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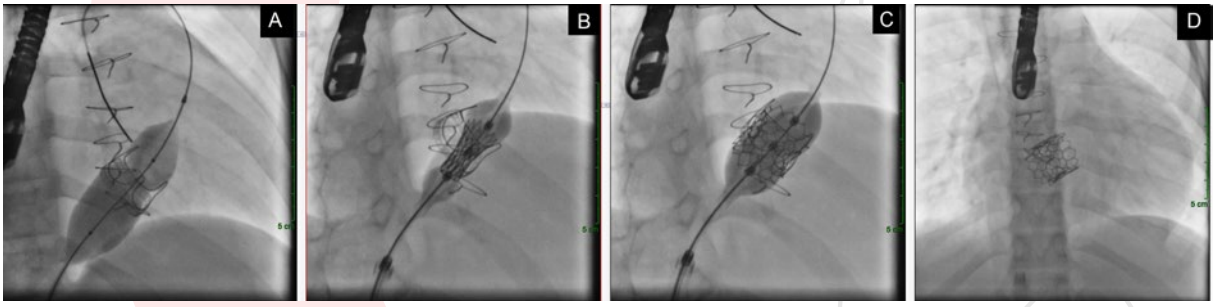

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EDITORIAL

Female physician empowerment

Empoderamiento de la mujer médica

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Cardiology, like the other fields of medicine, has experienced great advances throughout the course of mankind. The role of female physicians, particularly cardiologists, has changed the paradigms of many structures that were historically led by men, and today it is women who carry out true transformation. An article published in the Journal of the American College of Cardiology[1] highlights a concerning lack of female representation in the field of cardiology, in aspects like cardiovascular clinical trial leadership and the fact that most articles have a man as the principal author.

Based on these data, it is imperative to include women as research subjects, to make research inclusive and able to identify anatomical and pathophysiological differences between men and women, as well as different social and biological determinants of both sexes. This will contribute valuable information to individualize treatment approaches, promptly identify potential gender differences in the response to cardiovascular treatment and promote gender equality in health care[2].

To deal with these and other day-to-day situations, the Women's Cardiology Chapter of the Colombian Society of Cardiology and Cardiovascular Surgery developed the Cardio Woman project. This project included different female Colombian cardiologists with extensive experience, with the goal of raising awareness of the real risk of cardiovascular disease in women, providing the necessary information to foster a heart self-care culture, empowering Colombian women regarding the consequences and impact of these conditions, and thus reducing the incidence and prevalence of these diseases[3].

Despite all the activities women have carried out, the field of cardiology continues to have gender gaps. A small study published in the Archivos de Cardiología de México[4] journal (in which cardiologists from 19 Latin American countries, principally Mexico (69%), participated) showed that, compared to men, women did not receive the same recognition in this field and were not offered the same guarantees and rights. In addition, they were exposed to constant harassment and discrimination at work, which caused them anxiety and depression.

The limited number of female cardiologists in Latin America and the rest of the world continues to be concerning. Currently, the Colombian Association of Internal Medicine has 760 female internists and 175 female residents in its database. Therefore, many cardiovascular organizations around the world have proposed different strategies to highlight women's work in this field of medicine and thus experience the immense benefit it brings. One of these organizations is "Women as One," a non-profit agency whose goal is to promote the talent of female physicians, especially cardiology specialists, through a platform that functions as a database, from which they can obtain work resources and opportunities. In addition, they are given the opportunity to share their ideas and novel insights, which can be beneficial for the future of medical practice[5].

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The term "female empowerment" had its beginning at the Fourth World Conference on Women, in Beijing in 1995, which marked a milestone in the meaning of women's rights and gender equality today[6]. This concept entails many challenges for society and especially for women, who have left a mark throughout history, with most becoming icons in a struggle that has still not ended.

The 2023 Nobel Prize in Medicine was awarded jointly to Katalin Karikó and Drew Weissman "for their discoveries concerning nucleoside base modifications that enabled the development of effective mRNA vaccines against COVID-19"[7]. Karikó is a Hungarian biochemist who, since the 90s, has researched mRNA-based gene therapy, enabling more effective vaccines against coronavirus. This positions her as a central woman in the past health crisis, as her innovative findings have saved millions of lives[7].

The development of women's empowerment has been a dynamic and open change process that involves very solid power structures which should be reframed, understanding that women's role in society has become increasingly relevant and many women today are leaders, physicians, entrepreneurs, politicians, researchers and hold high government positions.

Narges Mohammadi, a brave journalist and defender of women's rights who dignifies women's empowerment, won the 2023 Nobel Peace Prize due to her commitment and dedication in the struggle against the oppression of women in Iran. Risking repression, harassment, violence and detection, she invites us to reflect on the role of women in the world and calls the international communities to make a serious commitment to the situation in Iran and many other parts of the world where women are still subjected to oppressive and degrading regimes[8].

In 1990, Claudia Goldin became the first woman to be given tenure in the Department of Economics at Harvard University. Today, Goldin has been awarded the 2023 Nobel Prize in Economics, recognized for "advancing our understanding of women's labor market outcomes"[9].

The Nobel Prize, which is awarded annually in recognition of intellectual and academic achievement, has been presented to more than 900 people throughout its history, from 1901 to 2023, and only 63 of these honored people have been women[7].

At a professional level, and considering only the health field, women play an essential role. Previously, men were the only ones who could study and practice medicine. Today we see that around 45% of medical students are women, which is an encouraging outlook that will open doors in the future and inspire other women to choose this path and contribute to the population's wellbeing. Despite this, and being the twenty-first century, there are still acts of male chauvinism and repression against women; most university professors are men who downplay the academic achievements of their female students, doubt their abilities and even sexually harass them.

Thus, it is crucial for women in the health field to be empowered and create change not only in office visits with their patients but also in academia. It has been proven that women are more caring, empathetic, disciplined, respectful, and expeditious, among other qualities, and that this, coupled with their knowledge of medicine, allows them to provide better patient care, which translates into more accurate diagnoses and treatments that have a positive impact on the population's quality of life.

In the educational setting, female professors have better tools and skills for communicating their knowledge, are more patient with their students and leave better lessons in medicine.

It is also important to reflect on how women contribute to medicine with their subjectivity, insofar as they are confident in their intuitive and intellectual capacity to heal, as this is something they have been granted by nature. They can play this role positively by believing in this skill and practicing the ancestral knowledge inherited from their culture together with their scientific knowledge. This knowledge should be gathered and shared with the community, and who better to carry out this task than women?

Another aspect to keep in mind and which may be negative, or limit women's medical practice, is the fact that most are responsible for their families and homes. Due to schedules and available time, this can lead to them not being able to specialize or being forced to choose a specialty that may not be the most interesting to them, but that provides more flexibility in line with their needs. Addressing these problems will help bolster and reclaim women's work in the medical setting.

In conclusion, women have had a long struggle over time, during which small and large advances have been made, which have led to them having access and opportunities that were formerly exclusively for men. However, the struggle continues, and all women have the duty to open doors for future generations and enable true gender equality to be achieved in the future.

In my specific case, I have been an undergraduate and graduate internal medicine university professor for

38 years, and I have personally had to live through difficult processes and face trials to be able to create leadership in academic representation positions and as a public servant for 10 years, working under four different mayors. The most important thing today is to recognize that, along the way, we always find physicians with a holistic vision and great ability to value the abilities of female physicians who, with their commitment and dedication, have proven to be on a par and many times have improved academic, research and scientific performance.

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ORIGINAL ARTICLE

The economic burden of pulmonary arterial hypertension in Colombia: A micro-costing analysis

La carga económica de la hipertensión arterial en Colombia: un análisis de micro-costeo

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Abstract

Introduction: *Pulmonary arterial hypertension (PAH) is an orphan disease, according to the Colombian Ministry of Health. Although there is evidence of studies assessing the cost of PAH in Colombia, update of the cost of illness estimation is necessary.* **Method:** *This study's objective was to estimate the annual cost of PAH in Colombia using the Colombian's Health Technology Assessment Agency methodology.* **Results:** *Clinical experts and opinion leaders consulted indicated that about 81% of the patients were in a moderate stage of the disease (FC II and III) and that the most frequent therapy is sildenafil in monotherapy or in combination. The average cost of diagnosing the disease in Colombia was US $ $2,088.23(COP $ 2,904,724.51), while the average annual treatment cost amounts to US $51,337.52(COP $71,410,480). Overall, costs and hospital admissions are higher in advanced stages of the disease.* **Conclusions:** *The results of this study indicate that even though drug therapy in PAH is expensive, administering adequate therapy can lead to an improvement in quality of life, a reduction in disease progression, hospitalizations and need for additional medication; reducing costs associated with the disease. This requires the creation of reference centers, and the dissemination of information about this pathology to health care professionals.*

Keywords: *Pulmonary arterial hypertension. Cost of illness. Colombia.*

Resumen

Introducción: *La hipertensión arterial pulmonar (HAP) es una enfermedad huérfana según el ministerio de salud colombiano. Aunque existen estudios de costo de la HAP en Colombia, es necesario una actualización del costo de enfermedad.* **Materiales y método:** *Este estudio estimó el costo anual de la HAP en Colombia utilizando metodologías de los manuales de evaluación de tecnologías.* **Resultados:** *Según la consulta a expertos clínicos y líderes de opinión alrededor del 81% de los pacientes se encontraban en estadio moderado de la enfermedad (FC II y III) y la terapia más frecuente es sildenafilo en monoterapia o combinación. El costo de diagnóstico promedio en Colombia fue de COP $2,904,724.51, mientras que el costo anual de tratamiento promedio asciende a COP $71,410,480. En general, los costos y hospitalizaciones son mayores en etapas avanzadas de la enfermedad.* **Conclusión:** *Según este estudio, aunque la medicación para el tratamiento de la HAP tiene un alto costo, administrar la terapia adecuada puede mejorar la calidad de vida, reducir la progresión de la enfermedad, las hospitalizaciones, el requerimiento de medicación adicional, llevando a reducir el costo asociado a la enfermedad. Esto requiere la creación de centros de referencia, y la difusión de información sobre esta patología a los profesionales de la salud.*

Palabras clave: *Hipertensión arterial pulmonar. Costo de enfermedad. Colombia.*

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Introduction

Pulmonary arterial hypertension (PAH) is a disease characterized by increased pulmonary vascular resistance and right ventricular dysfunction, which leads to right heart failure and death[1]. This condition is characterized by pulmonary arterial pressure (PAP) > 20 mmHg, pulmonary arterial wedge pressure ≤ 15 mmHg and pulmonary vascular resistance (PVR) ≥3 Wood units (WU)[2-4]. Vasoconstriction, inflammation, thrombosis and remodeling of pulmonary vessels are among the pathophysiological mechanisms leading to PAH[5].

In Colombia, some studies have estimated the prevalence of PAH, determining a range from 28 to 52 cases per million inhabitants[5,6]. Moreover, PAH has been regarded as an orphan disease by the Ministry of Health; therefore, patients diagnosed with PAH are covered by a special regulation that guarantees healthcare provision by the Colombian government[7].

The diagnosis of PAH usually involves imaging techniques, such as Doppler echocardiography or computed tomography for measuring PVR and pulmonary arterial wedge pressure, and the literature suggests that genetic tests are useful to rule out hereditary PAH (BMPR2 gene mutations are associated with the majority of hereditary PAH cases)[8,9]. But right heart catheterization (RHC) is required to establish the diagnosis, as it is used to measure the PAP[9]. Clinical classification and prognosis examination are usually carried out by measuring the clinical features, hemodynamic status, exercise capacity and brain natriuretic peptide[8]. In addition to the prognostic parameters mentioned above, the response to therapeutic interventions is an important variable for determining the prognosis[10,11].

Treatments are targeted to modify three key pathophysiological pathways: the endothelin-1 pathway, targeted by endothelin receptor antagonists (bosentan, ambrisentan, macitentan)[12]; the nitric oxide pathway, targeted by phosphodiesterase-5 inhibitors (sildenafil, tadalafil) and guanylate cyclase stimulators (riociguat)[13,14]; and the prostacyclin pathway, targeted by prostacyclin analogues (iloprost, treprostinil, epoprostenol) and prostacyclin receptor agonists (selexipag)[15,16]. In Colombia, only selexipag is not available.

Diagnosis, classification, treatment and follow-up are cost-generating items that, in Colombia, are assumed by the third-party payer, namely the public healthcare system (SGSSS – *Sistema General de Seguridad Social en Salud*). Some studies have tried to estimate the cost associated with PAH diagnosis and treatment in Colombia. For instance, one study conducted in 2013 estimated that the diagnostic cost of PAH was 112.52 United States dollars (USD) (217,788 Colombian pesos [COP], using the exchange rate applied in that study) per patient. For functional class (FC) I patients, the total annual disease cost per patient was 1,248.75 USD (about 2.3 million COP); it was 91,839 USD (about 174 million COP) for FC II and III patients, and 183,777.61 USD (about 349 million COP) for FC IV patients[17]. However, due to the changes in treatment protocols, especially with regards to upfront combinations and sequential approaches[18], it is pertinent for clinicians and decision-makers to analyze the current pharmacological and non-pharmacological costs of PAH treatment in Colombia. Therefore, the objective of this study was to estimate the economic burden of PAH in Colombia under the third-party payer perspective.

Methods

The following was a micro-costing study aimed at estimating the economic burden of PAH under the Colombian third-party payer perspective (SGSSS); therefore, only direct medical costs were included. In order to include all relevant costs, an initial phase of healthcare resource utilization (HCRU) estimation was conducted, followed by a cost estimation phase using recommended cost sources for economic evaluations in Colombia[19].

Healthcare resource utilization estimation

The HCRU was estimated through in-depth interviews with clinical experts. To guide these interviews, a questionnaire containing HCRU inquiries across all phases of PAH management was developed. Specifically, questions were aimed to gather data regarding diagnosis, pharmacological treatment, outpatient follow-up and inpatient treatment. Questions were elaborated based on current European Society of Cardiology (ESC) and European Respiratory Society (ERS) Guidelines for PAH treatment[3]. Clinical experts were also asked about the patient's profile, which was related to the WHO FC or ESC/ERS risk classification and tools required for diagnosis.

Micro-costing approach

The cost of each healthcare resource and drug identified in the previous phase was obtained from public sources, according to the guidelines for economic evaluations published by the national health technology assessment agency (IETS – *Instituto para la Evaluación de Tecnologías en Salud*)[18]. Costs of

Table 1. Main procedures and tests for each management step

Procedure	Quantity	Proportion	Annual cost per patient (PPP)
Diagnostic procedures			
RHC: right heart catheterization	1	100.0%	$ 452.54
Pulmonary angiography	1	100.0%	$ 284.27
Exercise RHC	1	58.5%	$ 264.64
LHC: left heart catheterization	1	70.2%	$ 150.81
Transesophageal echocardiography	1	73.7%	$ 144.86
Ventilation/perfusion (V/Q) lung scan	1	100.0%	$ 126.67
Volume loading	1	73.7%	$ 97.25
CT scan: computed tomography	1	96.5%	$ 91.07
6MWT: 6-minute walking test	1	100.0%	$ 73.71
ECG: electrocardiogram	1	88.3%	$ 64.02
Other procedures	1	-	$ 338.38
Outpatient follow-up			
RHC: right heart catheterization	2	100.0%	$ 905.07
6MWT: 6-minute walking test	4	100.0%	$ 294.86
BNP test	3	100.0%	$ 196.56
Transthoracic echocardiography	2.5	100.0%	$ 147.69
ECG: electrocardiogram	1.5	100.0%	$ 108.74
CPET: cardiopulmonary exercise test	1	100.0%	$ 73.71
Liver function tests	2.5	100.0%	$ 66.32
Medical assessment and FC determination	4	100.0%	$ 46.77
Electrolyte test	1.5	100.0%	$ 30.50
Troponin test	0.5	100.0%	$ 18.34
Other procedures	-	100.0%	$ 72.11
Adverse events			
Headache	1	60.6%	$12.24
Hypotension	1	4.1%	$0.50
Transaminase elevation	1	1.5%	$0.18
Pain at the application site	1	0.3%	$0.06
Knuckle swelling	1	0.3%	$0.04
Other outpatient treatments			
Oxygen therapy	1	63.0%	$ 279.55
Medical consultation - PAH specialist	4.6	100.0%	$ 53.90
Pneumococcal immunization	1	54.0%	$ 25.73
Physical activity and supervised rehabilitation at a hospital / specialist rehabilitation center training	1.6	100.0%	$ 28.38
Influenza immunization	1	95.00%	$ 19.56
Medical consultation - other specialists	0.9	100.00%	$ 10.29
Social assistance	1.4	100.00%	$ 7.51
Iron prescription due to anemia	1	77.00%	$ 7.50
Psychological assistance	1.2	100.00%	$ 7.10
Other healthcare professionals (e.g. nurse, nutritionist)	0.9	100.00%	$ 4.76

procedures, hospitalizations and consultations were obtained from the ISS tariff manual[20] plus a 30% increment, according to the IETS guidelines. Drug costs were obtained from the SISMED database. Cost is expressed in 2022 USD adjusted by purchasing power parity (PPP), since this measure is less sensitive to supply and demand changes. In 2022, 1 PPP-adjusted USD was equivalent to 1,390.99 COP. The following categories were considered in this analysis: diagnosis, outpatient follow-up, other outpatient treatments, hospital admissions, adverse events (AEs) and pharmacological treatment.

Results

Four pulmonologists were interviewed, with an average of 18 years of experience in treating PAH, comprising a universe of 342 patients with the disease treated. In the physicians' practice, most of the patients had idiopathic PAH (170 [49.7%]), followed by PAH associated with congenital heart disease (74 [21.6%]) and PAH associated with connective tissue disease (44 [12.9%]); this reflects the excellence center and high complexity setting in which the interviewed PAH experts work. With regard to the FC distribution of the patients, 21 (6%), 154 (45%),

123 (36%) and 44 (13%) of the patients were in FC I, II, III and IV, respectively, indicating that most patients are diagnosed in moderate stages of the disease.

The annual diagnostic cost was estimated at 2,088.23 USD, with RHC and pulmonary angiography being the costliest procedures at this stage. The average annual outpatient follow-up cost was estimated at 1,960.68 USD, almost half of which was related to RHC. In contrast, the annual cost of other outpatient treatments was estimated at 444.27 USD and was mainly related to oxygen therapy. On the other hand, the total annual AE cost per patient was 13.28 USD, with headaches constituting the main cost-generating event (Table 1).

Hospital admissions, cost and length of stay (LoS) were found to be different between the FC stages (Fig. 1). For instance, LoS for FC II patients was 7.5 and 4.0 days in the general ward (GW) and intensive care unit (ICU), respectively. Similarly, in FC III patients, LoS was 6.3 and 4.5 days in the GW and ICU, whereas LoS in FC IV patients was 11.0 and 12.8 days in the GW and ICU, respectively. The clinical experts reported no hospital admissions for FC I patients.

With regard to the PAH-specific pharmacological therapy, the data suggests that across all FCs, patients are mostly treated with dual combination therapies; 5 (23.8%), 8 (38.1%) and 8 (38.1%) of the FC I patients were treated with monotherapy, upfront combinations, and sequential approaches, respectively. In the case of FC II patients, this proportion was 46 (30%), 83 (54%) and 25 (16%), respectively. In FC III patients, this split was 16 (13%), 72 (59%) and 35 (28%), whereas all 44 FC IV patients were receiving upfront combinations. Therefore, upfront combinations appear to be the preferred option in combination therapy.

Moreover, sildenafil (both in monotherapy and combination therapy) is by far the most frequent pharmacological treatment prescribed across all FC stages, followed by endothelin receptor antagonists (Fig. 2). Overall, PAH-specific pharmacological treatment accounted for about 89% of the disease cost, which, on average, was 51,337.52 USD per patient (Fig. 3). Adjuvant treatment was comprised mainly of anticoagulants, diuretics and digoxin and had little impact on the overall disease cost.

Inpatient costs appear to be an important source of non-pharmacological costs for FC IV patients (Fig. 4).

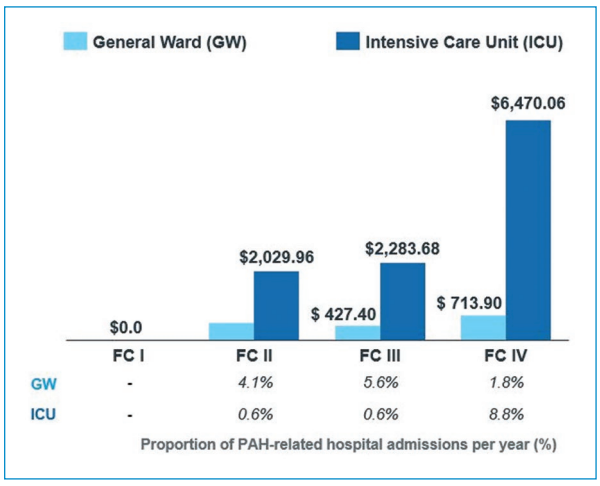

Figure 1. Average hospitalization costs per patient.

Discussion

Pulmonary arterial hypertension diagnosis requires a multidisciplinary approach, comprising, at least, cardiology, pulmonology, RHC and imaging[3], as the main identified procedures show. Moreover, centers of excellence within healthcare institutions are required to ensure an adequate and timely diagnosis and disease follow-up.

On the other hand, screening of at-risk patients can lead to more timely diagnoses and early initiation of pharmacological therapy, which is associated with better outcomes and quality of life[21]. An active screening approach has already been used in Colombia, leading to the identification of pulmonary hypertension in 25% of the patients with systemic sclerosis, 51% of the patients with end-stage kidney disease and 27.9% of the patients with cirrhosis and an indication for liver transplant[22]. This study shows that, in this sample of the Colombian population with PAH, 49% of the patients are in FC III and IV, which can be considered as moderate to advanced stages of the disease. This indicates that patients are still diagnosed in advanced stages of the disease (in which the prognosis is worse and the costs of inpatient and outpatient treatment are greater), thus highlighting the importance of early diagnosis and screening in populations and groups with known risk factors, which is associated with improved long-term survival[21,23]. Even though this study showed that RHC was responsible for the high cost of PAH diagnoses, it plays an important role in diagnostic certainty and timeliness, which enables more adequate pharmacological treatment and less likelihood of disease progression, which in turn allows for a better management of healthcare resources. Nevertheless, in order to achieve these diagnostic goals, centers of excellence should be implemented within healthcare institutions so as to deliver care expertise in a comprehensive and interdisciplinary fashion[24].

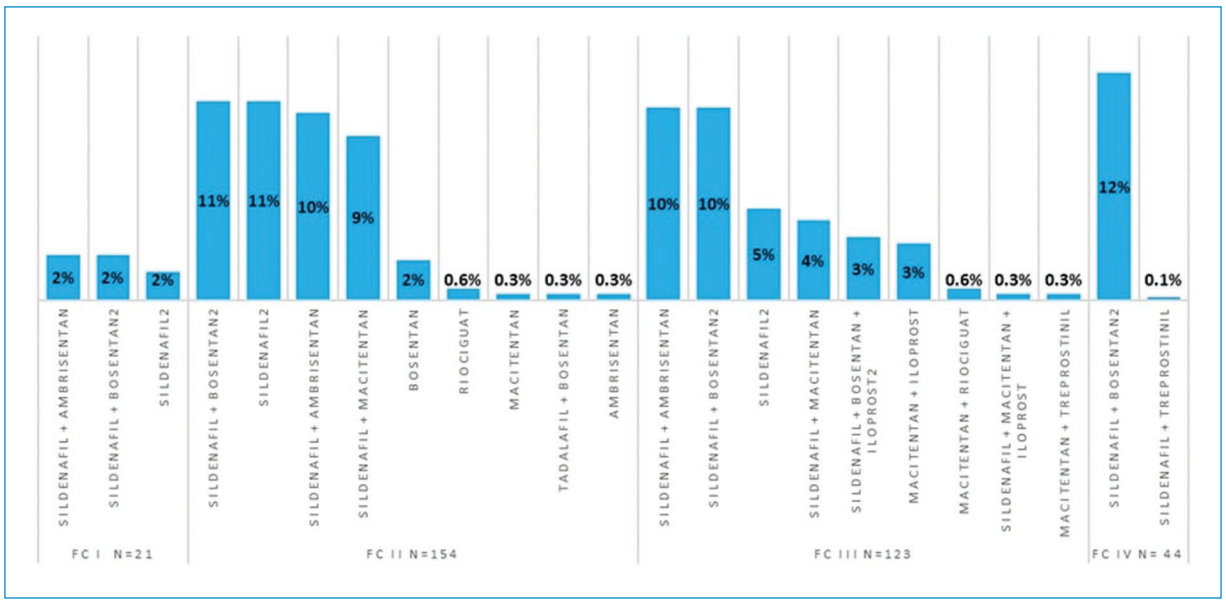

Figure 2. Pharmacological treatment distribution across all FC stages.

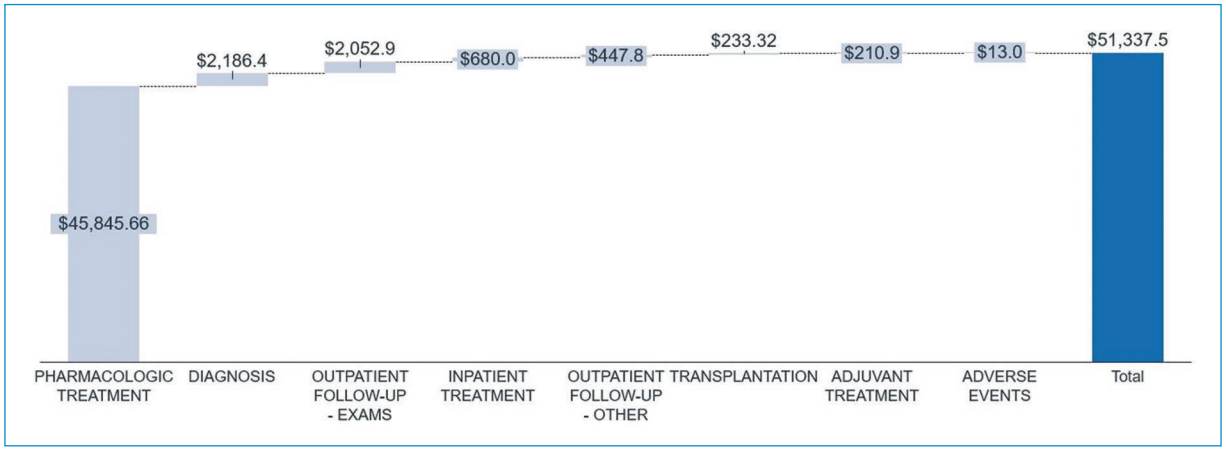

Figure 3. Average annual cost of PAH per patient.

Results also show that, regardless of the functional class, most patients currently receive combination therapy, as recommended by the expert consensus guidelines, with a lower percentage of patients treated with sequential combination therapy and monotherapy. This percentage decreases as the functional class worsens, with only 13% of patients in FC III receiving monotherapy, while 30% of the patients in FC II received this therapy and no class IV patients received it. Sequential therapy is mostly used in FC I, where it is just as frequent as upfront combinations (38%). Moreover, in FC IV patients, only 9.1% were receiving parenteral prostacyclin analogues, whereas the other 90.9% were treated with sildenafil + an endothelin receptor antagonist. This contrasts remarkably with what is currently recommended in the clinical guidelines, which state that patients in FC IV should start receiving IV or SC prostacyclin analogues[3].

Finally, the limitations of this study are related to its design and data sources, since the universe of patients explored was a small non-randomly selected subset of the national population diagnosed with PAH. Thus, we cannot ensure that it is representative of the Colombian PAH landscape. On the other hand, since this is a study based mainly on expert opinion, clinical practice bias is highly represented in proportion and HCRU

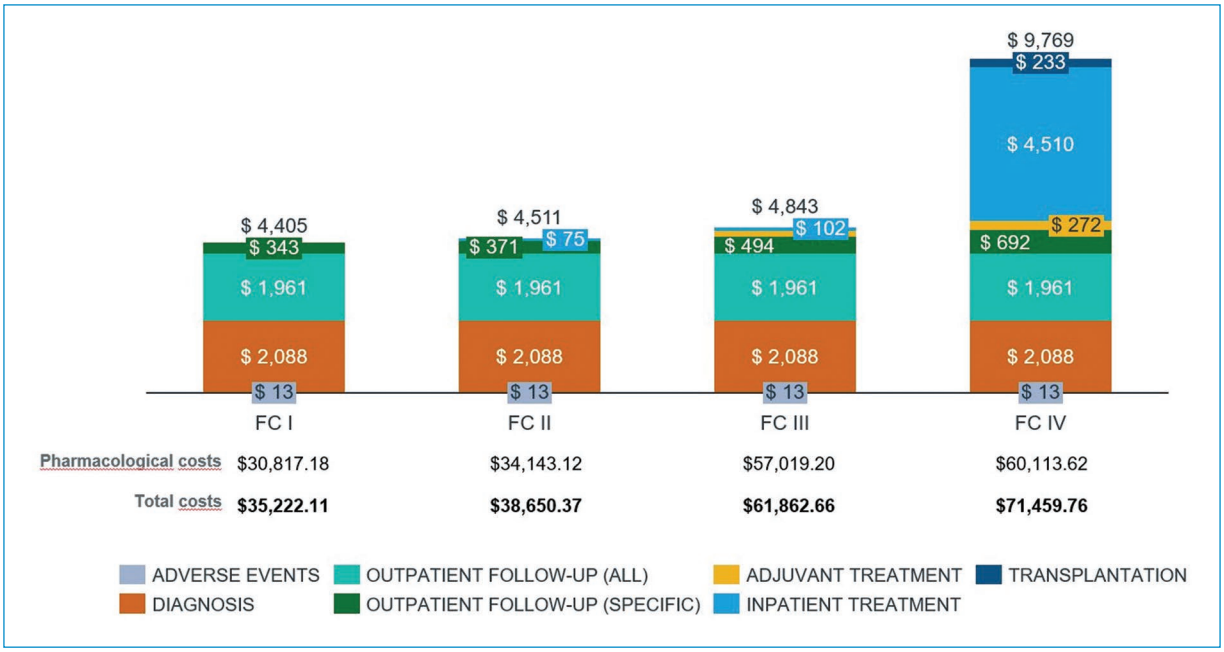

Figure 4. Components of non-pharmacological costs.

estimates; therefore, it is likely that treatment patterns and other HCRUs are not representative of the national clinical practice. Finally, as this study was conducted before the 2022 ESC/ERS updated guidelines[4], patient stratification and results were presented in accordance with the 2015 guidelines[3].

Conclusions

This study shows that patients are diagnosed in FC III and IV, which are moderate to advanced stages of the disease; as the disease progresses, hospitalization costs escalate, and in FC IV, the length of hospital stays as well as the ICU requirement are higher. Although drug therapy in PAH is expensive, its utilization is justified as it is effective in improving survival and quality of life and displays a reasonable safety profile. Hence, it is paramount that the right patients receive the right therapy, and that timely follow-up and therapy management is conducted in order to avoid adverse outcomes such as hospitalizations, the need for additional medications, transplantations and, less frequently, death. Nevertheless, this is an initial approach to unveil a commonly unknown reality of a low prevalence disease in Colombia.

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Conflicts of interest

Fabián Hernández, Julieta Larrosa, Jéssica Nacazume, Claudio Villaquirán, Rafael Conde, Catalina Rozo, Sarah Franco-Watanabe, Jorge Álvarez, and André Morais received grants from Janssen Pharmaceuticals during the study. Catalina Rozo, Jorge Álvarez, André Morais declare that they work for Janssen Pharmaceuticals.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Data confidentiality. The authors declare that no patient data appear in this article.

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ORIGINAL ARTICLE

Cardiac autonomic neuropathy in diabetic patients: An analytical cross-sectional study

Neuropatía autonómica cardiaca en diabéticos: estudio transversal analítico

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Abstract

Introduction: *Cardiac autonomic neuropathy is a little known and underdiagnosed condition in diabetic patients, characterized by damage to autonomic nerve fibers causing symptoms such as exercise intolerance and postural hypotension; the prevalence and risk factors in the Colombian diabetic population are unclear and understudied.* **Objective:** *To determine the prevalence of cardiac autonomic neuropathy and associated factors in diabetic patients in a Colombian population.* **Materials and method:** *This was an analytical cross-sectional study, in a population of 107 patients with type I and type II diabetes mellitus who were seen at a secondary care hospital in Colombia between April and September 2022. The diagnosis was made using the Ewing cardiovascular autonomic reflex tests. Descriptive and associative statistical analyses were performed using logistic regression, calculating odds ratios and 95% confidence intervals.* **Results:** *The study population had a mean age of 62 years, with 56.1% being women. Altogether, 94.4% (95% CI: 89.9-98.6) of the participants had a positive cardiac autonomic neuropathy test; 6.5% had early involvement, 26.2% had definite involvement and 61.7% had severe involvement; age is associated with the onset of cardiac autonomic neuropathy, aOR: 1.07 (95% CI: 1.03-1.11).* **Conclusions:** *The current study found a high prevalence of cardiac autonomic neuropathy (94.4%) when using the diagnostic gold standard. Patient age was associated with the presence and severity of this disease.*

Keywords: *Diabetes mellitus. Risk factors. Diabetic neuropathy.*

Resumen

Introducción: *La neuropatía autonómica cardíaca es una entidad poco conocida y subdiagnosticada en los pacientes diabéticos, la cual se caracteriza por el daño de las fibras nerviosas autónomas; ocasiona síntomas como intolerancia al ejercicio e hipotensión postural. La prevalencia y los factores de riesgo en la población diabética colombiana son poco claros y poco estudiados.* **Objetivo:** *Determinar la prevalencia de la neuropatía autonómica cardíaca y de los factores asociados en pacientes diabéticos de una población colombiana.* **Materiales y método:** *Estudio transversal analítico, en una población de 107 pacientes con diagnóstico de diabetes mellitus tipos I y II, que consultaron a un hospital de segundo nivel de atención en Colombia, entre abril y septiembre de 2022. Se realizó diagnóstico utilizando el test de Ewing de reflejo autonómico cardiovascular. Los análisis estadísticos fueron del orden descriptivo y de asociación mediante regresión logística calculando razón de disparidad e intervalos de confianza del 95%.*

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Resultados: *La población estudiada tuvo una edad promedio de 62 años; el 56.1% fueron mujeres. El 94.4% (IC 95%: 89.9-98.6) de los participantes presentaron una evaluación positiva para neuropatía autonómica cardíaca; el estado incipiente fue del 6.5%, la afectación confirmada del 26.2% y el compromiso grave del 61.7%. La edad está asociada con la aparición de neuropatía autonómica cardíaca (ORa: 1.07; IC 95%: 1.03-1.11).* **Conclusiones:** *Este estudio encontró alta prevalencia de neuropatía autonómica cardíaca (94.4%) cuando se utilizó el estándar de oro de diagnóstico. La edad de los pacientes tiene asociación con la presencia y la gravedad de esta enfermedad.*

Palabras clave: *Diabetes mellitus. Factores de riesgo. Neuropatía diabética.*

Introduction

Diabetes mellitus (DM) is a chronic disease which places a heavy burden on healthcare systems around the world. Its increased prevalence is concerning; in 2019, an estimated 500 million people had diabetes, and a 25 and 51% increase is predicted for 2030 and 2045, respectively[1].

The risk of morbidity and mortality is high, and it causes microvascular and macrovascular complications like peripheral artery disease, coronary disease, cerebrovascular accidents, heart failure, diabetic retinopathy, kidney disease and the little-known but very important cardiac autonomic neuropathy[1-6].

This last condition is characterized by damage to the autonomic nerve fibers that innervate the heart and blood vessels, leading to abnormal cardiovascular physiology both at rest and during exercise[7,8]. The most common clinical manifestations include resting tachycardia, exercise intolerance, orthostatic hypotension, syncope, intraoperative cardiovascular instability, silent myocardial infarction and ischemia. Despite its severe repercussions, cardiac autonomic neuropathy is a diabetic complication that is often overlooked and underdiagnosed[9,10].

Diabetes-induced cardiovascular autonomic neuropathy is a result of complex interactions, particularly glycemic control, disease duration, systolic and diastolic blood pressure, and neuronal death; the latter related to aging[7,8]. The Subcommittee of the Toronto Consensus Panel on Diabetic Neuropathy defines cardiac autonomic neuropathy as an impairment of cardiovascular autonomic control in patients with confirmed diabetes, after ruling out other causes[11,12].

In 1978, Ewing et al. published five non-invasive tests to measure cardiovascular autonomic changes based on the heart rate and blood pressure response to certain physiological maneuvers, to analyze sympathetic and vagal function. The tests are known as cardiovascular autonomic reflex tests (CARTs) and are considered the gold standard. These standardized tests are known as cardiovascular autonomic reflex tests (CARTs); they are simple, sensitive, specific and reproducible tests that are considered the gold standard for evaluating cardiovascular autonomic changes in response to simple clinical maneuvers[7,9,13,14].

There is a wide variety of literature on the epidemiology of cardiovascular autonomic neuropathy in diabetic patients, with prevalence rates ranging from 1.6% in patients with controlled diabetes up to 90% in patients waiting for a pancreatic transplant, with an average prevalence of 60%[9,15]. In Colombia, the cross-sectional study by Mendivil et al.[13] evaluating Neuropad® for detecting cardiac autonomic neuropathy in patients with type 2 DM recorded a 68% prevalence. The differences in cardiac autonomic neuropathy prevalence figures are due to factors like age, duration of the diabetes, and poor glycemic control, as well as the association with distal symmetrical polyneuropathy and microangiopathy[14,15].

Based on the limited information in our country's literature, and the wide variety in the prevalence of cardiac autonomic neuropathy and its associated risk factors, it is important to establish strategies for screening, diagnosing and treating this disease, in order to have a positive impact on the cardiovascular risk, mortality, reduction in relapses and hospital admissions, improved cardiopulmonary function, quality of life and prognosis of patients with DM[16]. Therefore, the objective of this study was to determine the prevalence and factors related to cardiac autonomic neuropathy in diabetic patients at a secondary care hospital in Colombia.

Materials and method

A cross-sectional analytical study was carried out from April to September 2022. The study population comprised people with type I and II DM who were seen at a secondary care hospital in Colombia.

Patients over the age of 18 who were diagnosed with type I and II DM as defined by the American Diabetes Association (ADA) 2021[17] were included. On the other hand, those with a diagnosis of neuropathy (like dorsolumbar and cervical spine injuries), cerebrovascular

accidents [CVAs], or Guillain-Barré syndrome), severe valve disease, a history of neurocardiogenic syncope, Parkinson's, or kidney failure, as well as pregnant women and patients with physical limitations, were excluded.

The open access OpenEpi program was used to calculate the sample size, considering an average prevalence of cardiac autonomic neuropathy of 60%[9,14], a 95% confidence interval and 10% estimated losses to obtain a sample of 107 participants through a non-probability convenience sample.

The study was approved by the hospital's Institutional Ethics Committee and the university's Ethics and Bioethics Committee (RECT-145/2022). Informed consent was also obtained from all participants. Furthermore, this study adheres to the current national and international clinical research norms derived from the Declaration of Helsinki[18].

Procedures

A pretest survey was applied to select the participants, analyzing prior conditions in the clinical history such as glycosylated hemoglobin values, glycemia, duration of diabetes and the selection criteria regarding previous medical conditions. Then, participants were scheduled for a medical-clinical assessment to collect sociodemographic information, anthropometric measurements like waist-hip ratio and body mass index, and hemodynamic variables like heart rate (HR), blood pressure and resting oxygen saturation. Subsequently, the standardized diagnostic assessment was performed with sympathetic and parasympathetic function tests using Ewing's CARTs[19], which measure beat-to-beat HR variability and the HR response to standing, as well as the systolic blood pressure response to standing and diastolic blood pressure response to isometric exercise[7,9]. Cardiac autonomic function was evaluated using a Welch Allyn® CardioPerfect® REF: SE-PRO 600 multiparameter electrocardiograph machine manufactured by Welch Allyn Inc., Skaneateles Falls, NY, USA, as well as a Baseline 200 LB Standard Head Hydraulic Hand Dynamometer, manufactured by Enterprises Inc, NY, USA. The tests were performed in the morning, in a calm setting, with a constant temperature between 22 and 24 °C. All procedures were performed by qualified medical staff.

The CARTs assessment was classified according to the following scale:

1. Normal (no abnormalities)
2. Early involvement when there was an abnormal HR test or two borderline results.
3. Confirmed involvement with two or more abnormal results.
4. Severe involvement with orthostatic hypotension.

First, a descriptive statistical analysis was performed according to the degree of severity of the phenomenon (normal, early, confirmed, or severe involvement); qualitative variables were described using absolute and percentage frequencies, and quantitative variables were expressed as means and standard deviation, since the Shapiro-Wilk test indicated that they were normally distributed. Second, to evaluate the association between cardiac autonomic neuropathy and the variables of interest, bivariate and multivariate regression models were developed which evaluated significance using the 95% confidence interval. The analyses were run using the SPSS 25.0 statistical program.

Results

The study population consisted of 107 patients, 56.1% of whom were women and 43.9% men, with an average age of 62 years. A total of 48.6% had a normal weight and most had a primary education (61.7%). There was a predominance of type II diabetes, the average time elapsed since diagnosis was 11 years, and 69.2% were insulin dependent (Table 1).

Altogether, 94.4% (95% CI: 89.9-98.6) of the participants had cardiac autonomic neuropathy, of whom 6.5% had early involvement, 26.2% had definite involvement and 61.7% had severe involvement.

Six patients did have a normal cardiovascular autonomic response, with an average duration of the disease of 3.7 ± 2.7 years. Considering the severity of the cardiac autonomic neuropathy, 63% of type II diabetic patients had acute involvement, as did 66.7% of women. The level of education was low (67.1%) and 64.3% had no marital partner (single, widowed or divorced). The patients with severe cardiac autonomic neuropathy had an average age of 65.5 years, compared with 39.4 years for those with early disease. The duration (in years) of diabetes was longer in those with greater cardiovascular autonomic response involvement. The average glycosylated hemoglobin level was not significantly different; however, poor glycemic control was found in all groups with cardiac autonomic neuropathy. The predominant body mass index category in the study population was overweight. The waist-hip ratio (WHR) was not markedly different (Table 2).

The evaluation of cardiac autonomic function highlighted that the immediate HR response to standing (a parasympathetic autonomic function test for

Table 1. Sociodemographic and clinical characteristics of the study population

Sociodemographic variables	n (%)
Sex	
Male	47 (43.9)
Female	60 (56.1)
Level of education	
No schooling	7 (6.5)
Primary	66 (61.7)
Secondary	18 (16.8)
Technical	14 (13.1)
Professional	2 (1.9)
Marital status	
Married	62 (57.9)
Divorced	2 (1.9)
Single	37 (34.6)
Cohabiting	3 (2.8)
Widowed	3 (2.8)
Occupation	
Homemaker	34 (31.8)
Unemployed	10 (9.3)
Employee	12 (11.2)
Student	3 (2.8)
Freelancer	45 (42.1)
Retired	3 (2.8)
Type of diabetes	
Type I	7 (6.5)
Type II	100 (93.5)
Body mass index	
Underweight	7 (6.5)
Normal weight	52 (48.6)
Overweight	36 (33.6)
Obesity	12 (11.2)
Age (years) *	62 (15)
Glycosylated hemoglobin %*	9.03 (2.0)
Time elapsed since diabetes diagnosis (years) *	11.9 (8.5)

*Mean (SD).

cardiovascular control) was abnormal in 83.2% of the patients, with an equal percentage of patients having an abnormal sympathetic autonomic function test (BP response, specifically changes in diastolic pressure response).

Table 3 shows the regression model for cardiac autonomic neuropathy, indicating that this was associated with age, with an adjusted odds ratio (aOR) of 1.07 (95% CI: 1.03-1.11).

Discussion

The objective of this study was to determine the prevalence of, and factors related to, cardiac autonomic neuropathy in diabetic patients at a secondary care hospital in Colombia. The main finding was a high prevalence of cardiac autonomic neuropathy, in 94.4% of the diabetic patients enrolled, diagnosed using what is currently considered to be the diagnostic gold standard. A second important finding was that older age is related to cardiac autonomic neuropathy.

The prevalence of this disease varies depending on the study and ranges from 2 to 91% in type I DM and from 25 to 75% in type II DM. Our study found a higher percentage than what has been published thus far in the literature. It is important to bear in mind that the wide variation in epidemiological data may depend on the study population and diagnostic test employed[8-10,13,14]. However, cardiac autonomic neuropathy is probably an underdiagnosed debilitating condition in patients with diabetes.

Pan et al.[15] reported lower cardiac autonomic neuropathy prevalences than those found in our study. In a multicenter cross-sectional study, they found that the prevalence for type I diabetics was 61.6%, while for type II diabetics it was 62.6%[15]. Likewise, a cross-sectional study by Dhumad et al.[19] at the University of Al-Nahrain in Baghdad, Irak, on the "The correlation of stratification and risk factors with cardiovascular autonomic neuropathy in patients with type II diabetes mellitus" (published in Scientific Reports in 2021[19]) reported a 52.82% prevalence of cardiac autonomic neuropathy.

In Colombia, despite limited studies on cardiac autonomic neuropathy, researchers like Mendivil et al.[13] found a prevalence of 68% in a cross-sectional study using Neuropad® to detect cardiac autonomic neuropathy in patients with type II DM.

We repeat that these different findings in the literature may be due to the diagnostic criteria for cardiac autonomic neuropathy, the size of the patient sample, the duration of the disease and the clinical and demographic characteristics of the study population in our study.

Regarding the association between risk factors and cardiac autonomic neuropathy, our study showed a trend (but without statistical evidence) toward a higher prevalence of cardiac autonomic neuropathy in female diabetic patients, people with a low level of education and those who are single, divorced or widowed. The time elapsed since the diabetes diagnosis, glycemic control (percentage of glycosylated hemoglobin and baseline blood sugar) and body mass index were also higher.

Table 2. Sociodemographic and clinical characteristics according to cardiac autonomic neuropathy status

Variables	Normal n = 6 (5.6%)	Early involvement n = 7 (6.5%)	Definitive involvement n = 28 (26.2%)	Severe involvement n = 66 (61.7%)
Sex n (%)				
Female	3 (5.0)	4 (6.7)	13 (21.7)	40 (66.7)
Male	3 (6.4)	3 (6.4)	15 (31.9)	26 (55.3)
Level of education n (%)				
No education/Primary	1 (1.4)	4 (5.5)	19 (26.0)	49 (67.1)
Secondary/Technical/Professional	5 (14.7)	3 (8.8)	9 (26.5)	17 (50.0)
Marital status n (%)				
Single/Widowed/Divorced	3 (7.1)	4 (9.5)	8 (19.0)	27 (64.3)
Married/Cohabiting	3 (4.6)	3 (4.6)	20 (30.8)	39 (60.0)
Type of diabetes n (%)				
Type I	2 (28.6)	2 (28.6)	0	3 (42.9)
Type II	4 (4.0)	5 (5.0)	28 (28.0)	63 (63.0)
Quantitative variables $\bar{x}$ [sd]				
Age years	38.2 (11.7)	39.4 (14.9)	63.7 (12.4)	65.6 (14)
Duration of diabetes (years)	3.7 (2.7)	6.3 (5.3)	13.9 (9.0)	12.4 (8.4)
Glycosylated hemoglobin (%)	9.0 (2.8)	10.3 (2.4)	8.6 (2.04)	9.1 (1.9)
Glycemia mg/dl	243.2 (185)	388.0 (117)	268.4 (118)	256.2 (110)
BMI kg/m^2	25.5 (3.8)	20.9 (3.1)	25.5 (4.3)	25.1 (4.7)
Waist-hip ratio	1.1 (0.05)	1.00 (0.08)	0.97 (0.07)	1.00 (0.08)

Table 3. Multivariate analysis of the sociodemographic and clinical characteristics and cardiac autonomic neuropathy

Variables	Simple model OR (95% CI)	Adjusted model* aOR (95% CI)
Sex		
Female	1.52 (0.71-3.26)	1.38 (0.61-3.15)
Male	Reference	Reference
Level of education		
No schooling/Primary	**2.45 (1.09-5.52)**	1.27 (0.50-3.18)
Secondary/Technical/Professional	Reference	Reference
Marital status		
Single/Widowed/Divorced	1.04 (0.47-2.29)	1.55 (0.63-3.81)
Married/Cohabiting	Reference	Reference
Type of diabetes		
Type I diabetes	Reference	Reference
Type II diabetes	**5.83 (1.18-28.9)**	0.38 (0.05-3.05)
Quantitative variables		
Age	**1.06 (1.03-1.09)**	**1.07 (1.03-1.11)**
Duration of diabetes	1.04 (0.99-1.09)	0.98 (0.92-1.04)
Glycosylated hemoglobin	1.00 (0.82-1.20)	1.11 (0.90-1.37)
Glycemia	1.00 (0.99-1.01)	1.00 (0.99-1.01)
BMI	1.03 (0.94-1.12)	1.02 (0.93-1.12)
Waist-hip ratio	1.02 (0.96-1.07)	1.03 (0.98-1.09)

*Model adjusted by age, type of diabetes and level of education.
Significant values are shown in bold type.

As far as age, Dhumad et al.'s[19] study showed a non-significant difference in the mean age of diabetics with and without cardiac autonomic neuropathy. In contrast, our study showed that the age of diabetic patients is associated with cardiac autonomic neuropathy evaluated in the adjusted model, with an OR: 1.07 (95% CI: 1.03-1.11). The increased prevalence of cardiac autonomic neuropathy with age in diabetics can be attributed

to the fact that these patients often have a long asymptomatic history, during which blood sugar peaks go unnoticed, without the disease being diagnosed or treated.[6] It is interesting to note that, just as in Dhumad et al.'s[19] study, women had a higher prevalence of cardiac autonomic neuropathy than men, which was not statistically significant.

Likewise, it should be noted that not all cardiovascular disease risk factors are associated with Ewing's score. However, Osailan's[20] cross-sectional study on cardiac autonomic neuropathy in people with type II diabetes and its association with cardiovascular risk factors in a group of 26 people at the Brierley Hill Health and Social Care Centre, Dudley, United Kingdom (published in December 2021), showed that the Ewing score was positively associated with resting SBP and inversely associated with cardiorespiratory fitness (CRF) (measured through peak VO_2)[20]. Similar to Osailan's study[20], our study reported a trend towards an association between a high SBP and DBP response and cardiac autonomic neuropathy. The correlation between SBP and cardiac autonomic neuropathy can be explained by the role of dominant sympathetic activity over parasympathetic activity in elevated blood pressure[9,21,22].

It is notable that our study did not find a statistically significant correlation between several risk factors and Ewing's scores. This is in line with the reports of other studies that analyze BMI as a cardiovascular risk factor, along with WHR[19,20]. The lack of correlation between BMI and WHR in this study is probably due to the sample size, the difference in study populations (type I and II diabetic patients, with different ages and sex) and the use of medications to control cardiovascular factors. This last item was not analyzed in this study, and therefore hypotheses are generated, and more studies must be done to clarify these parameters, where possible.

Unlike Dhumad et al.'s study[19], our study found that parasympathetic and sympathetic function analysis is necessary to identify autonomic dysfunction. In addition, the values of these two variables are altered or abnormal in 83.2% of the patients, which highlights the importance of evaluating both the HR response as well as the blood pressure response to stimuli during Ewing's tests. Reports have related the presence of cardiac autonomic neuropathy with two abnormal tests to higher CVD mortality rates[6,20]. Therefore, it is important to promptly and appropriately identify its related risk factors to help healthcare professionals mitigate these factors and implement strategies like professionally prescribed structured exercise programs, a nutrition plan, changes in eating habits, and smoking cessation, among other measures, to lower the risk of the disease and prevent future mortality.

From what is known in our country's literature, this is the first study to employ a cross-sectional methodology to analyze the behavior of the cardiovascular autonomic response and associated factors in type I and II diabetic patients, using standardized diagnostic assessment with sympathetic and parasympathetic function tests through Ewing's CARTs, showing a high prevalence of diabetic patients with abnormalities.

The study has some limitations due to its cross-sectional design which does not allow causal inferences between the variables. Another limitation is the study sample which included patients with diabetes from a single healthcare center, which affects the power of the statistical results and association of the variables.

It is important for future studies to expand the analyzed sample to include the analysis of other factors like medication consumption and the cardiorespiratory fitness response to exercise, with a cohort or case-control methodology.

Conclusions

This study found a prevalence of cardiac autonomic neuropathy as high as 94.4%, which indicates the DM-induced impairment, as well as a greater chance of having this neuropathy with increasing age. There was a trend toward an association between cardiac autonomic neuropathy and prevalence in women, people with a low educational level and being single, divorced or widowed, but without statistical evidence. Both sympathetic and parasympathetic impairment were found to be sensitive in detecting autonomic dysfunction.

Cardiac autonomic neuropathy is an important manifestation of DM involvement and is substantially associated with multiple sociodemographic, lifestyle and patient-specific conditions. Even knowing that cardiac autonomic neuropathy is a significant complication, its importance has not been completely clarified in clinical and academic settings, and it continues to fall within the field of research.

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Conflicts of interest

The authors have no conflicts of interest.

Ethical responsibilities

Human and animal protection. The authors declare that no experiments were conducted on humans or animals for this study.

Data confidentiality. The authors declare that they have followed their workplace protocols for patient data publication.

Right to privacy and informed consent. The authors have obtained informed consent from the patients and/or subjects referred to in this article. The corresponding author is in possession of this document.

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ORIGINAL ARTICLE

Heart valve replacement in Colombia: An analysis of official records

Reemplazo valvular cardíaco en Colombia: un análisis de los registros oficiales

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Abstract

Introduction: *Colombia is among the leading countries in cardiology and cardiovascular medicine in Latin America. The current demographic transition has generated greater demand for cardiovascular surgery procedures; however, with the COVID-19 pandemic situation, this has changed.* **Objective:** *to describe the demographic characteristics of patients undergoing heart valve replacements in Colombia.* **Materials and method:** *a descriptive cross-sectional study of data from the Sistema Integrado de Información de la Protección Social (SISPRO) [Integrated Social Protection Data System], taking into account the Clasificación Única de Procedimientos en Salud (CUPS) [Single Classification of Healthcare Procedures] in the category "Heart valve replacements" from 2017 - 2021.* **Results:** *10,023 heart valve replacements were performed, with a 3:2 male to female ratio, and 55% corresponded to the 60-79-year-old age group. There was a 23% reduction during the mandatory quarantine due to the pandemic. There was no significant difference between the contributory and subsidized health insurance regimens. The territorial entities with the most procedures were Bogotá, Valle del Cauca, Antioquia and Cundinamarca. The institution that performed the most procedures was Fundación Cardio Infantil in Bogotá.* **Conclusions:** *demographic and epidemiological information from SISPRO on heart valve replacements from 2017 to 2021 was reported.*

Keywords: *Colombia. COVID-19. Cardiovascular surgical procedures. Heart valves.*

Resumen

Introducción: *Colombia está entre los países líderes en cardiología y medicina cardiovascular en Latinoamérica. La transición demográfica actual ha generado mayor demanda de procedimientos de cirugía cardiovascular; sin embargo, con la situación de pandemia por la COVID-19, esta se vio afectada.* ***Objetivo:*** *describir las características demográficas de los pacientes sometidos a reemplazos valvulares cardíacos en Colombia.* **Materiales y método:** *estudio descriptivo de corte transversal, en el que se tomaron datos del Sistema Integrado de Información de la Protección Social (SISPRO) teniendo en cuenta la Clasificación Única de Procedimientos en Salud (CUPS) de la categoría «Reemplazos valvulares cardíacos» durante el período 2017 a 2021.* **Resultados:** *se realizaron 10.023 reemplazos valvulares cardíacos, con una relación hombres y mujeres de 3:2; el 55% correspondió al grupo etario entre 60 y 79 años. Se presentó una disminución del 23% durante el aislamiento obligatorio por la pandemia. No hay diferencia significativa entre el régimen contributivo y el subsidiado. Las entidades territoriales con más procedimientos fueron Bogotá, Valle del Cauca, Antioquia y Cundinamarca. La institución que más procedimientos realizó fue la Fundación Cardioinfantil de Bogotá.*

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Conclusiones: *se reportó información demográfica y epidemiológica de reemplazos valvulares cardíacos desde 2017 a 2021 del SISPRO.*

Palabras clave: *Colombia. COVID-19. Procedimientos quirúrgicos cardiovasculares. Válvulas cardíacas.*

Introduction

Cardiovascular surgery is a dynamic medical specialty that evolves with the rapid development of new technologies like extracorporeal membrane oxygenation, minimally invasive cardiac surgery, percutaneous procedures, or robotic heart surgery[1]. The leading countries in cardiology and cardiovascular medicine in Latin America include, in order, Brazil, Mexico, Argentina and Colombia[2]. This surgical discipline has developed rapidly in our country. According to the Sistema Nacional de Información de la Educación Superior (SNIES) [National Higher Education Data System], Colombia has six cardiovascular surgery training programs, two in Medellín and four in Bogotá[3]. In contrast with other Latin American countries like Brazil (where, citing epidemiological reasons, it was decided that general surgery and cardiovascular surgery needed to be separated, and a five-year training program is offered), two to three-year fellowship or super specialty programs are offered in Colombia, after obtaining a general surgery degree[4].

Older adults are the fastest-growing demographic group in western countries, and Latin America in particular[5]. The global population of people over the age of 65 is expected to increase from 10% in 2022 to 16% in 2050, when it is expected that the number of people 65 years old or older in the world will be more than double the number of children under the age of five[6]. This is important since it is estimated that 25% of those over the age of 75 have cardiovascular disease, which creates a higher demand for cardiovascular surgery procedures[7]. In this age group, the high-risk patients benefit the most from less invasive options[8].

In the early days of cardiovascular surgery, research focused on extracorporeal circulation[9]. Animal experiments explored oxygenators, blood pumps, tubes and cardioplegic solutions to maintain circulation and, at the same time, cause the least possible disturbance to blood and organ functions. With the development of modern molecular biology and genetic techniques, research in cardiac surgery, as in other disciplines, embarked on a new era[10].

With the healthcare system reform instituted by Law 100 of 1993, the Ministry of Health began to strengthen its centralized data system, known as Sistema Integrado de Información de la Protección Social (SISPRO) [Integrated Social Protection Data System][11,12]. One of SISPRO's components is the individual service provision record (RIPS, in Spanish), which has been widely used to estimate the prevalence of many rheumatologic diseases like rheumatoid arthritis[13] or Sjögren's disease[14]. Another SISPRO component is the Clasificación Única de Procedimientos en Salud (CUPS) [Single Classification of Healthcare Procedures], created to organize and arrange the procedures performed by all the different members of the system throughout the country, both public and private[15]. There is less research using CUPS than using RIPS. One example of the use of CUPS in research is the measurement of the effect of the COVID-19 pandemic on radiology procedures throughout the country[16]. The goal of this study was to review and analyze the national CUPS statistics corresponding to surgical heart valve replacement procedures, providing a description of both the patients undergoing the procedures as well as the healthcare institutions where the procedures were performed.

Materials and method

Using the Microsoft Excel program and Dynamic Tables tool, the SISPRO cubes were remotely accessed using the personal username and password of one of the researchers (DR). Data extraction was done under "CUPS classification," "surgical procedures and interventions," "circulatory system," "heart valve procedures," and "heart valve replacements." The following codes were selected from this last category: 3520: pulmonary valve replacement; 3521: aortic valve replacement; 3522: mitral valve replacement; 3523: tricuspid valve replacement; 3524: replacement or reconstruction of two or three valves; 3525: reintervention to replace prosthetic valves; 3526; replacement of the aortic valve and ascending aorta; and 3527: reintervention due to prosthetic valve dysfunction without replacement.

A "people seen" filter was used to avoid duplicate data if a person was seen on more than one occasion for the same reason or underwent the same procedure more than once. To analyze by age, the data was filtered by single ages and five-year age groups. An analysis was also done by sex and by type of healthcare system affiliation (contributory or subsidized). No patients were

Table 1. Valve replacements performed on females (F) and males (M) in Colombia between 2017 and 2021

Valve replacement	2017	2018	2019	2020	2021	Total	
						M	F
Pulmonary	4	10	17	18	21	46	24
Aortic	787	1,221	1,476	1,114	1,268	3,894	1,956
Mitral	359	618	858	1,341	701	1,909	1,960
Tricuspid	15	28	27	16	28	53	60
Two or three valves	23	30	28	3	7	48	43
Prosthesis replacement	79	76	110	85	111	261	198
Aortic valve and ascending aorta	121	89	24	8	13	180	74
Reintervention without replacement	10	3	3	2	0	9	9
Total	1,322	1,918	2,371	2,468	1,998	5,982	4,041

Source: SISPRO.

excluded. The years 2017 to 2021 were included, allowing the impact of the COVID-19 pandemic to be evaluated.

In addition, an analysis was done by department, using the option "provider location," and an analysis was done of the national administrative divisions (32 departments and Bogotá, D.C.) and the institutions that performed the most procedures, selecting those that reported a greater number of procedures performed.

Results

During the five-year period analyzed, 19,540,317 people underwent surgical procedures (including dental procedures), and 616,722 circulatory system surgical procedures were performed. Of these, 10,023 (males: 5,982; 59.7%) were heart valve replacements, equivalent to 0.05%. Table 1 shows the different valve replacement codes disaggregated by year and sex. Regarding the distribution by year, there were 1,322, 1,918, 2,371, 2,468 and 1,998 people seen per year during the five-year period from 2017 to 2021, respectively. The most reported procedure was aortic valve replacement, for which 5,850 procedures were performed (58.4% of all the valve replacements). Of these, 3,894 were in males (66.7%).

During the mandatory quarantine due to the COVID-19 pandemic, between March and July 2020, an average of 165.5 procedures were performed per month, compared to the six months prior, with an average of 215 procedures per month, and the six months after, with an average of 213 procedures per month.

Figure 1 shows the distribution by age of the patients undergoing these procedures, indicating that most valve replacements occur during the seventh and eighth decades of life (from 60 to 79 years); these account for 55% of all the procedures performed.

As seen in Table 2, the administrative divisions with the most valve procedures recorded were Bogotá (29.6%), Valle del Cauca (13.7%), Antioquia (12%), Santander (6.7%) and Atlántico (5.9%). These five territorial divisions account for more than 60% of all the procedures; if the top 10 administrative divisions are considered, they account for 86% of the total. As far as the disaggregation by procedure, Bogotá holds first place in five of the eight procedures (the four single valve replacements and reinterventions with replacement), while Antioquia leads in the replacement of two or more valves, Valle del Cauca in aortic valve and ascending aorta replacement, and Santander in reintervention due to prosthetic valve dysfunction without replacement.

Regarding the distribution according to healthcare system affiliation, 4,549 procedures were performed on patients in the contributory regimen and 4,343 in the subsidized regimen. However, disaggregating by territorial entities, the four territorial entities with the highest prevalence of procedures were found to have a higher proportion of contributory regimen affiliation. The most notable difference was found in Bogotá, where 1,791 procedures were performed on patients affiliated to the contributory regimen and 617 on subsidized regimen patients, with an approximately 3:1 ratio, while in Santander and Valle del Cauca there was a 3:2 ratio, and in Antioquia

Table 2. The 10 departments with the most valve replacements between 2017 and 2021

Departaments	PVR	AVR	MVR	TVR	R2V	RPVR	AV-AAR	RPDWR	Total
Bogotá, D.C.	34	1,508	1,286	37	11	199	29	2	2,968
Valle del Cauca	5	782	549	5	16	42	91	2	1,372
Antioquia	3	712	418	18	43	73	15	1	1,202
Santander	12	452	204	6	0	33	14	7	675
Atlántico	2	326	290	5	2	11	14	3	595
Huila	1	381	102	0	0	20	3	1	474
Tolima	1	292	112	3	0	3	2	0	388
Cundinamarca	3	203	178	16	2	33	3	0	380
Caldas	0	198	84	3	0	3	2	0	278
Nariño	2	154	76	4	5	4	46	0	273

PVR: pulmonary valve replacement; AVR: aortic valve replacement; MVR: mitral valve replacement; TVR: tricuspid valve replacement; R2V: replacement of two or more valves; RPVR: reintervention for prosthetic valve replacement; AV-AAR: aortic valve and ascending aorta replacement; RPDWR: reintervention for prosthetic dysfunction without replacement.

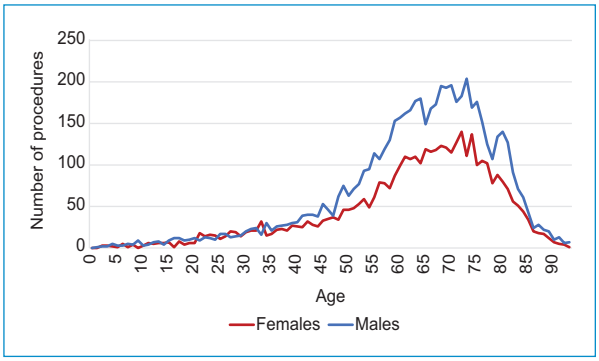

Figure 1. Distribution by sex and age of patients undergoing heart valve replacement in Colombia from 2017-2021. *Source: SISPRO.*

there were no significant differences. The opposite occurred in the rest of the territorial entities, where there was a higher proportion of patients affiliated to the subsidized regimen; Cundinamarca and Nariño had the highest ratios, with 7.5:1 and 6.8:1, respectively.

Finally, Table 3 shows the number of procedures recorded per institution. Fundación Cardioinfantil in Bogotá tops the list (5.3% of the country and 17.9% of the capital); this institution alone records more procedures than 28 of the country's 33 territorial entities, together. The list of the 20 institutions with the most procedures is filled out by another five institutions in Bogotá and its metropolitan area, two institutions in the metropolitan area of Medellín, two in Cali, two in the metropolitan area of Bucaramanga, two in Neiva and one each in Barranquilla, Ibagué, Villavicencio, Pereira, Pasto and Tunja.

Discussion

In Colombia, approximately 2,015 surgical heart valve replacements are performed every year, with a slight predominance of males over females, with an approximate 3:2 ratio. For aortic valve replacement, which is the most frequently performed procedure, this can be explained by the fact that aortic valve regurgitation also has an estimated 3:2 male to female ratio[17]. Another possible explanation is that female patients are underrepresented in the studies underlying the guideline recommendations regarding the left ventricular size limits for surgical intervention. These limits are mainly based on male patients who, on average, have significantly larger hearts, which limits female patients' access to this surgical intervention[18].

As far as healthcare system affiliation, it can be concluded that while there are no significant differences between the contributory regimen and the subsidized regimen at a national level, a difference is found when these are compared at the departmental level, with three times more procedures in the contributory regimen than in the subsidized regimen in the capital, Bogotá, as well as more cases in cardiovascular referral centers like Santander and Valle del Cauca. Meanwhile, other regions may have up to seven times more procedures performed in the subsidized regimen.

Table 3. The 20 healthcare institutions with the most valve replacements performed between 2017 and 2021

Institution	City	Total
Fundación Cardioinfantil	Bogotá	530
Clínica Colsubsidio Calle 100	Bogotá	406
Hospital Cardiovascular del Niño	Soacha	290
Clínica Las Américas	Medellín	266
Fundación Abood Shaio	Bogotá	255
Clínica Medilaser S.A.	Neiva	252
Clínica Avidanti Ibagué	Ibagué	239
Los Comuneros Hospital Universitario	Bucaramanga	235
Fundación Cardiovascular de Colombia	Floridablanca	234
Angiografía de Occidente S.A.	Cali	222
Hospital Universitario Mayor-Méderi	Bogotá	213
Organización Clínica General del Norte	Barranquilla	204
Especialidades Médicas Metropolitanas.	Bello	199
Unidad Cardioquirúrgica de Nariño	Pasto	190
Clínica Farallones	Cali	172
Clínica San Rafael Sede Cuba	Pereira	168
Hospital Universitario Hernando Moncaleano Perdomo	Neiva	134
Clínica Cardiovascular	Villavicencio	134
Clínica Mediláser Sucursal Tunja	Tunja	128
Unidad de Servicios de Salud Santa Clara	Bogotá	124

Source: SISPRO.

On another note, most cardiovascular procedures are performed on patients over the age of 60, secondary to the fact that most patients with mitral and aortic regurgitation are in this age bracket. There is a similar behavior in Japan with mitral valve replacement, where the highest prevalence is between 60 and 69 years, as opposed to aortic valve replacement, with this country reporting a higher prevalence in those 70 to 89 years old[19].

The Colombian population is facing an aging process due to a lower birth rate, which will exert pressure on the cardiovascular surgery programs, which are expected to face increased demand over the next few decades. In South Korea, a 50% increase in the demand for cardiovascular procedures is expected by 2040, with an estimated 25% increase in the number of specialists[20], a challenge which will not be foreign to our healthcare system.

The COVID-19 pandemic affected the trend in cardiovascular procedures after the mandatory quarantine began in March 2020, mainly for elective procedures. Studies show an up to 50% reduction in these procedures[21], with a similar trend in the behavior of valve procedures and a 23% reduction compared with the trend of the previous six months.

This behavior was similar in other countries like Germany, in which the cumulative number of heart procedures performed reduced significantly, including catheter ablations, percutaneous interventions and major cardiovascular surgery[22]. In England, studies reported a growing trend in cardiovascular procedures until February 2020, with a 25% increase in TAVR and 5% in other valve procedures compared with February 2019. However, with the beginning of the pandemic, the prevalence of TAVR was reported to decrease in March and June, with a 10.6 and 18% reduction, respectively, and a 45 and 89% reduction for other valve surgeries[23]. Likewise, in the United States and Canada, a study evaluating 67 hospitals in the two countries found a 10% reduction in heart valve procedures in institutions with more than 100 patients hospitalized for COVID-19, and a 5% reduction in valve procedures where there were fewer than 100 patients hospitalized for COVID-19, during April 2020[24].

One of the limitations of this study is possible under-reporting or diagnosis misclassification in the SISPRO database.

Conclusions

The information provided in this study, which was taken from SISPRO, is congruent with what is reported in the international literature.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical responsibilities

Human and animal protection. The authors declare that no experiments were conducted on humans or animals for this study.

Data confidentiality. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Use of artificial intelligence to generate text. The authors declare that they have not used any type of generative artificial intelligence in drafting this manuscript nor in creating figures, graphs, tables or their respective captions or legends.

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ORIGINAL ARTICLE

Characteristics and long-term follow-up of patients with acute myocardial infarction and non-obstructive coronary arteries: A cohort study (2015-2019)

Características y seguimiento a largo plazo de pacientes con infarto agudo de miocardio y arterias coronarias sin obstrucciones: un estudio de cohortes (2015-2019)

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Abstract

Objective: *to describe the characteristics of patients with acute myocardial infarction with non-obstructive coronary arteries (MINOCA), as well as their cardiovascular outcomes at 18 months.* **Materials and method:** *this was an ambispective cohort study that included patients who underwent coronary angiography after being diagnosed with acute myocardial infarction (AMI) between 2015 and 2019. The MINOCA group was selected, and outcomes such as readmissions and major cardiovascular events were obtained at 18 months.* **Results:** *data were obtained from 433 patients who met the inclusion criteria, 141 (33%) of whom met the criteria for MINOCA. The most prevalent clinical manifestations were chest pain and anginal equivalents (62% and 62.4%, respectively). The majority presented with non-ST elevation myocardial infarction (92.1%), with left ventricular ejection fraction (LVEF) ≥ 50% (42.6%). During the 18-month follow-up, data were obtained from 102 patients, 22% of whom had readmissions and 18% reinfarction; during follow-up, cardiovascular mortality was 12%, and all-cause mortality was 36%.* **Conclusions:** *there was a higher proportion of MINOCA in this study than described in the literature, with a predominance of atypical clinical manifestations. Equally striking was the significant percentage of pre-infarctions and cardiovascular deaths during this cohort's follow-up.*

Keywords: *Acute coronary syndrome. Acute myocardial infarction. Coronary angiography. Non-obstructive coronary disease. MINOCA.*

Resumen

Objetivo: *describir las características de los pacientes con infarto agudo de miocardio sin lesiones coronarias obstructivas (MINOCA), así como sus desenlaces cardiovasculares a dieciocho meses.* **Materiales y método:** *Estudio de cohortes, ambispectivo, de los pacientes que fueron llevados a angiografía coronaria por diagnóstico de infarto agudo de miocardio*

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(IAM), entre los años 2015 y 2019. Se seleccionó el grupo de MINOCA y obtuvieron datos de desenlaces como reconsultas y eventos cardiovasculares mayores a dieciocho meses. **Resultados:** *de los 433 pacientes incluidos, 141 (33%) cumplían definición de MINOCA; el dolor torácico y los equivalentes anginosos fueron las manifestaciones clínicas más prevalentes (62 y 62.4% respectivamente). La mayoría se presentaron con IAM sin elevación del ST (92.1%), con FEVI ≥ 50% (42.6%). En el seguimiento a dieciocho meses, se obtuvieron datos de 102 pacientes, de los que el 22% reconsultó y 18% presentó reinfarto. La mortalidad durante el seguimiento fue del 12% por causa cardiovascular y del 36% por todas las causas.* **Conclusiones:** *se encontró una mayor proporción de MINOCA respecto a lo descrito en la literatura y con predominio de manifestaciones clínicas atípicas. Es llamativo, igualmente, el alto porcentaje importante de preinfartos y muerte de origen cardiovascular durante el seguimiento de esta cohorte.*

Palabras clave: *Infarto agudo de miocardio. Angiografía coronaria. Enfermedad coronaria no obstructiva. MINOCA.*

Introduction

Acute myocardial infarction with non-obstructive coronary arteries (MINOCA) tends to be a diagnostic and therapeutic challenge for medical staff in their clinical practice. In simple terms, it refers to a clinical syndrome in which the criteria for acute myocardial infarction are met[1] but angiographic studies show no evidence of significant coronary artery obstruction (defined as > 50% stenosis) and there is no clear cause to explain the source of this clinical picture. The advent of diagnostic modalities like cardiac magnetic resonance imaging or intravascular ultrasound has provided a deeper understanding of this topic, as well as helped identify possible causes and develop and implement new proposed treatments[2,3]. Thus, interest in MINOCA research has grown over the last few decades, with population studies performed to try to identify potentially relevant clinical and paraclinical predictors of risk and improve the diagnostic and therapeutic approach. However, most of these studies are carried out in populations which are very different from the Latin American population, and therefore some results might not be applicable in our setting. Therefore, regional studies must be done to identify potential distinctive or differential MINOCA characteristics compared to the international population. This will help improve the diagnostic and therapeutic approach in our population in the future.

Objective

To describe the clinical, biochemical, electrocardiographic and echocardiographic characteristics of patients with acute myocardial infarction with non-obstructive coronary arteries, as well as their outcomes at 18 months, mainly in terms of reconsultation and major cardiovascular events (reinfarction, stroke, serious arrhythmias and death).

Materials and method

This was an observational, descriptive, ambispective study based on a medical record review in a cardiovascular unit and a hemodynamics unit between December 2015 and January 2019. A virtual form was used to record the different sociodemographic, clinical and paraclinical variables (Fig. 1), and the data was then stored in a database. The paraclinical variables included electrocardiographic, echocardiographic, angiographic and admission troponin level data (fourth generation troponin, ARCHITECT STAT TnI [Abbott] and ultrasensitive troponin I [bioMérieux VIDAS]). The coronary angiographies were all performed by the same interventionist cardiologist, following the established hospital protocol. The criteria from the Fourth Universal Definition of Myocardial Infarction, the 2019 American Heart Association MINOCA Consensus and the 2020 European Society of Cardiology Guidelines on the treatment of acute coronary syndrome without ST segment elevation were used for the operative definition of myocardial infarction. The MINOCA population was followed for 18 months (to June 2020) through medical charts and phone calls, and data was collected on variables like reconsults and major cardiovascular events (reinfarction, stroke, serious arrhythmias with hemodynamic instability or requiring immediate care, and death). Patients who did not meet the criteria for acute myocardial infarction or who had missing data during data collection were excluded (Table 1). The study was approved by the institutional ethics committee; informed consent was not required due to the study characteristics.

Results

A total of 433 patients who met the definition for acute myocardial infarction were included, 141 (32%) of whom did not have significant coronary artery

Table 1. Inclusion and exclusion criteria

Inclusion	Exclusion
Patients over the age of 18	
Patients with an official coronary angiography report between 2015 and 2019	Patients admitted only for coronary angiography
Patients with an official echocardiogram report	Patients with noncoronary angiographies (aortogram, lower extremities, carotid, etc.)
Patients with an official report of troponin levels drawn during the hospitalization itself or from an outside source	Patients without all the required variables, except at the investigators' discretion, on a case-by-case basis
Patients who have most of the variables for completing the tool available in the medical chart	

obstruction (Fig. 1); MINOCA occurred more often in women (56%); 67% (95/141) of the patients had arterial hypertension and a smaller proportion had diabetes mellitus (15.6%). Atypical chest pain and anginal equivalents were the most prevalent clinical manifestations (62 and 62.4%, respectively), followed by dyspnea in 54% (77/141). Syncope occurred in 2% (3/141) of the patients as the initial manifestation of MINOCA. ST elevation was found in 8.4% (11/141) of the cases; high-sensitivity troponin levels were lower in patients with MINOCA (none of the patients in this group had an elevation more than five times the 99th percentile on admission) and 15% (21/141) of the patients had some type of arrhythmia, with atrial fibrillation (12/21) being the most frequent. A significant proportion of the patients had an LVEF ≥ 50% (42.6%) (Table 2). All-cause mortality was 3.5% in the initial cohort (5/141).

At 18 months, data was obtained from 70.8% of the 141 patients (102/141). Of these, 28.4% (29/102) reported having had chest pain or dyspnea at some point during the follow up period, and 22% (23/102) reconsulted due to cardiovascular symptoms (Table 3); of this subgroup, 18.6% (19/102) met the criteria for reinfarction, and 8.8% (9/102) had a stroke or serious arrhythmia (Table 4). The cardiovascular mortality rate was 12% (12/102), with 25% mortality from other causes (25/102) (Table 5).

Discussion

This study found that, out of all patients undergoing coronary angiography in the context of AMI, 33% had coronary arteries with no significant obstruction, a significantly higher figure than reported in the literature. A study recently published in this country reported a prevalence of 7.11%, and, like our study, a higher frequency of MINOCA has been reported in women (56%)[4].

The clinical presentation in the MINOCA group was remarkable for more atypical or nonanginal chest pain and anginal equivalents (epigastric pain, dyspnea, etc.). In addition, there was a higher frequency of patients with a preserved ventricular ejection fraction (> 50%) and an admission electrocardiogram without ST elevation, in 91% of cases.

The initial mortality in patients with MINOCA was similar to the group with significant coronary disease. In general, the literature reports that MINOCA may occur in close to 6% of all acute myocardial infarctions and that it has an approximately 2 to 4% 12-month risk of reinfarction or death[5].

The data obtained during the 18-month follow up was remarkable for the considerable percentage of reconsultation and cardiovascular symptoms, such as chest pain or dyspnea, similar to what is reported in the literature[5]. Another relevant point was the number of patients who required percutaneous coronary intervention (16%), which we believe could be related to coronary lesions not seen on the initial coronary arteriograms, or new atherosclerotic and nonatherosclerotic events.

There was also a high percentage of readmissions (37%), and greater cardiovascular mortality in this subgroup (close to 12%), compared with 2 to 4% in similar studies, and greater all-cause mortality, which reached 36%.

In our study, the MINOCA group mortality was higher than that reported in the literature, which is no doubt partially due to being a more heterogeneous and less select group, with a greater number of patients in whom a more complete etiological study might have identified more extracardiac or nonischemic cardiac causes (false MINOCAs)[6]. Similar reasons could explain other findings, like left ventricular dysfunction in almost half the patients with MINOCA. The data from the SWEDEHEART Registry yielded an approximately 30% prevalence of heart failure with reduced LVEF in patients with MINOCA[7]. Other registries have shown similar findings regarding the adverse cardiovascular outcomes of MINOCAs. Taking data from the Korea Acute Myocardial Infarction Registry, the MINOCA group had similar major

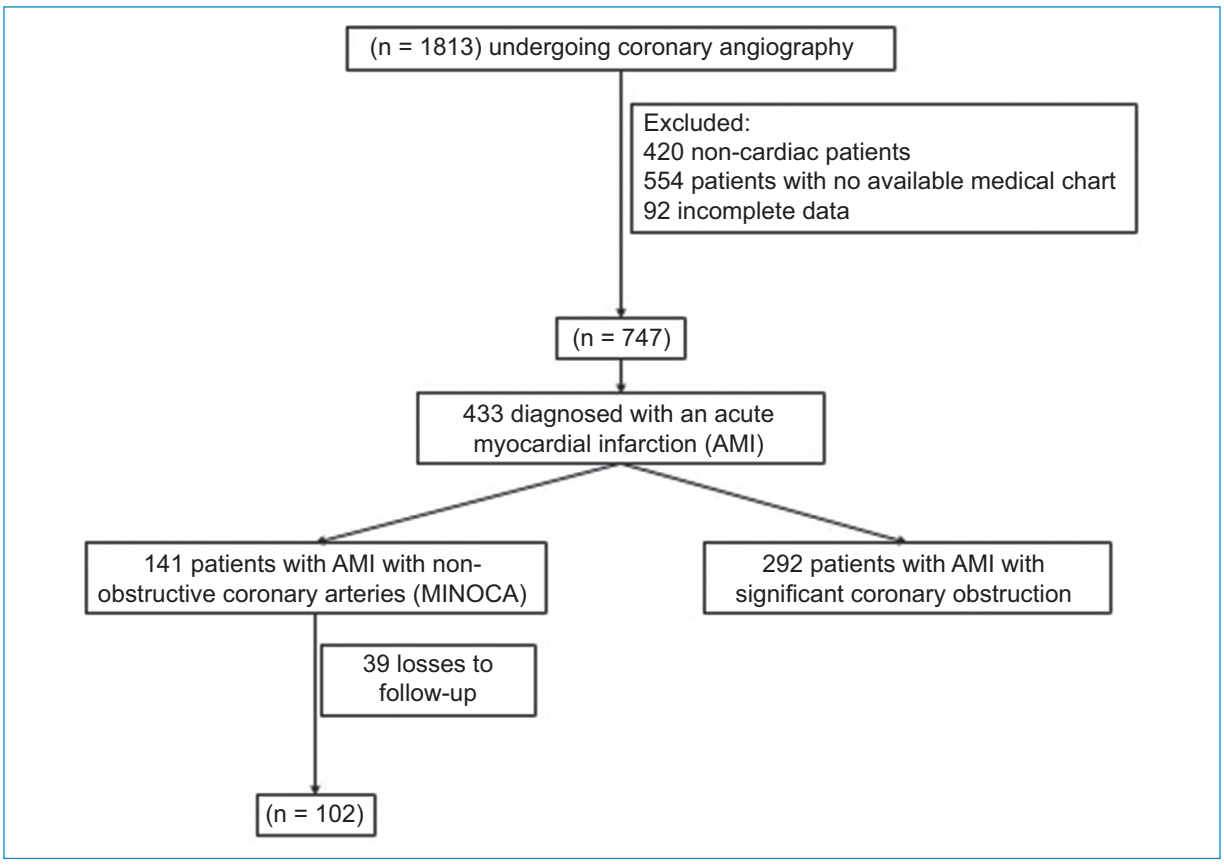

Figure 1. Recruitment flowchart.

adverse cardiovascular events (MACE) (infarction, bypass of the culprit vessel and cardiac death) to those of the group with involvement of one or two coronary vessels: 7.8 vs. 12%. Half of the MINOCA cases were of unknown etiology, and cardiac resonance imaging or intravascular imaging were rarely used[8].

Another factor that could explain the outcomes in this group (a comparison group was not used in follow-up) is the COVID-19 pandemic. The literature shows evidence of an increase in serious cardiovascular events (including death) related to the pandemic, not only due to the viral infection, but also to other phenomena related to healthcare system functioning during the pandemic (quarantine, social distancing, difficulties in accessing the healthcare systems, losses to follow up of patients with chronic illnesses, less access to medications and diagnostic tests, delayed consultation, and delays in coronary stratification), which may have had an impact[9].

This study included a significant national cohort of MINOCA patients, with very useful data for carrying out future studies, contributing to a better description of the clinical profiles of the Latin American population with MINOCA and identification of possible predictors which could be valuable in the diagnostic and therapeutic approach to this syndrome.

This study's limitations were its descriptive, observational nature, limited to a review of medical records and angiography reports, along with the unavailability of some diagnostic aids like cardiac resonance imaging or coronary intravascular imaging. Furthermore, since this study was carried out at a single healthcare center, there is selection bias. Having a single interventionist cardiologist to perform coronary arteriography causes an information or measurement bias, which affects the interpretation of the results and clinical decision-making based on the same. The difficulties in patient follow-up due to the COVID-19 pandemic should once again be mentioned.

Table 2. Comparison of the clinical and paraclinical characteristics of patients with MINOCA vs. AMI with significant obstruction

	MINOCA (n = 141)	Acute myocardial infarction with significant obstruction (n = 292)
	n (%)	n (%)
Demographic characteristics		
Sex Male Female	 61 (43.3%) 80 (56.7%)	 191 (65.4%) 101 (34.6%)
Age ≥ 75 years < 75 years	 40 (28.4%) 101 (71.6%)	 94 (32.2%) 198 (67.8%)
HTN	95 (67.4%)	213 (72.9%)
Diabetes mellitus	22 (15.6%)	102 (34.9%)
Clinical presentation		
Chest pain Anginal Nonanginal	 85 (60.3%) 56 (39.7%)	 198 (67.8%) 94 (32.2%)
Dyspnea	77 (54.6%)	145 (49.7%)
Anginal equivalents	88 (62.4%)	171 (58.6%)
Hemodynamic instability	25 (17.7%)	58 (19.9%)
Arrhythmias	21 (14.9%)	55 (18.8%)
Type of arrhythmias Atrial fibrillation AV block Bradycardia Ventricular tachycardia Supraventricular tachycardia	n = 21 12 (57.1%) 6 (28.6%) 1 (4.8%) 0 2 (9.5%)	n = 55 19 (34.5%) 15 (27.3%) 11 (20.0%) 5 (9.1%) 5 (9.1%)
Diagnostic aids		
EKG ST elevation No ST elevation	n = 131 11 (8.4%) 120 (91.6%)	n = 285 89 (31.2%) 196 (68.8%)
Ultrasenstivie troponin More than five times the 99th percentile (p99) Greater than p99 No data or qualitative report	 0 109 (77%) 32 (23%)	 239 (81.8%) 34 (11.6%) 14 (5%)
LVEF ≥ 50% < 50% No information	 60 (42.6%) 56 (39.7%) 25 (17.7%)	 106 (36.3%) 138 (47.3%) 48 (16.4%)

Table 3. Reconsults and symptom recurrence. Divided into the patients who had died at the end of follow-up vs. those who remained alive

	Deceased (n = 37)	Living (n = 65)	Total (n = 102)	p value
Reconsults, n (%)	8 (21.6)	15 (23.1)	23 (22.5)	0.720
Chest pain recurrence, n (%)	9 (24.3)	20 (30.8)	29 (28.4)	0.642
Pain with similar characteristics to the prior event, n (%)	7 (77.8)	6 (30.0)	13 (44.8)	0.217
Dyspnea, n (%)	7 (18.9)	22 (33.8)	29 (28.4)	0.168

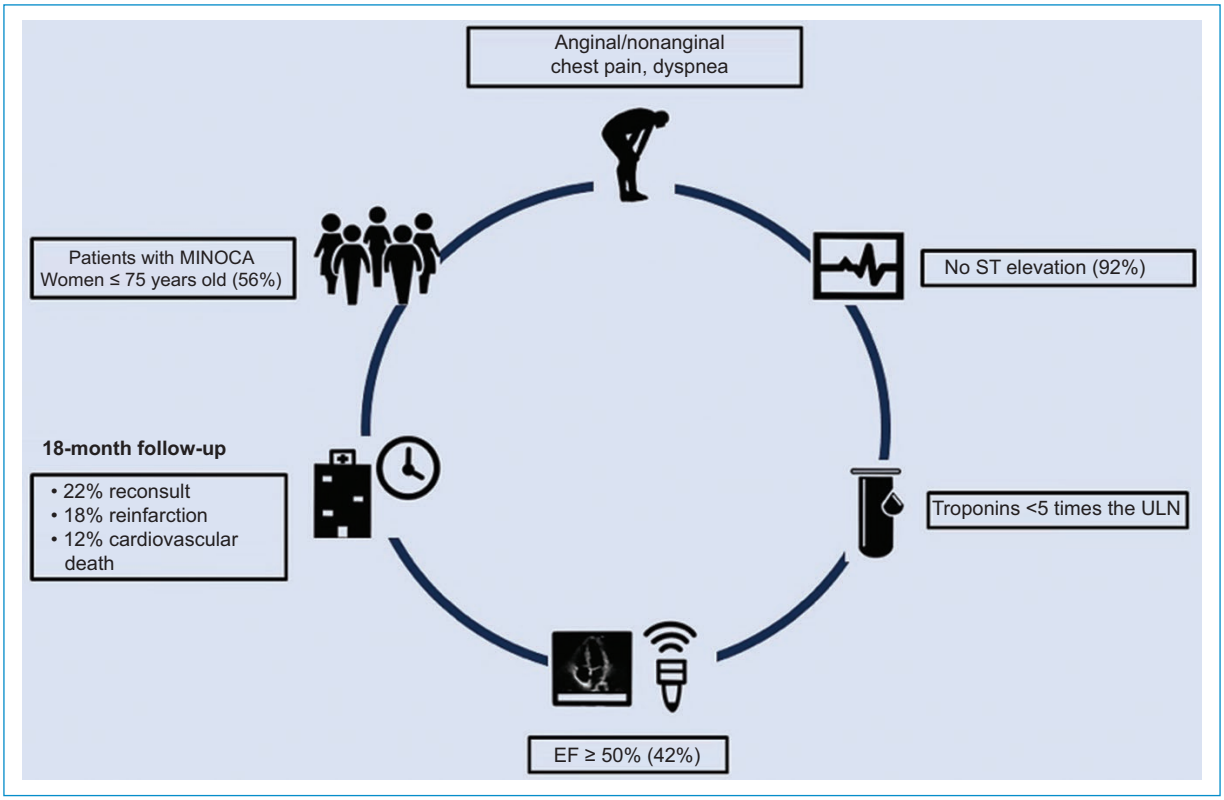

Figure 2. Main characteristics and outcomes in patients with MINOCA.

Table 4. Cardiovascular outcomes at 18 months in patients with MINOCA. Divided into patients who had died at the end of follow up vs. those who remained alive

	Deceased (n = 37)	Living (n = 65)	Total (n = 102)	p value
Rehospitalization, n (%)	9 (24.3)	29 (44.6)	38 (37.3)	0.068
Reinfarction, n (%)	12 (32.4)	7 (10.8)	19 (18.6)	0.015
Stroke/arrhythmia, n (%)	4 (10.8)	5 (7.7)	9 (8.8)	0.720
Percutaneous coronary intervention (%)	2 (5.4)	15 (23.1)	17 (16.7)	0.043

Table 5. Eighteen-month mortality in patients with MINOCA

	n (%)
Cardiovascular death	12 (12.2%)
All-cause mortality	37 (36.3)

Conclusion

We have presented the demographic description and clinical, paraclinical, electrocardiographic, echocardiographic and angiographic variables of a cohort of patients who met the MINOCA criteria, with 18-month follow-up. There was a significant percentage of recurrent events, including reconsults, reinfarctions and cardiovascular morbidity and mortality (Fig. 2). Multicenter studies with greater statistical power are needed in the local population.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Human and animal protection. The authors declare that no experiments were conducted on humans or animals for this study.

Data confidentiality. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Use of artificial intelligence to generate text. The authors declare that they have not used any type of generative artificial intelligence in drafting this manuscript or creating figures, graphs, tables or their respective captions or legends.

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CLINICAL CASE

Percutaneous tricuspid valve-in-valve implantation. First case report of a pediatric patient in Colombia

Implante valvular percutáneo valve-in-valve en tricúspide. Primer reporte de caso de paciente pediátrico en Colombia

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Abstract

Tricuspid valve abnormalities have a lower incidence than defects in the rest of the heart valves and may be due to primary or secondary causes. Recently, their pathophysiology and importance in cardiac morbidity and mortality have been widely studied. Open tricuspid valve surgery has a high rate of morbidity and mortality, and even more so when it comes to reoperation. For this reason, it is important to carry out these procedures endovascularly via a catheter, and some of these interventions around the world, using percutaneous tricuspid valve-in-valve implantation, have recently been published. We present the first reported case of this procedure in a pediatric patient in Colombia, whose procedure was uneventful and achieved significantly improved valve function, as an initial step toward continuing to develop the technique and perform the procedure in this country.

Keywords: *Tricuspid valve. Congenital heart disease. Tricuspid valve stenosis. Tricuspid valve regurgitation. Cardiac catheterization.*

Resumen

Las anormalidades de la válvula tricúspide tienen una incidencia menor respecto a los defectos del resto de válvulas cardiacas y pueden deberse a causas primarias o secundarias. Recientemente, se ha estudiado su fisiopatología y su importancia en la morbimortalidad por causas cardiacas. En este sentido, la cirugía valvular tricúspide abierta tiene una tasa de morbimortalidad elevada, más aún cuando se trata de una reoperación. Es por esto que estos procedimientos endovasculares transcatéter cobran relevancia y recientemente se han publicado a lo largo del mundo algunos casos de intervenciones por este método, por medio de implante valvular percutáneo valve-in-valve en posición tricúspide. Se presenta el primer caso reportado de este procedimiento en Colombia en una paciente pediátrica, el cual transcurrió sin complicaciones y con el que se logró una mejoría significativa en la función valvular como paso inicial para continuar desarrollando la técnica y realizando este procedimiento en el país.

Palabras clave: *Válvula tricúspide. Cardiopatía congénita. Estenosis valvular tricúspide. Insuficiencia valvular tricúspide. Cateterismo cardiaco.*

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Introduction

Tricuspid valve abnormalities have a wide variety of causes, including primary causes (either congenital or acquired) like Ebstein anomaly, tricuspid valve dysplasia and infective endocarditis[1,2]; or secondary causes, which are more common, like left heart disease, pulmonary hypertension, right ventricular failure or idiopathic causes[3-5].

When tricuspid valve replacement is needed, it is usually done using bioprosthetic valves, as these have been found to perform better with less risk than mechanical valves. However, bioprosthetic valves at this location last less than other prosthetic valves[6], with fewer than 60% of patients being intervention-free 15 years after the first procedure[1].

Thus, on most occasions, reintervention is required, either with open surgery or using a method described in some case reports around the world, which is valve-in-valve bioprosthetic tricuspid valve implantation. Since there are no dedicated tricuspid valve devices currently available, the reviewed case reports use valves originally manufactured for the aortic valve, on which this procedure is routinely performed[6,7]. However, this has some risks, like its location close to the conduction system, the risk of conduction system damage leading to heart block, and outflow tract obstruction, as well as endocarditis[7].

Nevertheless, when performed at specialized centers, it has a high success rate, thus constituting an excellent treatment option for these patients, since it reduces the invasive procedure that would otherwise be performed with open heart repair[6-8].

Clinical case

This was a 10-year-old female, mestizo patient with a history of atrial septal defect (ASD), ventricular septal defect (VSD) and infundibular stenosis diagnosed at age 2 years 11 months, when she underwent surgery to close the ASD and VSD and reconstruct the outflow tract. She had complications, with low cardiac output, a coagulation disorder, intraparenchymal cerebral hemorrhage and a right lamellar subdural hematoma. She was lost to follow up and, at age four, was admitted to our institution, referred with a diagnosis of supraventricular tachycardia. An echocardiogram showed significant atrial dilation and severe tricuspid regurgitation. She was diagnosed with bacterial endocarditis with significant valve involvement, and open tricuspid valve replacement was performed, using the PERIMOUNT 23 biological prosthesis.

The patient was once again lost to follow up and reconsulted at the age of 10 with a 24-hour complaint of palpitations, languor, decreased appetite, diaphoresis and nausea. On physical exam, she was alert and oriented, afebrile, and pale, with signs of poor perfusion and a heart rate of 218 bpm.

An electrocardiogram showed atrial flutter and significant right atrial enlargement. The tachyarrhythmia did not revert with pharmacological treatment, and she therefore required cardioversion followed by a continuous amiodarone infusion. An echocardiogram showed a severely dilated right atrium, with an area of 27 cm^2; a dilated right ventricle with systolic dysfunction; a TAPSE of 9 mm; prosthetic valve dysfunction with severe intravalvular regurgitation; a 78% LVEF; and a peak tricuspid gradient of 9 mmHg with a mean of 5 mmHg (Fig. 1).

A medical committee met to discuss the case and, given the patient's history and current status, she was not considered to be a candidate for mapping and ablation, due to severe valve damage and this being her third surgery, with a consequently greater surgical risk. Ultimately, percutaneous tricuspid valve-in-valve implantation with a bioprosthetic valve was selected as definitive treatment.

Technical description of the implantation

The right femoral vein was cannulated with a 14 Fr. introducer, and the left femoral vein with a 5 Fr. introducer. The guidewire was advanced under fluoroscopic guidance along with transesophageal echocardiography to the left pulmonary artery.

The diameter of the valve annulus was determined according to the medical manufacturer's specifications, in this case for a PERIMOUNT 23, stent ID 22 and true ID 21 valve. An ATLAS® GOLD 24 balloon was used for dilation and a Myval 23 prosthetic valve with a 21-22.5 mm ring diameter and 17.85 mm height was implanted. The valve was positioned at a maximum depth of 3 mm from the stent and attached to the ring. The procedure was guided by transesophageal echocardiography and fluoroscopy (Fig. 2).

The final gradient of the newly inserted prosthesis, as measured by echocardiography, was 4 mmHg. The patient was prescribed dual antiplatelet therapy and antibiotic prophylaxis.

The patient was discharged 48 hours after the procedure with a tricuspid gradient of 0.45 mmHg and a normally functioning valve with no paravalvular leaks. The right atrium measured 18.3 cm^2, with no postoperative complications (Fig. 3).

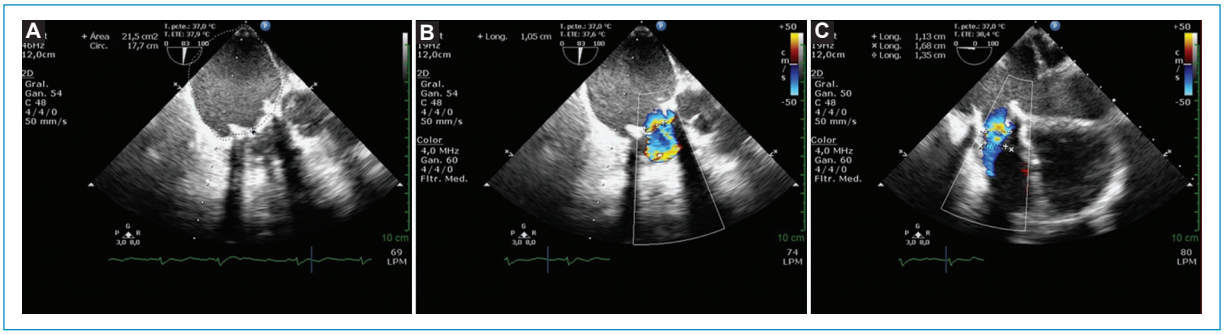

Figure 1. Echocardiogram prior to the procedure. **A:** the prosthetic tricuspid valve. **B:** color Doppler imaging showing flow acceleration corresponding to significant stenosis with right atrial enlargement. **C:** view of the valve that shows limited opening.

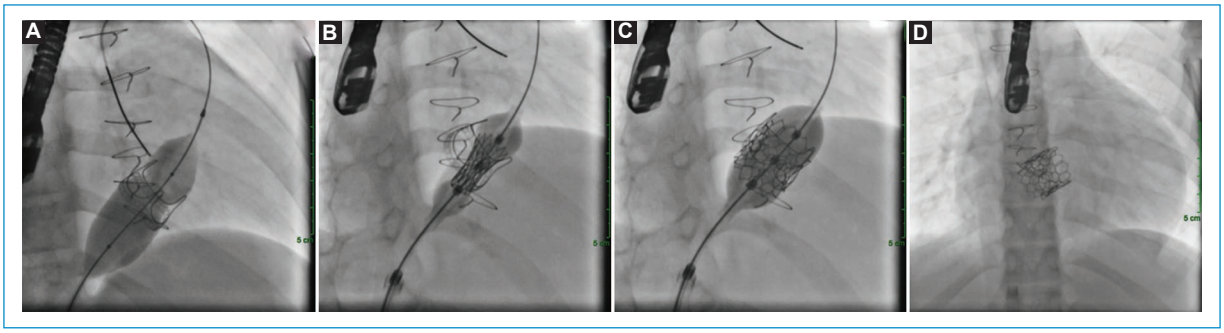

Figure 2. Implantation technique. **A:** rupture of the previous bioprosthetic valve. **B:** valve-in-valve insertion. **C:** valve-in-valve deployment. **D:** image of the final implanted valve.

Neither medium nor long-term follow up could be performed, as the patient was once again lost to follow up and could not be reached using any of the contact information provided.

Discussion

Percutaneous tricuspid valve-in-valve implantation is an infrequent procedure in children[7]. Although the tricuspid valve was given little importance in the past, today there are a growing number of options to treat its congenital, primary or secondary damage[1,2,9].

When a bioprosthetic tricuspid valve fails, reintervention surgery is considered as the first option. However, the percutaneous valve-in-valve procedure has been gradually introduced and is currently recommended for patients with severe heart failure symptoms caused by bioprosthetic valve regurgitation who are at high surgical risk[10].

We found multiple cases in the literature of this procedure performed on adults, most with a good clinical course. One international, multicenter registry study collected data from 156 patients with bioprosthetic tricuspid valve dysfunction who underwent catheterization for a new transcatheter bioprosthetic tricuspid

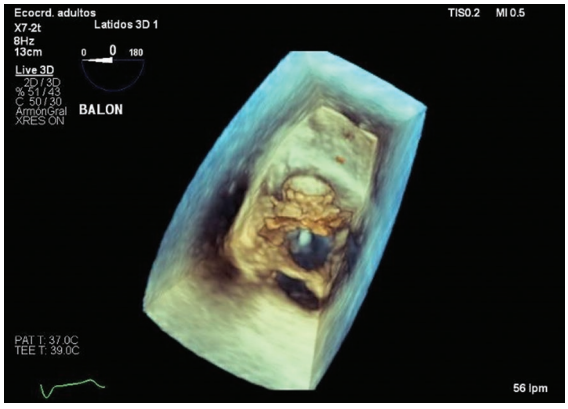

Figure 3. Implanted valve seen through transesophageal echocardiography.

valve-in-valve implantation, with a median age of 40 years. The procedure was successfully performed in 150 patients, with few serious complications. A total of 14% died, 8.6% required reintervention or had recurrent tricuspid valve dysfunction, and 77% showed evident clinical improvement with optimization of their New York Heart Association (NYHA) classification[11].

Reports of this procedure in children are scarce; we found a report of five cases in Greece, four of which involved patients under the age of 18 (6, 11, 12 and 17 years). All five patients had prior open-heart procedures, including tricuspid valve replacement with PERIMOUNT Carpentier-Edwards 25 mm (n = 4) and PERIMOUNT Carpentier-Edwards 29 mm (n = 1) valves, for different reasons.

These bioprosthetic valves had severe regurgitation in four patients and tricuspid stenosis in two cases, and all patients had a deteriorated functional class. The five patients underwent percutaneous tricuspid valve-in-valve replacement and had favorable short and medium-term outcomes, with an improved tricuspid gradient and NYHA classification, and no complications[12].

In the case we are presenting, the patient had a high surgical risk, as this was her third procedure; therefore, the risk of performing an open surgery was greater than the benefit. Thus, we opted for an innovative approach previously described in other countries using percutaneous tricuspid valve-in-valve implantation, which had not been reported to date in a pediatric patient in Colombia. There were no complications during the procedure, and the immediate postoperative course was favorable and complication-free, leading to functional and systemic function improvement.

It should be noted that a Myval THV was used in this case, which is more widely used in the aortic position. However, the success of this intervention in the tricuspid position suggests the need to develop new dedicated technologies and valves for this anatomical location. This fact is especially relevant given that tricuspid regurgitation is one of the most important valve diseases and its treatment is a challenge for the medical community.

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CLINICAL CASE

Percutaneous implantation of the Venus P self-expanding pulmonary valve in children; the first case in Colombia

Implante percutáneo de válvula pulmonar autoexpandible Venus P en niños; primer caso en Colombia

Ana M. Aristizabal[1,2], Sandra Galvis[1,2], Jaiber Gutiérrez[1] y Walter Mosquera[1,2]*

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Abstract

In patients with congenital heart disease, transcatheter pulmonary valve implantation is the treatment of choice in dysfunctional right ventricular outflow tracts (RVOT). The self-expandable Venus-P valve was approved recently for use in large native tracs. This study reports the experience of the first case of successful implantation of Venus-P pulmonary valve in Colombia. Ours was a 16-year-old patient with Tetralogy of Fallot, with complete correction at 11 months of life. The patient has severe pulmonary insufficiency and functional class deterioration. Cardiac catheterization was performed to place a 34X30 mm Venus-P valve, a procedure carried out without complications, evidencing significant improvement in the diastolic pressure of the pulmonary artery, without final gradient between the right ventricle and pulmonary artery. Reports exist of experiences in Venus-P valve implant globally with favorable results; percutaneous valve placement represents decreased procedure times and hospital stays. We believe percutaneous valve replacement in pulmonary position in native RVOTs is a possible and safe option to improve pulmonary insufficiency and right ventricular dysfunction in these types of patients.

Keywords: *Pulmonary regurgitation. Pulmonary valve. Right ventricle. Venus P-valve.*

Resumen

En pacientes con cardiopatía congénita, el implante percutáneo de válvula pulmonar es el tratamiento de elección en tractos de salida del ventrículo derecho (TSVD) disfuncionales. La válvula autoexpandible Venus-P, fue aprobada recientemente para su uso en tractos nativos de gran tamaño. El objetivo de este estudio es reportar la experiencia del primer caso de implantación exitosa de válvula pulmonar Venus-P en Colombia. Paciente de 16 años con Tetralogía de Fallot, con corrección completa a los 11 meses de vida. Presenta insuficiencia pulmonar severa y deterioro de la clase funcional. Se realiza cateterismo cardíaco para la colocación de válvula Venus-P 34X30 mm, procedimiento que se lleva a cabo sin complicaciones, evidenciando mejoría significativa de la presión diastólica de la arteria pulmonar, sin gradiente final entre el ventrículo derecho y arteria pulmonar. Existen varios reportes de experiencias en el implante de válvula Venus P a nivel mundial con resultados favorables. La colocación percutánea de la válvula representa disminución en tiempos del procedimiento y estancia hospitalaria. Consideramos el reemplazo valvular percutáneo en posición pulmonar en TSVD nativos es una opción posible y segura para mejorar la insuficiencia pulmonar y la disfunción ventricular derecha en este tipo de pacientes.

Palabras clave: *Insuficiencia pulmonar. Válvula pulmonar. Ventrículo derecho. Válvula Venus P.*

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Introduction

In recent years, percutaneous valve implantation has consistently progressed, achieving today's interventions that are less invasive and have lower morbidity, compared to surgical procedures[1]. For patients with congenital heart disease, percutaneous pulmonary valve implantation is the treatment of choice for dysfunctional right ventricular outflow tracts (RVOTs)[2]. There are several balloon-expandable pulmonary valves available for implantation in conduits, native tracts and prosthetic valves. The available valves (Melody or Edwards SAPIEN) are recommended for implantation only in RVOTs made with homografts or conduits[3,4]. However, most patients with tetralogy of Fallot undergo repair with a transannular patch, which leads to very pulsatile outflow tracts that are larger than the currently available balloon-expandable valves (22 mm for Melody, 29 mm for Edwards)[3,5].

This has led to the need for a valve that can be implanted in a native RVOT and is large enough for the wide diameters of RVOTs with a patch. The self-expanding Venus P-valve (MedTech, China) is a percutaneous valve recently approved for use in larger native tracts[6].

The structure of the Venus P-valve is made up of a nitinol stent, with the leaflets and stent covered in porcine pericardial tissue. The nitinol allows the stent to properly adapt to the pulmonary trunk without compressing neighboring structures, due to its lower radial force[7]. The available valve sizes range from 28 up to 36 mm in diameter, with 2 mm increments. The Venus P-valve stent is diabolo-shaped and measures 10 mm more on the ends than in the central area. Since it is wider on the ends, the valve is ideally designed to be implanted in tubular pulmonary trunks with no distal or pulmonary artery stenosis. The central area and proximal end are covered in porcine pericardial tissue to avoid paravalvular leaks, and the distal end is not covered, thus preventing pulmonary artery occlusion. The valve is crimped onto the delivery system under ice water. Under these conditions, the nitinol softens and can be crimped onto the delivery system. The valve is attached to the delivery system using two small hooks. Once hooked and compressed, the valve is covered with the delivery system´s sheath capsule so that it enters the patient covered. The sheath is a 22 Fr for 28- and 30-mm valves, and 24 Fr for larger valves (> 30 mm). Once situated at the chosen spot in the pulmonary tree, the valve recovers its diabolo shape when the delivery system capsule is removed, and it comes in contact with the blood stream at a temperature of 36-37°C[3].

The objective of this study is to report the experience of the first successful implantation of a Venus P-valve in Colombia.

Clinical case

The patient was 16 years old, weighed 63 kilos and had a history of tetralogy of Fallot for which he underwent complete repair at 11 months of age. He required reintervention a few days later to reconstruct the RVOT due to a transannular patch aneurysm and residual ventricular septal defect.

He was being followed for pulmonary valve regurgitation and had experienced clinical deterioration over the last six months, developing cyanosis with exercise and progressing from New York Heart Association (NYHA) functional class I to II.

An echocardiogram showed significant right ventricular dilation (right ventricular diastolic diameter: 47 mm, Z +3-07) with free pulmonary regurgitation. Cardiac magnetic resonance imaging reported a right ventricular diameter of 58 mm (Z +3.95), with a pulmonary regurgitant fraction of 56% and a right ventricular end-diastolic volume of 172 ml/m^2. The pulmonary valve annulus was measured at 29 mm on cardiac angiography tomography, with the course of the proximal anterior descending artery 4 mm from the plane of the pulmonary valve annulus.

Based on this, the case was discussed in a multidisciplinary committee and the patient was considered to be a candidate for self-expanding percutaneous pulmonary valve implantation.

With prior informed consent, a heart catheterization was performed under general anesthesia with the patient intubated and heparinized at 100 U/kg. The right and left femoral veins and left femoral artery were cannulated. Right and left heart catheterization was performed with a right ventricular pressure of 32/2 mmHg and right and left pulmonary artery pressures of 34/4/16 and 32/2/16 mmHg, respectively, along with RVOT sizing showing a 30 mm diameter (Sizing Balloon, AGA Medical Corp., United States), with a coronary test which was negative for obstruction (Fig. 1).

With this information, a valve was chosen that was 4 mm larger than the waist of the sizing balloon and long enough to leave the distal portion at the pulmonary bifurcation and the proximal tip of the diabolo in the RV, ultimately selecting a 34 x 30 mm valve.

The valve was loaded with no difficulties. The high-support Lunderquist guidewire (Cook Medical, Denmark) was advanced to the left pulmonary artery,

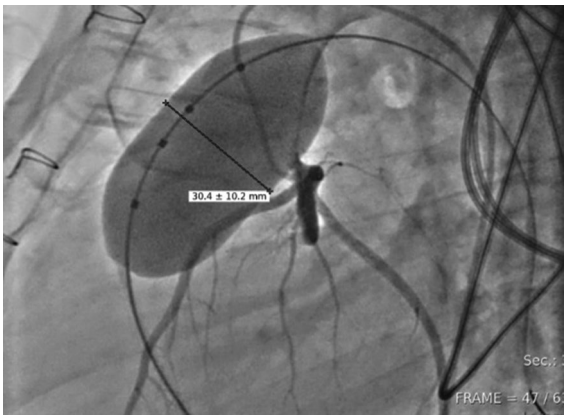

Figure 1. Coronary occlusion test with a 30 mm elastomer balloon.

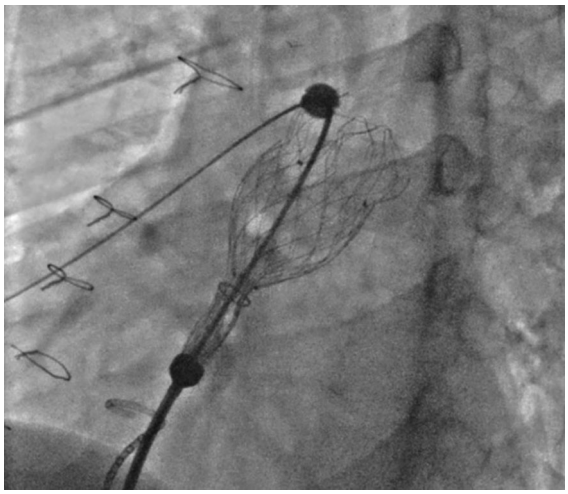

Figure 2. Initial valve deployment.

and the introducer was advanced through the artery to its origin.

Valve deployment was begun at the origin of the left pulmonary artery with serial angiographic monitoring. The initial position of the valve was not considered appropriate, and the guidewire was repositioned in the right pulmonary artery (Fig. 2). The complete valve was deployed in a controlled fashion from the right pulmonary artery, achieving an appropriate position (Fig. 3). No residual pulmonary regurgitation was found on angiography and a final coronary test showed no abnormalities. Pressures were taken after the procedure, with significantly improved diastolic pressure in the pulmonary artery, going from 4 to 14 mmHg after the procedure, with no significant gradient between the right ventricle and pulmonary artery (2 mmHg).

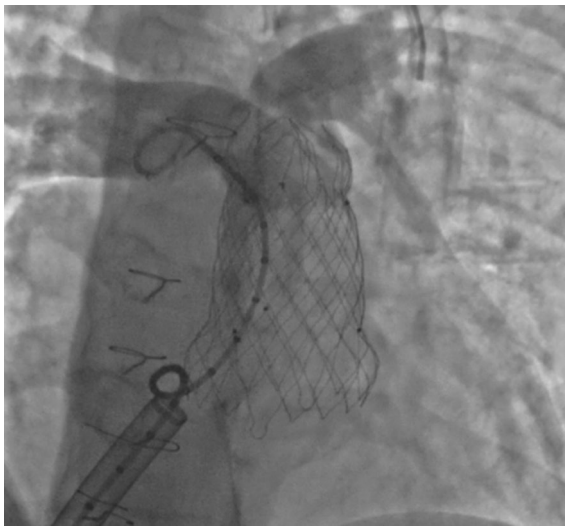

Figure 3. Final post-implant angiography.

Follow up after the procedure

One month after the procedure, the patient was asymptomatic, in NYHA functional class I, and had no cyanosis or dyspnea with activity. On physical exam, he had an oxygen saturation of 99%, with no abnormalities. The follow up echocardiogram reported trivial pulmonary regurgitation with no stenosis or paravalvular leaks, and adequate biventricular function.

Discussion

There are several reports to date of Venus P-valve implantation experiences around the world, with favorable outcomes[5,8-10]. Unlike the other available valves, Venus P-valve implantation does not require a stent to change the RVOT into a rigid conduit[11,12]. This reduces procedure time and exposure to radiation. In addition, radiopaque marks on the distal end of the straight part of the valve allow it to be precisely deployed and positioned, keeping it from protruding into the pulmonary trunk bifurcation[3].

Regarding the cost of the different expandable valves authorized by the regulatory agency in our country (INVIMA), the Melody valve (balloon-expandable) is less expensive than the Venus P (self-expanding).

However, the Melody valve is designed for "non-native" RVOTs with a diameter of up to 26 mm. For our patient, with a large RVOT, the self-expanding pulmonary valve available in this country is the Venus P-valve, which is why it was considered to be the ideal choice.

On another note, percutaneous valve implantation decreases orotracheal intubation times, intensive care unit stays and total hospital stays. As far as the cost of surgical replacement compared to the interventional procedure, percutaneous replacement is more expensive due to the cost of the valve. However, in specific cases, like that of our patient, who had already undergone two cardiothoracic surgeries, percutaneous replacement is considered to be the appropriate procedure, as it has lower morbidity and may have a lower risk of complications.

In patients with repaired or unrepaired congenital heart disease and secondary pulmonary regurgitation, the pulmonary valve may need to be replaced depending on the symptoms and hemodynamic repercussions of the regurgitation. Valve replacement candidates must undergo comprehensive assessment with an echocardiogram, cardiac magnetic resonance imaging, a stress test and a Holter electrocardiogram. When the diameter measurements are uncertain, angiography tomography may offer a more precise measurement to determine the size and length of the prosthesis to be implanted, as well as to evaluate the anatomical characteristics of the RVOT.

The selection of our patient, based on echocardiography, angiography tomography, magnetic resonance imaging and sizing balloon measurements through catheterization was effective and allowed the procedure to be successful. In our patient's case, there were no complications or hemodynamic decompensation during the procedure. An echocardiogram the next day showed a properly positioned valve with no stenosis or residual regurgitation. Furthermore, there were no local complications at the puncture sites and the patient was able to be discharged from the hospital 48 hours after the procedure.

Right ventricular volumes, right and left ventricular function and valve competence will be evaluated on follow up, as indicated in the international literature on implantation of this type of valves[8].

Based on this experience, we believe that percutaneous pulmonary valve replacement in dilated native RVOTs is a viable and safe option to improve pulmonary regurgitation and right ventricular dysfunction in this type of patient.

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Ethical responsibilities

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CARDIOLOGY IMAGES

Ventricular pericardial fistula secondary to endocarditis: Unusual complication

Fístula ventrículo-pericárdica secundaria a endocarditis: complicación inusual

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A 49-year-old male patient with no significant medical history consulted due to a 15-day history of recurrent fever with a deteriorated functional class associated with chest pain and loss of strength in his lower extremities, followed by altered consciousness. On cardiovascular physical exam, he had a mitral holosystolic murmur, for which a transthoracic echocardiogram was ordered. This showed vegetation on the mitral valve, with perforation of

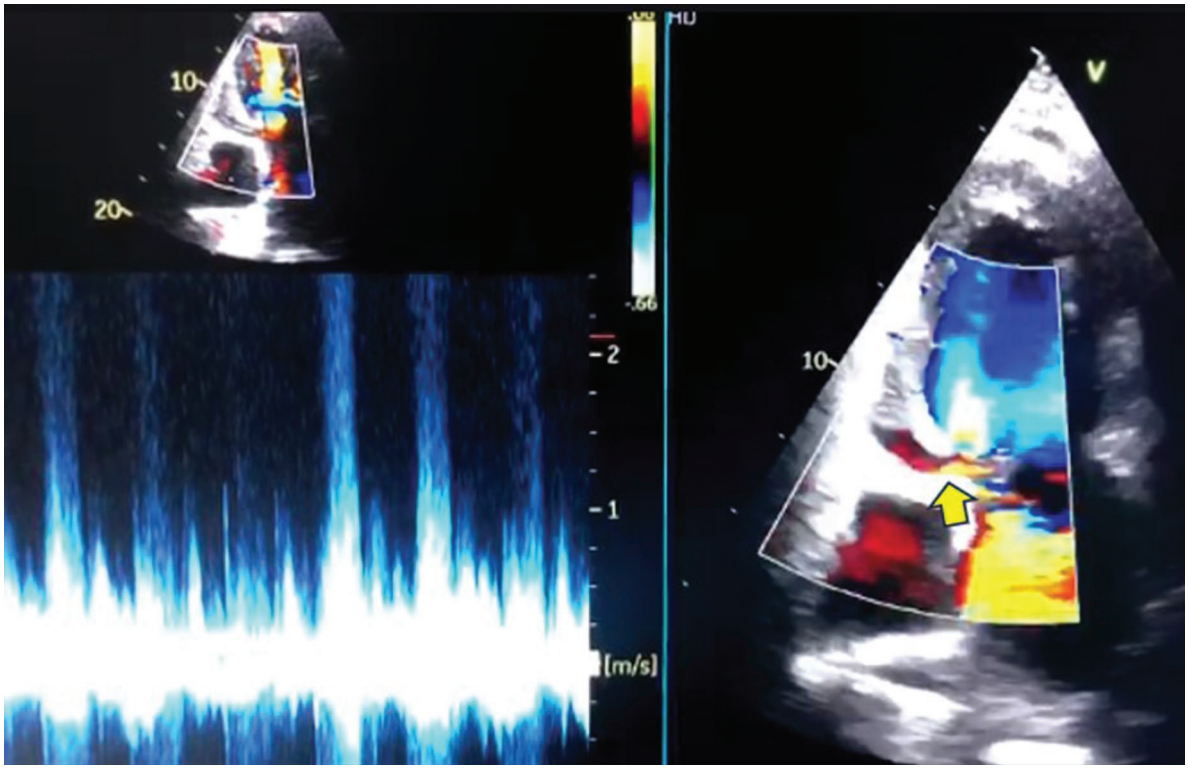

Figure 1. Apical transthoracic echocardiographic view. Evidence of anterior mitral annulus perforation relative to segment A3, causing a ventricular pericardial fistula.

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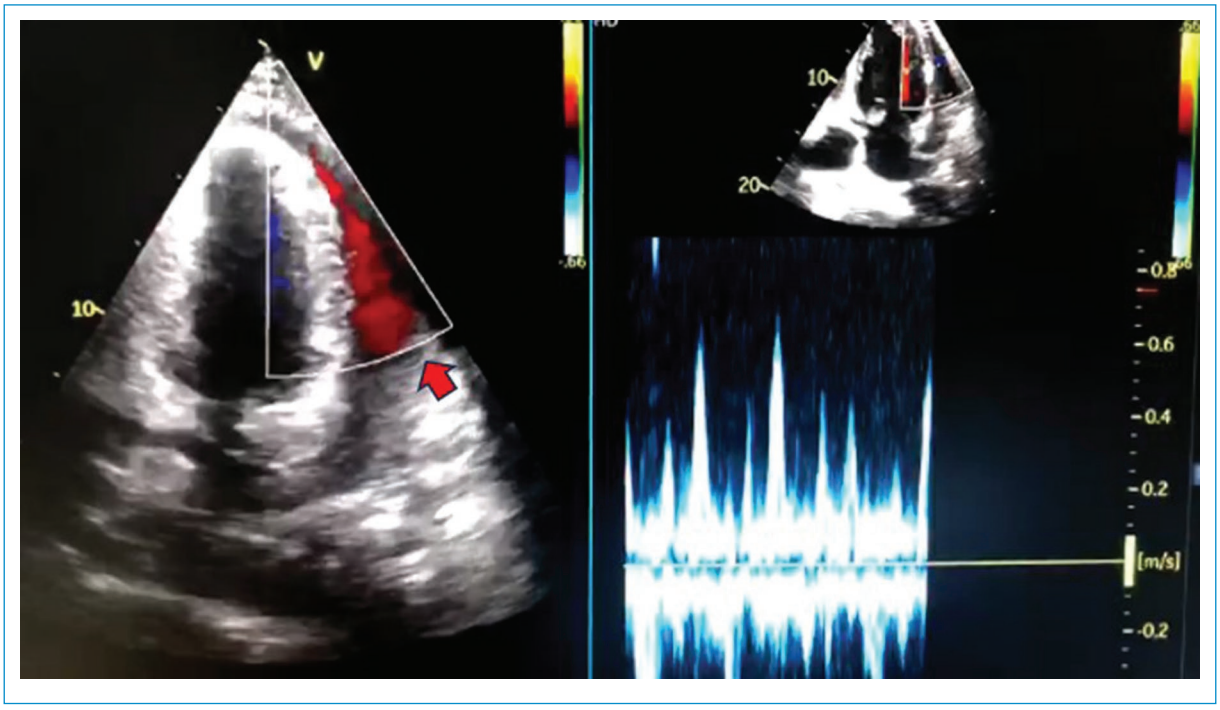

Figure 2. Transthoracic echocardiogram. The pericardial cavity shows signs of cardiac tamponade.

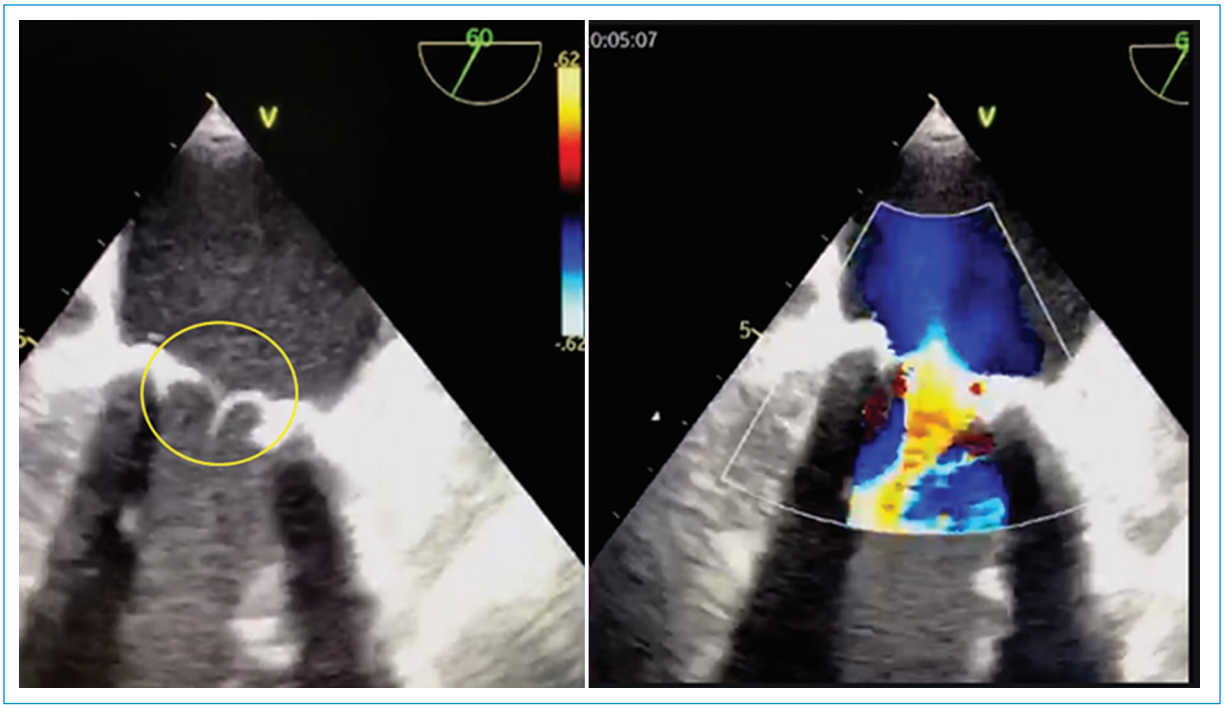

Figure 3. Apical transthoracic echocardiogram showing a normally functioning biological mitral prosthesis with no fistula.

the A3 segment, a severe mitral regurgitation jet, and anterior mitral annulus perforation relative to the A3 segment, causing a ventricular pericardial fistula with evidence of severe circumferential pericardial effusion with flow seen on color Doppler (Fig. 1; yellow arrow). The pericardial cavity showed signs of cardiac tamponade (Fig. 2; red arrow), and the left ventricle was hyperdynamic, with a 68% ejection fraction. Surgery was performed to resect the vegetation and confirm the fistula trajectory, closing it with an autologous pericardial patch and replacing the mitral valve with a #27 biological prosthesis. The patient recovered satisfactorily. A follow up echocardiogram prior to discharge showed a normally functioning biological mitral prosthesis (Fig. 3; yellow circle), with no periprosthetic leaks or evidence of a residual fistula (Fig. 3), a normal left ventricular thickness and chamber, global hypokinesia and mild systolic dysfunction (40% LVEF).

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CARDIOLOGY IMAGES

Use of rotational angiography with 3D reconstruction as a guide for stent aortoplasty in a pediatric patient with coarctation of the aorta

Uso de angiografía rotacional con reconstrucción 3D como guía para aortoplastia con stent en paciente pediátrico con coartación de aorta

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Departament of Hemodynamics, Clínica Neuro Cardiovascular, Cartagena, Colombia

Objective

To share the experience of using rotational angiography with 3D reconstruction as a guide for angioplasty with stenting in a pediatric patient with severe coarctation of the aorta.

Procedure

This was a 9-year-old male patient who weighed 30 kilograms and had a history of systemic hypertension and headaches. On physical examination, he had a 50 mmHg pressure gradient between his upper and lower limbs. Pediatric cardiology diagnosed coarctation of the aorta based on echocardiography, and referred him for aortoplasty with stenting. Rotational angiography was performed using Phillips Azurion 7 equipment, with a low radiation protocol at 30 images per second for five seconds, with contrast medium calculated at 1 cc/kg, diluted to 50% with 0.9% saline solution (Fig. 1). There was severe juxtaductal coarctation of the aorta, with a 40 mmHg peak-to-peak gradient. The acquired image was reconstructed and superimposed on live fluoroscopy, which guided the implantation of a 38 zig CP stent over a 12 x 45 mm balloon (Figs. 2, 3 and 4). At the end of the procedure, there was a residual 5 mmHg peak-to-peak gradient. A total of 60 milliliters of contrast was used, with a fluoroscopy time of 8 minutes; PDA (Product Dose - Area): 18.5 Gy.cm2.

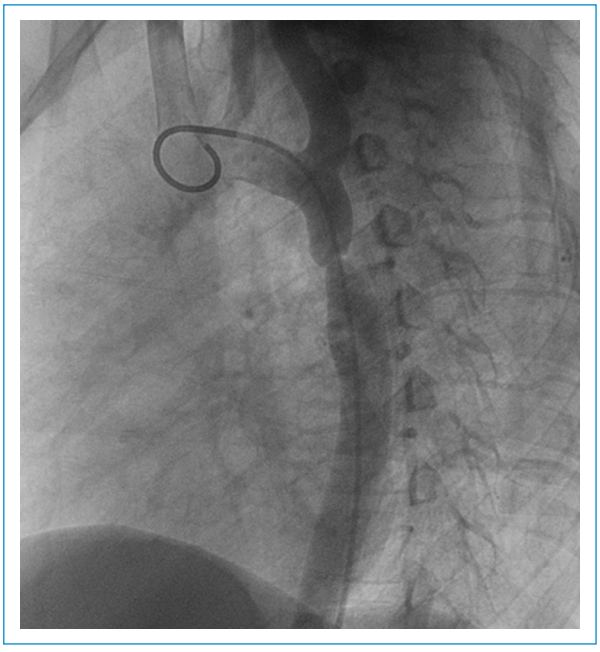

Figure 1. A rotational thoracic aortogram showing severe coarctation of the aorta, with post-stenotic dilation.

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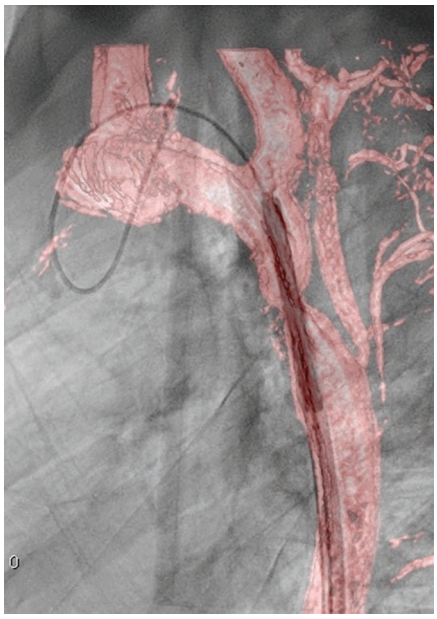

Figure 2. Three-dimensional reconstruction of the rotational aortogram superimposed over live fluoroscopy during stent implantation at the coarctation site.

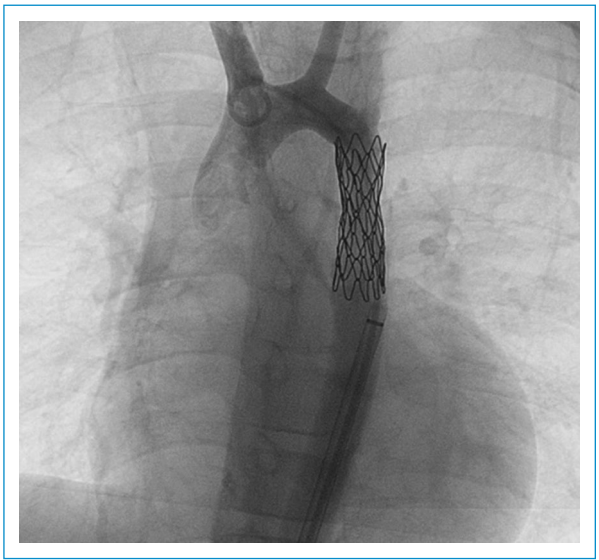

Figure 3. A rotational aortogram showing the stent implanted at the coarctation site.

Conclusion

This technique allows the operator to have a dynamic three-dimensional map, providing a useful anatomical reference during complex endovascular procedures. This reduces procedure time, radiation exposure and contrast medium volume when compared to traditional two-dimensional angiography.

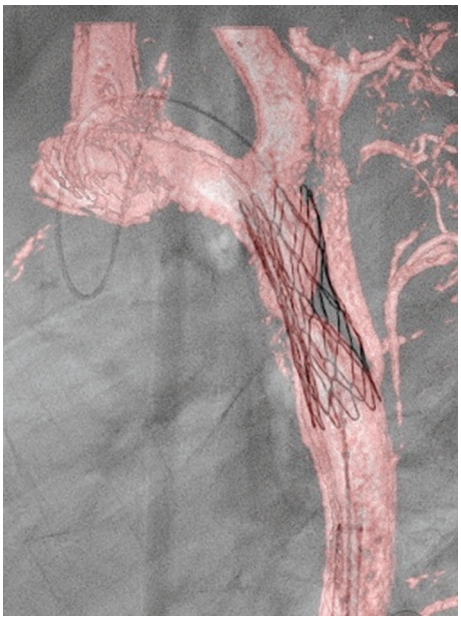

Figure 4. Three-dimensional reconstruction of the rotational aortogram superimposed over live fluoroscopy showing proper stent implantation at the coarctation site.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical responsibilities

Human and animal protection. The authors declare that no experiments were performed on humans or animals for this study.

Data confidentiality. The authors declare that they have followed their workplace protocols for the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Use of artificial intelligence to generate text. The authors declare that they have not used any type of generative artificial intelligence in drafting this manuscript nor in creating figures, graphs, tables or their respective captions or legends.

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LETTER TO THE EDITOR

Complementary information to the article: Recommendations for management and follow-up in patients with transthyretin-mediated hereditary amyloidosis

Información complementaria: recomendaciones de manejo y seguimiento en pacientes con amiloidosis hereditaria mediada por transtiretina

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Bogotá, D.C., Feburary 2, 2024

Dear Editor:

The following complements the declartion of conflicts of interest and provides some clarifications for the article titled “Recommendations for treatment and follow-up in patients with transthyretin-mediated hereditary amyloidosis,” published in Revista Colombiana de Cardiología, Volume 30, No. 6, 2023.

After reading the questions, the first thing we noted was that the document includes diagnostic and follow-up elements in patients with transthyretin-mediated amyloidosis and we did not consider any recommendations for specific treatment. Thus, the title that best reflects the content is “Recommendations for diagnosis and follow-up of patients with transthyretin (TTR)-mediated hereditary amyloidosis.”

The recommendations we have given for follow-up are (in order):

- The role of genetics in hereditary transthyretin-mediated (hATTR) amyloidosis.
- Neurological follow-up in symptomatic patients.
- Complementary tests in patients with hATTR and carpal tunnel syndrome.
- Complementary autonomic nervous system assessments in patients with hATTR.
- Cardiology assessment in patients with hATTR.
- Nephrological follow-up in patients with hATTR.
- Ophthalmological treatment of patients with hATTR (in which ophthalmologists recommend symptomatic treatment).

This working group began as an academic initiative among colleagues. We are a group of physicians from

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different specialties who began to diagnose patients with TTR amyloidosis in Colombia. As we needed the intervention of other specialties, we established an interest group that met at various gatherings focusing on this topic. Gradually, we became aware of the unmet need for establishing guidelines adapted to our healthcare setting, which could guide physicians throughout the country on a care route that would encompass the complexity and interdisciplinary work these patients require. Many of us were trained at international referral centers for this disease in the United Kingdom, Spain, Switzerland and Portugal. We contacted the PTC Therapeutics laboratory to request logistical support (travel and one night's stay) for the meeting to finalize the manuscript, following a literature review process conducted by the discussion panel members, in which Dr. Efraín Gómez (respected cardiology professor) participated, among others.

The criteria for selecting the participants were:

- Experience in managing neuromuscular diseases
- Experience in managing patients with amyloidosis
- Publications on the topic
- Knowledge of and interest in the disease
- Willingness to work on the project without receiving fees or compensations.

A multidisciplinary panel of experts was selected, consisting of 41 specialists in different medical fields (cardiology, pulmonology, physiatry, genetics, nephrology, ophthalmology, neurology and imaging) who were invited to participate in the meeting. This list was attached to the submission, in the publication credits.

Having previously collaborated with the Integralis firm in the consensuses on heart failure (in which the cardiologists of this group participated), we decided to approach them again for medical writing services so that PTC Therapeutics could stay removed from any activity related to drafting the meeting report and the article to be submitted for publication, a cost which the laboratory also decided to assume. With Integralis on the team, once the available evidence was reviewed by the specialists mentioned above, we met to draft the proposed recommendations for each of the areas. The relevant bibliography of the disease was sent to all meeting participants, including clinical practice guidelines. At the on-site meeting, the synopsis was presented by specialists in the fields of knowledge. The medical writer certified that the work was conducted independently of PTC Therapeutics.

Subsequently, the recommendations drafted for each specialty were presented and submitted to a vote. The Delphi methodology was used, with a cut-off point of 75% favorability. If this degree of favorability was not reached, the arguments in favor and against were presented by the panel and the recommendation was restructured according to the discussion. This revised recommendation was then submitted to a second vote. Once the recommendations were accepted, minor adjustments were made in their wording and content according to the participants' opinion. The main authors performed the literature review and drafted the first version of the recommendations, which was presented during the consensus meeting.

Considering that many of us have received, at some point in our practice, honorariums, scholarships, advisory boards and sponsorship of academic activities by the industry, we attach this declaration explicitly clarifying that PTC Therapeutics, in particular, never tried to influence the recommendations that appear in the article. In fact, the article revisions made by the authors after the meeting did not change the recommendations at all, since according to the established methodology, these changes required a new vote. A recording exists of the entire meeting. Therefore, we strongly reject the suggestion that this paper has been influenced by the pharmaceutical industry.

In addition, we declare, on our word of honor, that the medical writer's work was completely independent of PTC Therapeutics and only reflects information obtained during the meeting or suggested by the authors during the review process.

Regarding geneticist Diana Sánchez's current position at PTC Therapeutics, as stated by the doctor, we stipulate that when she participated in the consensus, she was not working for PTC Therapeutics, and the affiliations recorded in the article refer to her employment situation at that time.

When the article was submitted, the names of the participants who were not main authors were included in the acknowledgement section on the title page. The published article does not contain this section and, therefore, we believe that this was probably a typographical error, and therefore include the acknowledgments paragraph here.

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Ortega, Alba Marentes, Luis Fontanilla, Jenny Vicuña, Liliana Villareal, Diana Carolina Ramos, Sandra Castellar, Dora Inés Molina, Jaime Crump, Isabel Cárdenas, Jubby Marcela Gálvez, Gustavo Márquez, Marco Alvarado and Diego Jiménez for their participation in the consensus and contributions to the discussion.

After inquiring again about industry sponsorships received, we added the following changes to the Declaration of Conflicts of Interest:

- Erika Martínez has received honorariums from Abbott, Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Pfizer, PTC Therapeutics, Menarini, Merck S&D, Sanofi, Servier, MSD, Bristol, Novartis and Roche.
- Gina González Robledo has participated in conferences and advisory boards for Abbott/St. Jude, Astra Zeneca, Bayer (Colombia and Perú), Boehringer Ingelheim, CSL Vifor International, Farma Colombia and Ecuador, Novartis, Pfizer (Colombia, Honduras, Costa Rica), PTC Therapeutics, Menarini, Sanofi, Servier and Temis Lostalo Argentina, and has received a scholarship prize from the Asociación Colombiana de Medicina Interna with Vifor International for one year of training in heart failure and transplantation in Spain.

The remaining authors have nothing to declare besides PTC Therapeutics's logistical support for the meeting.