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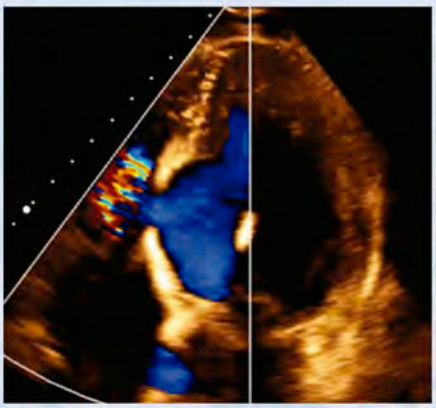

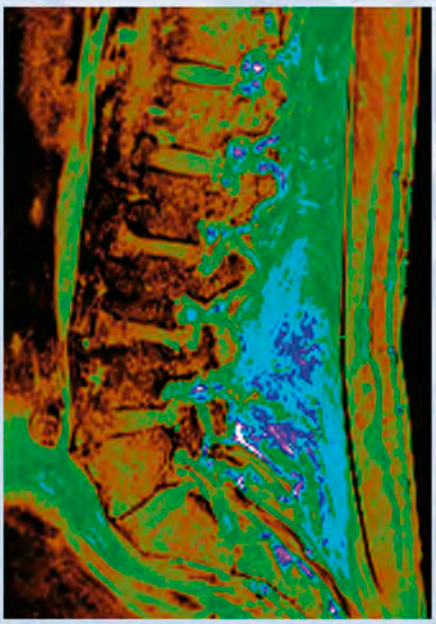

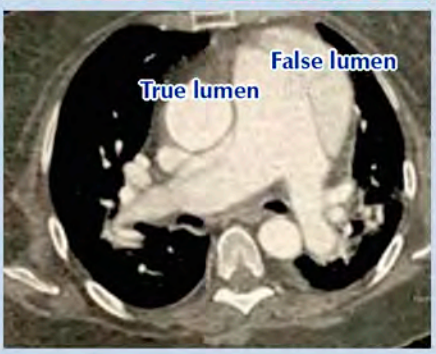

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Original research

Right ventricle dysfunction measured by echocardiogram and lactate levels in pulmonary embolism

Disfunción del ventrículo derecho medida por ecocardiograma y niveles de lactato en la embolia pulmonar

Josué Caleb Sarabia Salinas,* Enrique Alexander Berríos Bárcenas,*,‡ Dante Palacios Gutiérrez,‡ Karol Gema Hernández Gutiérrez,* Christian Alejandro Valdez Junco,* Laura María Bueno Repper,* Eduardo Viveros Rentería,* César Ricardo Kiamco Castillo,* José Benito Álvarez Mosquera*

* Cardiology, Hospital Español. Mexico.
‡ Outpatient Care Department, Instituto Nacional de Cardiología Ignacio Chávez. Mexico.

Correspondence:
César Ricardo Kiamco Castillo, MD
E-mail: rkiamco@gmail.com

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ABSTRACT. Introduction: In patients with pulmonary embolism, multiple risk stratification tools have developed in order to decrease short-term complications and mortality. Nonetheless, current instruments can underestimate the actual risk as prognosis largely depends on hemodynamic instability, which does not exclude the presence of right ventricular dysfunction, an independent predictor of mortality. **Objective:** This study aimed to determine the association between hyperlactatemia and right ventricular dysfunction by echocardiography in patients with pulmonary embolism. **Material and methods:** A single-center retrospective cohort study was conducted, including all patients older than 18 admitted to the coronary unit with objective pulmonary embolism diagnosis by imaging at the Emergency Department. All medical records from August 1st, 2013, to January 31th, 2020 were individually reviewed to identify eligible patients. Patients were stratified based on serum lactate levels and classified into < 2.0 and > 2.0 mmol/L. Baseline patient characteristics were collected, including all simplified pulmonary embolism severity index (sPESI) scale variables. The primary endpoint was right ventricular dysfunction by echocardiography. Secondary outcomes included death by any cause, mechanical ventilation, thrombolysis, and vasopressor agent use. Data collected included all Emergency Department discharge serum biomarkers values (lactate, NT-proBNP, and troponin I) and right ventricular function evaluation reports by imaging. Plasma lactate levels cut-point was used to determine the primary objective indicated by receiver operator characteristic (ROC) curve analysis. The odds ratio (OR) and 95% confidence intervals (CI) were estimated to define an association between hyperlactatemia and each sPESI scoring system variable and RV dysfunction occurrence. Significance was determined if the p-value was < 0.05. All data were analyzed with the SPSS program. **Results:** Overall, in-hospital mortality was 6.66% (n = 2). The primary outcome was observed in 70% (n = 21), while the secondary outcome was observed in 43% (n = 13). Elevated serum lactate levels (> 2 mmol/L) were associated with the presence of markers by echocardiography of right ventricular dysfunction in patients with PE (OR 8.7; 95% CI 1.3 to 54; p-value 0.02). Among its comparison with sPESI parameters, a significant association was found with hypotension (OR 13.2; 95% CI 2.1 to 82.5, p-value of 0.003) and age over 80 years (OR 4.76; 95% CI 0.9 to 23.8, p-value of 0.05). An area below the curve of 0.85 (95% CI from 0.71 to 0.99, p < 0.05) and a false-positive rate of 11% were found when considering a lactate value greater than 2.0 mmol/L as a marker of RV dysfunction. **Conclusion:** Hyperlactatemia could be used as an easy-to-perform and inexpensive marker of right ventricular dysfunction in patients with pulmonary embolism for early risk stratification, particularly when RV assessment by imaging is not available.

Keywords: Hyperlactatemia, right ventricular dysfunction, pulmonary embolism.

RESUMEN. ***Introducción:*** *En pacientes con tromboembolia pulmonar (TEP) se han desarrollado múltiples herramientas de estratificación de riesgo para disminuir las complicaciones y la mortalidad a corto plazo. Sin embargo, los instrumentos actuales pueden subestimar el riesgo real, ya que el pronóstico depende en gran medida de la inestabilidad hemodinámica, la cual no excluye la presencia de disfunción ventricular derecha, un predictor independiente de mortalidad.* ***Objetivo:*** *Determinar la asociación entre hiperlactatemia y disfunción ventricular derecha mediante ecocardiografía en pacientes con tromboembolia pulmonar.* ***Material y métodos:*** *Se realizó un estudio de cohorte retrospectivo, que incluyó a todos los pacientes mayores de 18 años ingresados en la Unidad Coronaria con diagnóstico comprobable de tromboembolia pulmonar por imagen en el Servicio de Urgencias. Todos los registros médicos desde el 1° de agosto de 2013 hasta el 31 de enero de 2020 fueron revisados individualmente para identificar a los pacientes elegibles. Los pacientes fueron clasificados en función de los niveles séricos de lactato y clasificados en < 2.0 y > 2.0 mmol/L. Se recogieron las características basales de los pacientes, incluyendo todas las variables de escala del índice de severidad de la embolia pulmonar simplificada (sPESI). El criterio de valoración primario fue la disfunción ventricular derecha por ecocardiografía. Los resultados secundarios incluyeron la muerte por cualquier causa, ventilación mecánica, trombólisis y uso de agentes vasopresores. Los datos recopilados incluyeron todos los valores de biomarcadores séricos al momento de alta de urgencias (lactato, NT-proBNP y troponina I) y reporte ecocardiográfico de la función ventricular derecha. Se utilizaron niveles plasmáticos de lactato para determinar el objetivo primario indicado por el análisis de curva ROC. Los odds ratio (OR) y los intervalos de confianza (IC) del 95% se estimaron para definir una asociación entre la hiperlactatemia y cada variable del sistema de puntuación sPESI y la ocurrencia de disfunción del VD. La significación se determinó si el valor p era < 0.05. Todos los datos se analizaron con el programa SPSS.* ***Resultados:*** *La mortalidad intrahospitalaria total fue de 6.66% (n = 2). El resultado primario se observó en 70% (n = 21), mientras que el resultado secundario se observó en 43% (n = 13). Los niveles elevados de lactato sérico (> 2 mmol/L) se asociaron a la presencia de marcadores por ecocardiografía de disfunción ventricular derecha en pacientes con TEP (OR 8.7; IC del 95%: 1.3 a 54; p = 0.02). En el análisis de hiperlactatemia con los parámetros de sPESI, se encontró una asociación significativa con la hipotensión (OR 13.2; IC del 95%: 2.1 a 82.5; p de 0.003) y la edad mayor de 80 años (OR 4.76; IC del 95%: 0.9 a 23.8; p de 0.05). Se encontró un área por debajo de la curva de 0.85 (IC del 95% de 0.71 a 0.99, p < 0.05) y una tasa de falsos positivos de 11% al considerar un valor de lactato superior a 2.0 mmol/L como marcador de disfunción del ventrículo derecho (VD).* ***Conclusión:*** *La hiperlactatemia podría ser utilizada como un marcador fácil de realizar y económico de la disfunción ventricular derecha en pacientes con embolia pulmonar para estratificación temprana de riesgo, particularmente cuando no se dispone de evaluación del VD por imágenes.*

Palabras clave: *Hiperlactatemia, disfunción ventricular derecha, embolia pulmonar.*

INTRODUCTION

Pulmonary embolism (PE) represents the third leading cardiovascular death cause worldwide, only behind acute myocardial infarction and stroke.[1] PE is associated with a significant mortality rate, primarily if adequate treatment is not initiated, affecting up to 30% as opposed to the 8% observed when properly managed.[2] Still, death is not unusual, with over 70% of deaths occurring within the first hour of disease onset due to hemodynamic instability,[3] reflecting the severe yet life-threatening character of the disease. Its prompt recognition and risk stratification allow decision-making and tailoring adequate management tools in order to decrease the burden of the disease.

In this regard, multiple risk stratification instruments, such as the pulmonary embolism severity index (PESI)[4] score and simplified pulmonary embolism severity index (sPESI),[5] have been developed to predict short-term mortality in PE. Still, these tools can underestimate the actual risk as prognosis largely depends on hemodynamic instability and right ventricular (RV) dysfunction, related to up to 24.5% 30-day mortality risk.[4] Furthermore, instability absence does not exclude the presence of RV dysfunction, an independent predictor of mortality.[6]

Plasma lactate concentration, a marker of severity and prognosis in sepsis, may provide valuable information for risk stratification of PE patients, reflecting tissue oxygen supply-to-demand mismatch secondary to right heart hypoperfusion and subsequent impairment.[3,7]

Therefore, a more significant risk assessment and stratification tool based on clinical and imaging evidence of hemodynamic instability and right ventricular dysfunction are required to decrease morbidity and mortality. Thus, the objective of this study was to determine the association between hyperlactatemia and right ventricular dysfunction by echocardiography and to explore its potential usefulness as a clinical tool in patients with PE.

MATERIAL AND METHODS

Study design and population. A single-center retrospective cohort study was conducted, including all patients older than 18 admitted to the coronary unit with PE diagnosis at Emergency Department discharge demonstrated by tomography or with high probability reported by ventilation/perfusion scintigraphy identified between August 1st, 2013, and January 31th, 2020. Patients with arterial blood gas at the emergency evaluation prior to treatment initiation and transthoracic echocardiography performed during hospital stay were included. Those with a history of previous PE or chronic venous thromboembolism (VTE) were excluded. All medical records from this period were individually reviewed to identify eligible patients.

Data collection and outcomes. The primary endpoint was right ventricular dysfunction by echocardiography. Secondary outcomes included death by any cause, mechanical ventilation, thrombolysis, and vasopressor agent use. Based on previous studies,[7] patients were stratified based on serum lactate levels and classified into < 2.0 and > 2.0 mmol/L. Baseline patient characteristics were collected, including all sPESI scale variables (age > 80 years, cancer, chronic cardiopulmonary disease, heart rate > 110 bpm, systolic pressure < 100 mmHg, and arterial oxygen saturation < 90%) and the presence or absence of right ventricular dysfunction.

Right ventricular dysfunction by transthoracic echocardiography was determined based on 2019 European Society of Cardiology guidelines demonstrated by the presence of any of the following: 1) RV dilation in the parasternal axis; 2) RV basal dilation with an RV/LV ratio > 1.0 in the 4-chamber view and McConnell's sign; 3) septal flattening in the parasternal short-axis; 4) dilatation of the inferior vena cava with decreased inspiratory collapse; 5) 60/60 sign (coexistence of a pulmonary systolic acceleration time > 60 ms and a midsystolic notch with a systolic peak gradient < 60 mmHg in the tricuspid valve); 6) presence of mobile thrombus in the right cavities, 7) tricuspid annular plane systolic excursion (TAPSE) < 16 mm; 8) decreased peak systolic velocity of tricuspid annulus < 9.5 cm/min.[6] All echocardiograms were performed by certified echocardiographers and following local protocols.

Statistical analysis. Data collected included all Emergency Department discharge serum biomarkers values (lactate, NT-proBNP, and troponin I) and RV function evaluation reports by imaging. Plasma lactate levels were used to determine the receiver operator characteristic (ROC) curve analysis, using the area under the curve, sensitivity, and specificity based on objective documentation of RV dysfunction.

Frequencies and percentages were used for categorical variables. According to their distribution, numerical variables are presented as mean and standard deviation or median and quartile 1 and 3. The odds ratio (OR) and 95% confidence intervals (CI) were estimated to define an association between hyperlactatemia and each sPESI scoring system variable and RV dysfunction occurrence. Significance was determined if the p-value was < 0.05. All data were analyzed with the SPSS program.

RESULTS

One hundred and fifty four medical records with PE diagnosis were reviewed, 82 of which were admitted to the Coronary Unit. After eliminating those with inconclusive criteria, 30 patients were included in the final registry. The median age was 67 ± 17 years. Approximately half of the patients presented with hemodynamic instability at admission, defined as systolic blood pressure < 100 mg.

Thrombolytic therapy was administered in 13% (n = 4) of the subjects. Overall, in-hospital mortality was 6.66% (n = 2). The primary outcome (right ventricular systolic dysfunction by echocardiography) was observed in 70%

(n = 21), while the secondary outcome (death by any cause, mechanical ventilation, thrombolysis, and vasopressor agent use) was observed in 43% (n = 13). Patient characteristics at coronary unit admission are compiled in *Table 1*.

Elevated serum lactate levels (> 2 mmol/L) were associated with the presence of at least one of the markers by echocardiography of right ventricular dysfunction in patients with acute pulmonary thromboembolism (OR 8.7; 95% CI 1.3 to 54; p-value 0.02).

The analysis between lactate values > 2.0 mmol/L and each sPESI scoring system variable and RV dysfunction occurrence are shown in *Table 2*. Among these parameters, a significant association was found between lactate values > 2.0 mmol/L and systolic blood pressure < 100 mmHg (OR 13.2; 95% CI 2.1 to 82.5) and age over 80 years (OR 4.76; 95% CI 0.9 to 23.8) with a p-value of 0.003 and 0.05 respectively.

A sensitivity and specificity analysis was performed using the ROC curve to evaluate hyperlactatemia > 2.0 mmol/L as a cutoff point for diagnosing RV systolic dysfunction, finding an area below the curve of 0.85 (95% CI from 0.71 to 0.99, p < 0.05). A false-positive rate of 11% was found when considering a lactate value greater than 2.0 mmol/L as a marker of RV dysfunction *(Figure 1)*.

DISCUSSION

This study showed an association between elevated serum lactate levels and echocardiographic documentation of RV dysfunction in patients with acute PE. These results are not dissimilar to those previously observed by Vanni et al., where the presence of RV dysfunction was more frequent in lactate levels greater than two mmol/L.[7] However, to our knowledge, this is the first study to observe a statistical association between lactate levels and RV dysfunction.

RV dysfunction is an independent predictor of mortality found in ≥ 25% of unselected patients with acute PE.[6] Likewise, it has been correlated with an elevated risk of short-term mortality in hemodynamically stable patients.[8] However, these findings are not limited to intermediate and high-risk patients. A metanalysis found that RV dysfunction on admission was associated with early mortality in low-risk patients.[9] Thus its sole presence sustains PE risk stratification. In the context of our findings, it seems reasonable to investigate RV dysfunction in those patients with elevated lactate concentrations, regardless of other clinical criteria and hemodynamic stability, to adequately stratify their risk in order to tailor the most appropriate management.

Although our study did not find an association between lactate levels and in-hospital short-term complications and mortality, hyperlactatemia has been associated with PE short-term complications as well, even in initially normotensive patients.[10] Galic et al. demonstrated that the lactate value could be used as an independent prognostic indicator of shock and right heart failure in patients diagnosed with intermediate to high-risk PE.[11]

Table 1: Patient baseline characteristics (N = 30).

Characteristics	n (%)
Male	11 (36)
Age (years)	67 ± 17
Hypertension	14 (46)
Diabetes mellitus	11 (36)
Coronary artery disease	2 (6)
sPESI	2.76 ± 1.13
Age > 80 years old	13 (43)
History of cancer	5 (16)
History of chronic cardiopulmonary disease	20 (66)
Heart rate > 100 bpm	20 (66)
Systolic blood pressure < 100 mmHg	14 (46)
Oxygen saturation < 90%	24 (80)
Vasopressor use	10 (33)
IMV	4 (13)
RVD	21 (70)
BNP (pg/mL)	18 (60)
TnI (ng/mL)	19 (63)

sPESI = simplified pulmonary embolism severity index; IMV = intermittent mandatory ventilation; RVD = right ventricular dysfunction; BNP = B-type natriuretic peptide; TnI = troponin I.

Table 2: Association between hyperlactatemia and clinical, biochemical and outcome variables in patients with acute pulmonary thromboembolism.

Variable	Lactate, n (%) < 2.0 mmol/L (N = 13)	Lactate, n (%) > 2.0 mmol/L (N = 17)	p	OR (CI 95%)
sPESI parameters				
Male	4 (30)	7 (41)	0.70	1.57 (0.3-7.2)
Age > 80 years	3 (23)	10 (58)	0.05	4.76 (0.9-23.8)
History of cancer	2 (15)	3 (17)	1.00	1.17 (0.1-8.3)
History of chronic cardiopulmonary disease	8 (61)	12 (70)	0.70	1.5 (0.3-6.9)
Heart rate > 100 bpm	9 (69)	11 (64)	1.00	0.81 (0.1-3.8)
Systolic blood pressure < 100 mmHg	2 (15)	12 (70)	0.003	13.2 (2.1-82.5)
Oxygen saturation < 90%	10 (76)	14 (82)	1.00	1.4 (0.2-8.4)
Other variables				
Hypertension	4 (30)	10 (58)	0.12	3.2 (0.7-14)
Diabetes mellitus	4 (30)	7 (41)	0.70	1.5 (0.3-7.2)
Coronary artery disease	1 (7)	1 (5)	1.00	0.7 (0-13)
Outcomes				
Vasopressor use	3 (23)	7 (41)	0.44	2.3 (0.4-11.6)
IMV	2 (15)	2 (11)	1.00	0.7 (0-6)
Thrombolysis	1 (7)	3 (17)	0.61	2.5 (0.2-28)
Death	0	2 (11)	0.49	–
RVD	6 (46)	15 (88)	0.02	8.7 (1.3-54)
BNP	6 (46)	12 (70)	0.17	2.8 (0.6-12.6)
TnI	9 (69)	10 (58)	0.70	0.6 (0.1-2.9)
Secondary outcome	11 (84)	16 (94)	0.56	2.9 (0.2-36)

sPESI = simplified pulmonary embolism severity index; IMV = intermittent mandatory ventilation; RVD = right ventricular dysfunction; BNP = B-type natriuretic peptide; TnI = troponin I; OR = odds ratio.

According to recent European Society of Cardiology guidelines, risk stratification tools such as PESI or sPESI score scale along with RV dysfunction imaging evaluation should be performed to identify patients with an intermediate-high risk of PE-related short-term complications or death.[6] Hemodynamic instability features such as low systolic blood, tachycardia, and respiratory insufficiency have also been associated with poor prognosis.[4-6] Our analysis seems to support this premise, as hypotension and age older than 80 were also associated with high lactate levels. Nonetheless, these parameters could underestimate the actual risk, as previous studies have reported.[8] Hence, the presence of hyperlactatemia could support PE risk stratification. Accordingly, previous studies observed an association between elevated lactate levels and 28-day mortality in ICU patients admitted for PE, independent of systolic blood pressure.[12]

Elevated serum lactate levels have been described as a prognostic survival factor in patients with PE, independent of acid-base status and RV dilation or positive biomarkers.[7,11,12]

In this study, we evaluated hypoperfusion manifested as hyperlactatemia and found this parameter could be a helpful, easy-to-perform, and inexpensive marker to identify high-risk patients in acute PE. Accordingly,

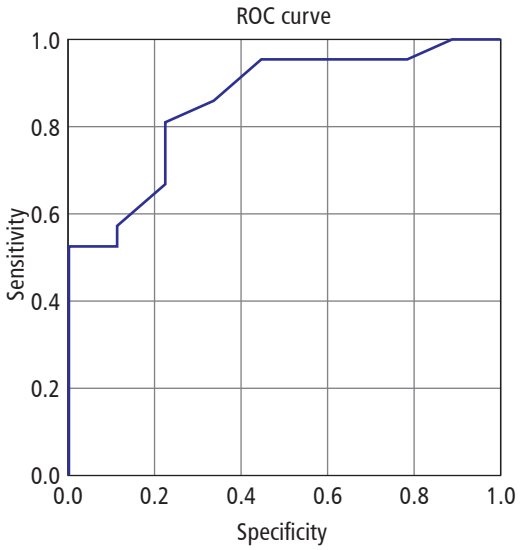

Figure 1: ROC curve analysis for hyperlactatemia and right ventricular dysfunction by echocardiography showing an AUC of 0.85%.

lactate association with RV dysfunction may be explained by the subsequent oxygen supply-demand imbalance secondary to thrombotic obstruction-related hypoxemia.[7] Lactate concentration might increase in acute PE before overt hemodynamic impairment as in other clinical settings like sepsis or trauma.[10] Hence, serum lactate could be used as a marker of hemodynamic severity in PE, particularly in the absence of RV assessment by imaging.

These results reflect the potential lactate application in PE early risk stratification to identify patients at high risk of complications and death who may benefit from more aggressive monitoring and management instruments. Nonetheless, to confirm our findings, a properly designed prospective study must be conducted to complement the results with a new registry with a larger number of patients.

We recognize several limitations in our study, in particular, its retrospective nature, as well as the small sample evaluated. In this regard, due to its convenience sample, no statistical significance sample size was reached. Although this study demonstrated association, no conclusions can be made based on its results as it is a hypothesis generator.

In summary, an association between elevated serum lactate levels and the objective documentation of RV dysfunction in patients with acute pulmonary thromboembolism was observed. Hyperlactatemia could be used as an easy-to-perform and inexpensive marker of RV dysfunction in patients with PE for early risk stratification, particularly when RV assessment by imaging is not available.

REFERENCES

1. Giri J, Sista AK, Weinberg I, et al. Interventional therapies for acute pulmonary embolism: Current status and principles for the development of novel evidence: A scientific statement from the American heart association. Circulation. 2019; 140 (20): e774-e801.
2. Belohlávek J, Dytrych V, Linhart A. Pulmonary embolism, part I: epidemiology, risk factors and risk stratification, pathophysiology, clinical presentation, diagnosis and nonthrombotic pulmonary embolism. Exp Clin Cardiol. 2013; 18 (2): 129-138.
3. Martinez Licha CR, McCurdy CM, Maldonado SM, et al. Current management of acute pulmonary embolism. Ann Thorac Cardiovasc Surg. 2020; 26 (2): 65-71.
4. Dentali F, Riva N, Turato S, et al. Pulmonary embolism severity index accurately predicts long-term mortality rate in patients hospitalized for acute pulmonary embolism. J Thromb Haemost. 2013; 11 (12): 2103-2110.
5. Jiménez D, Aujesky D, Moores L, et al. Simplification of the pulmonary embolism severity index for prognostication in patients with acute symptomatic pulmonary embolism. Arch Intern Med. 2010; 170 (15): 1383-1389.
6. Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Eur Heart J. 2020; 41 (4): 543-603.
7. Vanni S, Viviani G, Baioni M, et al. Prognostic value of plasma lactate levels among patients with acute pulmonary embolism: the thrombo-embolism lactate outcome study. Ann Emerg Med. 2013; 61 (3): 330-338.
8. Chen YL, Wright C, Pietropaoli AP, et al. Right ventricular dysfunction is superior and sufficient for risk stratification by a pulmonary embolism response team. J Thromb Thrombolysis. 2020; 49 (1): 34-41.
9. Barco S, Mahmoudpour SH, Planquette B, et al. Prognostic value of right ventricular dysfunction or elevated cardiac biomarkers in patients with low-risk pulmonary embolism: a systematic review and meta-analysis. Eur Heart J. 2019; 40 (11): 902-910.
10. Vanni S, Jiménez D, Nazerian P, et al. Short-term clinical outcome of normotensive patients with acute PE and high plasma lactate. Thorax. 2015; 70 (4): 333-338.

11. Galic K, Pravdic D, Prskalo Z, et al. Prognostic value of lactates in relation to gas analysis and acid-base status in patients with pulmonary embolism. Croat Med J. 2018; 59 (4): 149-155.

12. Urbina T, Bigé N, Nguyen Y, et al. Tissue perfusion alterations correlate with mortality in patients admitted to the intensive care unit for acute pulmonary embolism: an observational study. Medicine (Baltimore). 2018; 97 (42): e11993.

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Original research

Prognostic value of stress cardiac magnetic resonance. A third level hospital experience

Valor pronóstico de la resonancia magnética cardiaca de estrés. Una experiencia en hospital de tercer nivel

Juan Manuel Rebull-Isusi,* Jaime Galindo-Uribe,‡ Jorge Oseguera Moguel,‡ Sandra Rosales Uvera,‡ Alfonso Rafael Aldaco-Rodríguez,§ Dante Palacios Gutiérrez,§ Enrique Alexander Berríos-Bárcenas§

* Hospital Español. Mexico.
‡ Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán. Mexico.
§ Instituto Nacional de Cardiología Ignacio Chávez. Mexico.

Correspondence:
Enrique Alexander Berríos Bárcenas, MD, PhD
E-mail: berrios.md@gmail.com

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ABSTRACT. Introduction: Evaluating myocardial perfusion in patients with suspected coronary artery disease (CAD) is a widely accepted and recommended practice. In recent years, cardiac magnetic resonance imaging (CMR) with pharmacological stress has proven to be a better diagnostic performance than traditional tools (Echo and SPECT). However, there is limited evidence on the prognostic value of a positive CMR stress result. The present study aimed to determine the prognostic value of CMR and pharmacological stress (dipyridamole) for adverse events. **Material and methods:** This is a historical cohort, conducted between January 2011 and December 2014, which included patients over 18 years of age at the National Institute of Medical Sciences and Nutrition Salvador Zubirán, Mexico City. All underwent stress CMR (dipyridamole) and first-step perfusion evaluation. A 24-month follow-up was performed in search of an adverse event occurrence including death, non-fatal myocardial infarction, stroke, rehospitalization for cardiovascular causes, or heart failure decompensation. **Results:** A total of 97 patients were included, of which 47 were men. Hypertension (82%), dyslipidemia (56%), active smoking (53%) and diabetes (47%) were the most prevalent cardiovascular risk factors. The median age was 66 ± 13 years. 55% of patients had previous CAD. The stress CMR was positive in 33 patients and was associated with a higher proportion of adverse events without statistical significance (54% vs 31%, p = 0.1). The primary outcome was observed in 11 patients, with LVEF < 55% as predictor (OR: 5.6, 95% CI 1.5-20; p = 0.01). **Conclusion:** A positive stress test was not associated with adverse events in CAD intermediate to high-risk population. Nonetheless, more studies are needed to clarify its prognostic value in this clinical scenery.
Keywords: Myocardial perfusion, magnetic resonance imaging, coronary artery disease, ischemia.

RESUMEN. Introducción: *La evaluación de la perfusión miocárdica en pacientes con sospecha de enfermedad arterial coronaria (EAC) es una práctica ampliamente aceptada y recomendada. En los últimos años, la resonancia magnética cardiaca (RMC) con estrés farmacológico ha demostrado tener un mejor rendimiento diagnóstico que las herramientas tradicionales (Eco y SPECT). Sin embargo, hay pocas pruebas sobre el valor pronóstico de un resultado positivo de la RMC de estrés. El presente estudio tuvo como objetivo determinar el valor pronóstico de la RMC y el estrés farmacológico (dipiridamol) para los eventos adversos.* ***Material y métodos:*** *Se trata de una cohorte histórica, realizada entre enero de 2011 y diciembre de 2014, que incluyó a pacientes mayores de 18 años en el Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Ciudad de México. A todos se les realizó RMC de estrés (dipiridamol) y evaluación de perfusión de primer paso. Se realizó un seguimiento de 24 meses en busca de un evento adverso que incluyera muerte, infarto de miocardio no mortal, accidente cerebrovascular, rehospitalización por causas cardiovasculares o descompensación de la insuficiencia cardiaca.* ***Resultados:*** *Se incluyeron 97 pacientes, de los cuales 47 eran hombres. La hipertensión (82%), la dislipidemia (56%), el tabaquismo activo (53%) y la diabetes (47%) fueron los factores de riesgo cardiovascular más prevalentes. La edad media era de 66 ± 13 años. El 55% de los pacientes tenía una EAC previa. La RMC de estrés fue positiva en 33 pacientes y se asoció a una mayor proporción de eventos adversos*

sin significación estadística (54% frente a 31%, p = 0.1). El resultado primario se observó en 11 pacientes, con una FEVI < 55% como factor predictivo (OR: 5.6; IC del 95%: 1.5-20; p = 0.01). ***Conclusión:*** *Una prueba de esfuerzo positiva no se asoció con eventos adversos en la población de riesgo intermedio a alto de EAC. No obstante, se necesitan más estudios para aclarar su valor pronóstico en este escenario clínico.*
Palabras clave: *Perfusión miocárdica, resonancia magnética, enfermedad arterial coronaria, isquemia.*

INTRODUCTION

Ischemic heart disease (IHD) is characterized by myocardial supply-demand mismatch, which is often promoted by exercise, emotional disturbances, and induced or reproducible stress. Still, they also may develop suddenly without apparent underlying cause.[1,2]

IHD risk factors include hypertension, hypercholesterolemia, diabetes, sedentary lifestyle, obesity, smoking, and a family history of IHD at an early age.[3-7] Timely risk factors detection and management may reduce its incidence.

CMR has been widely studied in recent years, demonstrating good diagnostic performance in detecting IHD, superiority to single photon emission computed tomography (SPECT), and comparable to positron emission tomography (PET).[8] In patients with intermediate cardiovascular risk, a positive stress CMR has proven to be an independent risk factor for myocardial infarction and cardiac death.[9] Moreover, recent studies showed that CMR reduces unnecessary coronary angiography (CA) and revascularization with similar events rate compared to a fractional flow reserve guided strategy.[10,11]

2013 ESC guidelines on the management of stable coronary artery disease recommended CMR use in the IHD evaluation.[2] Most studies use regadenoson and adenosine as stress agents. Nevertheless, few studies have evaluated dipyridamole use, an inexpensive and more available agent.

MATERIAL AND METHODS

Study type and population: a historical cohort study was developed at the *Instituto Nacional de Nutrición y Ciencias Médicas Salvador Zubirán* in Mexico City between January 1st, 2011, and December 30th, 2014. Patients over 18 years old with angina or an equivalent who underwent CMR imaging with dipyridamole were included. A sequential non-probability sampling was performed. Sample size was not determined, and all available studies were included. Patients with severe valvular, pericardial, or aortic disease, and those with known neoplasia or a life expectancy of less than 12 months in their follow-up were excluded.

CMR protocol: this study was performed with a 6-hour fasting, without sedation and repeated apneas. T1 sequences were obtained with subsequent 2, 3, 4 cameras and short axes cardiac planes acquisition, following dipyridamole administration (56 mg/kg in 4 minutes). At minute 7, 0.1 mmol/kg of gadolinium was injected to obtain first pass perfusion stress.

Study variables: clinical variables were defined according to the Framingham risk scale. In addition, the total number of cardiovascular risk factors was determined by the presence of hypertension, dyslipidemia, diabetes, age (women > 55 years old and men > 45 years old), current or previous smoking history, previous IHD event, or IHD familial history. Laboratory analysis taken within a week prior to the CMR study were used. Basal heart rate, left ventricular ejection fraction (LVEF), wall motion abnormalities (WMA), and perfusion alterations data were obtained from CMR report.

Statistical analysis: numerical variables were determined by Kolmogorov-Smirnov test. According to their distribution, mean and standard deviation or median and interquartile range was used. The categorical variables were expressed in frequency and percentage. Bivariate analysis was performed depending on major adverse cardiovascular events (MACE) presence. Numerical variables were analyzed with Student's t-test or Mann-Whitney U. χ^2 or Fisher's test was used for categorical variables. Survival analysis was determined using Kaplan-

Meier curves and Log Rank test. A two-tailed $p < 0.05$ was considered significant. All analyzes were performed using SPSS v21 software.

RESULTS

Ninety-seven patients were included, of which 48% were male. The mean age was 66 ± 13 years.

Hypertension was present in 82%, dyslipidemia in 56%, smoking in 53%, and diabetes in 47% of the individuals. 53 patients had previous IHD. Regarding the lipid profile, the mean cholesterol was 176 ± 40 mg/dL, with median triglycerides of 144 mg/dL. The most common pharmacological treatment used were beta-blocker, aspirin, and statin. Patient's characteristics are shown in *Table 1*.

Table 1: General characteristics (N = 97).

Characteristics	n (%)
Age	66.6 ± 13.2
Males	47 (48.5)
Smoking	52 (53.6)
Diabetes mellitus	46 (47.4)
Heart failure	17 (17.5)
Arterial hypertension	80 (82.5)
Dyslipidemia	55 (56.7)
Hypothyroidism	17 (17.5)
Autoimmunity	15 (15.5)
Chronic kidney disease	21 (21.6)
Previous CAD	53 (54.6)
Family history of CAD	38 (39.2)
Framingham score	0.25 (0.13, 0.41)
Cholesterol (mg/dL)	176 ± 40
LDLc (mg/dL)	104 ± 40
HDLc (mg/dL)	46 ± 14
Triglycerides	144 (117, 191)
Creatinine serum	1 (1, 1)
Beta blocker	53 (54.6)
Calcium channel blocker	26 (26.8)
ACEi	25 (25.8)
ARB	25 (25.8)
Aspirine	47 (48.5)
Clopidogrel	18 (18.6)
Diuretic	20 (20.6)
Statin	49 (50.5)

CAD = coronary artery disease; LDLc = low density lipoprotein cholesterol; HDLc = high density lipoprotein cholesterol; ACEi = angiotensin-converting enzyme inhibitors; ARB = angiotensin receptor antagonist.

Table 2: Cardiac magnetic resonance parameters.

Characteristics	Value
Basal HR (bpm)	73.8 ± 15.3
LVEF (%)	63.5 ± 14.1
Heart failure	3 (3, 4)
WMA at rest	36 (37.1%)
WMA at stress	33 (34%)
Induced perfusion alterations	32 (33%)
Positive study for ischemia	33 (34%)

HR = heart rate; bpm = beats per minute; LVEF = left ventricle ejection fraction; WMA = wall motion abnormalities.

Table 3: Outcomes.

Event	n (%)
Fatal arrhythmias	1 (1.0)
New ACS	5 (5.2)
Hospital readmission	10 (10.3)
Heart failure decomposition	1 (1.0)
Emergency revascularization	0
Stroke	1 (1.0)
Death	3 (3.1)
Cumulative events	11 (11.3)

ACS = accurate coronary syndrome.

Regarding stress CMR characteristics, the mean initial LVEF was 63.5 ± 14%. 33 cases were positive for ischemia, and a third (37%) had WMA. *Table 2* displays all CMR parameters.

Mortality was observed in 3% of the population. The most frequent event was hospital readmission. The rest of the outcomes are presented in *Table 3*.

No difference in sociodemographic characteristics and risk factors was observed between both groups. Patients with MACE showed lower LVEF (65% vs 53%, $p < 0.05$) and greater use of clopidogrel. A positive stress test was not associated with MACE (31% vs 54%, $p = 0.17$). Both groups comparison is shown in *Table 4*.

Table 4: Comparison of groups according to MACE.

Characteristics	No MACE N = 86 n (%)	MACE N = 11 n (%)	p
Age	66.2 ± 13	69.5 ± 14	0.43
Males	42 (49.4)	5 (45.5)	0.80
Smoking	47 (54.7)	5 (45.5)	0.56
Diabetes mellitus	42 (48.8)	4 (36.4)	0.43
Heart failure	16 (18.6)	1 (9.1)	0.68
Arterial hypertension	71 (82.6)	9 (81.8)	1.00
Dyslipidemia	46 (53.5)	9 (81.8)	0.11
Hypothyroidism	16 (18.6)	1 (9.1)	0.68
Autoimmunity	13 (15.3)	2 (18.2)	0.68
Chronic kidney disease	19 (22.1)	2 (18.2)	1.00
Previous CAD	47 (54.7)	6 (64.5)	1.00
Family history of CAD	34 (39.5)	4 (36.4)	1.00
Framingham score	0.23 (0.12, 0.4)	0.4 (0.18, 0.6)	0.19
Cholesterol (mg/dL)	165 (143, 210)	185 (150, 195)	0.76
LDLc (mg/dL)	104.9 ± 38	96.9 ± 52	0.55
HDLc (mg/dL)	46.8 ± 13	46.3 ± 23	0.92
Triglycerides	141 (117, 185)	172 (127, 236)	0.24
Creatinine serum	1 (1, 1)	1 (1, 1)	1.00
Beta blocker	47 (54.7)	6 (54.6)	1.00
Calcium channel blocker	22 (25.6)	4 (36.4)	0.47
ACEi	20 (23.3)	5 (45.5)	0.14
ARB	22 (25.6)	3 (37.3)	1.00
Aspirine	40 (46.5)	7 (63.6)	0.28
Clopidogrel	13 (15.1)	5 (45.5)	0.02
Diuretic	18 (20.9)	2 (18.2)	1.00
Statins	43 (50.0)	6 (54.6)	0.77
LVEF (%)	64.8 ± 13	53.8 ± 18	0.01
Heart failure	3 (3, 4)	3 (2, 4)	0.21
Mobility disturbances at rest	29 (33.7)	7 (63.6)	0.09
WMA at rest	28 (32.6)	5 (45.5)	0.50
Induced WMA	26 (30.2)	6 (54.5)	0.17
Positive study for ischemia	27 (31.4)	6 (54.5)	0.17

MACE = major adverse cardiovascular events; CAD = coronary artery disease; LDLc = low density lipoprotein cholesterol; HDLc = high density lipoprotein cholestero; ACEi = angiotensin-converting enzyme inhibitors; ARB = angiotensin receptor antagonist; LVEF = left ventricle ejection fraction; WMA = wall motion abnormalities.

Kaplan-Meier curve *(Figure 1)* shows a favorable prognosis in negative stress CMR patients with an event-free survival at seven years of 91%, compared to 76% in those with a positive test, without statistical significance. There was no difference in patients with and without IHD with a p value of 0.08 for both groups.

DISCUSSION

The present study is, to our knowledge, the first in evaluating the prognostic performance of CMR stress with dipyridamole in a Mexican population.

Previous studies such as Bodi et al.,[12-14] observed a mean age of 64 ± 11 years, finding a hypertension in 50%, dyslipidemia in 44%, smoking history in 15% and previous coronary artery disease in 23%. These results might differ from ours due to ethnicity differences as their cohort was of Anglo-Saxon descent. Although mean age was similar, our population had a higher prevalence of risk factors, conferring a higher risk for cardiovascular disease. Conversely, the risk factor prevalence found in the present study is not dissimilar to those described in RENASICA II,[15] one of the largest Mexican cohorts published.

Regarding the outcomes, we observed that MACE events occurred in 11.3% of the population, with a mortality of 3.1%. Similar results were found by Bodi et al.,[13] with a MACE occurrence of 9.7%. When we compared patients' characteristics, those with positive events had significantly lower LVEF (65 vs. 53%, $p < 0.05$) and greater use of clopidogrel. The reduced ejection fraction has already been demonstrated in previous studies as one of the main prognostic factors. Nonetheless, the greater use of clopidogrel in the MACE group could be due to a higher angioplasty rate.

Although our data did not show statistical significance, a higher proportion of MACE was observed in those patients without previous CAD and positive stress-CMR with dipyridamole, suggesting its prognostic value. In agreement with this finding, several studies have demonstrated CMR prognostic value not solely in patients without previous CAD in middle-aged adults but in elderly patients (> 75 years old) as well.[16-18]

Moreover, during an eight-year follow-up of 6,095 patients, Pezel T et al. perceived an annual rate of MACE in 2.4% on those with a negative CMR compared to the 14.6% observed in those with IHD or late gadolinium enhancement. Furthermore, this study demonstrated a good prognostic value in diverse subgroups, including diabetes, obese and non-obese

subjects.[18] Thus, the small sample size and rate of patients lost to follow-up of our study, rather than dipyridamole efficacy, might explain the discrepancies observed between our analysis and previous literature. Nonetheless, all studies seem to converge in the good discriminative long-term prognostic value of CMR, which discloses the urgency of prospective studies to discern its value in the assessment and risk stratification in IHD, especially in high-risk individuals who could benefit from improved preventive and therapeutic instruments.

Limitation of the study

The limitations of the study are the «n» achieved and short-term follow-up, a longer follow-up time would be required to observe results with better statistical significance.

CONCLUSIONS

A positive stress test was not associated with adverse events in CAD intermediate to high-risk population. Nonetheless, more studies are needed to clarify its prognostic value in this clinical scenery.

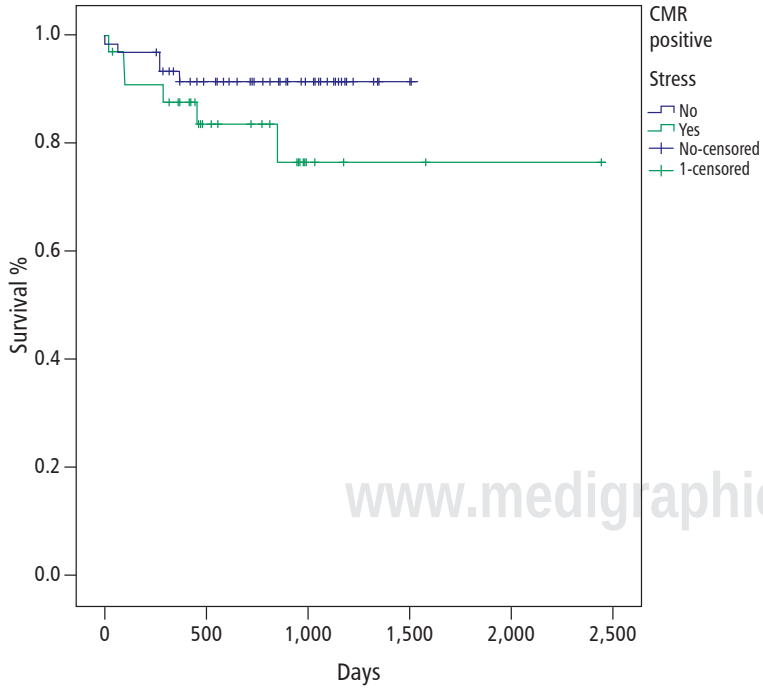

Figure 1: Kaplan-Meier event-free survival in the total population.

REFERENCES

1. Fihn SD, Blankenship JC, Alexander KP, Bittl JA, Byrne JG, Fletcher BJ, et al. 2014 ACC/AHA/AATS/PCNA/SCAI/STS focused update of the guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines, and the American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol. 2014; 64 (18): 1929-1949. doi: 10.1016/j.jacc.2014.07.017.
2. Task Force Members, Montalescot G, Sechtem U, Achenbach S, Andreotti F, Arden C, et al. 2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology. Eur Heart J. 2013; 34 (38): 2949-3003.
3. Pekkanen J, Linn S, Heiss G, Suchindran CM, Leon A, Rifkind BM, et al. Ten-year mortality from cardiovascular disease in relation to cholesterol level among men with and without preexisting cardiovascular disease. N Engl J Med. 1990; 322 (24): 1700-1707.
4. Bayturan O, Tuzcu EM, Uno K, Lavoie AJ, Hu T, Shreevatsa A, et al. Comparison of rates of progression of coronary atherosclerosis in patients with diabetes mellitus versus those with the metabolic syndrome. Am J Cardiol. 2010; 105 (12): 1735-1739.
5. Perk J, De Backer G, Gohlke H, Graham I, Reiner Z, Verschuren M, et al. European Guidelines on cardiovascular disease prevention in clinical practice (version 2012). The Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts). Eur Heart J. 2012; 33 (13): 1635-1701.
6. Frey P, Waters DD, DeMicco DA, Breazna A, Samuels L, Pipe A, et al. Impact of smoking on cardiovascular events in patients with coronary disease receiving contemporary medical therapy (from the Treating to New Targets [TNT] and the Incremental Decrease in End Points Through Aggressive Lipid Lowering [IDEAL] trials). Am J Cardiol. 2011; 107 (2): 145-150.
7. Otaki Y, Gransar H, Berman DS, Cheng VY, Dey D, Lin FY, et al. Impact of family history of coronary artery disease in young individuals (from the CONFIRM registry). Am J Cardiol. 2013; 111 (8): 1081-1086.
8. Jaarsma C, Leiner T, Bekkers SC, Crijns HJ, Wildberger JE, Nagel E, et al. Diagnostic performance of noninvasive myocardial perfusion imaging using single-photon emission computed tomography, cardiac magnetic resonance, and positron emission tomography imaging for the detection of obstructive coronary artery disease: a meta-analysis. J Am Coll Cardiol. 2012; 59 (19): 1719-1728.
9. Lipinski MJ, McVey CM, Berger JS, Kramer CM, Salerno M. Prognostic value of stress cardiac magnetic resonance imaging in patients with known or suspected coronary artery disease: a systematic

review and meta-analysis. J Am Coll Cardiol. 2013; 62 (9): 826-838.
10. Greenwood JP, Ripley DP, Berry C, McCann GP, Plein S, Bucciarelli-Ducci C, et al. Effect of care guided by cardiovascular magnetic resonance, myocardial perfusion scintigraphy, or nice guidelines on subsequent unnecessary angiography rates: the CE-MARC 2 randomized clinical trial. JAMA. 2016; 316 (10): 1051-1060.
11. Nagel E, Greenwood JP, McCann GP, Bettencourt N, Shah AM, Hussain ST, et al. Magnetic resonance perfusion or fractional flow reserve in coronary disease. N Engl J Med. 2019; 380 (25): 2418-2428.
12. Husser O, Monmeneu JV, Bonanad C, Lopez-Lereu MP, Nuñez J, Bosch MJ, et al. Prognostic value of myocardial ischemia and necrosis in depressed left ventricular function: a multicenter stress cardiac magnetic resonance registry. Rev Esp Cardiol (Engl Ed). 2014; 67 (9): 693-700.
13. Bodi V, Sanchis J, Lopez M, et al. Prognostic value of dipyridamole stress cardiovascular magnetic resonance imaging in patients with known or suspected coronary artery disease. J Am Coll Cardiol. 2007; 50 (12): 1174-1179.
14. Chattranukulchai P, Tumkosit M, Cholteesupachai J, et al. Diagnostic accuracy of combined dipirydamole stress perfusion and delayed enhancement cardiovascular magnetic resonance imaging for detection of coronary artery disease. Asian Biomedicine. 2010; 4 (1): 19-25.
15. García-Castillo A, Jerjes-Sánchez C, Martínez Bermúdez P, Azpiri-López JR, Autrey Caballero A, Martínez Sánchez C, et al. Registro mexicano de síndromes coronarios agudos: RENASICA II. Arch. Cardiol. Méx. 2005; 75 (Suppl 1): 6-19.
16. Pezel T, Hovasse T, Kinnel M, Unterseeh T, Champagne S, Toupin S, et al. Prognostic value of stress cardiovascular magnetic resonance in asymptomatic patients with known coronary artery disease. J Cardiovasc Magn Reson. 2021; 23 (1): 19.
17. Pezel T, Unterseeh T, Kinnel M, Hovasse T, Sanguineti F, Toupin S, et al. Long-term prognostic value of stress perfusion cardiovascular magnetic resonance in patients without known coronary artery disease. J Cardiovasc Magn Reson. 2021; 23 (1): 43.
18. Pezel T, Sanguineti F, Kinnel M, Hovasse T, Garot P, Unterseeh T, et al. Prognostic value of dipyridamole stress perfusion cardiovascular magnetic resonance in elderly patients >75 years with suspected coronary artery disease. Eur Heart J Cardiovasc Imaging. 2021; 22 (8): 904-911.

CARDIAC IMAGE UPDATED

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Clinical case

Pulmonary artery dissection in Chagas heart disease

Disección de la arteria pulmonar en cardiopatía chagásica

Juan Héctor Larios Lara,* Carlos Enrique Franco Cruz,‡ Verónica Gómez Leiva,‡ Gerson Jonathan Castillo Hernández§

* Chief Medical Resident. Internal Medicine Department.
‡ Cardiologist. Cardiology Service.
§ Fellow of Radiology. Department of Radiology.

Medical and Surgical Hospital, Salvadorean Social Security Institute. El Salvador.

ABSTRACT. Objective: To describe the presentation of a pulmonary artery dissection to the Emergency Unit, the sequence of events, and a literature review. **Case report:** A 59-year-old female patient with known Chagas heart disease presented at the Emergency Unit with an event of sudden, stabbing chest pain and progressive dyspnea, evolving rapidly to cardiogenic shock. A chest radiograph reported severe widening of the mediastinum and cardiomegaly; therefore, a thoracic angiotomography was performed to rule out acute aortic syndrome, in which a dissecting pulmonary artery aneurysm was diagnosed. Transthoracic echocardiogram showed an intimal flap at the pulmonary artery and severe dilatation. The patient died in less than four hours after arrival at the emergency room without being able to access surgical treatment due to the rapid evolution. **Conclusion:** Pulmonary artery dissection is a rare disease, with a high rate of mortality. Optimal management requires a rapid diagnosis with multiple imaging techniques. There is a lack of information about this topic.
Keywords: Pulmonary artery dissection, Chagas heart disease, thoracic angiotomography.

RESUMEN. Objetivo: *Describir la presentación de una disección de arteria pulmonar a la Unidad de Urgencias, la secuencia de eventos y revisión de la literatura.* ***Reporte de caso:*** *Paciente femenino de 59 años con cardiopatía chagásica conocida, quien acudió a urgencias por un episodio de dolor torácico repentino punzante y disnea progresiva, que evolucionó rápidamente a choque cardiogénico. Una radiografía de tórax informó un ensanchamiento severo del mediastino y cardiomegalia; por tanto, se realizó una angiotomografía torácica para descartar síndrome aórtico agudo, en la que se diagnosticó un aneurisma disecante de arteria pulmonar. El ecocardiograma transtorácico mostró un colgajo de la íntima a nivel de la arteria pulmonar y una dilatación severa. La paciente falleció en menos de 4 horas desde su llegada a urgencias sin poder acceder a tratamiento quirúrgico debido a la rápida evolución.* ***Conclusión:*** *La disección de la arteria pulmonar es una enfermedad rara, con una alta tasa de mortalidad. El manejo óptimo requiere un diagnóstico rápido con múltiples técnicas de imagen. Falta información sobre este tema.*
Palabras clave: *Disección de la arteria pulmonar, cardiopatía chagásica, angiotomografía torácica.*

Correspondence:
Carlos Enrique Franco Cruz, MD
E-mail: carlosenriquefranco@gmail.com

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INTRODUCTION

Pulmonary artery dissection (PAD) is a rare entity with high mortality. Since its first description by Helmbrecht in 1842,[1] less than 100 cases have been reported, most of them diagnosed post-mortem. Most of the patients die due to rapid-onset cardiogenic shock and sudden death. It usually occurs as a complication of chronic pulmonary hypertension.[2] In the largest case series reported, from 24 patients diagnosed alive, successful surgical repair was described only in seven subjects, attaining for the rapid evolution and fatal outcome.[2]

The present case report describes a middle-aged woman, previously diagnosed with chronic Chagas heart disease, with a dissecting

pulmonary artery aneurysm, cardiogenic shock and sudden death.

CASE PRESENTATION

The patient was a 59-year-old female, with a past medical history of arterial hypertension and Chagas heart disease.

She presented to the Emergency Unit with 1-month evolution of dysphonia, previously diagnosed as laryngitis, treated with prednisone 50 mg once a day for two weeks without improvement. One day prior to consultation, she suffers from a sudden onset of severe retrosternal pain, with stabbing characteristics, interscapular radiation, associated with progressive dyspnea at rest, that doesn't alleviate with analgesics.

On presentation, she was hemodynamically unstable, with pallor and acrocyanosis. Results on physical examination included a normal regular rhythm and a severe regurgitant tricuspid holosystolic murmur in addition to bilateral basal crackles. Arterial gasometry reports chronic respiratory acidosis and moderate acute respiratory distress syndrome (ARDS). Other laboratory tests are illustrated in *Table 1*.

Chest X-ray reveals marked mediastinal widening and vascular congestion with thickening at level of the aortic tract, an image suggestive of an aneurysm *(Figure 1)*.

As protocol to rule out acute aortic syndrome, a computed thoracic angiography was performed. In relation to the right ventricular outflow tract, an aneurysmal dilation of the pulmonary artery was reported, up to 5.3 cm diameter, with mass effect that compresses the aortic arch. It decreases the lumen to 1.3 cm causing pseudocoarctation. Also, an intimal flap was observed from pulmonary artery's origin, which extends to the right main pulmonary artery; true lumen gives rise to the left pulmonary artery, and incompletely to the right pulmonary artery, supplying only the right pulmonary upper lobe. Irrigation of the middle and lower right lobe origins from false lumen. A generalized cardiomegaly and a diffuse pulmonary mosaic pattern secondary to hypo perfusion were also described *(Figure 2)*.

Transthoracic, focused echocardiogram (TTE), describes a dilated cardiomyopathy, with reduced systolic function at rest, with a left ventricle ejection fraction of 25%, aneurysmal dilation of the pulmonary artery and the presence of an intimal flap. In addition, we identified a severe tricuspid regurgitation, with a peak velocity (Vmax) of 4.8 m/s, which stands to a high probability of pulmonary hypertension (PASP of 53 mmHg). There was no evidence of

Table 1: Laboratory tests at hospital admission.

Parameter	Value	Parameter	Value
White blood cells	17,000/mm^3	Glucose	96 mg/dL
Neutrophils	80%	Creatinine	0.77 mg/dL
Lymphocytes	13.7%	Uric acid	5.6 mg/dL
Eosinophils	2%	ALT	49 U/L
Monocytes	5.9%	AST	32 U/L
Hemoglobin	14.2 g/dL	CRP	24.9 mg/dL
Hematocrit	43.4%	ESR	62 mm/s
MCV	90.5 fL	LDH	290 U/L
MCH	29.6 pg	Sodium	139 mmol/L
MCHC	32.7 g/dL	Potassium	3.1 mmol/L
Platelets	234,000/μL	Phosphorus	3.7 mg/dL

MCV = median corpuscular volume; MCH = median corpuscular hemoglobin; MCHC = median corpuscular hemoglobin concentration; LDH = lactate dehydrogenase; CRP = C reactive protein; ALT = alanine aminotransferase; AST = aspartate aminotransferase; ESR = erythrocyte sedimentation rate.

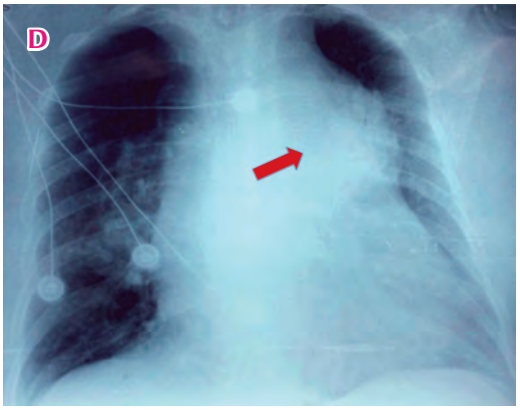

Figure 1: Chest X-ray. Cardiomegaly grade IV, mediastinal enlargement (red arrow) image suggestive of aneurysm.

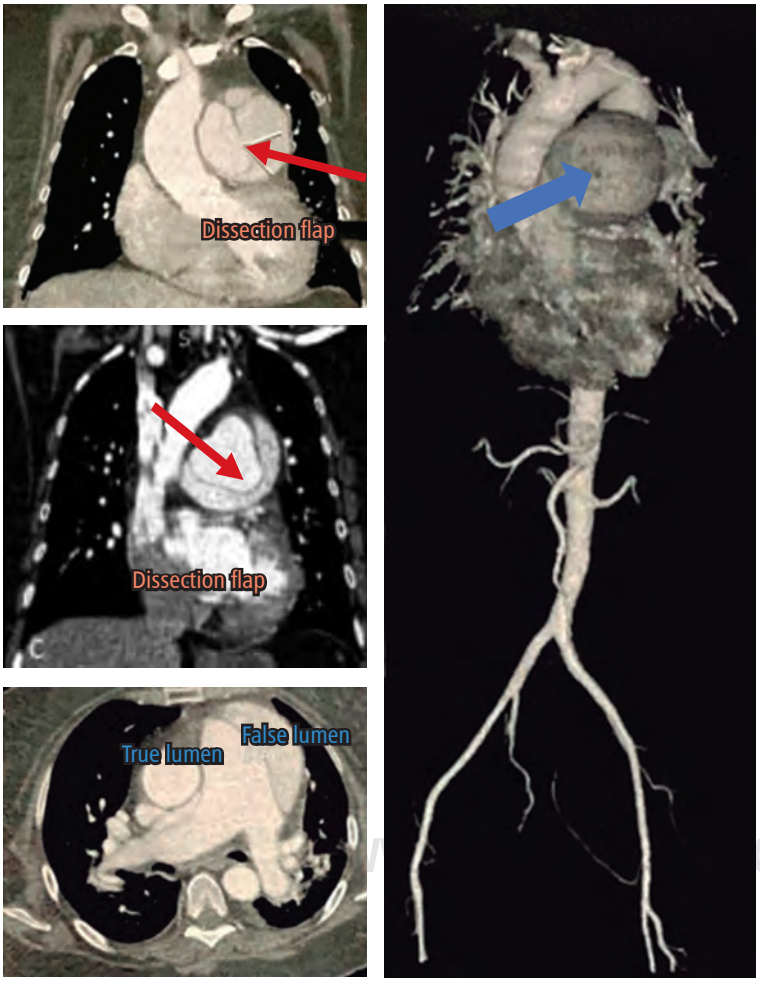

Figure 2: Thoracic angiography. Blue arrow indicates dissecting pulmonary artery aneurysm and its relationship with aortic arch (pseudocoarctation). Red arrow points to dissection flap.

pericardial effusion. Proximal aorta was normal *(Figure 3)*.

Due to its complexity, an evaluation by cardiovascular surgery was requested, recommending a surgical management; However, the patient presented a rapid evolution and dies in the Emergency Unit in less than 4 hours from arrival. For personal reasons, the autopsy was denied.

DISCUSSION

Pulmonary artery dissection (PAD) is an exceptionally rare condition with high mortality, frequently associated with pulmonary hypertension.[3,4] Occurs in both sex with a slight female predominance 1.2:1, with incidence peaks in the third and sixth decades of life.[5] The diagnosis is usually made in post-mortem studies due to the rapid progression that causes cardiogenic shock or sudden death.[6] The location of the dissection usually occurs in the major branches, predominantly in the trunk of the pulmonary artery in 72% of cases, followed by the intrapulmonary arteries in 10% and the involvement of the trunk and both main pulmonary arteries simultaneously in a minor percentage.[7]

Multiple causes of PAD are described, including chronic pulmonary hypertension leading to the development of a pulmonary artery aneurysm, congenital heart disease (mainly patent ductus arteriosus), chronic arteritis, pulmonary thromboembolism and rheumatic mitral valve stenosis.[8] Other less frequent causes are infections, trauma, atherosclerosis or connective tissue disorders.[9,10]

According to the literature, the clinical manifestations of PAD are nonspecific. The most frequent presentations are chest pain, dyspnea, cyanosis, hemoptysis, shock and death; dyspnea being the most common symptom in 82% of cases, while retrosternal chest pain and cyanosis have been described in 67% and 52% of cases, respectively.[11,12] Radiographic findings are nonspecific: cardiomegaly, dilatation of the trunk of the pulmonary artery and pleural effusion.[13] Computed tomographic angiography is a useful diagnostic tool in suspected pulmonary

artery dissection; however, its diagnostic performance has not been established due to the minority of reported cases.[14] Transthoracic echocardiography is an important imaging study in the initial approach by providing quantitative and qualitative information on cardiac function.

The optimal management of patients has not been defined due to the low number of cases in the literature. Based on anecdotal reports, surgical repair has been performed in few patients with variable results.[1] Medical treatment may include oxygen, analgesics, vasodilators, diuretics and inotropics.[15]

The patient has a medical history of chronic Chagas heart disease and hypertension who presented to the Emergency Unit with symptoms of atypical chest pain and physical examination with hemodynamic compromise; whose initial radiological findings led us to suspect an acute aortic syndrome; ruling out this cardiovascular emergency, the involvement of the pulmonary vasculature was documented in angiotomography, demonstrating a dissected aneurysm of the pulmonary artery of undetermined cause.

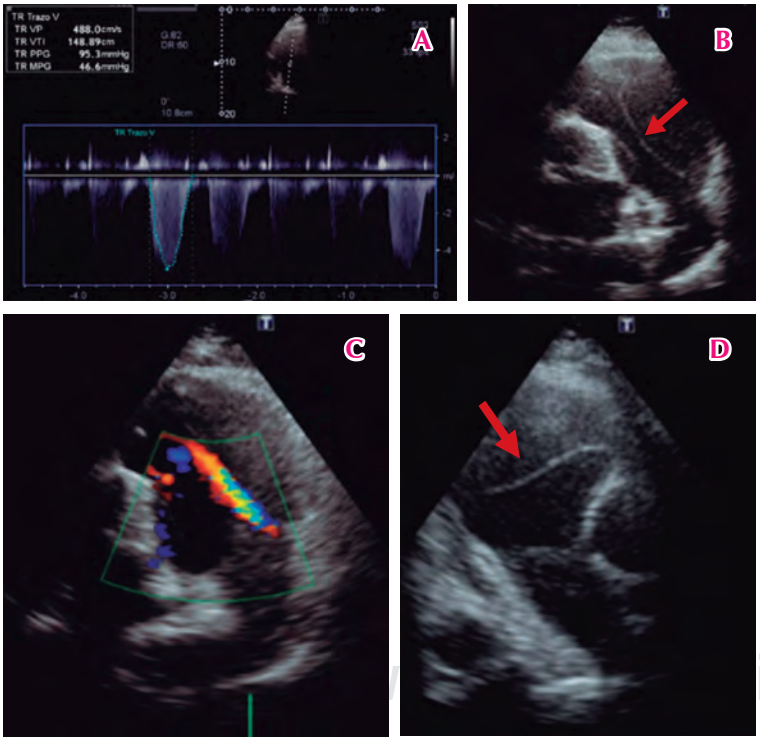

Figure 3: Transthoracic echocardiogram. **A)** Tricuspid regurgitation with a peak velocity (Vmax) of 4.8 m/s, and high echocardiographic probability of pulmonary hypertension. **B to D)** Great vessels short axis view. The arrow marks the dissecting flap in the pulmonary artery. **C)** Shows turbulence in Doppler color at the dissection point.

The series of events associated with aneurysmal dilation of the pulmonary artery is not known with certainty. Although there are no detailed studies in this regard, the development of aneurysms in the aorta, another large elastic artery, allows us to infer some common mechanisms. Thoracic aortic aneurysms are associated with classic cardiovascular risk factors, chest trauma, vasculitis (and other autoimmune diseases) and genetic factors in up to 25% of cases. Multiple genetic pathways are related to the development of aortic aneurysms and pulmonary hypertension, either in high penetrance familial forms (Marfan, Loeys Dietz, Ehlers-Danlos syndromes) or in sporadic mutations. The latter, perhaps more frequent in general population, requires a higher influence of environmental factors for phenotypic expression, among them, chronic left ventricule afterload alterations.[16]

In the case of our patient, hemodynamic overload due to type II pulmonary hypertension could favor the phenotypic expression of the pulmonary artery aneurysm, with unknown pathogenic mutations. Finally, case reports associate the chronic use of steroids with the presentation of aortic and pulmonary dissection, contributing to degeneration of the vascular media. Although the duration of therapy was short (only two weeks), high doses of corticosteroids (0.5 mg per kilogram of body weight) may be a predisposing factor in the presentation of this patient.[16]

Despite the fact that successfully surgical interventions are reported, the high risk that the intervention entails impoverishes the prognosis of patients, showing that even in conservative management despite optimal medical treatment, mortality is about 100%.[2]

We consider this case report of high academic value, given the unusual symptoms at presentation (dysphonia), treated erroneously as an upper respiratory infection. In addition, the high similarity with an acute aortic syndrome, with whom it shares a high mortality despite an adequate treatment instituted.

CONCLUSIONS

Pulmonary artery dissection is an extremely rare disease, generally with fatal outcome. Due to the few reported cases in the literature, there is a lack of management and treatment guidelines for this entity with high mortality, so the approach is based on case reports and clinical experiences. More studies are needed on this entity to improve the diagnostic and therapeutic approach.

REFERENCES

1. Perrotta S, Lentini S. Pulmonary artery dissection. J Card Surg. 2015; 30 (5): 442-447.
2. Malm CJ, Ternstrom L, Jorgensen K, Dellgren G. Pulmonary artery dissection in a patient with undiagnosed pulmonary hypertension--A case report and review of literature. Heart Lung. 2015; 44 (5): 453-457.
3. Navas Lobato MA, Martín Reyes R, Lurueña Lobo P, Maté Benito I, Guzmán Hernández G, Martí de Gracia M, et al. Pulmonary artery dissection and conservative medical management. Int J Cardiol. 2007; 119 (1): e25-e26.
4. Correa Rde A, Silva LC, Rezende CJ, Bernardes RC, Prata TA, Silva HL. Pulmonary hypertension and pulmonary artery dissection. J Bras Pneumol. 2013; 39 (2): 238-241.
5. Senbaklavaci O, Kaneko Y, Bartunek A, Brunner C, Kurkciyan E, Wunderbaldinger P, et al. Rupture and dissection in pulmonary artery aneurysms: incidence, cause, and treatment--review and case report. J Thorac Cardiovasc Surg. 2001; 121 (5): 1006-1008.
6. Shilkin KB, Low LP, Chen BT. Dissecting aneurysm of the pulmonary artery. J Pathol. 1969; 98 (1): 25-29.
7. Inayama Y, Nakatani Y, Kitamura H. Pulmonary artery dissection in patients without underlying pulmonary hypertension. Histopathology. 2001; 38 (5): 435-442.
8. Tonder N, Kober L, Hassager C. Pulmonary artery dissection in a patient with Eisenmenger syndrome treated with heart and lung transplantation. Eur J Echocardiogr. 2004; 5 (3): 228-230.
9. Degano B, Prevot G, Tetu L, Sitbon O, Simonneau G, Humbert M. Fatal dissection of the pulmonary artery in pulmonary arterial hypertension. Eur Respir Rev. 2009; 18 (113): 181-185.
10. Westaby S, Evans BJ, Ormerod O. Pulmonary-artery dissection in patients with Eisenmenger's syndrome. N Engl J Med. 2007; 356 (20): 2110-2112.
11. Zhang C, Huang X, Li S, Yao H, Zhang B. Pulmonary artery dissection: a fatal complication of pulmonary hypertension. Case Rep Med. 2016; 2016: 4739803.
12. Hako R, Fedacko J, Tóth S, Morochovic R, Kristian P, Pekárová T, et al. Rare presentation of left lower lobe pulmonary artery dissection. Case Rep Med. 2017; 2017: 2760535.
13. Hoye SL, Gale CP, Tolan DJ, Pepper CB. An unusual presentation of pulmonary artery dissection. Thorax. 2009; 64 (4): 368.
14. Neimatallah MA, Hassan W, Moursi M, Al Kadhi Y. CT findings of pulmonary artery dissection. Br J Radiol. 2007; 80 (951): e61-e63.
15. Khattar RS, Fox DJ, Alty JE, Arora A. Pulmonary artery dissection: an emerging cardiovascular complication in surviving patients with chronic pulmonary hypertension. Heart. 2005; 91 (2): 142-145.
16. Arul Rajamurugan PS, Panchapakesa Rajendran C, Rukmangatharajan S, Kanakarani P, Rajeswari S, Ravichandran R. Aortic dissection in a case of systemic lupus erythematosus. Lupus. 2007; 16 (12): 1001-1003. doi: 10.1177/0961203307081996.

CARDIAC IMAGE UPDATED

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Clinical case

Endocarditis and spondylodiscitis as a complication of postinfarction ventricular aneurysm rupture

Endocarditis y espondilodiscitis como complicación de ruptura de aneurisma ventricular postinfarto

Jesús Samuel Borges-López,* Emma Rosas-Munive,‡ José Luis Barón-Caballero,‡ Víctor Ochoa-Pérez,§ Rodolfo de Jesús Castaño-Guerra,¶ Eduardo Ayala-Hernández,¶ Abril Trejo-Caballero‖

* Department of Cardiology.
‡ Echocardiography Department.
§ Hemodynamics Department.
¶ Coronary Intensive Care Unit.
‖ Pathological Anatomy Department.

General Hospital of Mexico «Dr. Eduardo Liceaga», Mexico City, Mexico.

Correspondence:
Jesús Samuel Borges-López
E-mail:
jborgescardio@outlook.com

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ABSTRACT. Postinfarction ventricular aneurysm is defined as a dilatation of the left or right ventricle in a saccular form that can cause its rupture at the level of the ventricular wall or septum and can predispose to endocarditis due to the production of turbulence caused by short circuits that cause damage to the endocardial tissue. with the consequent bacterial colonization and systemic embolism. Once the diagnosis is confirmed, antibiotic treatment should be given and in case of complications, surgical treatment should be considered. We report the case of a male patient with a previous history of acute myocardial infarction, who attended the emergency room due to systemic inflammatory response data, showing endocarditis in the tricuspid valve and a ruptured ventricular aneurysm, causing embolic phenomena in the dorsal column, therefore which required surgical treatment.
Keywords: Ventricular aneurysm, infarction, endocarditis, spondylodiscitis.

RESUMEN. *El aneurisma ventricular postinfarto se define como una dilatación del ventrículo izquierdo o derecho en forma sacular que puede provocar su ruptura a nivel de la pared o septum ventricular y puede predisponer a endocarditis debido a la producción de turbulencias ocasionadas por cortocircuitos que ocasionan daño del tejido endocárdico con la consecuente colonización bacteriana y embolismos sistémicos. Una vez confirmado el diagnóstico, debe otorgarse tratamiento antibiótico y, en caso de complicaciones, valorarse el tratamiento quirúrgico. Se reporta el caso de un paciente masculino con antecedente previo de infarto agudo de miocardio, el cual acudió a urgencias por presentar datos de respuesta inflamatoria sistémica, evidenciándose endocarditis en válvula tricúspide y un aneurisma ventricular roto, condicionando fenómenos embólicos a columna dorsal, por lo que requirió tratamiento quirúrgico.*
Palabras clave: *Aneurisma ventricular, infarto, endocarditis, espondilodiscitis.*

INTRODUCTION

Post infarction ventricular aneurysm is defined as a non contractile and circumscribed dilation of the left or right ventricle in a saccular form, secondary to a large area of thinned necrotic tissue, as a consequence of an acute myocardial infarction (AMI). It is more common in males, between 50-60 years of age, predominating in the left ventricle in 95% of cases and 5% in the right ventricle.[1,2] A review of the pathophysiology, diagnostic approach and treatment of this serious complication.

CASE PRESENTATION

57 years old male with a history of smoking and cocaine use, lower ST segment elevation AMI 15 years ago *(Figure 1A)*, not revascularized, without treatment by own decision. He

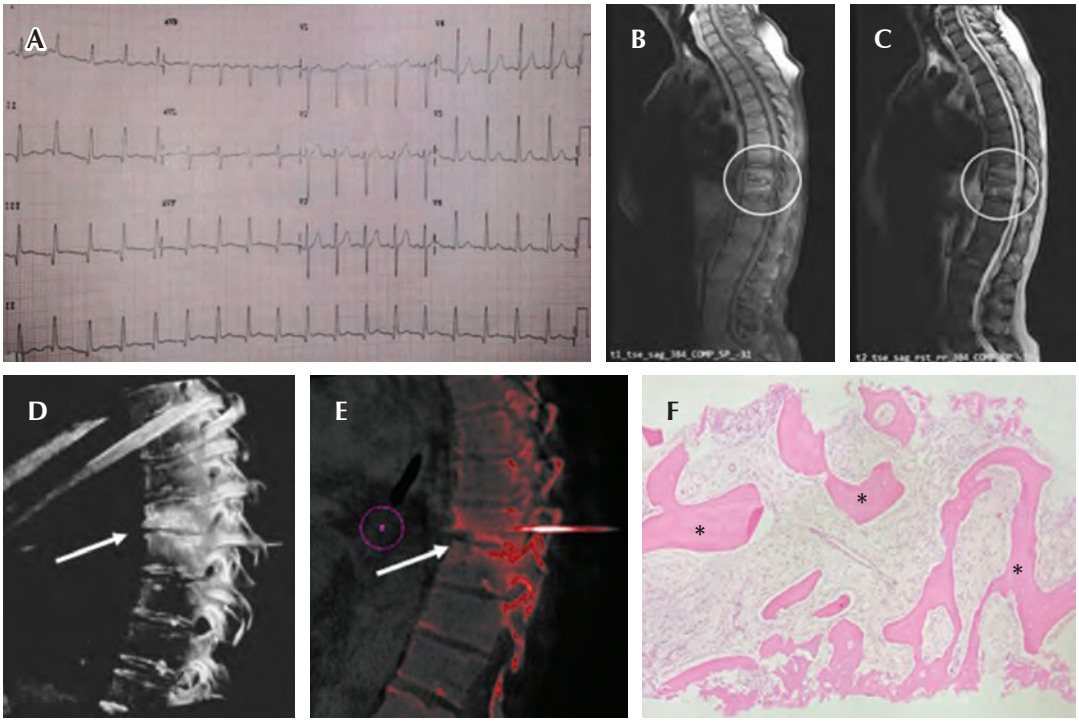

Figure 1: **A)** 12-lead electrocardiogram, HR 100 bpm, pathological Q waves in DII, DIII, aVF. **B, C)** MRI of the dorso lumbar spine showing destruction at the level of D9-D10 with T1, T2 and STIR sequences. **D, E)** Interventional-guided bone biopsy (arrows). **F)** Optical microscopy of bone marrow. Hematoxylin-eosin staining. Lymphocytes, plasma cells, macrophages, and myxoid degeneration are seen between the intertrabecular spaces (*).

began three months prior to admission with dyspnea with less effort than usual, fever of 38.5 ºC predominantly at night, myalgias, arthralgias and pain in the thoracic spine, asthenia, for which he went to the emergency room, deciding to hospitalize him in Internal Medicine. Cardiovascular exploration in the mitral and tricuspid focus revealed a holosystolic, regurgitant murmur, both of intensity III/VI. In the left parasternal region, a holosystolic murmur was auscultated, intensity IV/VI, low tone, radiating to the right parasternal region, accompanied by a thrill. Blood cultures were performed, having positive isolation to *Streptococcus mitis/Streptococcus oralis*, starting treatment with ceftriaxone 1 g IV every 24 hours for seven days, with subsequent control of blood cultures which remained positive. It was assessed by stomatology finding pulpal necrosis in upper left and right premolars, extracting said teeth. Given the persistence of pain in the spine, an MRI was requested, finding destruction of the vertebral bodies at D9-D10 *(Figure 1B and 1C)*, for which the Traumatology and Orthopedics service was consulted, indicating a percutaneous biopsy *(Figure 1D and 1E)*, who reported bone marrow with hypocellularity and myxoid degeneration between the intertrabecular spaces *(Figure 1F)*, reporting culture of said sample positive for *S. mitis/S. oralis*, adjusting treatment to vancomycin 1 g IV every 12 hours for six weeks. A transthoracic echocardiogram was performed, which reported dilated left cavities, LVEF 54%, inferior akinesia in its three segments, severe mitral regurgitation and moderate tricuspid regurgitation *(Figure 2A)*, in addition to an 11 mm ventricular septal defect, in the lower border, with flow from left to right, Qp/Qs 2.1, and an inferoseptal aneurysm in the basal segment *(Figure 2B and 2C)*. For persistence of fever and positive cultures, a transesophageal echocardiogram was performed, finding an oscillating mass of 10 × 8 mm, pedunculated,

hypermobile, at the base of the anterior valve of the tricuspid, which caused moderate tricuspid regurgitation, in addition to mitral valve with tenting that caused regurgitation severe mitral valve *(Figure 2D to 2F)*. Thoracoabdominal CT angiography was performed, finding data of multisegmental pneumonia *(Figure 3A and 3B)*, observing saccular calcification in the posterior region of the left ventricle *(Figure 3C and 3D)*. Coronary angiography was performed, which showed 75% stenosis in the anterior descending artery and total occlusion in the middle segment of the right coronary artery *(Figure 4A and 4B)*, corroborating skull and caudal LAO projection with saccular calcification suggestive of aneurysm *(Figure 4C)*. He was scheduled for surgical treatment where a left ventricular aneurysm was observed. Tricuspid valve with vegetation and perforation of the anterior leaflet was observed, performing bicuspidization with resection of the anterior leaflet plus vegetectomy, identifying a basal septal defect of 20 mm, deciding to close with a pericardial patch. Revascularization was performed with a bypass of the anterior descending artery distal to the aorta, observing mitral valve with myxomatous degeneration, which was replaced with a mechanical prosthetic valve, concluding the procedure without complications. The patient was subsequently discharged home, with follow up in outpatient Traumatology and Orthopedics, Cardiothoracic Surgery and Cardiology. A biopsy of the mitral valve was subsequently obtained, reporting data of myxomatous degeneration, and tricuspid anterior leaflet with fibrinoid necrosis and the presence of bacterial colonies *(Figure 4D and 4E)*.

DISCUSSION

The presence of a true ventricular aneurysm in the inferoposterior wall is rare (3%), since those located in this region are usually pseudoaneurysms.[3] Diagnosis is achieved with an echocardiographic study or at the time of cardiac catheterization, by means of left ventriculography, with CT and cardiac MRI

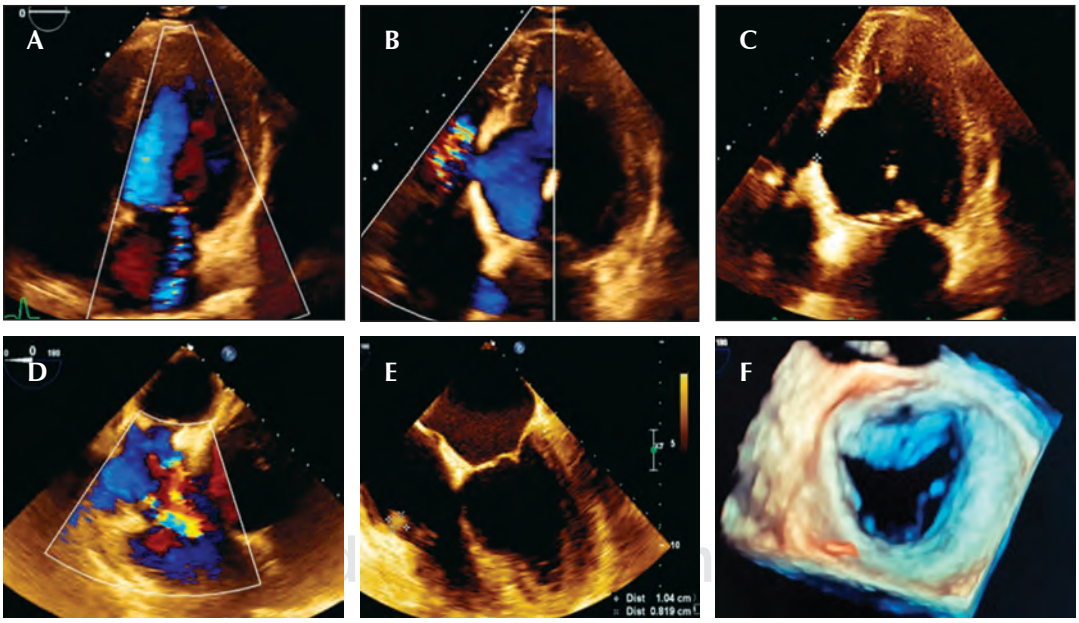

Figure 2: **A)** Transthoracic echocardiogram. Apical 4 chambers with Doppler color. Severe mitral regurgitation jet is observed. **B)** Apical 4 chamber Doppler color. Passage of flow through the ventricular septal defect is observed. **C)** Apical 4 chambers. Evidence of ventricular septal defect of 11 mm. **D)** Transesophageal echocardiogram with Doppler color. Ventricular septal defect is evident. **E)** Vegetation in the anterior tricuspid valve of 1.04 × 0.8 cm. **F)** 3D reconstruction of the mitral valve with tenting.

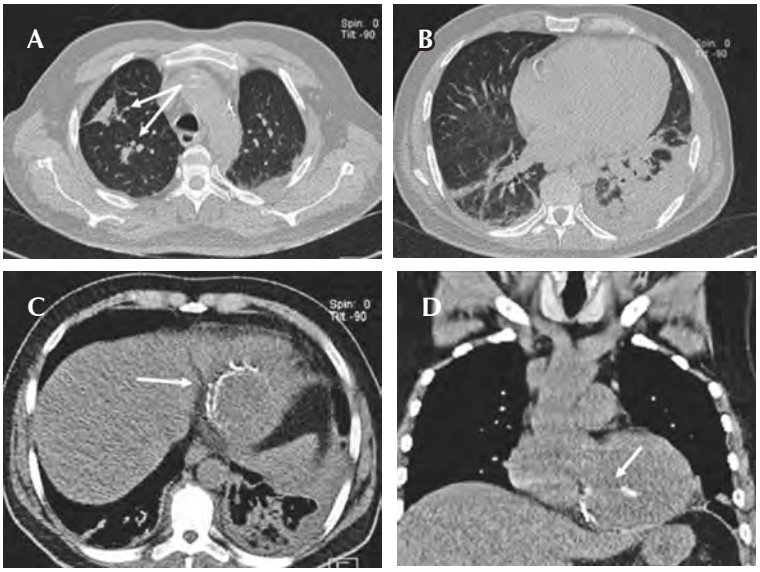

Figure 3: Chest CT. **A, B)** Multisegmental pneumonia data (arrows). **C, D)** Axial and coronal section. A calcified left ventricular aneurysm is observed at the basal level (arrows).

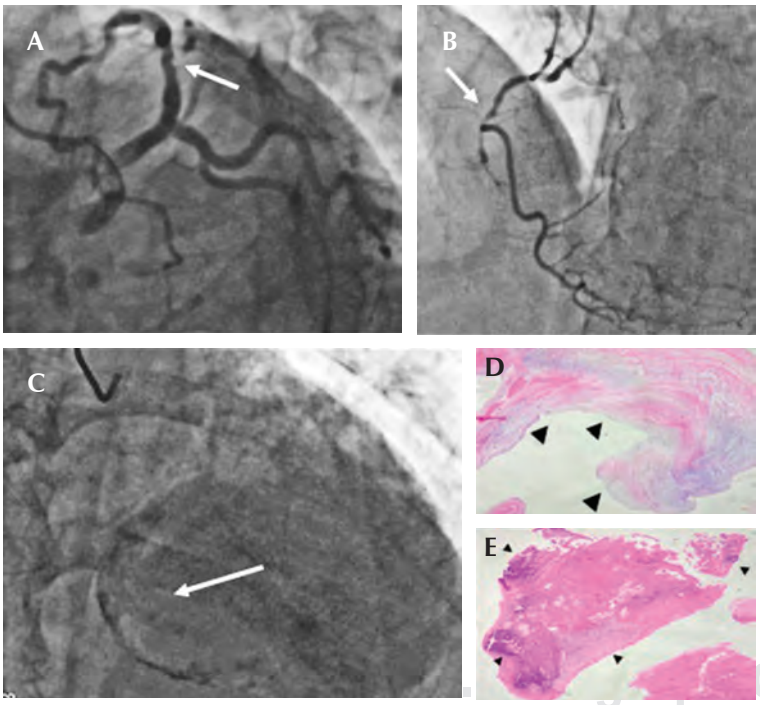

Figure 4: **A, B)** Angiography with coronary lesions in LAD and RCA arteries (arrows). **C)** Coronary angiography showing posterior saccular calcification of the left ventricle (arrow). **D)** Optical microscopy of the mitral valve. Hematoxylin-eosin staining. Myxomatous infiltration and disruption of elastic and collagen fibers are observed. **E)** Anterior tricuspid valve with fibrinoid necrosis and presence of hematoxylin-stained bacterial colonies (purple).

also being useful.[4,5] Surgical indications are the presence of angina, heart failure, arrhythmias or complications such as rupture, endocarditis or embolic phenomena as in the reported case.[6,7]

The patient in the reported case has a history of a non revascularized inferior AMI, in addition to not being under pharmacological treatment to reduce the complications of ventricular remodeling, having evidence of the formation of an inferoseptal left ventricular aneurysm.[8] Said ventricular aneurysm was complicated by rupture of the interventricular septum, despite its late presentation after AMI being infrequent.[9,10]

CONCLUSIONS

The previous case presents exceptionally as a late complication, in which, thanks to an adequate history, cardiovascular physical examination and imaging studies, a timely diagnosis and treatment was obtained.

REFERENCES

1. Arnaoutakis GJ, Zhao Y, George TJ, Sciortino CM, McCarthy PM, Conte JV. Surgical repair of ventricular septal defect after myocardial infarction: outcomes from the Society of Thoracic Surgeons National Database. Ann Thorac Surg. 2012; 94 (2): 436-443; discussion 443-444.
2. Cabrera-Rego J, Castañeda O, Valiente-Mustelier J, LLerena-Rojas R, López-Ferrero L, Mendoza-Rodríguez V. Presentación tardía de aneurisma ventricular post-infarto. Caracterización por múltiples modalidades de imagen. Revista Finlay [Internet]. 2011; 1 (3). Disponible en: http://www.revfinlay.sld.cu/index.php/finlay/article/view/57
3. Romero TL, Gutiérrez JL, Vasquez TG. Aneurisma ventricular calcificado en un paciente con cardiopatía isquémica y antecedente de trauma cerrado de tórax. Rev Costarric Cardiol. 2006; 8 (1): 27-29.
4. Walpot J, Peerenboom P, van Wylick A, Klazen C. Aneurysm of the membranous septum with ventricular septal defect and infective endocarditis. Eur J Echocardiogr. 2004; 5 (5): 391-393.
5. Alvarado Sánchez E, Lacayo González H, Siles Varela MA. Ruptura miocárdica y formación de aneurisma después de un infarto agudo de miocardio silente: Reporte de un caso. Rev Costarric Cardiol. 2011; 13 (2): 33-36.
6. Egbe AC, Poterucha JT, Rihal CS, Taggart NW, Cetta F, Cabalka AK, et al. Transcatheter closure of postmyocardial infarction, iatrogenic, and postoperative ventricular septal defects: The Mayo Clinic experience. Catheter Cardiovasc Interv. 2015; 86 (7): 1264-1270. doi: 10.1002/ccd.25989.

7. Ronco D, Matteucci M, Kowalewski M, De Bonis M, Formica F, Jiritano F, et al. Surgical treatment of postinfarction ventricular septal rupture. JAMA Netw Open. 2021; 4 (10): e2128309. doi: 10.1001/jamanetworkopen.2021.28309.
8. Blázquez González JA, Cortina JM, Centeno J, López MJ, Forteza A, Pérez de la Sota E, et al. Corrección quirúrgica de la comunicación interventricular postinfarto. Cir. Cardiov. 2009; 16 (2): 197-205.
9. Prior-Español A, Mateo L, Martínez-Morillo M, Riveros-Frutos A. Espondilodiscitis sin endocarditis causada por *Streptococcus mitis*. Reumatol Clin. 2016; 12 (6): 356-364.
10. Friedman BM, Dunn MI. Postinfarction ventricular aneurysms. Clin Cardiol. 1995; 18 (9): 505-511. doi: 10.1002/clc.4960180905.

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Clinical case

Paraspinal myositis and COVID-19, a case report

Miositis paraespinal y COVID-19, reporte de caso

Marlenet Olguín-Leyva,* Dante Palacios Gutiérrez,‡ Enrique A Berríos-Bárcenas,‡,§ José M Silva-Sánchez¶

* Medical Residency. Internal Medicine Service. Hospital Central Sur de Alta Especialidad PEMEX.
‡ Outpatient care Department. Instituto Nacional de Cardiología Ignacio Chávez.
§ Cardiology Department. Hospital Español.
¶ Imaging Department. Hospital General «Dr. Manuel Gea González».

Facultad de Medicina, UNAM. Mexico City, Mexico.

ABSTRACT. Viral myositis is characterized by the presence of fever, anorexia, myalgia, and muscle weakness. Few reports have described paraspinal myositis and myositis complicated with rhabdomyolysis as a manifestation of SARS-CoV-2 infection in adults. We present the case of a patient who developed paraspinal myositis secondary to COVID-19, confirmed by magnetic resonance imaging, characterized by intramuscular edema in paravertebral muscles. COVID-19 severe immune reaction and subsequent cytokine storm activation might play an important physiological role in muscle damage. Hence, in this pandemic, clinicians should consider COVID-19 myositis or rhabdomyolysis as a differential diagnosis in patients with focal muscle pain and fatigue.
Keywords: SARS-CoV-2, COVID-19, myositis, rhabdomyolysis, myalgia.

RESUMEN. *La miositis viral se caracteriza por la presencia de fiebre, anorexia, mialgia y debilidad muscular. Pocos informes han descrito la miositis paraespinal y la miositis complicada con rabdomiólisis como manifestación de la infección por SARS-CoV-2 en adultos. Presentamos el caso de una paciente que desarrolló una miositis paraespinal secundaria a COVID-19, confirmada por resonancia magnética, caracterizada por un edema intramuscular en los músculos paravertebrales. La grave reacción inmunitaria de la COVID-19 y la posterior activación de la tormenta de citoquinas podrían desempeñar un importante papel fisiológico en el daño muscular. Por lo tanto, en esta pandemia, los clínicos deberían considerar la miositis o la rabdomiólisis como diagnóstico diferencial en pacientes con dolor muscular focal y fatiga.*
Palabras clave: *SARS-CoV-2, COVID-19, miositis, rabdomiólisis, mialgia.*

Correspondence:
Marlenet Olguín-Leyva
E-mail:
marlenetolguin96@gmail.com

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INTRODUCTION

Viral myositis is characterized by fever, anorexia, myalgia, and muscle weakness, most frequently localized in the back and lower extremities, following an upper respiratory tract infection. Although the most frequently associated agents are Influenza A and B and enterovirus,[1] it has been observed that the SARS-CoV-2 virus can also be a potential cause of paraspinal myositis in adult patients.[2] In this report, we present the case of a patient who developed paraspinal myositis secondary to COVID-19, confirmed by magnetic resonance imaging.

CLINICAL CASE

A 71-year-old male with a history of diabetes, hypertension, and chronic heart failure with reduced ejection fraction (LVEF 32%) was admitted to our hospital with worsening respiratory distress and oxygen saturation of 88%. Chest X-ray revealed interstitial infiltrate with a diffuse distribution in both hemithorax with ground-glass opacity presumably consistent with COVID-19. Remarkable laboratory findings at his admission were DHL 387 U/L, D-dimer 524 μg/mL, CRP 274 mg/L, NT proBNP 2,484. A positive RT-PCR test for SARS-CoV-2 was obtained.

On day 22 of hospitalization, proximal muscle weakness and pain in lower extremities without CK elevation were disclosed. A contrasted MRI reported L4-L5 and L5-S1 discs herniation and edema in the medullary canal, compatible with acute myositis in paravertebral muscles *(Figures 1 and 2)*. Prednisone 20 mg and Pregabalin 150 mg were prescribed. Three days later, the patient was discharged without further complications.

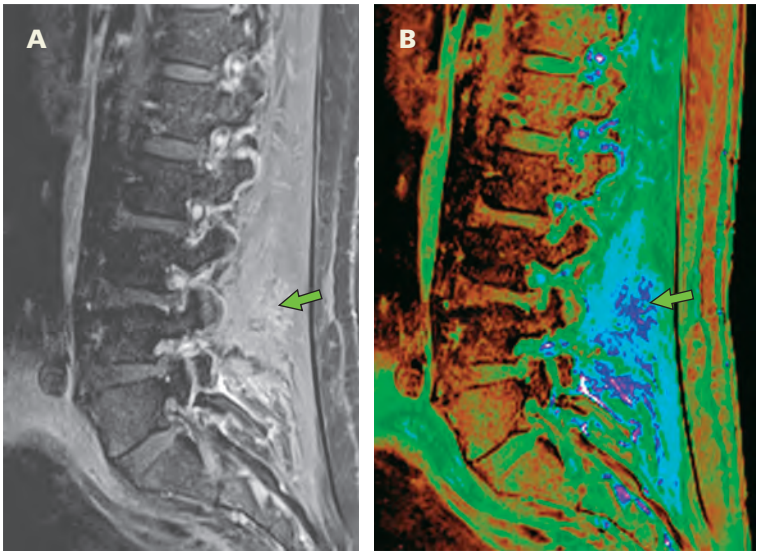

Figure 1: 71-year-old man with SARS-CoV-2. **A)** Fat-suppressed contrast enhanced T1-weighted sagittal MR image and **B)** color map, shows diffusely increased signal in paravertebral muscles of lumbosacral region at level to L3-L5 (green arrow), predominantly in rotators lumbar muscles, multifidus, lumbar iliocostals as well as, the lower insertion of longissimus thoracis muscle of bilateral form, suggesting acute myositis.

DISCUSSION

Among muscular COVID-related manifestations, myalgia, muscle weakness, and elevated alkaline phosphatase[3] are the most commonly found in adult patients. Myalgia prevalence was established to be between 35.86 and 50%,[2] while muscle weakness accounted for up to 30%. This muscular pain is usually symmetrical and involves trunk, proximal extremities, and neck muscles, persisting for up to 23 days after viral elimination.[4]

Besides the underlying SARS-CoV-2 pathogenic mechanism in muscular damage remains unclear, it has been hypothesized that skeletal muscle ACE-2 receptors and cytokine storm are involved. Viral infection induces immune T cells activation and clonal expansion, generating macrophage-mediated auto invasion of muscle fibers with abundant proinflammatory cytokines

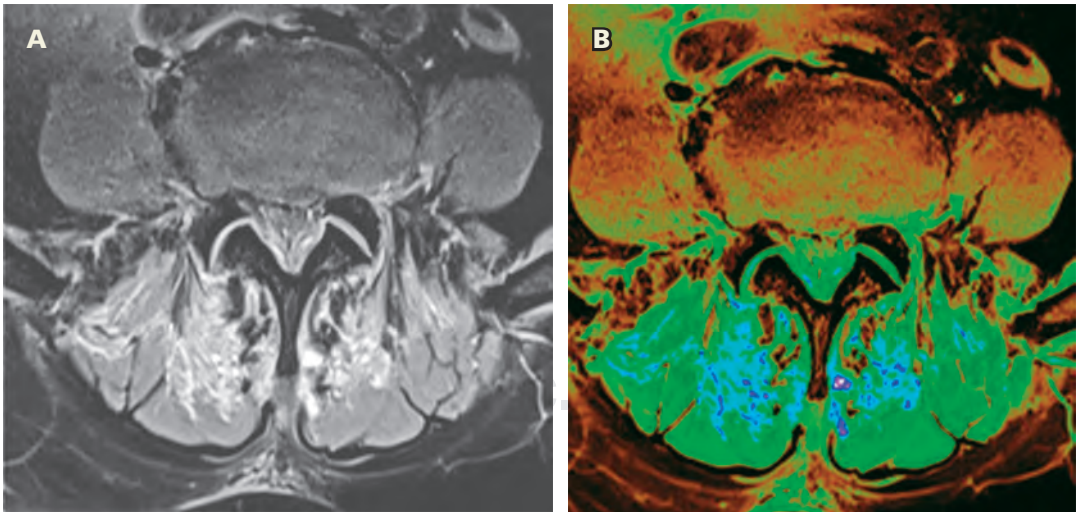

Figure 2: 71-year-old man with SARS-CoV-2. **A)** Fat-suppressed contrast enhanced T1-weighted axial MR image and **B)** color map, shows a reliable increase in the volumen and size of the intrinsic muscles of the lumbosacral region. Also, asymmetric bulging of the intervertebral disc can be observed.

in turn.[1] Nevertheless, no direct muscle infection has been demonstrated.[1,5] Thus, it is still unknown whether the mechanism of muscle necrosis and nerve tissue damage is due to direct viral infection, myotoxic immunological damage induced by cytokine release, or secondary to metabolic and systemic complications in view of a worsened underlying chronic disease.[6,7]

The present case is consistent with those reported by Mehan et al., where seven out of nine patients with COVID-19 presented intramuscular edema and myositis in MRI located bilaterally in the lumbar spine. In addition, the absence of spinal trauma discarded critical illness myopathy,[2] raising SARS-CoV-2 related viral myocarditis feasibility.

In this regard, pathological studies found a variable degree of focal necrosis on postmortem myofibrils without evidence of viral particles during the SARS pandemic in 2002,[8] suggesting that the most important physiological role of muscle damage is mediated by severe immune reaction and cytokine storm activation, which is recognized to occur in COVID-19.[6,9]

In conclusion, SARS-CoV-2 induced myocarditis and rhabdomyolysis should be considered a feasible differential diagnosis in those patients who present with focal muscle pain and fatigue,[10] as well as any patient with myositis or encephalomyelitis, an acute paralytic illness resembling Guillain-Barré syndrome, even in the absence of respiratory or systemic symptoms.[1] Still, due to COVID-19 novelty, studies are needed to elucidate the underlying viral pathogenesis and disease progression to tailor patient-targeted strategies for its diagnosis and management.

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REFERENCES

1. Dalakas MC. Guillain-Barré syndrome: the first documented COVID-19-triggered autoimmune neurologic disease: More to come with myositis in the offing. Neurol Neuroimmunol Neuroinflamm. 2020; 7 (5): e781. doi: 10.1212/NXI.0000000000000781.
2. Mehan WA, Yoon BC, Lang M, Li MD, Rincon S, Buch K. Paraspinal myositis in patients with COVID-19 infection. AJNR Am J Neuroradiol. 2020; 41 (10): 1949-1952. doi: 10.3174/ajnr.A6711.
3. Gulati A, Pomeranz C, Qamar Z, Thomas S, Frisch D, George G, et al. A comprehensive review of manifestations of novel coronaviruses in the context of deadly COVID-19 global pandemic. Am J Med Sci. 2020; 360 (1): 5-34. doi: 10.1016/j.amjms.2020.05.006.
4. Paliwal VK, Garg RK, Gupta A, Tejan N. Neuromuscular presentations in patients with COVID-19. Neurol Sci. 2020; 41 (11): 3039-3056. doi: 10.1007/s10072-020-04708-8.
5. Mao L, Jin H, Wang M, Hu Y, Chen S, He Q, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. JAMA Neurol. 2020; 77 (6): 683-690. doi: 10.1001/jamaneurol.2020.1127.
6. Suwanwongse K, Shabarek N. Rhabdomyolysis as a presentation of 2019 novel coronavirus disease. Cureus. 2020; 12 (4): e7561. doi: 10.7759/cureus.7561.
7. Berger JR. COVID-19 and the nervous system. J Neurovirol. 2020; 26 (2): 143-148. doi: 10.1007/s13365-020-00840-5.
8. Leung TW, Wong KS, Hui AC, To KF, Lai ST, Ng WF, et al. Myopathic changes associated with severe acute respiratory syndrome: a postmortem case series. Arch Neurol. 2005; 62 (7): 1113-1117. doi: 10.1001/archneur.62.7.1113.
9. Zhang H, Charmchi Z, Seidman RJ, Anziska Y, Velayudhan V, Perk J. COVID-19-associated myositis with severe proximal and bulbar weakness. Muscle Nerve. 2020; 62 (3): E57-E60. doi: 10.1002/mus.27003.
10. Jin M, Tong Q. Rhabdomyolysis as potential late complication associated with COVID-19. Emerg Infect Dis. 2020; 26 (7): 1618-1620. doi: 10.3201/eid2607.200445.

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Review

Plasticity and pathological remodeling of the mitral valve in ischemic mitral regurgitation. After an infarction, insufficiency with «normal valves»? Or structural damage to the mitral valve accompanying the remodeling of the ventricle?

Plasticidad y remodelación patológica de la válvula mitral en la regurgitación mitral isquémica. ¿Después de un infarto, insuficiencia con «válvulas normales»? ¿O daños estructurales en la válvula mitral que acompañan a la remodelación del ventrículo?

Luis Alberto Fernández Calix,* Wilman A de León López,* Alberto Aranda Fraustro,‡ Ricardo Álvarez Santana,§ Héctor Herrera-Bello,¶ Nydia Ávila-Vanzzini||

* Outpatient Care Department, Former Resident, National Institute of Cardiology Ignacio Chavez. Mexico City, Mexico.
‡ Pathology Department, National Institute of Cardiology Ignacio Chavez. Mexico City, Mexico.
§ Autonomous University of Ciudad Juarez. Mexico.
¶ Medica Sur Clinical Foundation. Mexico City, Mexico.
|| Department of Outpatient Care; National Institute of Cardiology Ignacio Chavez. Mexico City, Mexico.

Correspondence:
Nydia Ávila-Vanzzini
E-mail: vazzny74@yahoo.com

ABSTRACT. Ischemic mitral regurgitation (IMR) is a spectrum of mitral regurgitation with a complex mechanism; its presence increases the incidence of heart failure and mortality of patients. It is resulting from a displacement of the papillary muscles and tethering of the valve after a myocardial infarction. For many years it has been accepted that the mitral valve is essentially normal and in the context of an infarction, the left ventricle undergoes remodeling and displacement of the papillary muscles, which leads to the tethering of the valve and this conditions mitral regurgitation. There are many mechanisms associated with the poor mechanical coaptation of the valve that contribute to mitral regurgitation; but it is also true (considering multiple studies) that the valve undergoes a transformation of its structure and that therefore it is not structurally normal. In the late stages of IMR, the thickness and stiffness of the leaflets and the sub valvular apparatus contribute to the degree of mitral regurgitation, showing that the damage to the valve is clearly structural. The objective of this manuscript is to give an overview of the physio pathogenesis of IMR.
Keywords: Ischemic mitral regurgitation, plasticity, thickening, fibrosis.

RESUMEN. *La regurgitación mitral isquémica (RMI) es un espectro de regurgitación mitral con un mecanismo complejo; su presencia aumenta la incidencia de insuficiencia cardiaca y la mortalidad de los pacientes. Es el resultado de un desplazamiento de los músculos papilares y del anclaje de la válvula tras un infarto de miocardio. Durante muchos años se ha aceptado que la válvula mitral es esencialmente normal y que, en el contexto de un infarto, el ventrículo izquierdo sufre una remodelación y un desplazamiento de los músculos papilares, lo que provoca el anclaje de la válvula y condiciona la regurgitación mitral. Hay muchos mecanismos asociados a la mala coaptación mecánica de la válvula que contribuyen a la regurgitación mitral; pero también es cierto (teniendo en cuenta múltiples estudios) que la válvula sufre una transformación de su estructura y que, por tanto, no es estructuralmente normal. En las últimas fases de la RMI, el grosor y la rigidez de las valvas y del aparato subvalvular contribuyen al grado de regurgitación mitral, lo que demuestra que el daño de la válvula es claramente estructural. El objetivo de este manuscrito es ofrecer una visión general de la fisiopatogenia de la RMI.*
Palabras clave: *Regurgitación mitral isquémica, plasticidad, engrosamiento, fibrosis.*

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INTRODUCTION

Ischemic mitral regurgitation (IMR) is a spectrum of mitral regurgitation (MR), where segmental alterations and remodeling of the left ventricle (LV) due to a myocardial infarction result in displacement of the papillary muscles and tethering of the valve. In the case of inferior infarction, remodeling is asymmetric and is produced by the apical, posterior, and lateral displacement of the posteromedial papillary muscle, pulling the valve (this is named tethering) and generating an increase in the tension area (tenting); the same scenario occurs in anterior infarction, where both papillary muscles pull on the mitral valve (MV) through a symmetrical mechanism. All this pathophysiological mechanism alters the geometry of the valve, reducing the coaptation area and causing MR *(Figure 1)*.[1]

CELLULAR PLASTICITY OF THE VALVES

Currently it is known that MV is not an inert structure and has the ability to adapt to hemodynamic and traction stimuli, this versatility has been called «cellular plasticity» and in healthy valve tissue implies the ability to change its morphology, generally increasing the length and thickness of the leaflets to adapt to a new hemodynamic condition; the latter can occur during growth or pregnancy.[2] After embryonic development and during adult life, human valves maintain cell plasticity and their dynamic structure. Healthy heart valves can adapt to stress, and repair injury through connective tissue remodeling mediated by the synthesis, repair, and remodeling of extracellular matrix (ECM) components; in addition, interstitial valvular cells (IVCs) continually repair damage to collagen and other components of the extracellular matrix.[3]

IVCs comprise a diverse and dynamic population of resident cells that can modulate a spectrum of phenotypes regulated by environmental conditions. Although most IVCs in the normal valve are quiescent (inactive), IVCs are highly plastic and can shift from one phenotypic state to another during valve homeostasis, in response to adaptation to injury. The five distinct IVCs phenotypes include embryonic progenitor endothelial/mesenchymal

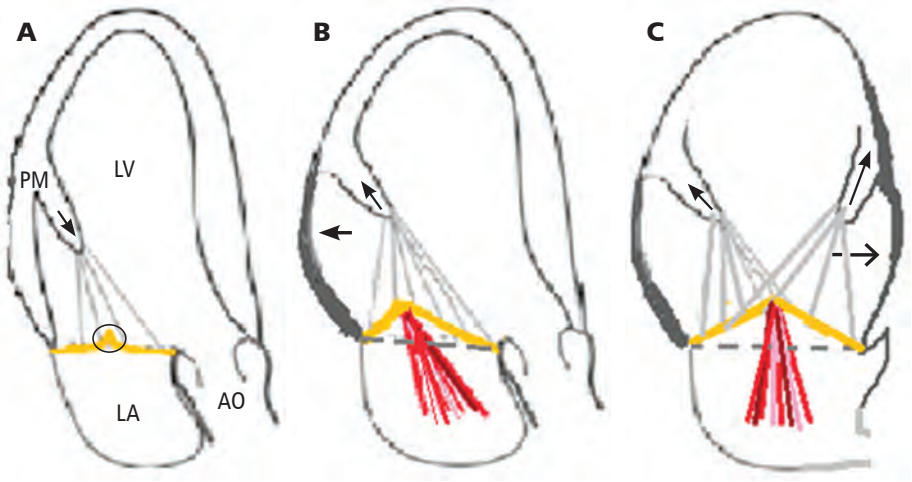

Figure 1: Schematic representation of the symmetric and asymmetric tenting area, and their evaluation by echocardiography. **A)** Schematic showing of apical long axis with normal coaptation of the mitral valve, close to its annulus, the red circle shows the coaptation surface of both leaflets. **B)** Schematic representation of an apical long axis, showing a lower infarct zone (dark gray area), observe the apical displacement of the papillary muscle and asymmetric tethering of the mitral valve. **C)** Representative diagram of a two-chamber axis with special angulation, showing both papillary muscles with apically displaced. The leaflet is pulled on both sides causing a symmetrical tethering of both leaflets, the dark gray areas represent areas of anterior and inferior infarction.
PM = papillary muscle; LV = left ventricle; LA = left atrium; AO = aortic valve.

cells (eIVCs), quiescent IVCs (qIVCs), activated IVCs (aIVCs), post developmental/ adult progenitor IVCs (pIVCs), and osteoblastic IVCs (ob-IVCs). The importance of knowing all these cellular components lies in the fact that they are the main protagonists of changes in the structure of the valve both in physiological and pathological scenarios.[4] Research suggest that IVCs in adult valves can be continually replenished through circulating endothelial or mesenchymal cell precursors derived from bone marrow. These precursors contribute to vascular healing and remodeling under physiological and pathological conditions.[5]

PATHOBIOLOGY OF VALVULAR HEART DISEASE

There are four types of pathological changes of valves: (1) disruption of the formation of the functional valve architecture, for example: congenital abnormalities; (2) damage or inadequate collagen leading to leaflets weakness, exemplified by degeneration of the myxomatous valve; (3) nodular calcification beginning in the IVCs, as in calcific aortic sclerosis/stenosis; and (4) fibrotic thickening with neovascularization.[3] Depending on the type of pathological change, the expression and mechanism of valve injury is different.

Regarding ischemic myocardiopathy, the ischemic myocardium can stimulate the growth of the MV leaflet and production of collagen through the secreting of TGF-β, which is elevated both in infarcted and remote non-infarcted myocardium.[5,6] Other research lines have showed that the turbulent MR jet may further signal the MV leaflets to change.[7,8] In the study by Dal-Bianco et al[9] using adult sheep in which a tethering of the MV was surgically generated, in order to simulate the effect of tethering in an infarction, the authors observed that mechanical stresses imposed at the valve increase the leaflet area and thickness, with cellular changes and they concluded that this suggest reactivated embryonic development pathways. On the other hand, in patients with chronically tethered leaflets evaluated by three-dimensional echocardiography, have been evident that MV leaflet surface area is greater by an average of 35% in compared with normal controls.[10] It would be reasonable to assume that in this pathologic IMR scenario an increase in surface mitral leaflet area might compensate for ventricular remodeling and tethering after myocardial infarction, and at least, decrease the degree of valvular regurgitation. However, not all patients have this valve plasticity, that is, they do not increase in size or thickness their mitral valve, some factors have already been associated with plasticity such as smoking associated with a loss of valve adaptability and diabetes mellitus of long evolution was associated with greater plasticity of the valve, possibly as a consequence of the trophic effects of insulin.[11] Ischemic and volume overload lesions, may have other local and paracrine effects on valve growth that may help explain the frequent failure of leaflet adaptation to prevent IMR.[7]

THE ECHOCARDIOGRAPHY AND EVALUATION OF MITRAL VALVE PLASTICITY

In a previous study of our research group, we defined plasticity in patients with inferior infarction as an increase in the length of the anterior and/or posterior mitral leaflets and first order posterior tendinous chords measuring these structures linearly on a parasternal long axis, with two-dimensional echocardiography.[11] The value accepted as normal for valve lengths was derived from anatomopathological studies of normal human hearts, where the length of the leaflets (measured from the annulus to the free edge of each leaflet) is 22-23 and 12-13 mm, for the anterior and posterior leaflets, respectively; normal length of tendinous cords is 18-22 mm.[12,13] In *Figure 2* there is an example of plasticity measure and some of the most important measurements in the IMR by bidimensional echocardiography.

ISCHEMIC MITRAL REGURGITATION WITH PLASTICITY AND / OR STRUCTURAL DAMAGE TO THE LEAFLETS

Ischemic mitral regurgitation had been considered as a «functional» valvular disease

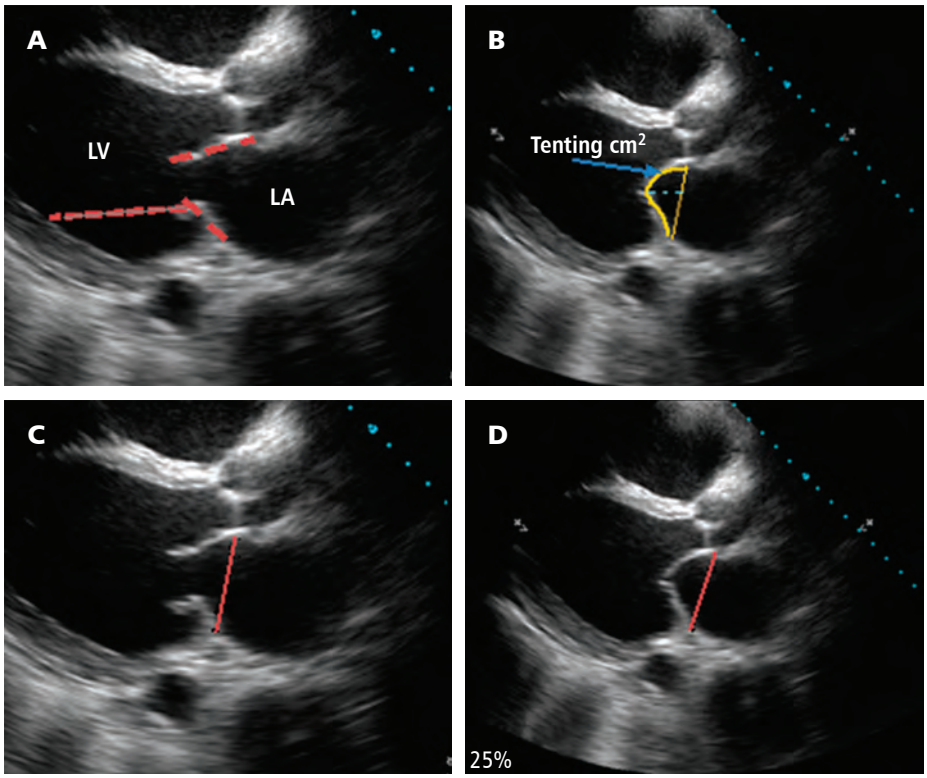

Figure 2: Evaluation by echocardiography 2D of ischemic mitral regurgitation. Long parasternal axis in a patient with inferior infarction and ischemic mitral regurgitation. **A)** Showing in diastole the longitudinal measurement of the anterior and posterior leaflets and chordae tendineae (from its union with the valve to the papillary muscle), dotted red line, the increase in the length of these structures denotes plasticity. **B)** Tenting is the area that borders the valve in the meso-systole (yellow line). The increase of it, denotes tethering of the valve; the dotted blue line shows the depth of coaptation going from the valve annulus to the coaptation site of both leaflets, both the tenting and the depth of coaptation denote the restrictive closure of the valve. **C** and **D)** Show how the annulus is measured in end-diastole **(C)** and early-systole **(D)**, red line, it should normally shorten antero-posteriorly at least 25%.
LV = left ventricle; LA = left atrium.

for many years, this meant that, there is no structural damage in the MV, and the leaflets are essentially reported as «normal», only with tethering due to ventricular remodeling; in others words, an abnormal left ventricular (LV) shape and function with a valvular manifestation.[14] This concept has been changing and in recent years the research has shown us that the advancement of IMR actually involves structural damage to the valves, that has been identified histologically, and also by echocardiography.[10,15]

In the study by Beaudoin[15] the investigators observed that the leaflets shown an increase in thickness in the cusps that is proportionally associated with the time of evolution of IMR. This thickening causes stiffness of the cusp of the leaflet, preventing normal coaptation and allowing regurgitation of Flow. In the experimental study in sheep, the post-myocardial infarction histopathology analysis showed expansion of the spongiosa central layer and focal subendothelial collagen deposition, mainly on the atrial leaflet surface, and expression of α-smooth muscle actin (α-SMA) point out endothelial mesenchymal transformation.[15] This study conclude MV thickness increases after myocardial infarction and correlates with MR, suggesting an organic component to IMR, and the fibrotic

remodeling of MV could be a focus of future treatments.

In *Figure 3* are showed the analysis the echocardiographic analysis of a patient before surgery of mitral valve replacement by severe ischemic mitral regurgitation. In *Figure 4* is showed the explanted mitral valve and its histological analysis of the same patient.

OPINION AND PERSPECTIVE

Analyzing the researchers' findings, it has led us to think that mitral valve remodeling has possibly several phases: the initial one is plasticity, that is, the increase in the length of the leaflets and with the passage of time it is possible that remodeling it becomes pathological and appears thickening of the valve and the insufficiency is greater.

Trying to find a logical order of the events that occur in the MV after a cardiac infarction, we can think that the remodeling in the LV causes the tethering of the valve; This pull of the valve activates the endothelial cells (VECs), which in turn, activate the interstitial cells (IVCs), this activation leads to the transformation of the extracellular matrix with endothelial-mesenchymal transformation, which also produces infiltration and transformation of the interstitial cells, mainly myofibroblasts.

Thus, changes begin in the cellular structure of the valves, mainly affecting the spongiosa layer, which begins to increase in

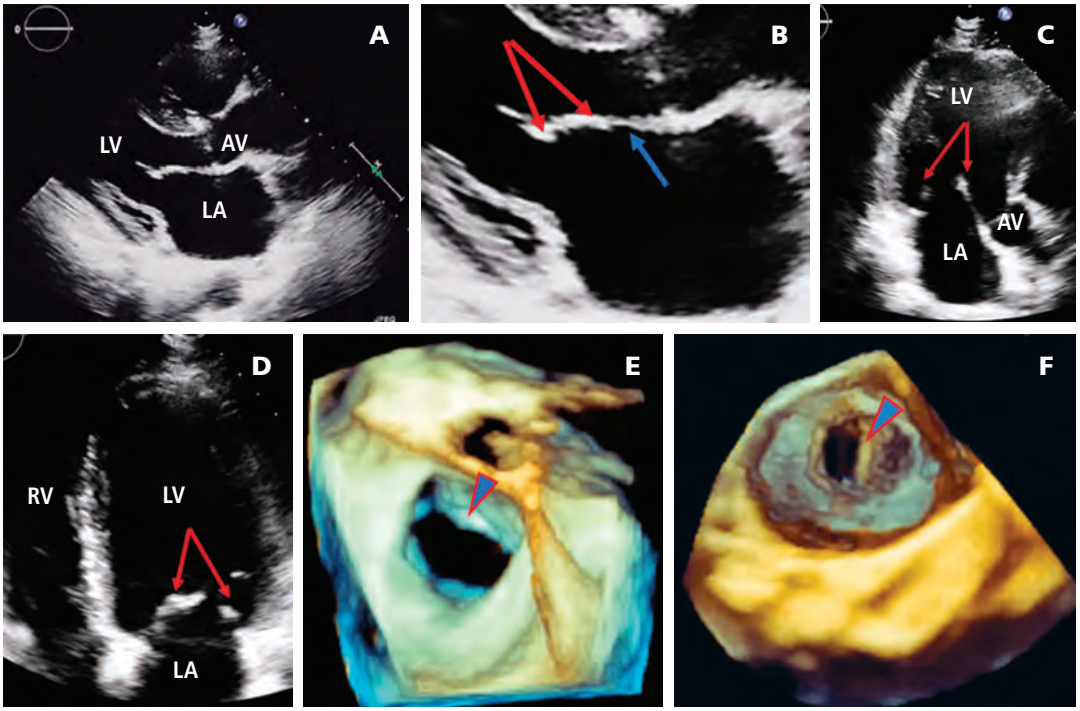

Figure 3: Echocardiographic analysis of explanted human valve in a patient with ischemic mitral regurgitation. **A)** 2D parasternal long axis shows increased length of the leaflets and dilation of the annulus (anterior leaflet 32 mm, posterior leaflet 22 mm, anulus in end diastole 39 mm). **B)** Approach to the mitral valve, the red arrows mark the thickening of the cusp and middle portion of the anterior leaflet (0.5 and 0.4 cm respectively) contrasting with the normal thickness of the base of the valve (0.2 cm) blue arrow. **C** and **D)** Apical long axis and four chambers showing the thickening of the cusps of the anterior and posterior leaflets in the same patient, red arrows. **E)** 3D echocardiography image of the mitral valve in face, arrow points to the site of distal thickening of the anterior leaflet. **F)** 3D echocardiography with approach from the ventricle. Note the anterior leaflet elongated, the posterior leaflet retracted, the arrow points to the site of distal valve thickening in anterior valve.
LV = left ventricle; AV = aortic valve; LA = left atrium; RV = right ventricle.

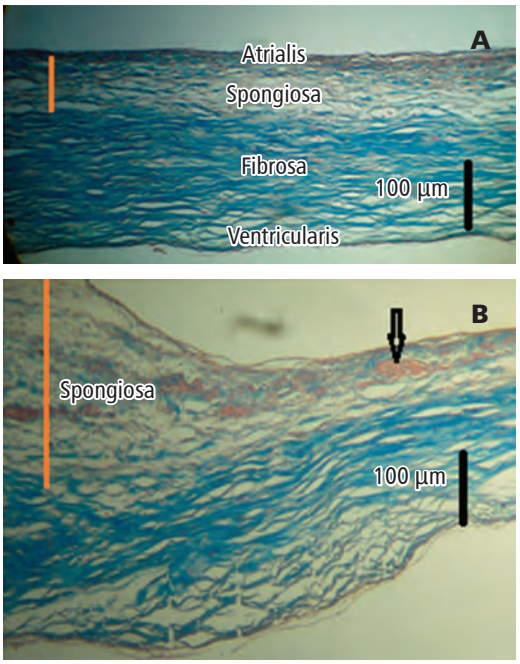

Figure 4: Histopathological analysis of the explanted valve in a patient with ischemic mitral regurgitation and its comparison with normal mitral valve. **A)** Histology of the anterior leaflet cusp with Masson's trichrome stain of normal human mitral valve. Notice the different layers and their normal proportion. Masson 2.5x. **B)** Histology of the anterior leaflet cusp with Masson's trichrome stain from a patient with ischemic mitral regurgitation who underwent valve replacement. Note the severe proliferation thickening of myxoid tissue in the Spongiosa layer (white and marked with the orange line). The arrow marks vascular neoformation in atrialis layer. Masson 2.5x.

size, but there is also a deposit of collagen fibers which give strength and support to the valve. At this point, and thanks to the transformation of the extracellular matrix, the valve increases its size and thickness, but it remains strong thanks to the joint deposition of collagen fibers, this has been recognized as cellular plasticity and is considered until now as a favorable compensatory or remodeling phenomenon.

At some point in the evolution of IMR and due to mechanisms not well understood, a disproportionate increase in the spongiosa layer begins as a consequence of a large number of fibroblasts and the generation of glycosaminoglycans and myxoid tissue, a deposition of fibrous tissue is produced, and the collagen fibers begin to decrease in quantity as do elastin fibers with the consequent loss of support and flexibility of the leaflets. This part appears to be the form of pathological remodeling and has been seen to occur late in IMR. Little is known about the triggers of this pathological evolution, possibly local or systemic factors are associated, but knowing more about pathophysiology opens up therapeutic possibilities to be able to stop the pathological course of IMR, if it exists; many more studies are needed to determine the events that occur in the physiology of this valve disease.

But at present, and analyzing the different investigations, we can affirm with certainty that in IMR the leaflets in late stages «are not normal» and have frank structural damage with thickening and fibrosis that contributes to the loss of adequate cooptation and forms a mechanism more associated with the degree of mitral regurgitation.

REFERENCES

1. Otsuji Y, Handschumacher MD, Liel-Cohen N, Tanabe H, Jiang L, Schwammenthal E, et al. Mechanism of ischemic mitral regurgitation with segmental left ventricular dysfunction: three-dimensional echocardiographic studies in models of acute and chronic progressive regurgitation. J Am Coll Cardiol. 2001; 37 (2): 641-648.
2. Wells SM, Pierlot CM, Moeller AD. Physiological remodeling of the mitral valve during pregnancy. Am J Physiol Heart Circ Physiol. 2012; 303 (7): H878-H892.
3. Schoen FJ. Evolving concepts of cardiac valve dynamics: the continuum of development, functional structure, pathobiology, and tissue engineering. Circulation. 2008; 118 (18): 1864-1880.
4. Liu AC, Joag VR, Gotlieb AI. The emerging role of valve interstitial cell phenotypes in regulating heart valve pathobiology. Am J Pathol. 2007; 171 (5): 1407-14018.
5. Visconti RP, Ebihara Y, LaRue AC, Fleming PA, McQuinn TC, Masuya M, et al. An *in vivo* analysis of hematopoietic stem cell potential: hematopoietic origin of cardiac valve interstitial cells. Circ Res. 2006; 98 (5): 690-696.
6. Deb A, Wang SH, Skelding K, Miller D, Simper D, Caplice N. Bone marrow-derived myofibroblasts are present in adult human heart valves. J Heart Valve Dis. 2005; 14 (5): 674-678.
7. Chester AH, Taylor PM. Molecular and functional characteristics of heart-valve interstitial cells. Philos Trans R Soc Lond B Biol Sci. 2007; 362 (1484): 1437-1443.

8. Mulholland DL, Gotlieb AI. Cell biology of valvular interstitial cells. Can J Cardiol. 1996; 12 (3): 231-236.
9. Dal-Bianco JP, Aikawa E, Bischoff J, Guerrero JL, Handschumacher MD, Sullivan S, et al. Active adaptation of the tethered mitral valve: insights into a compensatory mechanism for functional mitral regurgitation. Circulation. 2009; 120 (4): 334-342.
10. Chaput M, Handschumacher MD, Tournoux F, Hua L, Guerrero JL, Vlahakes GJ, et al. Mitral leaflet adaptation to ventricular remodeling: occurrence and adequacy in patients with functional mitral regurgitation. Circulation. 2008; 118 (8): 845-852.
11. Ávila-Vanzzini N, Michelena HI, Fritche Salazar JF, Herrera-Bello H, Siu Moguel S, Rodríguez Ocampo RR, et al. Clinical and echocardiographic factors associated with mitral plasticity in patients with chronic inferior myocardial infarction. Eur Heart J Cardiovasc Imaging. 2018; 19 (5): 508-515.
12. Levine RA, Hagége AA, Judge DP, Padala M, Dal-Bianco JP, Aikawa E, et al. Mitral valve disease--morphology and mechanisms. Nat Rev Cardiol. 2015; 12 (12): 689-710.
13. Rusted IE, Scheifley CH, Edwards JE. Studies of the mitral valve. I. Anatomic features of the normal mitral valve and associated structures. Circulation. 1952; 6 (6): 825-831.
14. Marwick TH, Lancellotti P, Pierard L. Ischaemic mitral regurgitation: mechanisms and diagnosis. Heart. 2009; 95 (20): 1711-1718.
15. Beaudoin J, Dal-Bianco JP, Aikawa E, Bischoff J, Guerrero JL, Sullivan S, et al. Mitral leaflet changes following myocardial infarction: clinical evidence for maladaptive valvular remodeling. Circ Cardiovasc Imaging. 2017; 10 (11): e006512.

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a) **Título:** representativo de los hallazgos del estudio. Agregar un título corto para las páginas internas (es importante identificar el diseño metodológico del estudio: registro, observacional de asociación cruzada, casos y controles, cohorte, ensayo clínico, estudio de prueba diagnóstica o revisión sistemática).
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c) **Introducción:** describe los estudios que permiten entender el objetivo del trabajo, mismo que se menciona al final de la introducción (no se escriben aparte los objetivos, la hipótesis ni los planteamientos).
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g) **Referencias:** deberá seguir las especificaciones descritas más adelante.
h) **Número máximo de caracteres sin espacio:** 8,000 (no incluye resumen).

Caso clínico o quirúrgico (1-3 casos) o serie de casos (más de tres casos clínicos)

a) **Título:** debe especificar si se trata de un caso clínico o una serie de casos clínicos.
b) **Resumen estructurado:** debe incluir objetivo de la presentación, descripción del caso y conclusiones, con palabras clave y *key words*. Máximo 1,200 caracteres sin espacios. En español e inglés.
c) **Introducción:** se trata la enfermedad o causa atribuible. Señalar el objetivo de la presentación del caso clínico.
d) **Presentación del(los) caso(s) clínico(s):** descripción clínica, laboratorio y otros. Mencionar el tiempo en que se reunieron estos casos. Las figuras o cuadros van en hojas aparte.
e) **Discusión:** se comentan las referencias bibliográficas más recientes o necesarias para entender la importancia o relevancia del caso clínico.
f) **Referencias:** deberá seguir las especificaciones descritas más adelante.
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b) **Resumen:** en español y en inglés, con palabras clave y key words. Máximo 1,200 caracteres sin espacios. En español e inglés.
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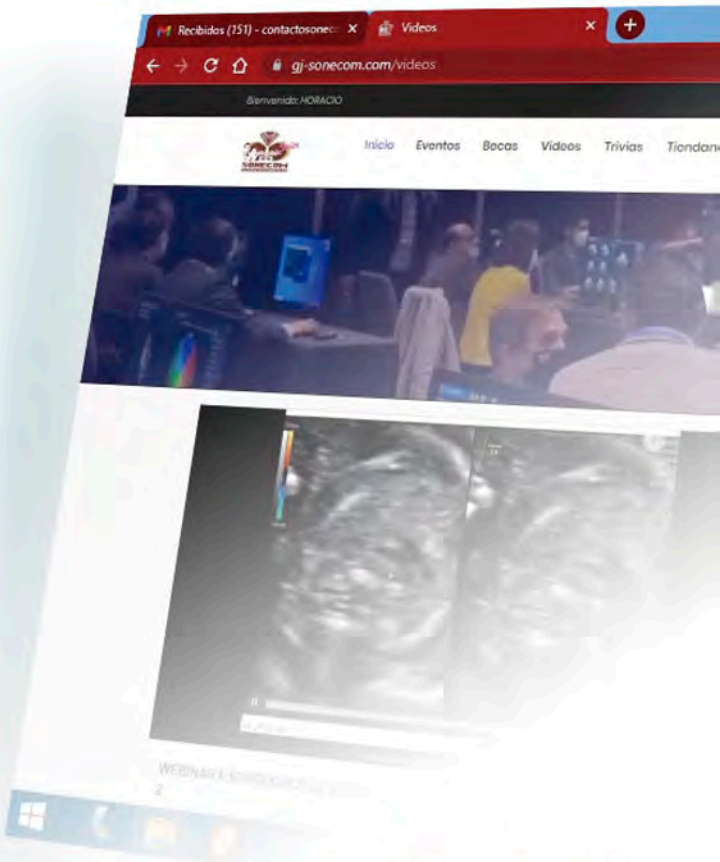

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