypertrophic cardiomyopathy – Strain - Cardiac magnetic resonance imaging - Oxygen consumption

RESUMEN

Introducción: El consumo pico de oxígeno (VO_2 pico) es un marcador clave para evaluar la capacidad funcional y el pronóstico en pacientes con miocardiopatía hipertrófica (MCH). Aunque múltiples factores pueden influir en este parámetro, su impacto relativo y valor predictivo no están completamente establecidos.
Objetivo: Analizar la asociación entre variables clínicas, ecocardiográficas y de resonancia magnética cardíaca (RMC) con el VO_2 pico en pacientes diagnosticados con MCH.
Material y métodos: Estudio retrospectivo, observacional y unicéntrico que incluyó pacientes con diagnóstico de MCH sarcomérica pertenecientes a un registro institucional entre 2017 y 2025, que contaran con ecocardiograma, RMC y prueba de consumo de oxígeno realizados en un intervalo menor a un año de diferencia entre sí. Se recolectaron de la historia clínica electrónica datos clínicos, imagenológicos y funcionales. Las exploraciones de RMC se realizaron con un imán de 1.5-T (Avanto, Siemens Medical Solutions®,

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Erlangen, Alemania). La cuantificación de realce tardío de gadolinio (RTG) y el *strain* longitudinal global por RMC (SLG-RMC) se efectuaron con el software Circle Cardiovascular Imaging (Tissue Tracking, cvi42). Se utilizaron modelos de regresión lineal univariados y multivariados para evaluar las asociaciones con el VO_2 pico.

Resultados: Se incluyeron 54 pacientes con una edad promedio de 53 ± 18 años, de los cuales el 59% eran hombres. El VO_2 pico promedio fue de 23,5 ± 9.6 mL/kg/min. En el análisis univariado, el sexo masculino (p=0,001), el volumen telediastólico del ventrículo derecho indexado (p<0,001) y el SLG-RMC (p=0,030) se asociaron significativamente con un mayor VO_2 pico. La edad presentó una asociación inversa con el VO_2 pico (p<0,001). No se hallaron asociaciones significativas con la fracción de eyección del ventrículo izquierdo, el gradiente obstructivo intraventricular, el índice de masa ventricular izquierda ni con el realce tardío de gadolinio. En el análisis multivariado, las variables que mostraron asociación independiente con un VO_2 pico más bajo fueron el sexo femenino (p=0,007), una mayor edad al diagnóstico (p<0,001) y un menor valor de SLG-RMC (p=0,033).

Conclusiones: En pacientes con MCH, el sexo femenino, una mayor edad y un menor *strain* longitudinal global del ventrículo izquierdo por RMC se asociaron de forma independiente con un menor VO_2 pico. Estos hallazgos resaltan la utilidad del *strain* miocárdico como marcador funcional complementario que podría contribuir a mejorar la estratificación pronóstica en esta población.

Palabras clave: Miocardiopatía hipertrófica - *Strain* - Resonancia magnética cardíaca - Consumo de oxígeno

INTRODUCTION

Hypertrophic cardiomyopathy (HCM) is a relatively common genetic clinical syndrome characterized by left ventricular (LV) hypertrophy in the absence of other cardiac, systemic, or metabolic disease (1). Its origin mainly lies in gene mutations of the sarcomere, and it is inherited in an autosomal dominant manner in most cases. (2) It presents a broad clinical spectrum, ranging from asymptomatic patients to those with advanced heart failure or sudden death. (3)

However, prognostic stratification in HCM remains challenging, given the heterogeneity in disease progression and the limited ability of conventional parameters to predict functional decline (3-5). Peak oxygen consumption (peak VO_2), obtained through cardiopulmonary exercise testing, is a robust marker of functional capacity and an independent predictor of morbidity and mortality in various heart diseases, including HCM (6). Thus, peak VO_2 was proposed as the primary endpoint in the main studies on this condition. (7-9) However, the clinical and imaging variables that determine lower peak VO_2 in this population are not clearly defined.

Cardiac magnetic resonance imaging (CMR) has become the gold standard for LV morphological and functional assessment, also allowing accurate quantification of fibrosis using late gadolinium enhancement (LGE) (1,2). Recently, the incorporation of global longitudinal strain analysis by cardiac magnetic resonance imaging (GLS-CMR) through feature tracking detects earlier stages of ventricular involvement, which are not evident with conventional techniques such as volumetric left ventricular ejection fraction (LVEF) measurement (10, 11). It should be noted that GLS was used in this study because it is the most reproducible parameter and the most widely used in clinical practice, with less variability than radial or circumferential strain (12, 13).

However, the prognostic value of this parameter in relation to functional capacity in HCM still requires further evidence. (14-17)

OBJECTIVES

We evaluated the association between GLS-CMR and other clinical, echocardiographic, and CMR variables with peak VO_2 measured in the cardiopulmonary exercise test in a contemporary cohort of patients with confirmed diagnosis of HCM, with the aim of identifying independent predictors of functional limitation that would optimize prognostic stratification in this group of patients.

METHODS

A retrospective, observational, single-center cohort study was conducted including patients belonging to an institutional HCM registry between January 2017 and March 2025. All patients gave informed consent prior to inclusion in the study. The data for the present analysis were obtained from a review of the institutional electronic medical records.

Hypertrophic cardiomyopathy was defined as the presence of increased thickness in any LV segment >15 mm, or >13 mm in first-degree relatives diagnosed with this disease, in the absence of any other justifiable cause. (1) Whenever possible, genetic studies were performed to confirm the sarcomeric etiology. Patients over 18 years of age with a confirmed diagnosis of sarcomeric HCM were included in the study, and phenocopies or other causes of ventricular hypertrophy were excluded.

For this study, only those patients who had echocardiogram, CMR, and cardiopulmonary exercise testing performed within an interval ≤ 12 months from each other were selected.

The following variables were collected: demographic (age, sex, height), clinical (NYHA functional class, treatment received), echocardiographic (LVEF, maximum intraventricular gradient, presence of obstructive HCM defined by a gradient ≥30 mmHg at rest and/or systolic anterior movement of the anterior mitral valve), and CMR-derived parameters (indexed ventricular volumes and mass, LVEF, and right ventricular ejection fraction, maximum wall thickness, presence and quantification of LGE, and LV GLS-CMR).

Cardiac magnetic resonance imaging was performed using a 1.5 T scanner (Avanto, Siemens Medical Solutions®, Erlangen, Germany) and LGE quantification (using a 5-threshold technique) and GLS-CMR were acquired using Circle Cardiovascular Imaging software (Tissue Tracking, cvi42, Figure 1). Peak VO_2 was obtained by cardiopulmonary testing on a cycle ergometer using an incremental protocol, expressed in mL/kg/min.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation (SD) or as median and interquartile range (IQR),

depending on their distribution as assessed by the Shapiro-Wilk test, and were compared using Student's t-test or the Mann-Whitney test, depending on data distribution. Categorical variables were presented as absolute frequencies and percentages and were compared using the Chi² test or Fisher's exact test, as appropriate.

Linear regression models were applied to explore the associations between clinical, echocardiographic, and CMR variables with peak VO_2. In the univariate analysis, each predictor was evaluated individually to identify significant correlations with peak VO_2. Subsequently, those variables with statistical significance ($p < 0.05$) or clinical relevance were incorporated into a multivariate linear regression model to identify independent predictors of lower peak VO_2. All statistical analyses were performed using STATA software version 13.1 (StataCorp LP, College Station, TX, USA), and p values <0.05 were considered as statistically significant.

Ethical considerations

The study protocol follows the ethical guidelines of the Declaration of Helsinki, (18) and the design of the institutional hypertrophic cardiomyopathy registry from which the data were obtained was approved by the institutional ethics committee.

RESULTS

A total of 54 patients diagnosed with sarcomeric HCM were included in the study. Mean age was 53±18 years, and 59.2% (n=32) were men. The obstructive form of the disease was recorded in 26 patients (48.1%). Mean peak VO_2 in the population was 23.5±9.6 mL/kg/min.

Cardiac magnetic resonance parameters

Mean LVEF was 72±10% and mean maximum wall thickness 17±4 mm. Late gadolinium enhancement was present in 94.4% (n=51) of patients, with a median mass of 15 grams and a 95% confidence interval (CI) of 6.84-33.59 (no discrimination was made according to LGE percentage). Mean LV GLS-CMR was -13±3.3%. Figure 1 shows an example of GLS-CMR measurement in one cohort patient. The remaining clinical, echocardiographic, CMR, and cardiopulmonary exercise test variables are detailed in Table 1.

Univariate analysis

In the univariate linear regression model, significant associations were observed between peak VO_2 and age at diagnosis (β = -0.35; 95% CI: -0.46 to -0.24; $p < 0.001$), male sex (β= +8.26; 95% CI +3.37 to +13.14; $p = 0.001$), indexed right ventricular end-diastolic volume (β= +0.31; 95% CI +0.15 to +0.46; $p < 0.001$), and LV GLS-CMR (β= -0.85; 95% CI -1.62 to -0.08; $p = 0.034$). No significant associations were found with NYHA functional class, the presence of dynamic intraventricular obstruction, maximum intraventricular gradient, LVEF, LV volumes, LV mass, maximum wall thickness, or LGE. Table 2 details the variables

Fig. 1. Example of left ventricular global longitudinal strain analysis using Circle Cardiovascular Imaging (Tissue Tracking, cvi42).

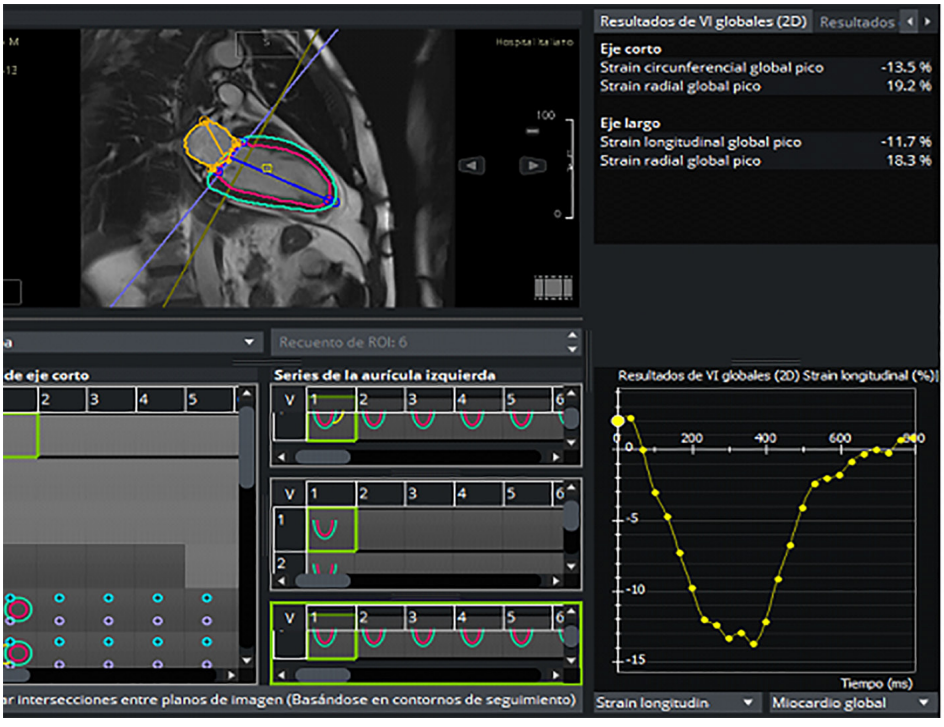

Table 1. General characteristics of the population

Clinical variables	
Age at diagnosis, years, mean ± SD	53 ±18
Male sex, n (%)	32 (59.3)
Height, centimeters, mean ± SD	161 ±33
NYHA functional class* ≥ 2, n (%)	16 (29.6)
BMI*, kg/m², mean ± SD	28.4 ± 5.1
Hypertension, n (%)	21 (38.9)
Diabetes mellitus, n (%)	6 (11.1)
Atrial fibrillation, n (%)	7 (13.0)
Dyspnea, n (%)	31 (57.4)
Angina, n (%)	12 (22.2)
Atrial fibrillation, n (%)	7 (13.0)
Beta-blockers, n (%)	38 (70.4)
Calcium channel blockers, n (%)	7 (13.0)
Myosin inhibitors, n (%)	3 (5.6)
ICD*, n (%)	6 (11.1)
Septal myectomy, n (%)	3 (5.6)
Septal alcoholization, n (%)	2 (3.7)
Ecocardiographic variables	
Wall thickness, mm, mean ± SD	17.4 ± 3.9
Left atrial anteroposterior diameter, mm, median (IQR)	42 [38-46]
Intraventricular gradient, mmHg, median (IQR)	30 [6-58]
SAM, n (%)	25 (46.3)
LVOTO, n (%)	32 (59.3)
Cardiac resonance variables	
LVEF, %, mean ± SD	72 ±10
Indexed LV end-diastolic volume, mL/m², mean ± SD	72 ±18
Indexed LV end-systolic volume, mL/m², median (IQR)	69 [60-78]
Maximum thickness, mm, mean ± SD	17 ±4
Presence of LGE, n (%)	51 (94.4)
LGE mass, grams, median (IQR)	15 [6.84-33.59]
Left ventricular GLS, %, mean ± SD	-13 ± 3.3
Right ventricular ejection fraction, %, mean ± SD	66 ±7
RV end-diastolic volume, mL, mean ± SD	71 ±15
RV end-systolic volume, mL, mean ± SD	27 ±24
LV mass, grams	86 ±24
Oxygen consumption variables	
Peak VO_2 (mL/kg/min), mean ± SD	23.5 ± 9.6
VO_2 (% of predicted), mean ± SD	83.3 ± 19.5
Heart rate at peak VO_2 (bpm), mean ± SD	133.7 ± 30.7
OUES, [(mL/min)/log10], mean ± SD	2156.8 ± 954.7

BMI: body mass index; ICD: implantable cardioverter defibrillator; IQR: interquartile range; LGE: late gadolinium enhancement; LV: left ventricular; LVEF: left ventricular ejection fraction; LVOTO: left ventricular outflow tract obstruction; NYHA: New York Heart Association; OUES: oxygen uptake efficiency slope; RV: right ventricular; SAM: systolic anterior mitral valve movement; SD: standard deviation.

included in the univariate analysis and their relationship with peak VO_2.

Multivariate analysis

In the multivariate linear regression model (Table 3), the independent predictors of lower peak VO_2 were: female sex (β = -6.1; 95% CI -10.56 to -1.75; p = 0.007), older age at diagnosis (β= -0.26; 95% CI: -0.37 to -0.15; p <0.001), and lower LV GLS-CMR (β= -0.59, 95% CI: -1.14 to - 0.04; p = 0.033).

DISCUSSION

In this contemporary cohort of patients with HCM, we observed that a lower LV-GLS-CMR value was independently associated with lower functional capacity, as measured by peak VO_2 in the cardiopulmonary exercise test. This finding could provide a relevant pathophysiological perspective, based on the hypothesis that functional limitation in HCM would depend not only on the degree of hypertrophy or the presence of dynamic obstruction, but also on both clinical and subclinical myocardial contractile failure, detectable by GLS-CMR, even in patients with preserved LVEF. Global longitudinal strain, by reflecting the longitudinal deformation capacity of the myocardium, is a sensitive marker of contractile efficiency and allows the detection of early mechanical dysfunction before global LVEF alterations or advanced symptoms become apparent (19, 20). It is noteworthy that all patients in our cohort had preserved LVEF.

Abnormal GLS probably represents the functional expression of the distinctive molecular mechanisms of HCM, characterized by a progressive loss of contractile efficiency, which translates into reduced myocardial shortening and, consequently, a limited ability to increase cardiac output during exercise. In other words,

Table 2. Univariate linear regression model

Variable	Univariate linear regression β coefficient (95% CI)	p value
Age at diagnosis	-0.35 (-0.46 to -0.24)	<0.001
Male	+8.26 (+3.37 to +13.14)	0.001
NYHA dyspnea	-2.59 (–5.35 to +0.17)	0.065
Maximum intraventricular gradient (mmHg)	-0.06 (–0.15 to +0.02)	0.110
Obstructive HCM	-1.14 (–6.44 to +4.17)	0.669
LVEF %	+0.11 (–0.16 to +0.38)	0.425
Indexed left ventricular end-diastolic volume, (mL/m²)	+0.08 (–0.06 to +0.23)	0.265
Indexed LV end-systolic volume, (mL/m²)	–0.05 (–0.15 to +0.05)	0.320
Left ventricular mass (g/m²)	–0.0007 (–0.11 to +0.11)	0.921
Maximum wall thickness (mm)	+0.09 (–0.60 to +0.79)	0.781
Quantitative LGE (%)	–0.004 (–0.10 to +0.09)	0.934
LGE (present)	+2.35 (-18 to 23.2)	0.821
RVEF (%)	+0.25 (–0.10 to +0.60)	0.162
Indexed RV end-diastolic volume (mL/m²)	+0.31 (+0.15 to +0.46)	<0.001
Indexed RV end-systolic volume (mL/m²)	–0.018 (–0.13 to +0.09)	0.743
CMR strain (%)	-0.85 (-1.6 to -0.08)	0.034

CMR: cardiac magnetic resonance; HCM: hypertrophic cardiomyopathy; LGE: late gadolinium enhancement; LV: left ventricular; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; RV: right ventricular; RVEF: right ventricular ejection fraction.

Table 3. Multivariate linear regression model

Variable	Multivariate linear regression β coefficient (95% CI)	p value
Age at diagnosis (years)	-0.26 (–0.37 to –0.15)	<0.001
Female sex	-6.10 (–10.56 to –1.75)	0.007
LV global longitudinal strain	-0.59 (–1.14 to –0.04)	0.033

LV: left ventricular

reduced GLS implies a lower contractile reserve and, therefore, a limitation in sustaining cardiac output, which translates into decreased peak VO_2. (14,19) This phenomenon could explain the association between greater GLS-CMR alteration and lower peak VO_2 observed in our study, in accordance with the findings of the STRAIN-HCM study, where GLS behaved as an independent predictor of adverse events. (14, 21)

On the other hand, we found no correlation between peak VO_2 and the amount of myocardial fibrosis measured by LGE, a finding that reinforces the idea that GLS identifies an earlier functional stage of myocardial damage. (22, 23) It should be noted that in our cohort, almost all patients had some degree of LGE, suggesting that the differential prognostic value of GLS does not depend exclusively on the presence or absence of fibrosis, but on the degree of underlying mechanical dysfunction.

The lower functional capacity observed in women in this study is consistent with reports from other series, where female sex is associated with more symptomatic phenotypes, smaller ventricular cavities, and greater predisposition to dynamic obstruction. (24) These anatomical features, combined with a frequently later diagnosis, could partly explain the functional gap observed. Similarly, older age was a negative determinant of peak VO_2, probably reflecting the cumulative impact of diffuse fibrosis, myocardial stiffness, and associated comorbidities. (25, 26)

From a clinical perspective, incorporating GLS-CMR into the evaluation of HCM may provide additional prognostic value and allow for a more accurate characterization of the functional phenotype. In patients with preserved LVEF, a significant reduction in GLS could anticipate clinical deterioration and guide early interventions. This integrated approach is in line with the current trend in the AHA/ACC international guidelines, (1) which promote personalized pathophysiological stratification, prevailing over a purely morphological approach.

In the future, it will likely be necessary to develop prognostic models that integrate clinical, imaging, and functional variables to refine risk prediction in this population.

Although this study has limitations inherent to its retrospective design and the single-center nature of the sample, the availability of high-quality complementary studies—echocardiogram, CMR, and cardiopulmonary testing— strengthens the robustness of the results. Furthermore, our population represents a clinical profile characteristic of HCM, with the presence of obstructive forms, which reinforces the representativeness of the sample and the applicability of the findings. Taken together, our data consolidate the notion that HCM is essentially a disease of myocardial mechanics rather than hypertrophy per se, and position GLS-CMR as a potentially important marker for understanding, quantifying, and monitoring contractile efficiency in clinical practice.

CONCLUSIONS

In this contemporary cohort of patients with HCM, female sex, older age, and reduced GLS-CMR were independently associated with lower peak VO_2.

These results highlight the usefulness of GLS-CMR as a complementary tool for prognostic stratification and functional assessment, beyond conventional parameters such as LVEF or LGE. Its systematic implementation could optimize the early identification of patients at higher risk of functional deterioration.

Limitations

The limitations of this study include its retrospective nature and the lack of stratification of peak VO_2 according to patient sex. It is also important to note that no comparison was made between strain measured by cardiac magnetic resonance imaging and strain assessed by echocardiography.

Conflicts of interest

None declared.

(See authors' conflict of interests forms on the web).

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