- **40 years beating with Colombian cardiology**
- **Decongestion in acute heart failure**
- **Hospital neurovascular complications after cardiovascular surgery**
- **COAPT score in MitraClip therapy**
- **Heart transplantation in Colombia**

11002ACOL256

EDITORIAL

Forty years beating with Colombian cardiology: trajectory and future of the Colombian Journal of Cardiology

Cuarenta años latiendo con la cardiología colombiana: trayectoria y proyección de la Revista Colombiana de Cardiología

Darío Echeverri

Editor en Jefe, Revista Colombiana de Cardiología

Miembro Honorario, Sociedad Colombiana de Cardiología y Cirugía Cardiovascular.

Introduction

Revista Colombiana de Cardiología (RCC) [Colombian Journal of Cardiology] published its first issue for the national scientific community in November 1985 (Fig. 1), under the direction of Dr. Jorge León-Galindo (Fig. 2A), its first editor-in-chief, and while Dr. Bernardo Tovar Gómez was president of the Society (Fig. 2B). Today, it celebrates four decades of continuous publication, establishing itself as the official scientific organ of the Sociedad Colombiana de Cardiología y Cirugía Cardiovascular [Colombian Society of Cardiology and Cardiovascular Surgery]. This commemorative article intends to highlight the fundamental milestones of its publishing history and its scientific and technological evolution, as well as project the challenges and opportunities it faces as a platform for scientific dissemination in a more globalized academic and scientific setting. *Revista Colombiana de Cardiología* represents not only a record of the progress of cardiology in Colombia and Latin America, but also a testament to the cardiovascular medicine community's commitment to research, continuing education and academic excellence, over several generations.

Today, RCC is the Society's official scientific publication. It is issued every two months, is open access (available free of charge for authors and readers), and undergoes peer review. It is published electronically and accepts manuscripts for review in both Spanish and English on basic, epidemiological, surgical and clinical topics within the broad spectrum of cardiovascular medicine. It consists of an editor-in-chief, an editorial committee, an arbitration committee, an international committee, a digital communications committee and an administrative and editorial assistance department.

Four decades of living history

In 1985, RCC was born in response to the urgent need for an academic medium that would collect, organize and disseminate the knowledge produced by Colombian cardiologists. Its foundation coincided with a crucial time in the Society´s history in which modern cardiology was growing in this country, different specialties and subspecialties were emerging and being consolidated, and technology was beginning to
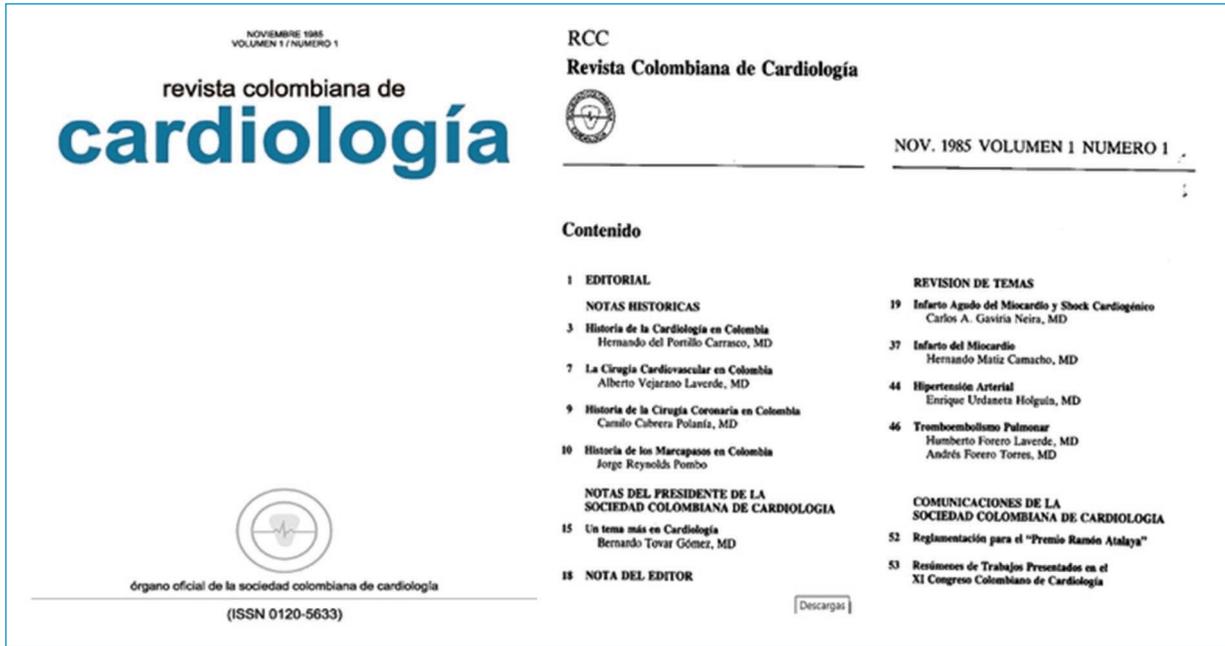
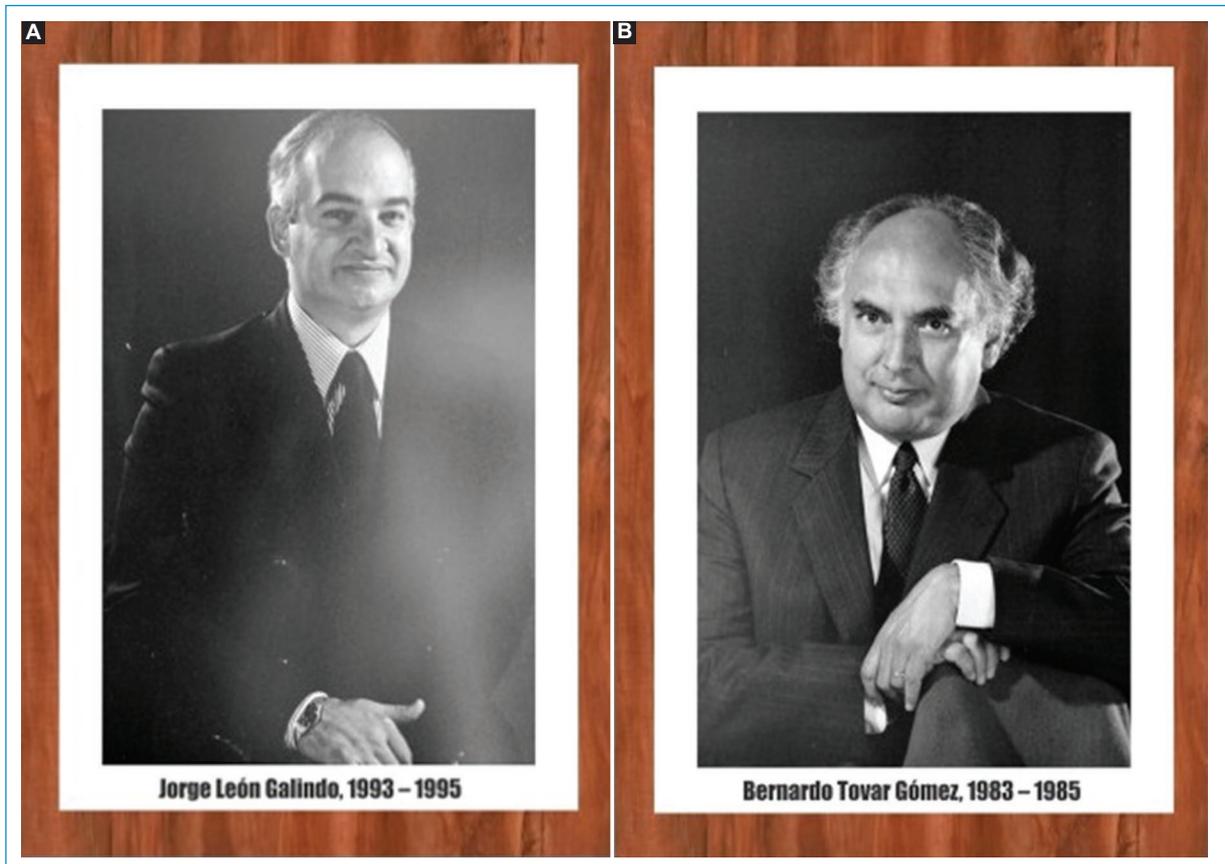**Figure 1.** Content of the first issue of *Revista Colombiana de Cardiología*. Published in November 1985.

Figure 2. A: Dr. Jorge León-Galindo, former president of *Sociedad Colombiana de Cardiología*, Founder and Editor Emeritus of *Revista Colombiana de Cardiología*. **B:** Dr. Bernardo Tovar Gómez, President of *Sociedad Colombiana de Cardiología* (1983-1985).

be introduced in the diagnosis and treatment of cardio-vascular diseases.

Since then, RCC has witnessed and played a leading role in the development of clinical and preventive, interventional, imaging and surgical cardiology, serving as a mirror of the scientific and technological advances that have marked our region and the world.

Editorial and scientific evolution: From a bulletin to an indexed journal

The journal´s first issues reflected the enthusiasm of a growing medical community, with original articles, case reports, reviews and short papers. Over time, RCC adopted international publishing standards, implemented peer review processes and achieved indexation in regional and international databases.

The initial phase covered a long period of approximately 30 years, during which the staff worked hard to achieve structure and maturity, consolidate a team of highly committed specialists and administrative staff, create a publishing process and attain national ranking.

Over the last decade, the journal has experienced key transformations, initially supported by the Elsevier publishing house and now by Permanyer, achieving a great impact in terms of the professionalization of the editorial committee; more participation of the associated editors, international reviewers and methodological experts; and the adoption of digital tools to transition from a paper version to an electronic, online setting. At the same time, it extended its reach due to inclusion in databases like SciELO, LILACS and Latindex and, most recently, in search engines that are more visible and open to international authors, maintaining its focus on Latin American cardiovascular problems. Simultaneous publication in Spanish and English have allowed greater visibility for both the journal and the authors, which have also made it a more attractive medium for publishing articles from different continents around the world.

A pillar of continuing medical education and national research

Throughout these 40 years, RCC has been much more than a scientific journal. It has been a vehicle of visibility for young researchers; a setting for continuing medical education, by conveying the clinical guidelines and consensuses adapted to the Colombian setting; a platform for academically positioning the nation´s

universities and medical centers; and a historical archive for studying the evolution of medical thinking and cardiovascular challenges in our population. In 2020, it participated in the call for indexation of specialized Colombian scientific journals – Publindex 2020 –, and was classified in Category C, as it scored in the fourth quartile of the SCImago Journal Rank.

Furthermore, RCC is part of the Society's Quality Management System under the ISO 9001:2015 Standard and certified by Bureau Veritas, due to its high-level processes in planning, organization, tracking, final product and client satisfaction. It also has an established social media plan (Instagram, Facebook, X), in line with the current needs, and provides specific education microsites on its web page (www.revcolcard.org) with the industry, achieving continuing education, survey modules and podcasts. Likewise, it has implemented an article search system through its web site to offer access to all the content published throughout its 40 years of existence.

Over this last decade, which has been a time of strategizing and continuous improvement, RCC has been especially interested in training its editors and arbitrators and has offered online courses in scientific writing and critical analysis of scientific articles to help authors construct a better product. Finally, it has created internal policies, restructured its web page (www.revcolcard.org), created information microsites, trained reviewers and committee members, strengthened digital activities (the digital ecosystem), involved young cardiologists who belong to the Society in the publishing process, and entered into an agreement with the Learning and Research Resource Center at Universidad del Rosario and the indexation "Plan" on PubMed Central.

Challenges and opportunities for the future

The next few years will bring several demands: maintaining the journal´s regional identity without losing relevance within the global scientific setting. In this regard, some of the key challenges arise, as expected, from trying to adapt to a demanding world with increasingly fast communication. As one of its projects, RCC is planning to advance in the indexation process for high-impact international databases (Scopus, PubMed Central, DOAJ) and continue to foster bilingual publication (Spanish-English) to broaden its global reach; strengthen author and reviewer training on topics pertaining to ethics, transparency, scientific writing, and

statistical analysis; integrate technologies – like artificial intelligence – in publishing processes and article review, in order to facilitate and shorten the entire process, seeking greater immediacy; and, finally, increase interinstitutional and international collaboration to improve the quality and variety of the articles.

Along with the challenges, there are great opportunities for improvement with a journal that is changing and growing. These opportunities include conducting training courses for students and young cardiologists in writing scientific articles, as well as capacity building courses for arbitrators and authors; drafting and publishing RCC policies in line with the international recommendations and guidelines of the Committee on Publication Ethics and the International Committee of Medical Journal Editors, with a plan for improvement of our editorial practices; and achieving gender equality in authorship, the group of reviewers, and the editorial and executive committee.

As with all scientific journals, RCC has a plan for improvement of its editorial practices, understood as specific national and international codes of conduct for research. These emphasize complaints of misconduct; authorship and the contribution of coauthors; responses to complaints and appeals, declarations of conflicts of interest, intellectual property, adequate, efficient and transparent peer review processes, and post-publication discussions and corrections. Continuous improvement strategies have been considered that attempt to attract people in training in Colombia and internationally. Other strategies include having a greater presence on social media with the creation of creative, attractive and scientifically responsible content; improving the quality of the articles; constantly updating its web page; and involving artificial intelligence in the publishing process.

In summary, a journal with a solid past and a vibrant future

Revista Colombiana de Cardiología has been a faithful witness of scientific-cardiovascular development in Colombia. After 40 years, it presents itself as a mature, rigorous, modern publication that is committed to academic excellence. As the official organ of *Sociedad Colombiana de Cardiología y Cirugía Cardiovascular*, it has the mission and privilege of continuing to be the editorial heart of cardiovascular medicine in Colombia and one of the main journals in Latin America.

The cardiovascular medical community is called to continue supporting this journal, either as authors, reviewers or readers, because a scientific journal is not just edited, it is built as a team. The Society's members should be permanent auditors and monitor its protection and growth; it is the Society's most valuable asset. We invite you to work for it along with us.

Acknowledgement

Application of a rapid decongestion protocol for patients with acute heart failure

Aplicación de un protocolo de descongestión rápida para pacientes con falla cardíaca aguda

Natalia Henao, Yuly J. Rojas, Mónica Zuluaga, Juan C. Chavarriaga*, and Natalia A. Arboleda

Department of Internal Medicine and Medical Specialties, Hospital Pablo Tobón Uribe, Medellín, Colombia

Abstract

Introduction: *Heart failure has a high prevalence and mortality and is the cause of frequent hospitalizations due to acute decompensation with congestion. Diuretics are the cornerstone of treatment.* **Objective:** *To describe the results of applying a decongestion protocol in a population with acute decompensated heart failure in a tertiary care center.* **Methods:** *Descriptive, retrospective study that included patients > 18 years old with decompensated heart failure and congestive signs, hospitalized for more than 24 hours in a high complexity center and in whom an institutional decongestion protocol was applied.* **Results:** *Fifty-five patients with decompensated heart failure were included. There was 85% adherence to the protocol with the initial bolus administration of furosemide and, in 82% of cases, the door-to-diuretic time was less than 1 hour. Urine sodium was below target in 3.6% of patients. A median diuresis of 2.4 L was achieved. None of the patients developed acute kidney injury during hospitalization or upon discharge. The median hospitalization was five days, with 3.6% mortality and 9% readmissions for heart failure within 30 days.* **Conclusions:** *The aggressive decongestion protocol resulted in a short hospital stay, low mortality, and few readmissions. The risk of hypotension, renal failure, or electrolyte disorders did not increase.*

Keywords: Heart failure. Diuretics. Furosemide.

Resumen

Introducción: *La falla cardíaca tiene alta prevalencia y mortalidad, y es causa de frecuentes hospitalizaciones por descompensación aguda con congestión. Los diuréticos son la piedra angular del tratamiento.* **Objetivo:** *describir los resultados de la aplicación de un protocolo de descongestión en una población con falla cardíaca con descompensación aguda en un centro de alta complejidad.* **Métodos:** *Estudio descriptivo, retrospectivo que incluyó pacientes mayores de dieciocho años con falla cardíaca descompensada y signos congestivos, hospitalizados por más de veinticuatro horas en un centro de alta complejidad y en quienes se aplicó un protocolo institucional de descongestión.* **Resultados:** *Se incluyeron 55 pacientes con falla cardíaca descompensada. La adherencia al protocolo con administración de bolo inicial de furosemida fue del 85% y en el 82% de los casos el tiempo puerta-diurético fue menor a una hora. El sodio urinario estuvo bajo la meta en el 3.6% de los pacientes. Se logró una mediana de diuresis de 2.6 litros. Ningún paciente desarrolló lesión renal aguda, durante la hospitalización o al egreso. La mediana de hospitalización fue de cinco días, la mortalidad fue del 3.6% y los reingresos por falla*

cardíaca a treinta días fueron del 9%. **Conclusiones:** *El protocolo agresivo de descongestión resultó en una estancia hospitalaria corta, baja mortalidad y reingresos. No se incrementó el riesgo de hipotensión, falla renal ni trastornos electrolíticos.*

Palabras clave: Insuficiencia cardíaca. Diuréticos. Furosemida.

Introduction

Heart failure is a large-scale health problem due to its high prevalence of 2.3% in Colombia, according to data from the Ministry of Health and Social Protection[1], and a mortality of up to 10% per year[2]. In many cases it ends up being progressive, with deteriorated function and recurrent hospitalizations. Within the group of patients hospitalized for congestion, those who are discharged with residual congestion (up to 48% of cases) and those with persistent congestion and hypotension have a worse prognosis, with up to 50% one-year mortality[3].

Intravenous (IV) loop diuretics are the cornerstone of treatment for acute decompensated heart failure (ADHF) with congestive signs. Several studies have been published over the last 15 years, seeking to determine the optimal use of IV diuretics as far as dose, method of administration, length of administration and response assessment. In the DOSE-AHF[4] study, IV furosemide was administered to patients with ADHF; bolus administration was compared to continuous infusion, and low doses (the same as the outpatient oral dose) were compared to high doses (2.5 times the ambulatory oral dose). There were no significant differences in the main outcomes (patient-evaluated symptoms and creatinine changes) in the four evaluated groups. However, within the secondary outcomes, there was greater diuresis in the high-dose group. The study has been questioned for delaying IV diuretic dose adjustments for up to 48 hours. The ADVOR[5] study also found a better diuretic response and decongestion after three days in patients who received high doses of IV diuretics (twice the ambulatory oral dose) in addition to acetazolamide. Some registries have evaluated the importance of early IV diuretic administration and have found lower mortality when it is administered within 60 minutes of admission[6-8]. In addition, natriuresis has proven to be a better parameter for evaluating the diuretic response than body weight and fluid balance alone. A spot urine sodium (UNa) level below 50-70 mmol/L two hours after administering the first IV furosemide bolus in patients with congestive ADHF has been shown to indicate a poor prognosis[9]. The American College of Cardiology (ACC) and the European Society of Cardiology (ESC) have proposed some decongestion protocols[10,11] based on three pillars: 1) early administration of diuretics – an IV bolus within an hour of admission – ; 2) a high initial dose – twice the ambulatory dose – and 3) dose review and adjustment every six hours according to diuresis and UNa levels. This study describes the results of applying this decongestion protocol in a population with acute decompensated heart failure at a tertiary care center.

Methods

We conducted a retrospective, descriptive study of a cohort that included patients over the age of 18 with a diagnosis of ADHF and congestive signs, who were hospitalized for more than 24 hours at a tertiary care facility in the city of Medellín. They were managed with the institution's established decongestion treatment protocol. These patients were selected by ICD-10 code over a period of six months from July to December 2022. Acute decompensated heart failure was defined as new onset or worsening signs and symptoms of heart failure[1] in patients with altered cardiac structure and function. Patients with reduced and preserved ejection fraction (EF) were included; while patients with a diagnosis of acute myocardial infarction, hypersensitivity to loop diuretics, advanced kidney disease on dialysis, nephrotic syndrome or decompensated cirrhosis and patients hospitalized in the intensive care unit or special care unit since hospital admission were excluded. Patients with prolonged hospitalization for a diagnosis other than decompensated heart failure and those admitted to the emergency room for reasons other than ADHF were also excluded.

After reviewing the medical charts, the following variables were recorded in the REDCap database: sex, age, heart failure etiology, ejection fraction, valve disease, creatinine, blood urea nitrogen (BUN), electrolyte panel on admission, weight on admission, weight at discharge, Stevenson hemodynamic classification, cause of heart failure decompensation, initial furosemide dose, door-to-diuretic time, SU two hours after admission, maximum furosemide dose, maximum

diuresis recorded, use of other diuretics, furosemide dose at discharge, mechanical ventilation and treatment with vasodilators, inotropes, dialysis, or both. Inpatient and 30-day mortality were evaluated, as well as readmissions within 30 days. The last three variables were evaluated through telephone follow-up which was recorded in the medical chart and was done 72 hours and 30 days after discharge.

The decongestion protocol was based on the ESC and ACC guidelines[10,11]. A special alert, known as a "failure code" was set up in the institution to rapidly identify patients with ADHF. This code is a medical order activated by nursing staff at the triage desk which allows the physicians to provide priority care and begin diuretics within one hour of admission. To ensure that the protocol and failure code orders were followed, training was provided for the medical and paramedical staff in the emergency room. This code also included an order for the nurses to sequentially ask the patient to empty his/her bladder through spontaneous urination, record his/her weight on admission, and administer the first dose of furosemide. At that point, a record of urine output and daily weight was begun on the medical chart. The initial furosemide dose was administered as a bolus, with a dose equal to or double the dose the patient was receiving as an outpatient. If the patient was not on ambulatory oral furosemide, 20 to 40 mg were administered IV. Along with the order for the first dose of furosemide, UNa was ordered at two hours, and urine output was evaluated at six hours. The physician evaluated whether the patient met the target for two parameters: UNa greater than 70 mEq/L and 600 ml of urine output (100 ml/h). For patients who met these two parameters, the initial furosemide dose was maintained every 12 hours, and target accomplishment (three to five liters of urine output) was reassessed in the following 24 hours. If the patients did not meet the target urine output, the furosemide dose was doubled, and they were reassessed in six hours. If the target urine output (600 ml) was achieved, the furosemide dose was ordered on a schedule. If the expected urine output was not achieved, the furosemide dose was doubled up to a maximum of 320 mg IV, since the maximum recommended dose in 24 hours is 600 mg of furosemide IV. If patients reached the ceiling dose without achieving the target urine output, a third diuretic was added; the first choice was hydrochlorothiazide at 25 mg per day. On admission, all patients received 25 mg of spironolactone and a sodium-glucose cotransporter-2 (SGLT-2) inhibitor, if not contraindicated, regardless of their type of heart failure. If, despite triple nephron blocking, the patients continued to have congestion and did not achieve the target urine output, they were considered refractory and transferred to the special care unit to continue treatment with advanced strategies which included IV vasodilators, IV inotropes, or dialysis support, depending on the case. For those who achieved the target urine output, the same IV dose was maintained until decongestion was achieved. At that point, they were switched to oral dosing which was maintained for at least 24 hours before granting discharge.

All patients were educated by a heart failure nurse on diet, exercise, daily weight recording at home and how to adjust the oral furosemide dose before having to go to the emergency room.

Descriptive statistics were used to calculate measures of central tendency and frequencies. Absolute and relative frequencies were reported for qualitative variables. The mean, standard deviation and median with interquartile ranges were reported for normally distributed variables, or minimum and maximum values when normality was not proven. Statistical analysis was done using the SPSS 21 program.

The study adhered to the principles established in the Declaration of Helsinki and was approved by the institution's Ethics Committee.

Results

During the period from July to December 2022, 307 patients with a diagnosis of acute heart failure were found. A total of 252 patients were excluded for the following reasons: 110 patients had a reason for admission other than acute heart failure, or the described decongestion protocol was not applied. Another six patients had prolonged hospitalization related to a diagnosis other than decompensated heart failure; 36 patients were initially admitted to the intensive care unit or special care unit; 25 patients were admitted for acute myocardial infarction; 22 patients had advanced kidney disease on dialysis, nephrotic syndrome or decompensated cirrhosis; and three patients had heart failure that was being managed in palliative care.

Fifty-five patients were included, with an average age of 77 ± 13 years, 58% of whom were female, mostly from urban areas (78%). The baseline characteristics are presented in table 1. Altogether, 34.5% were admitted for new onset failure; the most common etiology was hypertension in 36.4%, followed by valve problems in 30.9%, tachycardiomyopathy in 23.6%, ischemic cardiomyopathy in 14.5% and, other

etiologies like dilated cardiomyopathy, amyloidosis, human immunodeficiency virus, obesity and toxicity in smaller percentages. A total of 27.3% had had at least one hospital admission in the previous year. Altogether, 36.4% were classified in New York Heart Association (NYHA) functional class III, 32.7% in II, and 1.8% in I; information on the prior functional class was not available for 29% of cases. Heart failure with reduced EF was found in 43.6% of the patients, and heart failure with preserved EF was found in 45.5%. Altogether, 21.8% had electrical stimulation devices, and the main comorbidities were: hypertension 81.8%, atrial fibrillation 36.4%, dyslipidemia 36.4%, diabetes 27.3%, kidney disease 27.3%, chronic obstructive pulmonary disease 27.3%, smoking 12.7%, thyroid disease 12.7%, peripheral artery disease 9.1%, coronary disease 9.1%, cerebrovascular disease 7.3%, cancer 5.5% and flutter 1.8%. The most frequent causes of decompensation were disease progression 29.1%, poor adherence 21.8%, arrhythmia 12.7%, infection 9.1% and uncontrolled hypertension 3.6%. The cause of decompensation could not be determined in 50% of the patients.

The laboratory tests and medications the patients were taking on admission are described in table 1.

Regarding the decongestion protocol (Table 2), there was 85% adherence in the administration of the initial IV furosemide bolus. This bolus was 40 mg in 45.5% of the patients and 80 mg in 42%. The median door-to-diuretic time was 1.07 hours and was less than one hour in 82% of cases. A UNa level was obtained two hours after the diuretic bolus in 94.5% of the patients. Only two patients had a level under 70 mmol/l (3.6%) (Fig. 1). Urine output was less than 100 ml/h in 6% of patients on the first assessment following the initial bolus. Sixty-seven percent had treatment adjustments due to not achieving the target diuresis or natriuresis or both. Thirty percent achieved a urine output of more than three liters in the first 24 hours. Fifteen percent received high doses of furosemide (more than 300 mg/24 hours). A median 24-hour urine output of 2,650 (1,575-3,700 ml) was achieved. Intravenous furosemide was administered for a median of four days (2-10 days). A median weight loss (admission-discharge) of 4.9 kg was achieved. A total of 70.9% were treated with SGLT-2 inhibitors and 9.1% with hydrochlorothiazide.

Altogether, 47.3% of the patients had a baseline creatinine of 1.0 mg/dl or less on admission, with an overall average creatinine on admission of 1.2 ± 0.57 mg/dl, reaching an average maximum inpatient value of 1.5±

Table 1. Baseline patient characteristics

Demographics	n = 55
Age (median in years)	81 (70-86)
Sex, n (%)	
Male	32 (58)
Female	23 (42)
Comorbidities, n (%)	
Hypertension	45 (81.8)
Atrial fibrillation/flutter	21 (38.2)
Dyslipidemia	20 (36.4)
Diabetes mellitus	15 (27.3)
Chronic kidney disease	15 (27.3)
Chronic obstructive pulmonary disease	15 (27.3)
Smoking	7 (12.7)
Thyroid disease	7 (12.7)
Chronic arterial occlusive disease	5 (9.1)
Coronary disease	5 (9.1)
Cerebrovascular disease	4 (7.3)
Cancer	3 (5.5)
Heart failure classification according to EF, n (%)	
EF > 50% (preserved)	27 (49.1)
EF < 40% (reduced)	24 (43.6)
EF 40-50% (intermediate)	4 (7.3)
Etiology of heart failure, n (%)	
Hypertensive	20 (36.4)
Valvular	12 (30.9)
Arrhythmic	13 (23.6)
Ischemic	8 (14.5)
Other etiologies	15 (27.3)
NYHA classification, n (%)	
NYHA I	1 (1.8)
NYHA II	18 (32.7)
NYHA III	20 (36.4)
NYHA IV	0 (0)
No information	16 (29.1)
Decompensation classification, n (%)	
Stevenson B (warm-wet)	55 (100)
Use of electrical stimulation devices, n (%)	12 (21.8)
Outpatient medications, n (%)	
ACE inhibitors/ARBs	25 (45.4)
Beta blockers	32 (58.2)
Mineralocorticoid receptor antagonists	13 (23.6)
Angiotensin receptor-neprilysin inhibitors (ARNIs)	2 (3.6)
Furosemide	30 (54.5)
SGLT-2 inhibitors	12 (21.8)
None	9 (16.4)
Hospitalization for heart failure during the last year, n (%)	15 (27.3)
Cause of decompensation, n (%)	
Disease progression	16 (29.1)
Poor adherence	12 (21.8)
Arrhythmia	7 (12.7)
Infection	5 (9.1)
Poorly controlled hypertension	2 (3.6)
Undetermined	28 (50.9)
Laboratory tests	
Serum sodium, mEq/L	138±4.63
Serum potassium (K), mEq/L	4.12±0.63
Serum creatinine, mg/dl	1.2±0.57
Hemoglobin, mg/dl	12.7±2.3)
TSH (mIU/L)	2.29
	(1.25-4.7)

EF: ejection fraction; NYHA: New York Heart Association; ACE inhibitors: angiotensin converting enzyme inhibitors; ARBs: angiotensin receptor blockers; SGLT-2 inhibitors: sodium-glucose cotransporter-2 inhibitors; TSH: thyroid stimulating hormone; mIU/L: milli-international units per liter.

0.7 mg/dl and 1.34 ± 0.59 mg/dl at discharge. No patients developed kidney injury requiring dialysis due to the treatment, nor did they have persistent impaired renal function at discharge. A total of 3.6% required venous vasodilator support during their treatment, and only one patient (1.8%) required a transfer to intensive care and noninvasive ventilation. None of the patients required vasopressor or inotropic support or dialysis. An electrical stimulation device was implanted in 7.1% of the patients.

Table 3 shows the study's main clinical outcomes. The median hospitalization was 5.2 (3-10 days). One patient died during hospitalization due to heart failure progression and advanced disease, and another patient died within 30 days after discharge from a noncardio-vascular cause.

The discharge prescriptions included: beta blockers 78.2%, SGLT-2 inhibitors 74.5%, furosemide 72.7%, ACE inhibitors 41.8%, ARBs 23.6%, MRAs 60%, ARNIs 10.9%, and ivabradine 1.8%. The percentage of readmissions for heart failure within 30 days was 9%; two cases were readmitted for impaired kidney function and disease progression, one case for uncontrolled hypertension, one case for nonadherence to fluid restrictions and one case for nonadherence to treatment due to medications not being provided.

Discussion

This study describes the application of a rapid decongestion protocol in 55 patients through early use of high-dose loop diuretics and close monitoring of the diuretic response through UNa and urine output measurement every six hours until the expected results were achieved.

Several studies evaluating the impact of IV diuretic adjustment based on natriuresis were ongoing during the course of this study and are now published. The PUSH-AHF[12] study evaluated the effect of adjusting diuretics in patients with ADHF according to UNa levels above or below 70 mmol/L and found no significant difference in mortality or hospitalization at 180 days, but did obtain a greater diuretic response (greater natriuresis) at 24 hours. The ENACT-HF[13] study showed a 64% increase in natriuresis at 24 hours when a cohort of patients with conventional treatment was compared to another cohort in which a protocol of IV diuretic adjustment based on UNa results was applied (the furosemide dose was

Table 2. Decongestion protocol

Protocol adherence, n (%)	n = 55
Initial furosemide dose according to the protocol	47 (85.5)
Initial furosemide bolus within one hour of admission	45 (82)
UNa measurement two hours after the furosemide bolus	52 (94.5)
Treatment modification six hours after the initial bolus	39 (71)
Initial IV furosemide bolus, n (%) 20 mg to 40 mg 80 mg to 120 mg 160 mg to 340 mg	 25 (46) 25 (46) 4 (8)
Maximum furosemide dose in 24 hours, n (%) 40 mg to 80 mg 120 mg to 240 mg 320 mg to 480 mg	 18 (32.7) 29 (52.7) 8 (14.6)
Furosemide administration times Time (hours) of the initial bolus administration (median) Time (days) of inpatient IV furosemide (median)	 1.07 4 (2-10)
UNa two hours after the initial furosemide bolus, n (%) Less than 70 mmol/L More than 70 mmol/L Not done	 2 (3.6) 50 (90.9) 3 (5.5)
Urine output (ml) in 24 hours (median)	2,650 (1,575-3,700)
Weight loss (kg) (mean/SD)	4.9 ± 6.07
Use of other diuretics, n (%) Spironolactone SGLT2 inhibitors Hydrochlorothiazide Chlorthalidone	 29 (52.7) 39 (70.9) 9 (16) 0 (0)

n: number of patients; IV: intravenous; mmol/L: millimoles per liter; UNa: urine sodium in a spot sample; kg: kilogram; mg: milligram; SD: standard deviation.
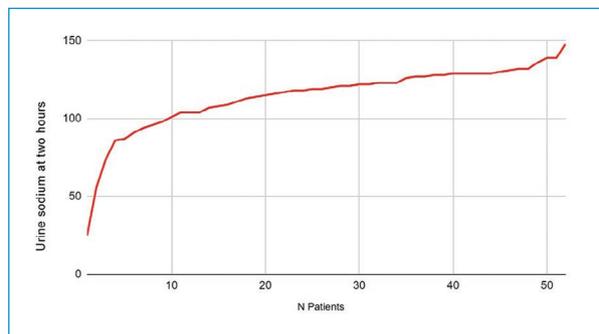

Figure 1. Urine sodium in a spot sample two hours after the initial diuretic bolus.

Table 3. Clinical outcomes

Length (days) of hospitalization (median)	5.2 (3-10)
Inpatient mortality, n (%)	1 (1.8)
Mortality within 30 days of discharge, n (%)	1 (1.8)
Readmissions for heart failure, n (%)	5 (9)

doubled six hours after the initial bolus if the UNa was less than 50 mmol/L). In addition, the length of hospital stay decreased (5.8 vs. 7 days), with no increase in adverse events like electrolyte disorders, hypotension or renal impairment. Other ongoing studies are DECONGEST[14] and ESCALATE[15], which will evaluate the use of UNa as a guide for adjusting diuretics in ADHF, as they are still in the patient recruitment phase and their results have not been published.

It is challenging to follow this protocol in our setting, due to overcrowding in emergency rooms. However, the furosemide dose was able to be applied within the first hour in 82% of the patients, and a daily urine output of 2.6 L was achieved, with only 15% of the patients requiring doses over 300 mg/d. There was no kidney injury, fluid or electrolyte abnormalities or hypotension, and the hospital stay was 5.2 days, which is very low compared to previous data from the same institution (unpublished) and data from recent studies like ENACT-HF[13], with a length of stay of 5.8 days. Likewise, the 9% readmission rate within 30 days and 1.8% inpatient mortality rate are similar to those reported by ENACT-HF.

In this study, UNa measurement two hours after the first furosemide bolus had a low impact on treatment modification six hours after the bolus, as only 3.6% of the patients had a level below 70 mmol/L. This contrasts with the PUSH-AHF study, in which 80% of the patients had a low UNa, which indicated treatment modification at six hours. On the other hand, only 12% of the patients in ENACT-HF had this result, which could be explained by the difference in populations, since 100% of the patients in ENACT-HF had received furosemide as outpatients, compared to 56.4% of our patients (34.5% had new onset heart failure). Other important differences between the populations in ENACT-HF, PUSH-AHF and our study were age (70 years, 74 years vs. 81 years, respectively), the fact that there were more women in our study (37.7%, 41% vs. 58%) and reduced EF < 40% (55.6, 35 vs. 43.6%).

Our study included 27.3% of patients with kidney failure (vs. 50.1% in ENACT-HF), and there were no patients in NYHA IV (vs. 71% in PUSH-AHF). These differences can explain why treatment modifications six hours after the initial bolus in our study population were based on urine output and that the UNa had marginal value.

In this cohort of patients with ADHF, we found that it is possible to apply the decongestion protocol suggested by ESC and ACC in our setting, and that this protocol leads to short hospital stays and lower mortality and 30-day readmissions. Furthermore, the risk of cardiogenic shock, kidney failure or electrolyte disorders did not increase.

Conclusions

In a cohort of patients with ADHF in whom an aggressive decongestion protocol was applied based on early use of high-dose IV furosemide (within one hour of admission) adjusted every six hours until the target urine output was achieved, there was a short hospital stay (5.2 days) as well as low mortality and readmissions (1.3% and 9%, respectively). The risk of kidney failure, hypotension or electrolyte disorders did not increase.

Funding

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 in the course of this study.

Confidentiality, informed consent and ethical approval. The study was evaluated by the ethics and research committee at Hospital Pablo Tobón Uribe. The study did not involve personal patient information or require ethical approval. The SAGER guidelines did not apply.

Use of artificial intelligence to generate text. The authors declare that they did not use any type of generative artificial intelligence in writing this article nor for

creating figures, graphs, tables or their respective titles or captions.

References

1. Rivera-Toquica A, Saldarriaga-Giraldo CI, Echeverría LE, Buitrago A, Mariño A, Arias-Barrera CA, et al. Actualización 2022 del Consenso colombiano de insuficiencia cardíaca con fracción de eyección reducida. Rev Colomb Cardiol. 2022;29(Supl2):1-19.

2. Gerber Y, Weston SA, Redfield MM, Chamberlain AM, Manemann SM, Jiang R, et al. A contemporary appraisal of the heart failure epidemic in Olmsted County, Minnesota, 2000 to 2010. JAMA Intern. Med. 2015;175:996-1004.

3. Lala A, McNulty SE, Mentz RJ, Dunlay SM, Vader JM, AbouEzzeddine OF, et al. Relief and Recurrence of Congestion during and after Hospitalization for Acute Heart Failure: Insights from Diuretic Optimization Strategy Evaluation in Acute Decompensated Heart Failure (DOSE-AHF) and Cardiorenal Rescue Study in Acute Decompensated Heart Failure (CARESS-HF). Circ. Heart Fail. 2015;8:741-8.

4. Felker GM, Lee KL, Bull DA, Redfield MM, Stevenson LW, Goldsmith SR, et al. Diuretic Strategies in Patients with Acute Decompensated Heart Failure (DOSE-AHF). N Engl J Med. 2011;364:797-805.

5. Mullens W, Dauw J, Martens P, Verbrugge FH, Nijst P, Meekers E, et al. Acetazolamide in Acute Decompensated Heart Failure with Volume Overload (ADVOR). N Engl J Med. 2022;387:1185-95.

6. Matsue Y, Damman K, Voors AA, Kagiyama N, Yamaguchi T, Kuroda S, et al. Time-to-furosemide treatment and mortality in patients hospitalized with acute heart failure. J Am Coll Cardiol. 2017;69:3042-51.

7. Park JJ, Kim SH, Oh IY, Choi DJ, Park HA, Cho HJ, et al. The effect of door-to-diuretic time on clinical outcomes in patients with acute heart failure. JACC Heart Fail. 2018;6:286-94, Erratum in JACC Heart Fail. 2018;6:812.

8. Wong YW, Fonarow GC, Mi X, Peacock WF, Mills RM, Curtis LH, et al. Early intravenous heart failure therapy and outcomes among older patients hospitalized for acute decompensated heart failure: findings from the Acute Decompensated Heart Failure Registry Emergency Module (ADHERE-EM). Am Heart J. 2013;166(2):349-56.

9. Singh D, Shrestha K, Testani JM, Verbrugge FH, Dupont M, Mullens W, et al. Insufficient natriuretic response to continuous intravenous furosemide is associated with poor long-term outcomes in acute decompensated heart failure. J Card Fail. 2014;20:392-9.

10. Hollenberg SM, Stevenson LW, Ahmad T, Amin VJ, Bozkurt B, Butler J, et al. 2019 ACC Expert consensus decision pathway on risk assessment, management, and clinical trajectory of patients hospitalized with heart failure. J Am Coll Cardiol. 2019;74:1966-2011.

11. Mullens W, Damman K, Harjola VP, Mebazaa A, Brunner-La Rocca HP, Martens P, et al. The use of diuretics in heart failure with congestion — a position statement from the Heart Failure Association of the European Society of Cardiology. Eur J Heart Fail. 2019;21:137-55.

12. TerMaaten JM, Beldhuis IE, van der Meer P. Natriuresis-guided diuretic therapy in acute heart failure: A pragmatic randomized trial (PUSH-AHF). Nat Med. 2023;29:2625-32.

13. Dauw J, Charaya K, Lelonek M. Protocolized Natriuresis-Guided Decongestion Improves Diuretic Response: The Multicenter (ENACT-HF) Study. Circ Heart Fail. 2024;17:e011105.

14. Verbrugge FH. Diuretic Treatment in Acute Heart Failure With Volume Overload Guided by Serial Spot Urine Sodium Assessment (DECONGEST). Status: recruiting. ClinicalTrials.gov ID NCT05411991.

15. Cox ZL, Siddiqi HK, Stevenson. Randomized controlled trial of urinEchemiStry guided aCuteheArtfaiLuretreATmEnt (ESCALATE): Rationale and design. Am Heart J. 2023;265:121-31.

Postoperative neurovascular complications and risk factors associated with adult patients after cardiovascular procedures

Complicaciones neurovasculares posoperatorias y factores de riesgo asociados en pacientes adultos llevados a procedimientos cardiovasculares

Camilo A. Romero[1], Jorge L. Molinares[2]*, Jaime Camacho-Mackenzie[3], Ivonne G. Pineda[3], and Lina M. Ramírez[3]

[1]Department of Neurology; [2]Universidad del Rosario; [3]Department of Cardiovascular Surgery. Hospital Fundación Cardioinfantil-La Cardio, Bogotá, Colombia

Abstract

Introduction: Neurovascular events after cardiovascular surgery are major complications and increase morbidity and mortality. In Colombia, there is limited information on the incidence and risk factors for these complications. **Objective:** To determine the incidence, type, and risk factors for postoperative neurovascular complications following cardiovascular surgery in adults. **Methods:** A prospective database of 7,063 adult patients undergoing cardiovascular surgery at a tertiary care hospital was retrospectively analyzed between 2012 and 2022. **Results:** The incidence of postoperative neurovascular complications was 1.6% (n = 113). The most frequent type of neurovascular complication was cerebral infarction with 73.5% (n = 83), followed by intracranial hemorrhage with 13.3% (n = 15), spinal cord ischemia with 9.7% (n = 11), and transient ischemic attack with 3.5% (n = 4). Risk factors for postoperative neurovascular complications were atheromatous carotid artery disease (OR: 170; 95% CI: 40.8-714.2), chronic kidney disease (OR: 44.2; 95% CI: 24.9-78.4), heart transplantation (OR: 9.1; 95% CI: 3.1-26.6), and aortic surgery (OR: 6.5; 95% CI: 4.2-10.3). Postoperative length of stay (14 days vs. 6 days) and in-hospital mortality (29.2 vs. 3.6%) were higher in patients with neurovascular complications. **Conclusions:** The incidence of postoperative neurovascular complications was low but associated with a longer hospital stay and mortality. Atheromatous carotid artery disease, chronic renal failure, and the type of cardiovascular surgery were risk factors for these postoperative complications.

Keywords: Risk factors. Incidence. Stroke. Postoperative complications. Colombia.

Resumen

Introducción: los eventos neurovasculares en el posoperatorio de cirugía cardiovascular son complicaciones mayores que aumentan la morbimortalidad. En Colombia hay escasa información sobre la incidencia y los factores de riesgo de estas complicaciones. **Objetivo:** determinar la incidencia, el tipo y los factores de riesgo de las complicaciones neurovasculares en el posoperatorio de cirugía cardiovascular en una población adulta. **Métodos:** se hizo un análisis retrospectivo de una base de datos prospectiva de 7063 pacientes adultos sometidos a cirugía cardiovascular en un centro hospitalario de alta complejidad, entre los años 2012-2022. **Resultados:** la incidencia de complicaciones neurovasculares posquirúrgicas fue de 1.6% (n = 113). El infarto cerebral fue la más frecuente en 73.5% (n = 83), seguido de hemorragia intracraneal en 13.3% (n = 15), isquemia medular en 9.7% (n = 11) y ataque isquémico transitorio en 3.5% (n = 4). Los factores de riesgo

de estas complicaciones posquirúrgicas fueron la enfermedad carotidea ateromatosa (OR: 170; IC 95%: 40.8-714.2), la enfermedad renal crónica (OR: 44.2; IC 95%: 24.9-78.4), el trasplante cardiaco (OR: 91; IC 95%: 3.1-26.6) y la cirugía de aorta (OR: 6.5; IC 95%: 4.2-10.3). La estancia posoperatoria (14 vs. 6 días) y la mortalidad hospitalaria (29.2 vs. 3.6%) fueron mayores en los pacientes con complicaciones neurovasculares. **Conclusiones:** *la incidencia de complicaciones neurovasculares posquirúrgicas fue baja y se asoció a mayor tiempo de estancia y mortalidad hospitalaria. La enfermedad carotidea ateromatosa, la falla renal crónica y el tipo de cirugía cardiovascular son factores de riesgo para estas complicaciones posquirúrgicas.*

Palabras clave: Factores de riesgo. Incidencia. Infarto cerebral. Complicaciones posoperatorias. Colombia.

Introduction

An estimated 170 adults per million undergo open heart surgery every year, globally. In the United States, 1,220 open heart surgeries are performed per million inhabitants[1]. According to data from the Ministry of Health and Social Protection, 10,703 cardiac procedures were performed in Colombia in 2019[2]. Neurological complications are the second most frequent complications after cardiovascular surgery, with an incidence rate between 0.4 and 14%, exceeded only by cardiovascular complications[3]. Understanding the etiology of neurological complications requires a knowledge of the incidence, type, risk factors and mechanisms of the lesions[4].

Neurological complications after cardiovascular surgery can be classified into three types: a) neurovascular, b) encephalopathy or neuropsychiatric complications, and c) those involving the peripheral nervous system. Neurovascular complications include ischemic or hemorrhagic cerebrovascular accidents (CVAs), transient ischemic attacks (TIAs) and spinal cord ischemia or hemorrhage[5,6].

The incidence of neurovascular complications after cardiovascular surgery varies depending on the procedure performed, ranging from 7.4 to 7.9% for concomitant coronary artery bypass grafting (CABG) and valve procedures, 4.7 to 7.2% for aortic surgery, 1.4 to 8.8% for aortic or mitral valve interventions, and 0.18 to 0.5% for percutaneous coronary interventions and heart transplants[7].

Inpatient neurovascular complications following cardiovascular surgery are associated with worse short-, medium-, and long-term clinical outcomes, up to nine times greater inpatient mortality, and longer hospital and intensive care unit stays (an average of three to nine more hospital and two more intensive care unit days)[8].

There are many reported predictors for these complications, including demographic (age), clinical (peripheral vascular disease, a history of CVA, and a history of vascular risk), and procedural factors (urgent/ emergency surgery, cardiopulmonary bypass time, and aortic surgery)[4,6,7].

There is little information available in Colombia about these complications in adults. The purpose of this study was to determine the incidence, type and risk factors for inpatient neurovascular complications following cardiovascular surgery at a tertiary care facility in Bogotá, Colombia.

Methods

We conducted a retrospective, analytical, cohort study evaluating subjects over the age of 18 who underwent different types of cardiovascular surgery at a tertiary care institution from 2012-2022 and were included in the cardiovascular surgery department´s database. This database systematically and prospectively collects the administrative and clinical data of all patients undergoing cardiovascular surgery, with online storage on the institutional server.

The analysis included data from the index surgery during its respective hospitalization, and patients were divided into two groups: Group 1: postoperative cardiovascular surgery patients without neurovascular complications, and Group 2: postoperative cardiovascular surgery patients with neurovascular complications. Those with index or extrainstitutional cardiovascular procedures or with incomplete data were excluded.

Inpatient neurovascular complications were classified as ischemic cerebral infarction CVAs, hemorrhagic CVAs, TIAs, and spinal cord ischemia/hemorrhage. Cerebrovascular accidents were defined as focal neurological deficits persisting for more than 24 hours, confirmed by neuroimaging (simple head computed tomography or brain magnetic resonance imaging), while TIAs were defined as focal neurological deficits lasting less than 24 hours and with no acute lesions on neuroimaging. Finally, spinal cord ischemia/hemorrhage was defined as postoperative acute paraparesis with or without neuroimaging correlation.

Variables were collected for all patients, which included but were not limited to: demographic-anthropometric data (age, sex, body mass index), preoperative clinical data (medical history, pharmacological history, paraclinical tests), surgical data (indication for the procedure, elective-urgent-emergency procedure, type of surgery, pump time, aortic clamping time, use of external oxygenation or hemodynamic support – ECMO – , use of intra-aortic balloon), and postoperative outcomes of the cardiovascular surgery (hospital stay, intensive care unit [ICU] stay, mortality, discharge destination).

The types of surgery were classified into six categories: a) isolated CABG, b) CABG along with another procedure, c) valvular surgery, d) aortic surgery, e) heart transplant, and f) other cardiovascular procedures.

Continuous variables are presented using measures of central tendency (mean ± standard deviation or median and interquartile range, depending on their distribution). Categorical variables are presented using frequencies and proportions.

Chi-square or Fisher's exact test were used for comparisons between the two groups (with and without neurovascular complications), while Student's T or the Mann-Whitney U test were used for categorical and continuous variables, depending on their distribution. A bivariate and multivariate logistic regression analysis was run to determine the risk factors associated with the complications being studied. The odds ratios (ORs) with their 95% confidence intervals (CIs) were calculated for each risk factor identified in the logistic regression. The statistical analyses were done using StataCorp Version 15.0 Stata statistical software.

The study followed the current normative guidelines for health research in Colombia (Resolution 8430 of 1993 and Law 23 of 1981). Since this was a health study with no interventions or risk, informed consent was not required (Resolution 8430 of 1993). The protocol was approved by the institutional research and ethics committee. The authors certify the veracity and accuracy of the information presented and report no conflicts of interest.

Results

From 2012 to 2022, 7,063 cardiovascular procedures were performed at the institution; 66.9% (n = 4,726) were on males with a mean age of 64.9 years. The main prior medical conditions were systemic hypertension, dyslipidemia, recent myocardial infarction, diabetes, heart failure, chronic kidney disease and smoking. The mean cardiac ejection fraction in both groups was 51%, with 70.5% (n = 4,978) of the patients in functional class II, according to the New York Heart Association (NYHA) classification. The most frequent procedures were valvular surgery, in 38.6% (n = 2,731) and isolated CABG, in 33% (n = 2,337); 23.3% (n = 1,646) received preoperative heparin. Intra-aortic balloon pumps were used perioperatively in 5.5% (n = 393) and ECMO in 0.6% (n = 41) of the procedures. The overall inpatient mortality rate was 4% (n = 286) (Table 1).

The incidence of neurovascular complications following cardiovascular surgery was 1.59% (n = 113). A comparison of the two groups, patients with or without neurovascular complications, showed no statistically significant differences in the demographic-anthropometric variables. Among the preoperative clinical variables in patients with neurovascular complications, there was a statistically significantly higher frequency of prior cerebrovascular disease (15.9 vs. 4%), atrial fibrillation (16.8 vs. 8.6%), chronic kidney disease (86 vs. 13.4%), atheromatous carotid disease (15 vs. 0.1%) and the use of warfarin (11.5 vs. 1.4%). As far as surgical variables, there was a statistically significantly higher frequency of CABG associated with other procedures (8 vs. 5.5%), aortic surgery (40.7 vs. 13.7%), heart transplantation (4.4 vs. 1.1%), postoperative use of ECMO (4.4 vs. 0.3%) and emergency procedures (17.7 vs. 4.6%). Among the postoperative outcomes of cardiovascular surgery, the following were statistically significantly higher in patients with neurovascular complications: mean ICU stay in days (6.1 vs. 2 days), mean postoperative stay in days (14 vs. 6 days) and inpatient mortality (29.2 vs. 3.6%) (Table 1).

Aortic surgery was the type of procedure with the highest number of neurovascular complications following cardiovascular surgery, with 47 patients (41.6%). By type of surgery, the incidence of neurovascular complications was highest for aortic surgery and heart transplantation (Table 2).

Altogether, 97.3% (n = 110) of the patients with neurovascular complications following cardiovascular surgery were seen by neurology. Cerebral infarction, with 73.5% (n = 83), was the most common neurovascular complication. A total of 84.3% (n = 70) of the infarctions were cardioembolic, 62.6% (n = 52) of which were minor or moderate, according to the National Institute of Health Stroke Scale (NIHHS) (score of 1-15); 90.3% (n = 75) were in the anterior territory or multiple, and only 3.6% (n = 3) underwent thrombectomy; 11 (73.3%) of the 15 hemorrhagic CVAs were intraparenchymal (Tables 3 and 4).

Table 1. Characteristics of patients with and without neurovascular complications following cardiovascular surgery: 2012-2022

Characteristics	Patients without neurovascular complications after cardiovascular surgery (n = 6,961) 98.4%	Patients with neurovascular complications after cardiovascular surgery (n = 113) 1.59%	p
Sex, male	4,653 (66.8)	73 (64.6)	0.616
Age, years	64.3 (55-72.3)	65.4 (55-74.6)	0.321
BMI, kg/m^2	26 (23.5-29.4)	25.7 (23-28.8)	0.134
Dyslipidemia	2,068 (29.7)	34 (30.1)	0.919
HTN	3,850 (55.3)	66 (58.4)	0.444
CVA	220 (3.2)	12 (10.6)	< 0.001
TIA	59 (0.8)	6 (5.3)	< 0.001
COPD	483 (6.9)	9 (8)	0.671
Smoking	987 (14.2)	21 (18.6)	0.184
OSAHS	214 (3.1)	1 (0.9)	0.289
AF	599 (8.6)	19 (16.8)	0.002
CKD	932 (13.4)	88 (86)	< 0.001
Dialysis	259 (3.7)	6 (5.3)	0.319
Diabetes	1369 (19.7)	23 (20.4)	0.855
Carotid disease	5 (0.1)	17 (15)	< 0.001
Peripheral vascular disease	182 (2.6)	4 (3.5)	0.543
Heart failure	1,043 (15)	12 (10.6)	0.196
AMI < 90 days	1,754 (25.2)	27 (23.9)	0.751
LVEF, n (%)	51 (44-57)	51 (45-55)	0.442
NYHA			
I	521 (7.5)	7 (6.2)	
II	4,899 (70.4)	79 (69.9)	
III	1,314 (18.9)	24 (21.2)	
IV	227 (3.3)	3 (2.7)	
Anticoagulation			
Warfarin	95 (1.4)	13 (11.5)	< 0.001
DOAC	85 (1.2)	4 (3.5)	0.054
Heparin	1,638 (23.5)	8 (7.1)	< 0.001
Type of cardiovascular surgery			
CABG + other procedures	385 (5.5)	9 (8)	< 0.001
Isolated CABG	2,311 (33.2)	26 (23)	
Valvular surgery	2,707 (38.9)	24 (21.2)	
Aortic surgery	951 (13.7)	46 (40.7)	< 0.001
Heart transplant	75 (1.1)	5 (4.4)	< 0.001
Others	532 (7.6)	3 (2.7)	

(*Continues*)

Table 1. Characteristics of patients with and without neurovascular complications following cardiovascular surgery: 2012-2022 *(continued)*

Characteristics	Patients without neurovascular complications after cardiovascular surgery (n = 6,961) 98.4%	Patients with neurovascular complications after cardiovascular surgery (n = 113) 1.59%	p
Need for IABP			
Preoperative	122 (1.8)	8 (7.1)	< 0.001
Intraoperative	171 (2.5)	5 (4.4)	< 0.001
Postoperative	84 (1.2)	3 (2.7)	< 0.001
ECMO			
Preoperative	13 (0.2)	1 (0.9)	
Postoperative	22 (0.3)	5 (4.4)	< 0.001
Type of admission to the operating room			
Elective	2712 (39)	34 (30.1)	
Urgent	3,923 (56.4)	59 (52.2)	
Emergency	326 (4.6)	20 (17.7)	< 0.001
Other surgical times, min. (ranges)			
CPB	114 (89-152)	105 (26-173.5)	0.088
Aortic clamping	90 (70-119)	77 (0-120)	< 0.001
Hospital stay, days (ranges)			
Preoperative	4 (1-7)	3 (1-8)	0.194
ICU	2 (1-3.8)	6.1 (3-11)	< 0.001
Total POP	6 (4-9)	14 (8-26.5)	< 0.001
Mortality	253 (3.6)	33 (29.2)	< 0.001

CKD: chronic kidney disease; AF: atrial fibrillation; COPD: chronic obstructive pulmonary disease; BMI: body mass index; TIA: transient ischemic attack; AMI: acute myocardial infarction; DOAC: direct oral anticoagulant; CABG: coronary artery bypass graft; POP: postoperative, IABP: intra-aortic balloon pump; ECMO: extracorporeal membrane oxygenation; CPB: cardiopulmonary bypass pump; ICU: intensive care unit.

Postoperative ICU and hospital stays were longer for patients with ischemic/hemorrhagic spinal cord neurovascular complications, with a mean of 8 and 20 days, respectively. These patients had an inpatient mortality rate similar to those with CVAs, with 27.2% (n = 3) of 11 patients (Table 3).

The multivariate logistic regression analysis indicated the following risk factors for inpatient neurovascular complications following cardiovascular surgery: atheromatous carotid disease (OR: 170; 95% CI: 40.8-714.2), chronic kidney disease (OR: 44.2; 95% CI: 24.9-78.4), heart transplantation (OR: 9.1; 95% CI: 3.1-26.6) and aortic surgery (OR: 6.5; 95% CI: 4.2-10.3) (Table 5).

Discussion

This study, with 7,063 cardiovascular procedures, found a 1.6% incidence of postoperative inpatient neurovascular complications. The most frequent type of neurovascular complication was cerebral infarction. The risk factors for neurovascular complications following cardiovascular surgery were atheromatous carotid disease, chronic kidney disease, aortic surgery and heart transplantation (Fig. 1). Patients with neurovascular complications following cardiovascular surgery had worse outcomes, longer stays and higher inpatient mortality.

Table 2. Incidence of neurovascular complications following cardiovascular surgery according to the type of surgery: 2012-2022

Type of cardiovascular surgery	n	Patients without neurovascular complications after cardiovascular surgery, n (%)	Patients with neurovascular complications after cardiovascular surgery, n (%)	Incidence
CABG + other procedures	394	385 (5.5)	9 (8)	2.2%
Isolated CABG	2,337	2,311 (33.2)	26 (23)	1.1%
Valvular surgery	2,731	2,707 (38.9)	24 (21.2)	0.8%
Aortic surgery	997	951 (13.7)	46 (40.7)	4.6%
Heart transplant	80	75 (1.1)	5 (4.4)	6.2%
Others	535	532 (7.6)	3 (2.7)	0.5%

CABG: coronary artery bypass graft.

Table 3. Description of neurovascular complications in postoperative cardiovascular surgery patients: 2012-2022

Variables	Total (n = 113)	CVA* (n = 98) (86.7%)	TIA (n = 4) (3.5%)	Spinal cord ischemia/hemorrhage (n = 11) (9.7%)	p
Etiology, n (%)					
1: atherothrombotic	5 (4.4)	5 (5.2)	0 (0)	-	0.133
2: cardioembolic	72 (63.7)	70 (72.2)	2 (66.7)	-	
3: small vessel	2 (1.8)	1 (1.1)	1 (33.3)	-	
4: other causes	2 (1.8)	2 (2.1)	0 (0)	-	
5: undetermined	19 (16.8)	19 (19.6)	0 (0)	-	
Intervention, n (%)					
Reperfusion	3 (2.7)	2 (2)	1 (25)	0 (0)	0.103
Hemicraniectomy	4 (3.5)	4 (4.1)	0 (0)		1
Neurology assessment	110 (97.3)	96 (98)	4 (100)	10 (91)	0.35
Main outcomes, n (%)					
Death	33 (29.2)	30 (30.6)	0 (0)	3 (27.3)	0.681
Discharged to home	79 (69.9)	67 (68.4)	4 (100)	8 (72.7)	
Discharged to home hospitalization	1 (0.9)	1 (1.0)	0 (0)	0 (0)	
Hospital stay, days (ranges)					
Preoperative	3 (1-8)	3 (1-8)	5 (2-8)	2 (1-9)	0.73
ICU	6.1 (3-11)	6 (3-12)	4 (1.2-7.6)	8 (4-10)	0.475
Total postoperative time	14 (8-26.5)	13 (8-26)	8 (4-23)	20 (10-27)	0.286

CVA: ischemic and hemorrhagic cerebrovascular accident; TIA: transient ischemic attack; ICU: intensive care unit.

The incidence of neurovascular complications following cardiovascular surgery may be as high as 6%, depending on whether the study is retrospective or prospective[9]. In a cardiovascular surgery study from 2014-2015, Arribas et al.[9] reported a CVA incidence of 2.5% in 647 patients. In 2,569,597 CABG surgeries

Table 4. Type and characteristics of neurovascular complications in postoperative cardiovascular surgery patients: 2012-2022

Variables	Ischemic CVA (n = 87) 75%	Acute cerebral infarction (n = 83) 73.5%	TIA (n = 4) 3.5%
NIHSS (score)	**n (%)**	**n (%)**	**n (%)**
Minor (0-4)	34 (39.1)	30 (36.1)	4 (100)
Moderate (5-15)	22 (25.2)	22 (26.5)	0
Serious (16-20)	8 (9.2)	8 (9.6)	0
Very serious (21-42)	8 (9.2)	8 (9.6)	0
Not reported	15 (17.2)	15 (18.1)	0
Territory			
Multiple	34 (39.1)	34 (40.9)	0
Anterior	45 (51.7)	41 (43.9)	4 (100)
Posterior	8 (9.2)	8 (9.6)	0
Etiology			
Atherothrombotic	2 (2.3)	2 (2.4)	0 (0)
Cardioembolic	71 (81.6)	69 (83.1)	2 (50)
Small vessel	2 (2.3)	1 (1.2)	1 (25)
Other causes	2 (2.3)	2 (2.4)	0
Indeterminate	10 (11.4)	9 (10.8)	1 (25)
Intervention			
Mechanical thrombectomy	3 (3.4)	3 (3.6)	0
Hemicraniectomy	4 (4.6)	4 (4.8)	0
None	80 (91.9)	76 (91.5)	4 (100)
Hemorrhagic CVA (n = 15) 15%	SAH	2 (13.3)	
	Intraparenchymal	11 (73.3)	
	Subdural hematoma	4 (26.6)	

CVA: cerebrovascular accident; TIA: transient ischemic attack; NIHSS: National Institutes of Health Stroke Scale.

performed between 2004 and 2015, there was a 1.8% incidence of ischemic CVA[10]. Heart valve surgery differs from CABG and requires cardiopulmonary bypass and opening of the heart chambers, which can increase the risk of brain hypoperfusion. A study of left chamber valve replacements that enrolled 2,085 patients from 2005 to 2015 showed a 2.6% incidence of ischemic CVA[11]. On the other hand, a meta-analysis of 222 studies with 43,720 aortic arch surgery patients found a 5.3 to 6.9% incidence of CVA with disability[12]. Van de Beek

Table 5. Logistic regression model of risk factors for neurovascular complications in postoperative cardiovascular surgery patients: 2012-2022

Risk factor	OR	p	95% CI
History of CKD	44.2	< 0.001	24.9-78.4
Atheromatous carotid disease	170	< 0.001	40.8-714.2
Aortic surgery	6.5	< 0.001	4.2-10.3
Heart transplant	9.1	< 0.001	3.1-26.6

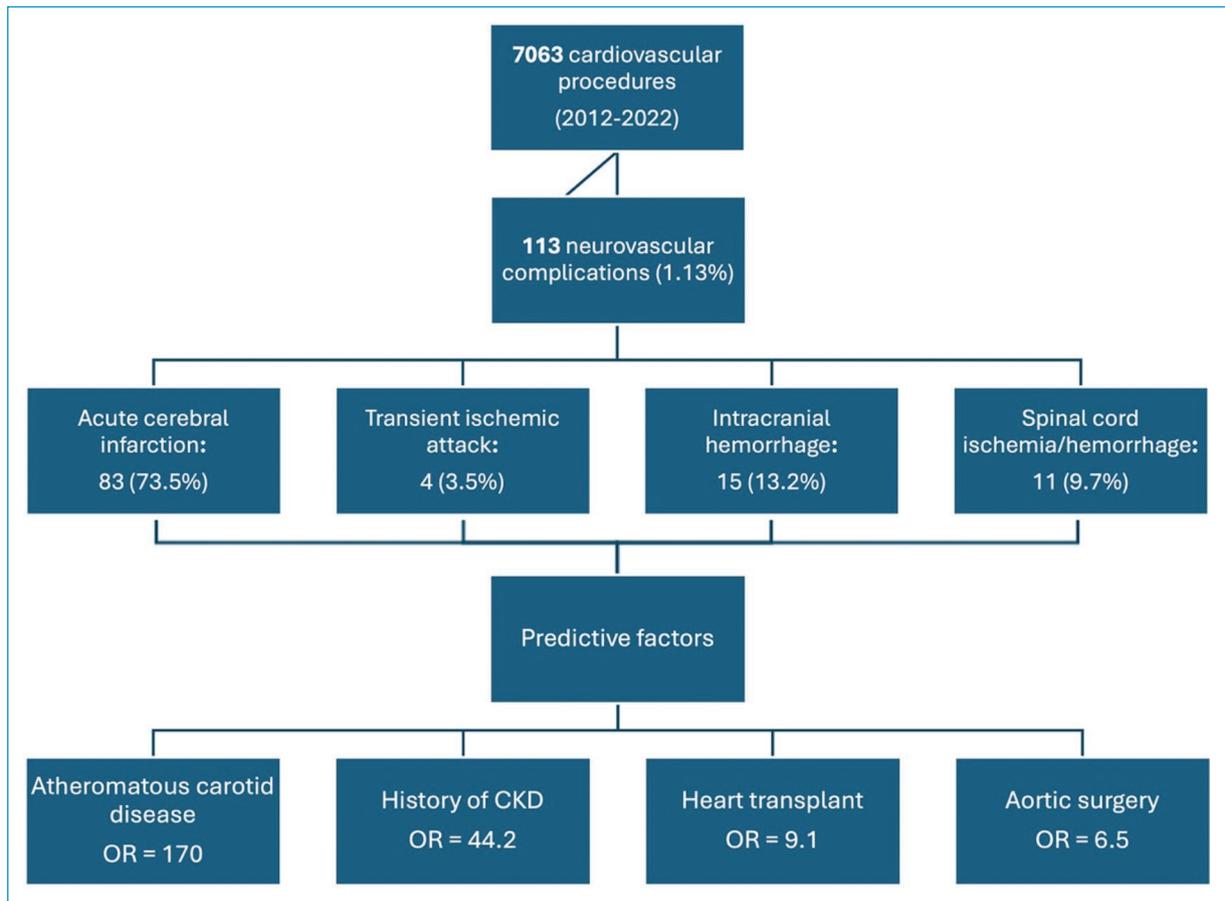OR: odds ratio; CI: confidence interval; CKD: chronic kidney disease.

Figure 1. Central figure. Distribution of neurovascular complications following cardiovascular surgery and factors that predict their onset. CKD: chronic kidney disease; OR: odds ratio.

et al.[13] reported a 5% incidence of perioperative cerebrovascular complications in heart transplant patients; most occurred after the second post-transplant day and were related to external circulatory support. The frequency of neurovascular complications reported after cardiovascular surgery depends on the reporting center, study method, analysis period and cardiovascular procedure. In our cohort, the incidence of neurovascular complications after cardiovascular surgery was similar to that in the literature. This could be due to the institution's high volume of cardiovascular surgery, highly trained specialists, and safety and quality parameters.

Cerebral infarction is the most frequently reported neurovascular complication following cardiovascular surgery. A meta-analysis and systematic review of CVAs following cardiac surgery by Gaudino et al.[14], with 174,969 subjects (63% undergoing isolated CABG) and a 3% incidence of perioperative or early CVAs, found that 88% were ischemic. In this same study, the incidence of TIAs was 1.38%. This complication could be due to embolic and cerebral hypoperfusion mechanisms[15], in which case aortic manipulation and external hemodynamic support would favor its onset[15]. Likewise, atrial fibrillation may occur in up to 60% of patients after cardiac surgery and has been associated with perioperative cerebral infarction (OR: 2.17; 95% CI: 1.90-2.49)[16]. However, although there is no direct causal relationship between atrial fibrillation following cardiovascular surgery and adverse outcomes, its presence should be assumed to be a risk factor for postoperative morbidity and mortality and not a transient disturbance[17].

As previously mentioned, patients undergoing cardiovascular surgery have multiple risk factors for cerebral infarction[18]. In our cohort, 73.5% of the neurovascular complications after cardiovascular surgery were cerebral infarctions. In the assessment of the etiological mechanism, 84.3% were attributed to cardioemboli,

perhaps due to the high frequency of pre and perioperative transient atrial fibrillation, or to mistaken attribution by the clinician. Hemorrhagic CVAs, while less frequent, are associated with greater morbidity and mortality[19]. In postoperative cardiovascular surgery patients, hemorrhagic CVAs may be related to the use of perioperative anticoagulation, the indication for surgery (endocarditis) and the prevalence of systemic hypertension in patients with cardiovascular disease. Iatrogenesis is the principal cause of spinal cord infarction, with aortic surgery as the main culprit[20-22]. Spinal cord ischemia may occur due to hypoperfusion with clamping or hyperperfusion of the radicular arteries on clamp removal[22]. Given its frequency in aortic surgery and high level of disability, multiple intraoperative strategies have been studied to prevent it. However, once an iatrogenic spinal cord injury has occurred after cardiovascular surgery, there is little indication of how to treat it[22].

The literature describes multiple clinical and surgical risk factors for neurovascular complications following cardiovascular surgery. In a prospective study of 10,250 postoperative cardiovascular surgery patients, Sultan et al.[23] reported age, a history of cerebrovascular disease, diabetes mellitus and emergency surgery as CVA predictors. The predictive factors for neurovascular complications after cardiovascular surgery may vary depending on the study population, type of procedure, timing of CVA and type of neurovascular complication. In an English population undergoing CABG, age over 60 and female sex were the most important predictive factors for CVAs after cardiovascular surgery[10]. In a study of transcatheter aortic valve implantation (TAVI), the predictors of a CVA within the first 30 days were triglyceride levels over 117.5 mg% and dilation during the procedure[24]. Early CVAs following cardiovascular surgery, defined as those detected upon awakening or after extubation, are associated with cardiopulmonary bypass times rather than patient characteristics[14], suggesting risk factors related to the surgical technique. Late CVAs following cardiovascular surgery, defined as those occurring after normal awakening from anesthesia, have been associated with atrial fibrillation or cerebrovascular disease[14]. Attempts have been made to create scales with scores to predict the risk of CVAs after cardiovascular surgery, using variables such as age, urgent/emergency surgery, occlusive peripheral artery disease, a history of CVA and cardiopulmonary bypass time[25], with greater weight for age over 66 and a history of CVA[25]. Although the risk factors for hemorrhagic CVAs and spinal cord injuries (as neurovascular complications of cardiovascular surgery) have demographic, vascular risk and postoperative aspects in common with ischemic CVAs, they also include procedural aspects[5,9].

Furthermore, intra and extracranial atherosclerotic disease has been associated with a higher likelihood of a CVA following cardiovascular surgery[26]. Carotid stenosis is an independent factor for CVAs following cardiovascular surgery; the risk increases with the degree of stenosis and is highest for patients with 80-99%[26]. Patients with intracranial atherosclerotic disease have a 3.6 times greater likelihood of having a CVA following cardiovascular surgery[27]. In this regard, strategies have been studied to predict or reduce CVAs after cardiovascular surgery in patients with suspected or confirmed atheromatous carotid disease. The most frequently used techniques for this are preoperative ultrasound, intraoperative neurophysiological monitoring, transoperative transcranial Doppler, modified surgical techniques, embolus trapping devices and perioperative treatment of carotid stenosis[26,27]. Fifteen percent of our patients with neurovascular complications had atheromatous carotid disease (OR: 170; 95% CI: 40.8-714.2).

On the other hand, kidney disease has been included in multiple models for predicting mortality and complications following cardiovascular surgery[28,29]. It affects cardiovascular outcomes and heart structure[30] and increases the risk of cardiovascular surgery complications, coronary disease, atheromatous aortic disease and heart valve disease[30,31]. A study of 1,209 patients with ischemic heart failure found an inverse relationship between the glomerular filtration rate and the risk of death, death from cardiovascular disease and hospitalizations[32]. Among 529 patients who underwent heart transplantation, older age at the time of transplant, diabetes, kidney dysfunction and cytomegalovirus infection were associated with a higher risk of CVA[33]. Patients with kidney disease often have cardiovascular risk factors like systemic hypertension and diabetes[34]. In addition, atheromatous plaques in patients with chronic kidney disease have a higher calcium density, and vascular disease is the biggest contributor to mortality and morbidity[34]. Measures for improving postoperative outcomes following cardiovascular surgery in patients with chronic kidney disease include hydration, low-dose dopamine infusion, increased perfusion pressure during cardiopulmonary bypass, fluid and electrolyte monitoring, postoperative hemofiltration, and prophylactic dialysis[34]. It is important to note that the relationship between kidney dysfunction and

cardiovascular surgery is bidirectional, as up to 30% develop acute kidney injury following cardiovascular surgery[35]. Only 2 to 3% of patients with acute kidney injury after cardiovascular surgery require renal replacement therapy[35]. Eighty-six percent of our patients with neurovascular complications after cardiovascular surgery had chronic kidney disease, with 5.3% on renal replacement therapy.

Out of 54,995 adult patients undergoing heart transplantation between 1987 and 2018, 2.1% had a CVA in the first 30 days after cardiovascular surgery[36]. The annual incidence of CVA is 0.7% in transplant patients vs. 2.4% in patients on the heart transplant waiting list (HR: 0.4; 95% CI: 0.2-0.6%)[37]. In the retrospective study of the United Network for Organ Sharing (UNOS) database conducted between 2009 and 2020 with 25,015 heart transplant patients, 2.9% had a CVA after cardiovascular surgery[38], a percentage that increased from 2.1% in 2009 to 3.7% in 2019. Age, prior heart surgery, a history of CVA, the use of a left ventricular assist device, ECMO, ischemic time and mechanical ventilation at the time of transplant were independent predictive factors for CVA following cardiovascular surgery[38]. A CVA after transplant was associated with greater 30-day and all-cause mortality[38]. Our cohort´s 6.2% incidence of neurovascular complications in heart transplantation could be related to the change in criteria for assigning heart transplants, the number of transplants performed (75 in 10 years), the availability of new hemodynamic support technologies prior to transplant, and greater survival of patients in need of a transplant[39].

Neurovascular complications are not uncommon following aortic cardiovascular surgery and are associated with worse outcomes. Out of 704 thoracic aorta surgery patients, 533 with ascending aortic aneurysms and 171 with type A dissections, the incidence of CVAs after cardiovascular surgery was 4.5% (95% CI: 2.9-6.6) for the former and 12.3% (95% CI: 7.8-18.16) for the latter[40]. Lower hemoglobin levels, longer cardiopulmonary bypass, deep hypothermic circulatory arrest and hypothermia were identified as potential factors for CVA following cardiovascular surgery[40]. Harky et al.[41] reported a 7 and 0% incidence of CVA following cardiovascular surgery and paraplegia, respectively, in 157 patients undergoing descending thoracic aortic aneurysm repair. The same authors[41] showed a 9.9 and 3.3% incidence of CVA after cardiovascular surgery and paraplegia, respectively, in 273 patients undergoing thoracoabdominal aneurysm repair[41]. To develop a risk model for morbidity and mortality in aortic surgery, 24,051 patients with different arterial procedures were enrolled at 905 hospitals, and a 2.4% incidence of CVA after cardiovascular surgery was found[42]. Circulatory arrest and a history of CVA were associated with CVAs following cardiovascular surgery[42]. Given the high impact and frequency of neurovascular complications following aortic cardiovascular surgery, various neuroprotective strategies have been implemented[43]. These include hypothermic circulatory arrest, anterograde and/or retrograde cerebral perfusion, intraoperative spinal cord and cerebral blood flow monitoring, cerebrospinal fluid drainage, surgical technique modifications and embolism prevention devices[43,44]. However, the risk of spinal cord lesions with paraparesis or paraplegia has not dropped substantially over the last three decades, especially for patients with thoracoabdominal aortic repair[44]. In our cohort, the 1.1% incidence of spinal cord injuries in 997 postoperative aortic cardiovascular surgery patients is lower than described in other studies[40-44]. The reason for this was not a focal point of this study and requires a subgroup analysis of the enrolled patients.

The impact of neurovascular complications following cardiovascular surgery is reflected in mortality, ICU stay, hospital stay, costs, discharge destination, systemic complications, functionality and quality of life. In a study of 8,291 postoperative cardiovascular surgery patients, with 165 CVAs (1.99%) and incidences of 0.85% for CABG and up to 8.14% for aortic surgery, ICU stay (8 vs. 1.1 days), hospital stay (12.94 vs. 8 days) and inpatient mortality (17 vs. 5.9%) were higher for subjects with neurovascular complications[45]. Santos et al.[46] reported a 3.7 times higher mortality rate (OR: 5.06; 95% CI: 3.5-7.33) in patients with CVAs following cardiovascular surgery. Furthermore, in a comparative study[47] of 44 postoperative cardiovascular surgery patients and 626 without CVAs, hospital stay was longer (25 vs. 9.5%) (OR: 3.2; 95% CI: 1.5-6.6). Likewise, ICU stay (17 vs. 2 days) and total hospital stay (26 vs. 8 days) were longer in patients with neurovascular complications following cardiovascular surgery[47]. There was an increase of 1.1 days of hospital stay and 0.8 days of ICU stay for each point increase on the NIHSS[47]. Similar to what has been reported, in our cohort, inpatient mortality (29.2 vs. 3.6%), ICU stay (6.1 vs. 2 days) and total hospital stay (14 vs. 6 days) were greater in patients with neurovascular complications following cardiovascular surgery.

The diagnosis of inpatient neurovascular complications following cardiovascular surgery can be complicated by sedation, pain, restricted mobility, availability

of neurological consults, and other variables. In addition, there is little information and no established treatment guideline for managing neurovascular complications following cardiovascular surgery. Some of the treatments for CVAs are contraindicated in patients recovering from cardiovascular surgery[5]. Awareness of the incidence, type, and risk factors for neurovascular complications following cardiovascular surgery will help in understanding the pathophysiological mechanisms and establishing primary, secondary, and tertiary measures to reduce their short- and long-term impact.

This study had the following strengths: it included a significant number of patients undergoing cardiovascular surgery (7,063), and it was conducted at an institution with a high volume of cardiovascular surgeries (approximately 700 per year) over a lengthy and recent period (2012-2022), with data extracted from a registry that adheres to the Society of Thoracic Surgeons (STS) guidelines. It also included a variety of cardiovascular procedures divided into groups, a description of the neurovascular complications, inpatient outcome measurements, neurology assessments in 97% of cases, and imaging confirmation of neurovascular complications.

Its limitations include the following:
− It was conducted at a single center, which could limit generalization of its results.
− It was retrospective.
− There was no ambulatory follow-up of the patients.
− Data is lacking on the timing of the neurovascular complication in relation to the procedure.
− There is no record of functional neurological assessment scales.
− Information on the NIHSS score was not available for 18% of patients with CVAs.
− A subgroup analysis by cardiovascular procedure or type of neurovascular complication was not performed.

In patients who are scheduled for aortic surgery or heart transplantation, atheromatous carotid disease and chronic kidney disease, or both, predict a high likelihood of neurovascular complications postoperatively. The most frequent type of neurovascular complication is cerebral infarction. Awareness of these and other variables will help clinicians determine the risk/benefit of preventive measures and have a clearer conversation regarding the surgical prognosis with patients or their relatives.

Conclusions

The incidence of neurovascular complications following cardiovascular surgery is low (1.59%). Cerebral infarction is the most frequent neurovascular complication following cardiovascular surgery. Atheromatous carotid disease, chronic kidney disease, aortic surgery and heart transplantation are risk factors for its occurrence. Neurovascular complications following cardiovascular surgery are associated with a longer hospital stay, longer intensive care unit stay and greater inpatient mortality. More studies are needed to understand their pathophysiological mechanisms, investigate preventive measures and establish treatment strategies when they occur.

Funding

The authors declare that they received no funding for this study.

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 in the course of this study.

Confidentiality, informed consent and ethical approval. The authors were granted approval by the Ethics Committee for the analysis of routinely obtained and anonymized clinical data, and therefore informed consent was not required. The pertinent guidelines were followed.

Declaration on the use of artificial intelligence. The authors declare that they did not use any type of generative artificial intelligence in writing this article.

References

1. Zilla P, Yacoub M, Zühlke L, Beyersdorf F, Sliwa K, Khubulava G, et al. Global unmet needs in cardiac surgery. Global Heart. 2018;13(4):293-303.
2. Pérez-Rivera CJ, Rincón-Tello FM, Vervoort D, Acosta-Buitrago LM, Maldonado-Escalante J. Acceso a la cirugía cardíaca en Colombia: Un análisis situacional. Rev Colomb Cardiol. 2024;31(3):134-42 doi:10.24875/rccar.22000098.
3. O'Brien SM, Shahian DM, Filardo G, Ferraris VA, Haan CK, Rich JB, et al. The Society of Thoracic Surgeons 2008 cardiac surgery risk models: Part 2—isolated valve surgery. The Ann Thorac Surg. 2009;88(Supl. 1):S23-42: doi:10.1016/j.athoracsur.2009.05.056.
4. Gottesman RF, McKhann GM, Hogue CW. Neurological complications of cardiac surgery. Sem Neurol. 2008;28(5):703-15. https://doi.org/10.1055/s-0028-1105973.
5. Sheth KN, Nourollahzadeh E. Neurologic complications of cardiac and vascular surgery. Hand Clin Neurol. 2017;141:573-92. doi:10.1016/b978-0-444-63599-0.00031-4.

6. Raffa GM, Agnello F, Occhipinti G, Miraglia R, Lo Re V, Marrone G, et al. Neurological complications after cardiac surgery: A retrospective case-control study of risk factors and outcome. J Cardiothorac Surg. 2019;14(1). doi:10.1186/s13019-019-0844-8.

7. Hrdlicka CM, Wang J, Selim M. Neurological complications of cardiac procedures. Sem Neurol. 2021;41(04):398-410. doi:10.1055/s-0041-1728761.

8. Tuman KJ, McCarthy RJ, Najafi H, Ivankovich AD. Differential effects of advanced age on neurologic and cardiac risks of coronary artery operations. J Thorac Cardiovasc Surg. 1992;104(6):1510-7. doi:10.1016/s0022-5223(19)33877-2.

9. Arribas JM, Garcia E, Jara R, Gutierrez F, Albert L, Bixquert D, et al. Incidencia y mecanismo etiológico de ictus en cirugía cardiaca. Neurol. 2020;35(7):458-63. doi:10.1016/j.nrl.2017.10.004.

10. Mohamed MO, Hirji S, Mohamed W, Percy E, Braidley P, Chung J, et al. Incidence and predictors of postoperative ischemic stroke after coronary artery bypass grafting. Int J Clin Pract. 2021;75(5). doi:10.1111/ijcp.14067.

11. Kim HJ, Lee EJ, Jung SH, Lee JW, Kim JS, Kim JB, et al. Cerebral atherosclerosis and early ischemic stroke after left-sided valve replacement surgery. J Thorac Cardiovasc Surg. 2022;163(3). doi:10.1016/j.jtcvs.2020.05.002.

12. Abjigitova D, Veen KM, van Tussenbroek G, Mokhles MM, Bekkers JA, Takkenberg JJ, et al. Cerebral protection in aortic arch surgery: systematic review and meta-analysis. Int Cardiovasc Thorac Surg. 2022;35(3). doi:10.1093/icvts/ivac128.

13. Van de Beek D, Kremers W, Daly RC, Edwards BS, Clavell AL, McGregor CG, et al. Effect of neurologic complications on outcome after heart transplant. Arch Neurol. 2008;65(2). doi:10.1001/archneurol.2007.52.

14. Gaudino M, Rahouma M, Di Mauro M, Yanagawa B, Abouarab A, Demetres M, et al. Early versus delayed stroke after cardiac surgery: A systematic review and meta-analysis. J Am Heart Assoc. 2019;8(13). doi:10.1161/jaha.119.012447.

15. Ferrante M, Pisano C, Van Rothem J, Ruvolo G, Abouliatim I. Cerebrovascular events after cardiovascular surgery: Diagnosis, management and prevention strategies. Polish J Cardio-Thorac Surg. 2023;20(2):118-22. doi:10.5114/kitp.2023.130020.

16. Caldonazo T, Kirov H, Rahouma M, Robinson NB, Demetres M, Gaudino M, et al. Atrial fibrillation after cardiac surgery: A systematic review and meta-analysis. J Thorac Cardiovasc Surg. 2023;165(1). doi:10.1016/j.jtcvs.2021.03.077.

17. Hussain ST, Kalimi R. Commentary: Atrial fibrillation after cardiac surgery: More than just a nuisance! J Thorac Cardiovasc Surg. 2023;165(1):106-7. doi:10.1016/j.jtcvs.2021.03.104.

18. Marchesan LQ, Saffi MA, Silveira LF, Lovato MC, Araujo PC, Chemello D. Risk factors associated with ischemic stroke in the immediate postoperative period of cardiac surgery. Braz J Cardiovasc Surg. 2023;38(4). doi:10.21470/1678-9741-2022-0072.

19. Montaño A, Hanley DF, Hemphill JC. Hemorrhagic stroke. Hand Clin Neurol. 2021;229-48. doi:10.1016/b978-0-444-64034-5.00019-5.

20. Robertson CE, Brown RD, Wijdicks EFM, Rabinstein AA. Recovery after spinal cord infarcts. Neurol. 2012;78(2):114-21. doi:10.1212/wnl.0b013e31823efc93.

21. Salvador de la Barrera S, Barca-Buyo A, Montoto-Marqués A, Ferreiro-Velasco M, Cidoncha-Dans M, Rodriguez-Sotillo A. Spinal cord infarction: Prognosis and recovery in a series of 36 patients. Spinal Cord. 2001;39(10):520-5. doi:10.1038/sj.sc.3101201.

22. Naik A, Moawad CM, Houser SL, Kesavadas TK, Arnold PM. Iatrogenic spinal cord ischemia: A patient level meta-analysis of 74 case reports and series. NASSJ. 2021;8:100080. doi:10.1016/j.xnsj.2021.100080.

23. Sultan I, Bianco V, Kilic A, Jovin T, Jadhav A, Jankowitz B, et al. Predictors and outcomes of ischemic stroke after cardiac surgery. Ann Thorac Surg. 2020;110(2):448-56. doi:10.1016/j.athoracsur.2020.02.025.

24. Castelo A, Grazina A, Teixeira B, Mendonça T, Rodrigues I, Garcia Brás P, et al. Outcomes and predictors of periprocedural stroke after transcatheter aortic valve implantation. J Stroke Cerebrovasc Dis. 2023;32(5):107054. doi:10.1016/j.jstrokecerebrovasdis.2023.107054.

25. Magedanz EH, Guaragna JC, Albuquerque LC, Wagner MB, Chieza FL, Bueno NL, et al. Risk score elaboration for stroke in cardiac surgery. Braz J Cardiovasc Surg. 2021;36(6). doi:10.21470/1678-9741-2020-0331.

26. Ruka E, Lesur O, Gingras M, Buruian M, Voisine E, Marzouk M, et al. Relationship between the degree of carotid stenosis and the risk of stroke in patients undergoing cardiac surgery. Can J Cardiol. 2022;38(3):347-54. doi:10.1016/j.cjca.2021.11.007.

27. Yang A, Nguyenhuy M, Seevanayagam S. Intracranial atherosclerosis increases the risk of postoperative stroke after cardiac surgery: A Review and meta-analysis. Heart, Lung and Circulation. 2023;32(12):1417-25. doi:10.1016/j.hlc.2023.09.022.

28. Shahian DM, O'Brien SM, Filardo G, Ferraris VA, Haan CK, Rich JB, et al. The Society of Thoracic Surgeons 2008 cardiac surgery risk models: Part 1—coronary artery bypass grafting surgery. Ann Thorac Surg. 2009;88(1). doi:10.1016/j.athoracsur.2009.05.053.

29. Hein OV, Birnbaum J, Wernecke K, England M, Konertz W, Spies C. Prolonged intensive care unit stay in cardiac surgery: Risk factors and long-term-survival. Ann Thorac Surg. 2006;81(3):880-5. doi:10.1016/j.athoracsur.2005.09.077.

30. Zhou X, Ruan W, Zhao L, Lin K, Li J, Liu H, et al. Causal links between renal function and cardiac structure, function, and disease risk. Global Heart. 2024;19(1):83. doi:10.5334/gh.1366.

31. Bangalore S, Maron DJ, O'Brien SM, Fleg JL, Kretov EI, Briguori C, et al. Management of coronary disease in patients with advanced kidney disease. N Engl J Med. 2020;382(17):1608-18. doi:10.1056/nejmoa1915925.

32. Doenst T, Haddad H, Stebbins A, Hill JA, Velazquez EJ, Lee KL, et al. Renal function and coronary bypass surgery in patients with ischemic heart failure. J Thorac Cardiovasc Surg. 2022;163(2). doi:10.1016/j.jtcvs.2020.02.136.

33. Alnsasra H, Asleh R, Kumar N, Lopez C, Toya T, Kremers WK, et al. Incidence, risk factors, and outcomes of stroke following cardiac transplantation. Stroke. 2021;52(11). doi:10.1161/strokeaha.121.034874.

34. An X, Ye N, Bian W, Cheng H. Prophylactic dialysis improves short-term clinical outcome in patients with non-dialysis-dependent chronic kidney disease undergoing cardiac surgery: A meta-analysis of randomized controlled trials. Coronary Artery Disease. 2021;33(1). doi:10.1097/mca.0000000000001080.

35. Cheruku SR, Raphael J, Neyra JA, Fox AA. Acute kidney injury after cardiac surgery: Prediction, prevention, and management. Anesthesiol. 2023;139(6):880-98. doi:10.1097/aln.0000000000004734.

36. Liou L, Mostofsky E, Lehman L, Salia S, Gupta S, Barrera FJ, et al. Racial disparities in post-transplant stroke and mortality following stroke in adult cardiac transplant recipients in the United States. PLOS One. 2023;18(2). doi:10.1371/journal.pone.0268275.

37. Merkler AE, Chen ML, Parikh NS, Murthy SB, Yaghi S, Goyal P, et al. Association between heart transplantation and subsequent risk of stroke among patients with heart failure. Stroke. 2019;50(3):583-7. doi:10.1161/strokeaha.118.023622.

38. Alvarez P, Kitai T, Okamoto T, Niikawa H, McCurry KR, Papamichail A, et al. Trends, risk factors, and outcomes of postoperative stroke after heart transplantation: An analysis of the UNOS database. ESC Heart Failure. 2021;8(5):4211-7. doi:10.1002/ehf2.13562.

39. Lin A, Feng I, Zhao Y, Kurlansky P, Vinogradsky A, Wang C, et al. Increased prevalence of stroke after heart transplant in the New Allocation System Era. Ann Thorac Surg. 2025;120(1):130-9. doi:10.1016/j.athoracsur.2025.02.006.

40. Zaaqoq AM, Chang J, Pothapragada SR, Ayers L, Geng X, Russell JL, et al. Risk factors for stroke development after thoracic aortic surgery. J Cardiothorac Vasc Anesth. 2023;37(12):2524-30. doi:10.1053/j.jvca.2023.08.135.

41. Harky A, Othman A, Shaw M, Nawaytou O, Harrington D, Kuduvalli M, et al. Contemporary results of open thoracic and thoracoabdominal aortic surgery in a single United Kingdom Center. J Vasc Surg. 2021;73(5). doi:10.1016/j.jvs.2020.09.027.

42. Desai ND, Vekstein A, Grau-Sepulveda M, O'Brien SM, Takayama H, Chen EP, et al. Development of a novel society of thoracic surgeons aortic surgery mortality and morbidity risk model. Ann Thorac Surg. 2025;119(1):109-19. doi:10.1016/j.athoracsur.2024.09.025.

43. Manoly I, Uzzaman M, Karangelis D, Kuduvalli M, Georgakarakos E, Quarto C, et al. Neuroprotective strategies with circulatory arrest in open aortic surgery – a meta-analysis. Asian Cardiovasc Thorac Ann. 2022;30(6):635-44. doi:10.1177/02184923211069186.

44. Kouchoukos NT. Commentary: Rates of spinal cord ischemic injury after aortic surgery: One size does not fit all. J Thorac Cardiovasc Surg. 2022;163(2):566-7. doi:10.1016/j.jtcvs.2020.05.053.

45. Karunanantham J, Ali JM, Evans NR, Webb S, Large SR. Impact of stroke on outcomes following cardiac surgery: Propensity matched analysis. J Cardiac Surg. 2020;35(11):3010-6. doi:10.1111/jocs.14964.

46. Santos HN, Magedanz EH, Guaragna JC, Santos NN, Albuquerque LC, Goldani MA, et al. Predictors of stroke in patients undergoing cardiac surgery. Braz J Cardiovasc Surg. 2014;29(2):140-7. doi:10.5935/1678-9741.20140025.

47. Messe SR, Kasner SE, Mullen MT, Cummings S, Leibowitz L, Weimer J, et al. Abstract TP120: The impact of stroke on cost and length of stay after cardiac surgery. Stroke. 2022;53(Suppl. 1). doi:10.1161/str.53.suppl_1.tp120.

Check for updates

Application of the COAPT (Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy) score in patients with severe functional mitral regurgitation and percutaneous management with the MitraClip device

Aplicación del puntaje COAPT (Evaluación de resultados cardiovasculares del tratamiento percutáneo con MitraClip) en pacientes con insuficiencia mitral funcional grave y tratamiento percutáneo con dispositivo MitraClip.

Diego A. Salas-Márquez[1]*, Edgar F. Hurtado[1], Wilmer A. Cely[2], and Fernán Mendoza[3]

[1]Department of Hemodynamics and Interventional Cardiology; [2]Department of Noninvasive Cardiology; [3]Department of Clinical Cardiology. Fundación Clínica Shaio, Bogotá, Colombia

Abstract

Introduction: *Functional mitral regurgitation is defined as blood backflow from the left ventricle to the left atrium during ventricular systole. In the short-term, this causes heart failure due to geometric alteration, leading to poor papillary muscle and chordae tendineae function as a result of blood flow compensation. Percutaneous treatment with MitraClip (Abbott Vascular) has shown improved mortality, morbidity and quality of life in patients with severe functional mitral regurgitation.* **Objective:** *To describe COAPT scores in patients with functional mitral regurgitation after being treated with the MitraClip device at a cardiovascular institution between July 2016 and May 2024.* **Methods:** *An observational descriptive study was performed with the application of a risk index score.* **Results:** *Fifty-nine patients met the inclusion criteria for the study. The mean age was 71 ± 8.3 years, 83% had hypertension, 74.5% had hypercholesterolemia, 57.6% had coronary heart disease and 23% had previous myocardial revascularization. There were 25 heart failure hospitalizations (42.3% of the population), and 4 deaths (6.77%). A left ventricular ejection fraction (LVEF) less than 25% (OR: 7.38; 95% CI: 1.83-28.9), left ventricular end-systolic diameter greater than 5.5 cm (OR: 3.56; 95% CI: 1.1-10.9), and left ventricular end-diastolic diameter greater than 7.5 cm (OR: 25.3; 95% CI: 1.2-509) were significant predictors of hospitalization for heart failure, but not of mortality.* **Conclusions:** *The COAPT score did not significantly predict mortality results in the study population, although left ventricular diameter measurements (both systolic and diastolic) as well as LVEF less than 25% were predictors of hospitalization for heart failure over two years of follow up.*

Keywords: Heart failure. Mortality prediction. Transcatheter edge-to-edge repair. Functional mitral regurgitation.

Resumen

Introducción: *La insuficiencia mitral secundaria (o también llamada funcional) se define como la regurgitación de flujo sanguíneo desde el ventrículo izquierdo hacia la aurícula izquierda durante la sístole ventricular, la cual produce insuficiencia cardíaca a corto plazo como resultado de la alteración en la geometría del ventrículo izquierdo, lo que, a su vez, conlleva a mal funcionamiento de*

los músculos papilares y cuerdas tendinosas por compensación del flujo sanguíneo. El manejo percutáneo con el dispositivo MitraClip (Abbott Vascular) ha demostrado mejoría en mortalidad, morbilidad y calidad de vida en pacientes con insuficiencia mitral funcional grave. **Objetivo:** *Describir el comportamiento del puntaje de riesgo COAPT en pacientes con insuficiencia mitral funcional grave y manejo percutáneo con dispositivo MitraClip en una institución cardiovascular entre junio de 2016 y mayo de 2024.* **Métodos:** *Estudio observacional descriptivo con aplicación de puntaje de riesgo.* **Resultados:** *en el análisis se incluyeron 59 pacientes, con promedio de edad de 71 ± 8.3 años, de los cuales el 83% tenía hipertensión arterial, el 74.5% hipercolesterolemia, el 57.6% enfermedad coronaria y el 23% revascularización miocárdica previa. Se presentaron veinticinco hospitalizaciones por insuficiencia cardíaca (42.3% de la población) y cuatro muertes (6.77%). La fracción de eyección del ventrículo izquierdo (FEVI) menor a 25% (OR: 7.38; IC 95%: 1.83-28.9), el diámetro de fin de sístole (dFSVI) mayor a 5.5 cm (OR: 3.56; IC 95%: 1.1-10.9) y el diámetro de fin de diástole del ventrículo izquierdo (dFDVI) mayor a 7.5 cm (OR: 25.3; IC 95%: 1.2-509) son predictores significativos de hospitalización por insuficiencia cardíaca, pero no de mortalidad.* **Conclusiones:** *El puntaje COAPT en la población en estudio no mostró resultados significativos para mortalidad, aunque las medidas de diámetro del ventrículo izquierdo (tanto sistólico como diastólico) al igual que la FEVI menor al 25%, sí fueron predictores para hospitalización por insuficiencia cardíaca.*

Palabras clave: Insuficiencia cardíaca. Predicción de mortalidad. Reparo borde a borde transcatéter. Insuficiencia mitral funcional.

Introduction

Mitral regurgitation (MR) is defined as blood backflow from the left ventricle (LV) to the left atrium during ventricular contraction or systole. It is one of the most frequent valve diseases in the world, with an estimated prevalence of 1 to 2% in adults in the United States and a poor clinical prognosis[1].

Almost one third of patients with heart failure have moderate or severe MR[2]. The global prevalence of MR in the general population is close to 2%, and its etiology may be primary (organic) or secondary (functional). Primary MR is caused by a primary lesion of one or more of the mitral apparatus components. Degenerative (fibroelastic deficiency and Barlow's disease), rheumatic and endocarditis etiologies are the main primary causes[3].

The treatment of choice for primary MR is surgical mitral valve repair or replacement. Urgent surgery is indicated for patients with severe MR. Generally, papillary muscle rupture requires valve replacement. For patients with chronic MR, the decision is based on the presence of symptoms, reduced left ventricular ejection fraction (LVEF), left ventricular end-systolic diameter (LVESD), recent onset of atrial fibrillation and pulmonary artery systolic pressure (PASP), based on the clinical practice guidelines of European and American scientific societies[3,4].

On the other hand, secondary or functional MR refers to valve dysfunction with regurgitation without structural damage to the mitral apparatus. It is more frequent than primary MR and is due to left ventricular dilation and dysfunction, mainly in patients with reduced LVEF, in whom structural abnormalities lead to poor leaflet coaptation despite a normal structure, causing the chronic pathophysiological condition of ventricular-atrial regurgitation[5].

Mitral transcatheter edge-to-edge repair (M-TEER) with a MitraClip device (Abbott Vascular) has been proposed for secondary MR correction[6]. This device has a polyester-covered cobalt-chromium nitinol clip with hooks to anchor the mitral valve and a maneuvering system to help position the clip. Different version of the clip have been available since its introduction: MitraClip NTR and MitraClip XTR (only available in the United States). It is implanted using a venous catheter and transseptal puncture and is designed to capture the anterior and posterior valve leaflets to correct or decrease MR[7]. It was approved by the Food and Drug Administration (FDA) in March 2019 for treating secondary or functional MR.

There is limited information on the predictors of death and hospitalization for heart failure in patients with heart failure and secondary or functional MR. In 2022, a simple predictive risk score (COAPT Score)[8] was proposed based on data from the Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation (COAPT) clinical trial[9]. This score uses clinical, echocardiographic and treatment variables to provide useful prognostic information for patients with heart failure and severe functional MR.

The COAPT score includes clinical variables: New York Heart Association (NYHA) functional class, the presence of chronic obstructive pulmonary disease (COPD), atrial fibrillation or flutter, and chronic kidney disease (CKD). It also includes echocardiographic variables: LVEF, LVESD, left ventricular end-diastolic diameter (LVEDD), right ventricular systolic pressure (RVSP), and the presence of tricuspid regurgitation (TR); as well as a treatment variable corresponding to the presence or absence of MitraClip treatment (with all patients in our case scoring for treatment). Score are assigned as follows: for CKD stage 3 (+1 point), for CKD stage 4 or

more (+3 points), NYHA functional class III or IV (+1 point), COPD (+1 point) and a history of atrial fibrillation or flutter (+1 point). For the echocardiographic variables, the scoring is as follows: RVSP > 45 mm Hg (+3 points), LVEF 25% to 35% (+1 point), LVEF < 25% (+2 points), LVESD: > 5.5 cm (+2 points) and TR ≥ 2+ (at least moderate) (+2 points). Finally, -3 points are assigned to patients with MitraClip treatment. Combining these values, the COAPT score ranges from -3 to +15 points.

The objective of this study was to describe the COAPT risk scores in patients with severe functional MR treated percutaneously with the MitraClip device at a cardiovascular facility between June 2016 and May 2024.

Results

From June 2016 to May 2024, 59 mitral transcatheter edge-to-edge repair procedures were performed with the MitraClip device at Fundación Clínica Shaio.

The included patients had an average age of 71 ± 8.3 years, of whom 64.4% were males and 83% had essential hypertension. The main heart disease etiology was ischemia (57.6%), with a history of percutaneous coronary intervention (52.5%) and surgical myocardial revascularization (23.7%). Altogether, 52.5% had undergone percutaneous coronary intervention (PCI) prior to the index hospitalization, and only one patient had peripheral artery disease with manifest signs and symptoms (Table 1).

The average LVEF was 27.6% (minimum of 10 and maximum of 67%), and the degree of TR was moderate (2+) in 27.1% and severe in 30.5%. Fifty-nine patients underwent the procedure, with a total of 117 clips implanted, for an average of 1.98 clips per patient (range of 1-4). During the index hospitalization, most of the patients were in NYHA functional classes II to IV. As far as comorbidities and treatments, 13.5% had a glomerular filtration rate of less than 30 ml/min; 20.3% (12 patients) were on cardiac resynchronization therapy with a defibrillator (CRT-D); and 57.6% had implantable cardioverter-defibrillators (ICDs). Fifty-seven of the 59 patients had a transthoracic echocardiogram prior to discharge.

This group of patients had a mortality rate of 6.78% (4 patients) and a heart failure hospitalization rate of 42.7% (n = 25) two years after the procedure (Table 2). The clinical variables were used to calculate the COAPT score, with the following results: 13 patients had COPD, 27 had atrial fibrillation or flutter; 23 were in NYHA functional class III and 6 were in functional class IVa;

Table 1. Demographic and clinical characteristics of patients with severe functional mitral regurgitation and the MitraClip device (n = 59)

Variable	p
Age (years)	71.0 ± 8.3
Male sex	38 (64.4%)
Body mass index (kg/m²)	23.7 ± 3.5
Body surface area (m²)	1.68 ± 0.16
Essential hypertension	49 (83.0%)
Hypercholesterolemia	44 (74.5%)
Coronary disease	34 (57.6%)
Diabetes mellitus	19 (32.2%)
History of surgical myocardial revascularization	14 (23.7%)
PCI	31 (52.5%)
Previous stroke	6 (10.1%)
Transient ischemic attack	4 (6.78%)
Peripheral artery disease	1 (1.69%)
History of atrial fibrillation or flutter	27 (45.7%)
CRT D	12 (20.3%)
ICD	34 (57.6%)
COPD	13 (22.0%)
CKD	33 (55.9%)
Baseline creatinine, mg/dl	1.27 ± 1.02

Baseline glomerular filtration rate, ml/min
  Between 30-60 ml/min
  Less than 30 ml/min
	
	26 (44.0%)
	8 (13.5%)

PCI: percutaneous coronary intervention; CRT D: cardiac resynchronization therapy with a defibrillator; ICD: implantable cardioverter-defibrillator; COPD: chronic obstructive pulmonary disease. CKD: chronic kidney disease.

33 patients had stage 3 and 4 CKD; and only two patients were recorded to be on renal replacement therapy with hemodialysis. Among the echocardiographic variables, 52.5% (n = 31 patients) had an LVEF < 25%, and 18.6% (n = 11 patients) had an LVEF between 25-35%. A total of 52.5% (n = 31 patients) had an LVESD > 5.5 cm, 50.8% (n = 30 patients) had an LVEDD between 6.1 and 7.5 cm, 10.1% (n = 6 patients) had an LVEDD > 7.5 cm, and 66.1% (n = 39) had an RVSP > 45 mmHg (Table 2).

Table 3 shows hospitalizations for heart failure and mortality after two years of follow-up for each clinical variable. There were four deaths in two years (6.67%). One patient died after six months due to heart failure

progression secondary to non-ST segment elevation myocardial infarction. The second patient died after one year from community-acquired pneumonia; the third and fourth patients developed septic shock with a fatal outcome after almost two years of follow-up.

After evaluating each of the COAPT score characteristics against the risk of hospitalization for heart failure and mortality two years after the MitrClip device procedure, both LVEF less than 25%, as well as LVESD greater than 5.5 cm and LVEDD greater than 7.5 cm were significant predictors of hospitalization for heart failure, but not mortality, in the study population (Tables 3 and 4).

COAPT score in the study population

Table 5 describes the COAPT score application in the study population. All the patients had –3 points due to undergoing the MitraClip procedure. COAPT scores 4, 5 and 6 had the most hospitalizations for heart failure after two years, but were not related to mortality (Table 5, Fig. 1).

Grouped by COAPT score categories (quartiles), the category with COAPT scores between –3 and +2 had eight hospitalizations for heart failure and 16 patients who did not need to be hospitalized. In the +3 and +4 category, five patients had to be hospitalized and nine did not. The +5 and +6 category had the highest number of hospitalizations, while only two of four patients in the +7 to +15 category had to be hospitalized (Fig. 2).

When grouped by COAPT score categories (quartiles), the category with COAPT scores between –3 and +2 recorded two deaths after two years, with 22 patients still living. There were no deaths in the +3 and +4 group. There was one death in the +5 and +6 group, and 14 patients were still living after two years. The +7 to +15 category had one death, with three patients still living (Figs. 3 and 4).

As far as complications in patients with M-TEER using the MitraClip device, seven patients had complications from the procedure, and one patient did not have follow-up data. One patient had an atrial septal defect that had to be closed percutaneously with an Amplatzer (Abbott Cardiovscular) device, and one patient had leaflet tearing and rupture, causing severe acute mitral regurgitation, which was corrected with another clip. One patient experienced chordae tendineae rupture, and two patients had severe residual MR. One patient had a left atrial thrombus that required monitoring and systemic anticoagulation before proceeding with the intervention. In the last patient, posterior leaflet discontinuity was found at the end of the

Table 2. Echocardiographic and clinical characteristics of patients with severe functional mitral regurgitation and the MitraClip device

Characteristics	p
Baseline NYHA	
I	5 (8.47%)
II	24 (40.6%)
III	23 (38.9%)
IVa	6 (10.1%)
None	1 (1.69%)
LVEF, n (%)	
More than 35%	17 (28.8%)
Between 25-35%	11 (18.6%)
Less than 25%	31 (52.5%)
LVESD greater than 5.5 cm	31 (52.5%)
LVEDD	
Less than 6.1	21 (35.5%)
Between 6.1 and 7.5	30 (50.8%)
More than 7.5	6 (10.1%)
RVSP greater than 45 mmHg	39 (66.1%)
TR	
Mild	23 (38.9%)
Moderate	16 (27.1%)
Severe	18 (30.5%)
Number of clips implanted	
One	14 (23.7%)
Two	34 (57.6%)
Three	9 (15.2%)
Four	2 (3.3%)
Hospitalizations for heart failure after two years	25 (42.3%)
Deaths	4 (6.77%)

NYHA: New York Heart Association; LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic diameter; LVEDD: left ventricular end-diastolic diameter; RVSP: right ventricular systolic pressure; TR: tricuspid regurgitation.

procedure; he is therefore being followed and has been symptom-free (Table 6).

During the two-year follow-up, there were four patient deaths, none of which were related to the procedure. All the patients were treated by the center's heart failure group, which ensured medical management based on clinical practice guidelines; 100% of the patients received beta blockers, empagliflozin or dapagliflozin, spironolactone or eplerenone, and sacubitril-valsartan (maximum tolerated dose). This was done before being presented to the multidisciplinary heart team.

Discussion

Transcatheter edge-to-edge repair with MitraClip devices has proven to improve morbidity, mortality and quality of life in patients with severe MR. In 2022, a risk

Table 3. Relationship between clinical and paraclinical characteristics and hospitalization for heart failure and mortality in the study population two years post-intervention with a MitraClip device (n = 59)

Variable	Hospitalization for heart failure at two years		Mortality at two years	
	(n = 25)	(n = 34)	(n = 4)	(n = 55)
	Yes	No	Yes	No
Age < 60 Between 60-75 years > 75 years	3 (5.08%) 17 (28.8%) 5 (8.47%)	3 (5.08%) 16 (27.1%) 13 (22.0%)	0 (0.0%) 3 (5.26%) 1 (1.75%)	6 (10.5%) 30 (52.6%) 17 (29.3%)
Male sex	15 (25.4%)	10 (16.9%)	2 (3.51%)	2 (3.51%)
BMI	23.2±3.5	23.9±3.6	27.8±3.4	23.3±3.4
Essential hypertension	22 (37.9%)	25 (42.3%)	4 (7.02%)	43 (75.4%)
Hypercholesterolemia	18 (30.5%)	24 (40.6%)	4 (7.02%)	38 (66.6%)
Diabetes mellitus	7 (11.8%)	12 (20.3%)	1 (1.75%)	18 (31.5%)
Coronary disease	14 (23.7%)	18 (30.5%)	3 (5.26%)	29 (50.8%)
History of revascularization	5 (8.47%)	8 (13.5%)	2 (3.51%)	11 (19.3%)
Prior PCI	14 (23.7%)	16 (27.1%)	3 (5.26%)	27 (47.3%)
History of acute myocardial infarction	14 (23.7%)	16 (27.1%)	3 (5.26%)	27 (47.3%)
Previous stroke	3 (5.05%)	3 (5.08%)	0 (0.0%)	6 (10.5%)
Previous transient ischemic attack	3 (5.08%)	1 (1.69%)	0 (0.0%)	4 (7.02%)
Peripheral vascular disease	0 (0.0%)	1 (1.69%)	0 (0.0%)	1 (1.69%)
COPD	4 (6.78%)	9 (15.2%)	2 (3.39%)	11 (18.6%)
History of atrial fibrillation or flutter	10 (16.9%)	15 (25.4%)	1 (1.69%)	24 (40.6%)
CRT D	6 (10.1%)	5 (8.4%)	2 (3.39%)	9 (15.2%)
ICD	20 (33.9%)	13 (22.0%)	3 (5.08%)	30 (50.8%)
CKD	9 (15.2%)	10 (16.9%)	2 (3.39%)	17 (28.8%)
NYHA functional class I II III IV	1 (1.69%) 12 (20.3%) 8 (13.5%) 4 (6.78%)	3 (5.08%) 11 (18.6%) 15 (25.4%) 2 (3.39%)	0 (0.0%) 3 (5.08%) 1 (1.69) 0 (0.0%)	4 (6.78%) 20 (33.9%) 22 (37.2%) 6 (10.1%)
LVEF > 35% 25-35% < 25	3 (5.08%) 3 (5.08%) 19 (32.2%)	14 (23.7%) 6 (10.1%) 12 (20.3%)	1 (1.69%) 0 (0.0%) 3 (5.08%)	16 (27.1%) 9 (15.2%) 28 (47.4%)
RVSP > 45 mm Hg	18 (30.5%)	19 (32.2%)	2 (3.39%)	35 (59.3%)
LVESD > 5.5 cm	18 (30.5%)	7 (11.8%)	3 (5.08%)	28 (47.4%)
LVEDD < 6.1 6.1-7.5 cm > 7.5 cm	7 (11.8%) 12 (20.3%) 6 (10.1%)	14 (23.7%) 17 (28.8%) 0 (0.0%)	1 (1.69%) 1 (1.69%) 2 (3.39%)	20 (33.9%) 28 (47.4) 4 (6.78%)
TR Mild Moderate Severe	8 (14.5%) 7 (12.7%) 9 (16.3%)	15 (27.2%) 9 (16.3%) 7 (12.7%)	1 (1.75%) 2 (3.51%) 1 (1.75%)	22 (38.6%) 14 (24.5%) 15 (26.3%)

BMI: body mass index; PCI: percutaneous coronary intervention; COPD: chronic obstructive pulmonary disease; CRT D: cardiac resynchronization therapy with a defibrillator; ICD: implantable cardioverter-defibrillator; LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic diameter; LVEDD: left ventricular end-diastolic diameter; CKD: chronic kidney disease. NYHA: New York Heart Association functional classification; TR: tricuspid regurgitation.

Table 4. Predictors of death or hospitalization for heart failure at two years (n = 59)

Variable	Hospitalization for heart failure		Death	
	OR	P	OR	P
LVEF, n (%)				
> 35% reference	1.00	-	1.0	-
25-35% vs. reference	2.33 (0.36-15.0)	0.33	Insufficient data	
< 25% vs. reference	7.38 (1.83-28.9)	0.000	1.7 (0.16-17.8)	
LVESD > 5.5 cm vs. less	3.56 (1.15-10.9)	0.02	2.5 (0.25-26.3)	0.39
LVEDD				
< 6.1 (reference)	1.00	-	1.0	-
6.1-7.5 cm vs. reference	1.44 (0.43-4.54)	0.39	0.75 (0.06-7.4)	0.66
> 7.5 cm vs. reference	25.3 (1.24-509)	0.000	7.59 (0.78-73.2)	0.11

LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic diameter; LVEDD: left ventricular end-diastolic diameter.

Table 5. COAPT score in the study population, by groups (mortality and hospitalization for heart failure at two years)

COAPT score	Hospitalizations for heart failure at two years (n)	No hospitalization (for heart failure) (n)	Mortality at two years (n)	Survival at two years (n)
-3	0	1	0	1
-2	0	4	0	4
-1	0	1	0	1
0	1	2	1	2
1	4	4	1	7
2	3	4	0	7
3	0	4	0	4
4	5	5	0	10
5	6	3	0	9
6	4	2	1	5
7	2	2	1	3
Total	25	32	4	53

COAPT: Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation.

score was developed for this population derived from the COAPT trial. This was the first study to develop a risk score for predicting death or hospitalization for heart failure in patients undergoing M-TEER with a MitraClip device[8].

The M-TEER risk stratification is key for decision making to properly select patients with severe functional MR. The current risk scores for functional (also secondary) MR are suboptimal. Scores designed specifically for M-TEER, like MitraScore[10], do not differentiate between patients with primary or secondary MR.

The COAPT score is derived from four clinical variables, four echocardiographic variables and one treatment-related variable; the latter applied for all patients. We underscore the usefulness of this procedure based on the COAPT study, which showed a significant reduction in the primary outcome of hospitalization for heart failure in the intervention group (35.8 vs. 67.9%; HR: 0.53; 95% CI: 0.40-0.70; p < 0.001), after two years of follow-up, compared with medical treatment.

This is the first descriptive study to date to apply the COAPT risk score in a population undergoing a
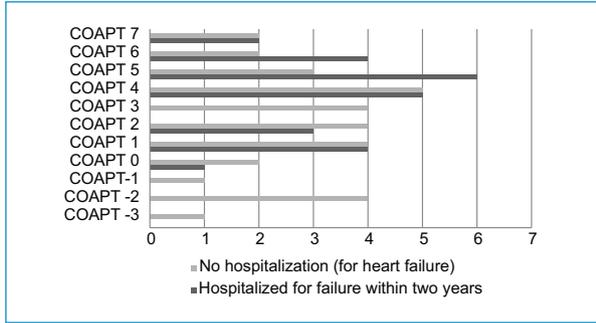
Figure 1. COAPT scores for heart failure hospitalization in the two years post-intervention (n = 59).
COAPT: Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation.
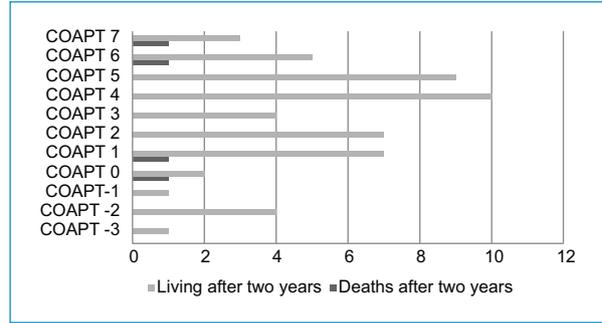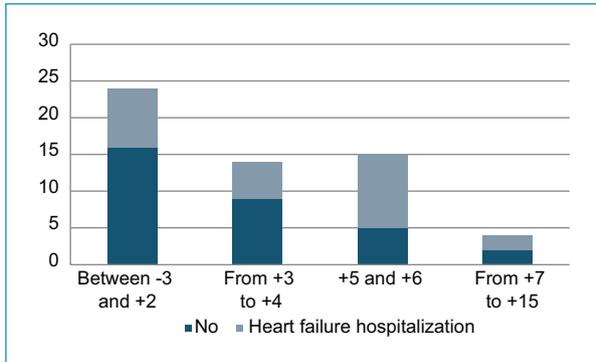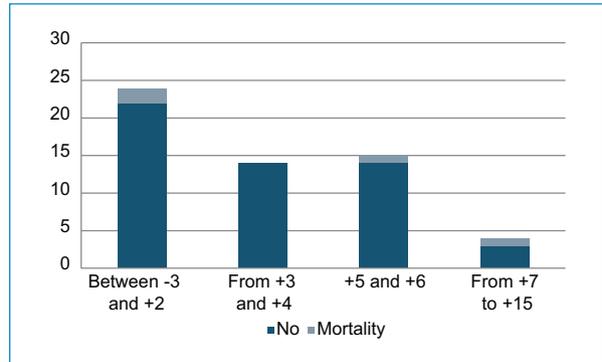

Figure 3. COAPT score for mortality in the two years post-intervention (n = 59).
COAPT: Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation.

Figure 2. COAPT scores for heart failure hospitalization in the two years post-intervention, by COAPT score categories (quartiles) (n = 59).
COAPT: Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation.

Figure 4. COAPT score for predicting mortality in the two years post-intervention, by COAPT score categories (quartiles) (n = 59).
COAPT: Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation.

procedure at a cardiovascular facility. The goal was to describe the results of applying the COAPT score to patients with severe functional MR undergoing edge-to-edge repair with a MitraClip device at Clínica Shaio from June 2016 to May 2024.

The main findings of this study were the demographic, clinical and echocardiographic descriptions of the 59 patients who underwent the procedure at our center, whose average age was similar to the original study (71 years); most of the patients were male (64%) and had no significant cardiovascular history, similar to the population in the original study[8]. It also reports the COAPT scores of patients undergoing the procedure, individually and by quartiles, against the frequency of hospitalization for heart failure and mortality during

follow-up. There were 25 hospitalizations for heart failure (42.4%) after two years of follow-up, and four deaths (6.6%). Relating each of the score's characteristics to the study population showed that an LVEF less than 25% (OR: 7.38; 95% CI: 1.83-28.9), an LVESD greater than 5.5 cm (OR: 3.56; 95% CI: 1.1-10.9), and an LVEDD greater than 7.5 cm (OR: 25.3; 95% CI: 1.2-509) are significant predictors of hospitalization for heart failure but not of mortality.

Mitral regurgitation affects the prognosis of patients with heart failure. Previous management only included optimal medical treatment and resynchronization, if indicated. The COAPT study was able to show improved outcomes after M-TEER with a MitraClip device, compared to optimal medical treatment in symptomatic

Table 6. Relationship between mortality and complications in the study population (n = 59) after the intervention

Mortality and complications post-intervention	n	% among patients with complications (n = 12)	% among the total study population (n = 59)
Mortality	4	33.3%	6.77%
Severe residual MR	2	16.6%	3.38%
Left atrial thrombus	1	8.3%	1.69%
Posterior leaflet continuity (P2)	1	8.3%	1.69%
No follow-up data	1	8.3%	1.69%
Leaflet tearing and rupture (severe MR)	1	8.3%	1.69%
Rupture of chordae tendineae	1	8.3%	1.69%

patients with heart failure and moderate to severe functional MR who were on guideline-directed medical treatment with maximum tolerated doses and cardiac resynchronization therapy, with a two-year follow-up[9]. The frequency of hospitalization for heart failure was 35.8% of patients per year in the MitraClip group compared to 67.9% in the optimal medical treatment group. Furthermore, the MitraClip procedure significantly reduced two-year mortality compared to optimal medical treatment (29.1 vs. 46.1%; HR: 0.62; 95% CI: 0.46-0.82; p < 0.001)[9]. The benefits after M-TEER have been extended to up to five years after randomization[11].

In contrast, the MITRA-FR clinical trial showed no significant benefits with MitraClip compared to optimal guideline-directed medical treatment in a heart failure population that was different from the COAPT patients[12].

Other risk scores have been developed for patients with primary MR, like MIDA, which was validated in the MIDA-BNP registry[13]. This score predicts mortality one and five years after medical treatment and mitral cardiovascular surgery using the following variables: age over 65 years, heart failure symptoms, atrial fibrillation, left atrial enlargement, RVSP greater than 50 mmHg, LVEF less than 60% and LVESD greater than 4 centimeters. Thus far, severe functional mitral disease is known to be different from primary mitral disease, and therefore only two scores for predicting mortality and heart failure hospitalization have been published for patients with transcatheter interventions using the MitraClip device[8,13].

The patients in our study had a similar average age, functional class symptoms and comorbidities as those in COAPT. The rate of implantation was more than 95% (the procedure only had to be suspended in one patient, due to a thrombus) similar to what occurred in COAPT[9], and a post-procedural reduction in MR of at least one degree was achieved in more than 95% of cases.

The study also described the complications during follow-up. The number of patients undergoing the procedure positions Clínica Shaio as an experienced cardiovascular center for treating patients with mitral disease related to heart failure with reduced ejection fraction.

We consider that echocardiographic measurements must continue to be standardized and a committee should be established to evaluate the outcomes, to promote validation of the COAPT score at our institution as well as other institutions that currently perform M-TEER with the MitraClip device. This instrument can estimate the risk of heart failure hospitalization and mortality in patients with a MitraClip after two years of follow-up. Thus, early identification and referral of patients with severe functional MR who are eligible for MitraClip treatment (who meet the COAPT criteria) is important, but it should also be noted that there are patients who do not benefit from this treatment, such as those with advanced or end-stage heart failure, as shown by the MITRA-FR[12] clinical trial.

It is very important to create a multidisciplinary group including cardiologists specializing in heart failure, cardiac imaging specialists, anesthesiologists, electrophysiologists, cardiovascular surgeons and interventional cardiologists experienced in structural disease, to analyze cases and ensure optimal medical treatment, cardiac resynchronization needs and echocardiographic criteria, including disproportionate MR, based on the effective regurgitant orifice area (EROA):LVEDD ratio. The data from the COAPT study must be considered for proper patient selection; these include LVEF $\geq$ 20%, LVESD $\leq$ 70 mm, PASP $\leq$ 70 mmHg, nonsevere TR, TAPSE $\geq$ 15 mm and no hemodynamic instability or end-stage heart failure.

We recognize the prognostic usefulness of stratifying patients with heart failure and severe functional MR treated with MitraClip, as well as its usefulness for inpatient follow-up. We highlight that, in the description by quartiles, patients with COAPT +5 and +6 had the most hospitalizations for heart failure, but the mortality rate was no different from the original article, which is probably related to the number of patients at our institution compared to those in COAPT[8,9].

The study's limitations include the fact that few institutions in Colombia perform M-TEER with MitraClip. Therefore, patients who could be treated with this

device should be actively sought out, and the selection criteria should correspond to the COAPT criteria. The COAPT risk score needs to be validated with a larger group of patients, perhaps combining experience groups from cardiovascular centers around the country who have treated more than 50 patients since 2016. The number of patients may not allow causal association factors to be determined, like hospitalization for heart failure and mortality. This was a descriptive study that applied the COAPT score and observed its behavior in a population of patients treated with MitraClip at a single high-quality cardiovascular center.

There are no external validation studies of the COAPT score to date, but some are in the publishing process, drawn from an independent registry of other international centers with patients treated with MitraClip, which are necessary for its reproducibility and applicability.

Conclusions

Severe functional MR presents a higher risk of complications in patients with heart failure with reduced ejection fraction.

Guideline-directed medical therapy is the first step in patients with reduced ejection fraction and functional MR. If it persists, multidisciplinary assessment is needed to consider transcatheter edge-to-edge repair based on technological advances and the experience of centers dedicated to these procedures. A risk score is needed for these cases, and the COAPT score may be a good tool.

In our study, the COAPT score did not show significant results for mortality, although left ventricular diameter measurements (both systolic and diastolic) as well as an LVEF less than 25% did predict hospitalization for heart failure in the study population.

Funding

The authors declare that they received no funding for this study.

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 in the course of this study.

Confidentiality, informed consent and ethical approval. The authors followed their institution's confidentiality protocols, obtained informed consent from the patients, and received approval from the ethics committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that they did not use any type of generative artificial intelligence in writing this article.

References

1. Nkomo V, Gardin J, Skelton T, Gottdiener J, Scott C, Enriquez-Sarano M. Burden valvular heart diseases: a population-based study. Lancet. 2006;(368):1005-11.
2. Varadarajan P, Sharma S, Heywood J, Pai R. High prevalence of clinically silent severe mitral regurgitation in patients with heart failure: role for echocardiography. J Am Soc Echocardiogr. 2006;(19):1458-61.
3. Vahanian A, Beyersdorf F, Praz F, Milojevic M, Baldus S, Bauersachs J, et al. ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J. 2022;43(7):561-632.
4. Otto CM, Nishimura RA, Bonow RO, Carabello BA, Erwin JP, Gentile F, et al. 2020 ACC/AHA guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/ American Heart Association Joint Committee on Clinical Practice Guidelines. J Am Coll Cardiol [Internet]. 2021;77(4):e25-197. Disponible en: https://doi.org/10.1016/j.jacc.2020.11.018.
5. Asgar A, Mack M, Stone G. Secondary mitral regurgitation in heart failure: pathophysiology, prognosis, and therapeutic considerations. J Am Coll Cardiol. 2015;65(12):1231-48.
6. Pibarot P, Delgado V, Bax JJ. MITRA-FR vs. COAPT: Lessons from two trials with diametrically opposed results. Eur Heart J Cardiovasc Imaging. 2019;20(6):620-4.
7. Benítez LM, Náder CA, Lores AJ, Rodríguez AM, Cadena J, Cucalón ÁM, et al. Endovascular mitral valve repair with MitraClip®. Rev Colomb Cardiol. 2019;26:161-70.
8. Shah N, Madhavan M V., Gray WA, Brener SJ, Ahmad Y, Lindenfeld JA, et al. Prediction of death or HF hospitalization in patients with severe FMR: The COAPT Risk Score. JACC Cardiovasc Interv. 2022;15(19):1893-905.
9. Stone GW, Lindenfeld J, Abraham WT, Kar S, Lim DS, Mishell JM, et al. Transcatheter mitral-valve repair in patients with heart failure. N Engl J Med. 2018;379(24):2307-18.
10. Raposeiras-Roubin S, Adamo M, Freixa X, Arzamendi D, Benito-González T, Montefusco A, et al. A score to assess mortality after percutaneous mitral valve repair. J Am Coll Cardiol. 2022;79(6):562-73.
11. Stone GW, Abraham WT, Lindenfeld J, Kar S, Grayburn PA, Lim DS, et al. Five-year follow-up after transcatheter repair of secondary mitral regurgitation. N Engl J Med. 2023;388(22):2037-48.
12. Obadia J-F, Messika-Zeitoun D, Leurent G, Iung B, Bonnet G, Piriou N, et al. Percutaneous repair or medical treatment for secondary mitral regurgitation. N Engl J Med. 2018;379(24):2297-306.
13. Hausleiter J, Lachmann M, Stolz L, Bedogni F, Rubbio AP, Estèvez-Loureiro R, et al. Artificial intelligence-derived risk score for mortality in secondary mitral regurgitation treated by transcatheter edge-to-edge repair: The EuroSMR risk score. Eur Heart J. 2024 [Internet]; 45(11):922-36. Disponible en: https://doi.org/10.1093/eurheartj/ehad871.

Annual report on heart transplantation in Colombia: 1985-2023

Reporte anual de trasplante cardíaco en Colombia: 1985-2023

Francisco L. Uribe-Buritica[1,2], Noel A. Flórez Alarcón[1,2], Pastor Olaya-Rojas[1,2], Diana C. Carrillo-Gómez[1,2], Juan D. López-Ponce de León[,2,3], Edilma L. Rivera-Muñoz[1,3], Álvaro M. Quintero-Ossa[3,4], Luis E. Echeverría[3,5], Fernán Mendoza[3,6], Alejandro Mariño[3,7], Mª. Juliana Rodríguez-González [3,8], Carlos Arias-Barrera[3,9], Eduardo J. Echeverri-Navarrete[3,10], and Juan E. Gómez-Mesa[1,2,3]*

[1]Department of Cardiology, Fundación Valle del Lili, Cali; [2]Department of Clinical Sciences, Universidad Icesi, Cali; [3]Heart Failure, Heart Transplant and Pulmonary Hypertension Chapter, Asociación Sociedad Colombiana de Cardiología y Cirugía Cardiovascular, Bogotá; [4]Department of Cardiology, Clínica CardioVid, Medellín; [5]Department of Cardiology, Fundación Cardiovascular de Colombia, Floridablanca; [6]Department of Cardiology, Fundación Clínica Shaio, Bogotá; [7]Department of Cardiology, Hospital Universitario San Ignacio, Bogotá; [8]Department of Cardiology, LaCardio, Bogotá; [9]Department of Cardiology, Clínica Universitaria Colombia, Bogotá; [10]Department of Cardiology, Centro Médico Imbanaco, Cali. Colombia

Abstract

Introduction: *Heart transplantation is a treatment option for advanced heart failure. The Colombian Heart Transplant Registry (RECOLTRACA) compiles relevant data on this procedure. In 2023, statistical data on the current state of heart transplantation was updated.* **Objectives:** *To describe heart transplantation activity in 2023 and the cumulative data since the first procedure was performed in Colombia in 1985.* **Methods:** *A retrospective cross-sectional study was conducted through interinstitutional collaboration among transplant centers in Colombia. Data was collected electronically via confidential communication channels of the Heart Failure, Heart Transplant, and Pulmonary Hypertension Chapter of the Sociedad Colombiana de Cardiología y Cirugía Cardiovascular [Colombian Society of Cardiology and Cardiovascular Surgery].* **Results:** *Ten institutions performed at least one heart transplant between 1985 and 2023. According to the SCC evaluation, a total of 1,618 heart transplant procedures had been recorded in Colombia up to 2023. In that year, 8 of these 10 institutions performed 97 heart transplant procedures, the majority in adult patients (87%), with a low percentage of heart retransplantation (5%) and combined heart transplants (2%).* **Conclusions:** *Heart transplantation has been performed in Colombia for nearly four decades. The sustained efforts of transplant institutions, interinstitutional collaboration, and governmental support were crucial in ensuring that this procedure remained accessible to a significant number of patients in 2023.*

Keywords: Heart transplantation. Institutions. Colombia.

Resumen

Introducción: *El trasplante cardíaco es una opción de tratamiento para la falla cardíaca avanzada. El Registro Colombiano de Trasplante Cardíaco (RECOLTRACA) recopila datos relevantes sobre este procedimiento. Para el año 2023, se actualizaron datos estadísticos sobre el estado actual del Trasplante cardíaco.* **Objetivo:** *Describir la actividad de trasplante cardíaco en el año 2023 y la información acumulada desde que se realizó el primer procedimiento en el territorio colombiano en el*

año 1985. **Métodos:** *Estudio transversal retrospectivo, con colaboración interinstitucional entre entidades trasplantadoras en Colombia. La información fue recolectada en formato electrónico a través de los canales de comunicación confidenciales del Capítulo de Falla Cardíaca, Trasplante Cardíaco e Hipertensión Pulmonar de la Sociedad Colombiana de Cardiología y Cirugía Cardiovascular.* **Resultados:** *Desde el año 1985 hasta el año 2023, diez instituciones en Colombia realizaron al menos un trasplante cardíaco, y se idenficaron un total de 1618. Para el año 2023, se realizaron 97 trasplantes cardíacos en ocho de estas instituciones, la mayoría en población adulta (87%), con un porcentaje bajo de retrasplante cardíaco (5%) y de trasplante cardíaco combinado (2%).* **Conclusiones:** *En Colombia se realizan trasplantes cardíacos desde hace casi cuatro décadas. El esfuerzo continuo de las instituciones trasplantadoras y la colaboración interinstitucional, junto con el apoyo gubernamental, fueron determinantes para que durante el año 2023 se realizara este procedimiento a un número significativo de pacientes.*

Palabras clave: *Trasplante cardíaco. Instituciones. Colombia.*

Introduction

Heart transplantation, considered to be the definitive treatment for advanced or refractory heart failure, was first performed in Colombia in 1985. Since then, a growing number of patients have undergone this treatment as result of increased medical/surgical staff training and the establishment of more transplant facilities around the country.

The Heart Failure, Heart Transplant, and Pulmonary Hypertension Chapter of Sociedad Colombiana de Cardiología y Cirugía Cardiovascular (SCC) [Colombian Society of Cardiology and Cardiovascular Surgery] has been working for several years on a national heart transplant registry (Registro Colombiano de Trasplante Cardíaco – RECOLTRACA), which seeks to record information relevant to the donation process, perioperative management, and short- and long-term follow-up of patients undergoing this procedure. This registry is expected to provide updated, consolidated, and multicenter information on the performance of this procedure in our population, which will also help improve our understanding of the extent of its benefits for patients with advanced or refractory heart failure.

Continuing with the initiative of implementing this heart transplant registry, in 2023, the SCC's Heart Failure, Heart Transplant, and Pulmonary Hypertension Chapter gathered information on the status of heart transplantation in Colombia through a questionnaire sent to the centers that had performed this procedure that year.

Objective

To record the number of heart transplants and the characteristics of their recipients in Colombia from 1985 to 2023, underscoring the information on procedures performed in 2023.

Methods

A cross-sectional study was conducted using a survey sent out by the SCC's Heart Failure, Heart Transplant, and Pulmonary Hypertension Chapter to transplant centers in Colombia, which were eligible if they had performed at least one heart transplant between 1985 and 2023. The survey collected data on the type of heart transplant (single, retransplant, or combined), age and sex of the recipient, and number of heart transplants performed at each participating institution for each registry year. The frequency of heart transplantation was reported as the absolute number of heart transplants performed per year in the country, and the number of heart transplants performed by the participating institution. Finally, the heart transplant information was reported by sex and the geographical location of the institution, categorized by year of transplantation (2023 or previous years). The transplant regions were classified according to the guidelines of the Network of Organ and Tissue Donation and Transplantation. Region 1 comprised the catchment area of the departments of Cundinamarca, Tolima, Boyacá, Casanare, Meta, Caquetá, Vichada, Vaupés, Guaviare, Guainía, Putumayo, and Amazonas; Region 2 comprised the departments of Antioquia, Caldas, Córdoba, Chocó, and San Andrés y Providencia; Region 3 comprised the departments of Valle del Cauca, Risaralda, Quindío, Cauca, and Nariño; Region 4 comprised the departments of Santander, Norte de Santander, Cesar, and Arauca; Region 5 comprised the departments of Atlántico, Bolívar, Magdalena, Guajira, and Sucre; and Region 6 comprised the department of Huila. The information was collected in an electronic database and analyzed with descriptive statistics using Microsoft Excel®.

The study was approved by the Biomedical Research Ethics Committee at Fundación Valle del Lili, in Cali,

Colombia, which coordinated and supervised the study. It was considered a no risk study according to Resolution No. 8430 of 1993 under Colombian law and therefore received informed consent exemption.

Results

In Colombia, nine institutions performed at least one heart transplant during 2023 (Table 1). Of these, eight answered the survey; the consolidated information from these eight institutions is the data presented in this paper. The information regarding heart transplant activity in the previous years (1985 to 2022) was obtained from previous publications, built on this same database created by SCC[1,2]. In 2023, we obtained information on a total of 97 heart transplants performed in eight institutions (Figs. 1 and 2), 93% of which were single heart transplants (Fig. 3), 5% were heart retransplants, and 2% were combined heart transplants (Table 2).

Recipient characteristics

The number of heart transplants increased in 2023, both in adults and children, compared to the previous five years. This increase could be partly related to the increase in procedures performed after 2020 and 2021, when the national and global situation was affected by the COVID-19 pandemic. However, it is interesting that this reduction in the number of heart transplants had also been seen in the years prior to the pandemic (Fig. 1).

In 2023, among adult heart transplant patients (n = 85), men accounted for 72% (n = 61), while women represented 28% (n = 24). There were 12 pediatric heart transplant recipients, half of whom were males. Compared to previous years, there was a notable increase in the proportion of female pediatric heart transplant recipients in 2023. However, considering the cumulative number of procedures from the first heart transplant up to 2023, males continue to have a higher rate of heart transplantation. These results suggest a persistent trend of male predominance in heart transplantation, with the single exception being the proportion of female children transplanted in 2023 (Table 3).

Heart transplant regions

The national distribution of transplant centers, considering the six transplant zones or regions in 2023, showed a tendency to concentrate heart transplant activity for both adults and children in Regions 2

Table 1. Institutions that performed heart transplants in 2023

Bogotá	Clínica Universitaria de Colombia (CUC)
	Fundación Cardioinfantil (FCI)
	Fundación Clínica Shaio
	Hospital Universitario San Ignacio (HUSI)
Bucaramanga	Fundación Cardiovascular de Colombia (FCV)
Cali	DIME Clínica Neurocardiovascular (DIME)*
	Centro Médico Imbanaco (CMI)
	Fundación Valle del Lili (FVL)
Medellín	Clínica CardioVid (CCVid)

*Did not provide data for this article.

Table 2. Type of procedure and year in which it was performed

Type of transplant	1985-2022	2023	Total
Heart transplant	1,476	90	1,566
Heart retransplant	16	5	21
Combined heart transplant Heart-kidney Heart-lung	27 2	2 0	29 2
Total	1,521	97	1,618

(Antioquia) and 4 (Valle del Cauca). These two regions accounted for 59% of the procedures performed in the country.

In an analysis of the consolidated transplant activity to date in Colombia (1985-2023), Region 2 (Antioquia) stood out as having the most heart transplants in adults (41%), while Regions 2 and 4 had the most heart transplants in children (approximately 40% for each region) (Table 3).

Discussion

In 2021, SCC's Heart Failure, Heart Transplant, and Pulmonary Hypertension Chapter began the process of gathering heart transplant information from the entire country, as part of an initiative to obtain detailed information on this procedure and work on implementing a national registry (RECOLTRACA). Through this process and ongoing data collection from different transplant centers, this paper was able to compile general heart
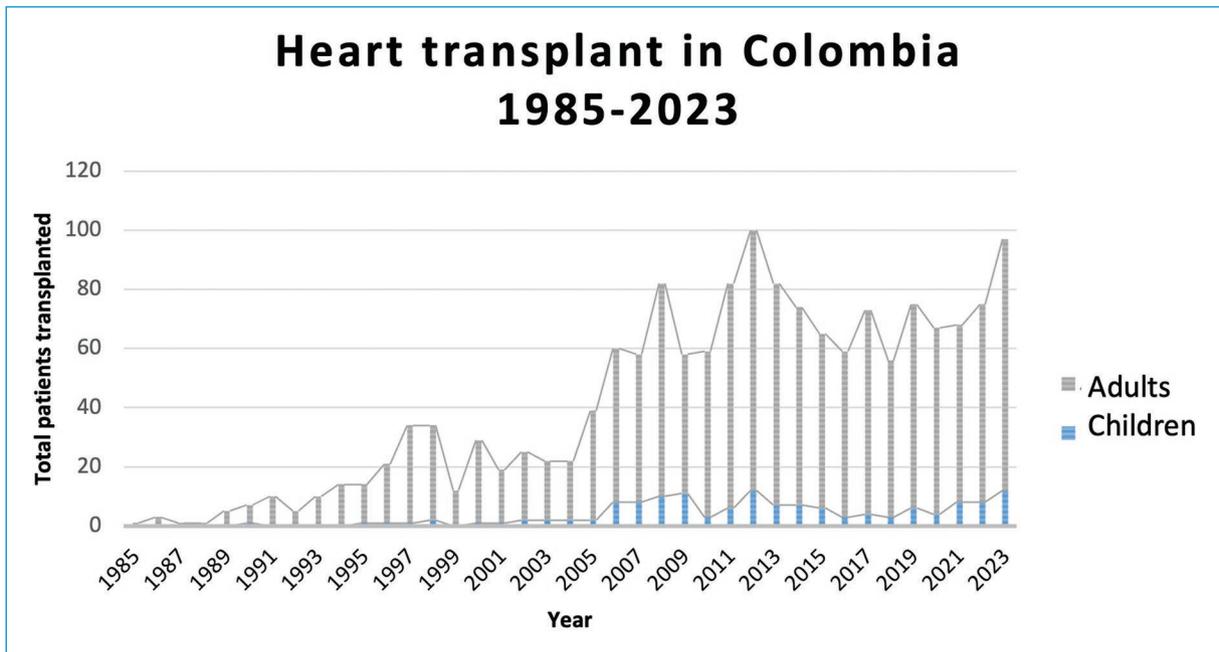
Figure 1. Frequency of heart transplantation by year (adult and pediatric).

transplant information in Colombia up to 2023. The efforts made by the transplant centers to ensure accessibility to this procedure, as well as training and progress in the learning curve, evidenced in the consistent performance of these procedures during 2022-2023[1,2].

Due to the obstacles posed by the SARS-CoV-2 pandemic, the population of transplanted patients dropped during the two years after the pandemic began (2020-2021). However, with global stabilization of this situation, the number of heart transplants performed worldwide has rebounded[3].

Males continue to represent the highest number of adult and pediatric patients transplanted in our study. In adults, this may be due to the higher prevalence of cardiovascular diseases in males than females. Risk factors like smoking, hypertension, and diabetes, which are more frequent in males, contribute to the severity of heart disease, which, in turn, increases the need for heart transplantation in this group of people[4,5].

In our country, transplant centers are concentrated in the main cities. The analysis of regional results since the first heart transplant in Colombia shows an increase in the number of transplanted patients, not only in the institutions that pioneered this procedure, but also in other regions in the country. This has led to optimization of the national coverage for this procedure.

However, it continues to be insufficient for the number of patients with advanced and refractory heart failure, whose prevalence is estimated to be 1% of the population, with an incidence of approximately 199 cases per 100,000 people per year[5].

Despite advances in the treatment of cardiovascular diseases, more diagnostic and therapeutic efforts are needed in rural areas, where the incidence of cardiovascular diseases is greater than in urban areas, which may be related to differences in access to healthcare services and the prevalence of risk factors. Strategies to improve healthcare infrastructure in rural areas and raise awareness of cardiovascular disease prevention are essential for reducing the incidence of heart failure and improving health outcomes in these regions[4].

No new Thoracic Organ Transplant (TTX) Registry reports on heart transplant activity have been published by the International Society of Heart and Lung Transplantation (ISHLT) since 2019. Due to privacy laws enacted in Europe in 2018 (the General Data Protection Regulation [GDPR]), this registry (TTX ISHLT) was halted to ensure compliance with these laws, and it is currently being relaunched[6]. Therefore, heart transplant activity in our country in 2023 cannot be compared to regional, continental or global information.
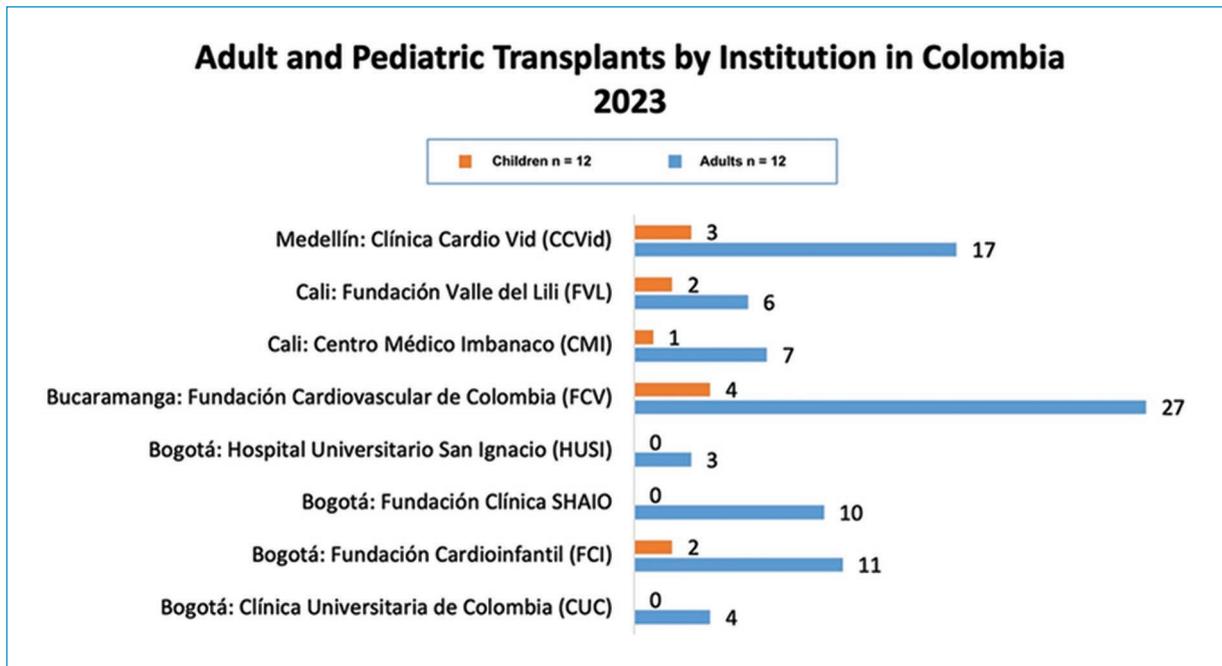
Figure 2. Heart transplants by transplant center in 2023.

Furthermore, at the moment, isolated institutions cannot participate in this international report (ISHLT) but rather must do so through national or multinational registries. Therefore, one of the goals of implementing the RECOLTRACA registry is to include Colombian data in this global database and provide a direct contribution from SCC and our country to the overall global statistics.

Over the last decade, the incidence of new heart transplants and retransplants has increased nationally. Transplant centers, together with the National Health Institute, have overcome the socioeconomic barriers of a low- and middle-income country, ensuring that patients who need these procedures receive them. Sustained effort and interinstitutional cooperation are decisive factors in carrying out these processes, and thus the establishment of a heart transplant registry will facilitate a better description of this population.

It is extremely important to show the heart transplant activity in each country, as this provides a comprehensive view of the advances and challenges in local health care. It also helps identify areas for improvement aimed at promoting policies that will benefit the patients. The documentation and analysis of this data not only improve clinical practice and resource planning but also strengthen national and international cooperation and knowledge exchange.

These findings underscore the need to continue strengthening national transplant registries and promoting policies that will facilitate data collection and analysis at a national and international level. This will not only contribute to improving clinical outcomes and resource management but will also allow better adaptation to the changing needs of transplanted patients.

One of this study's main strengths is the ongoing effort to collect and consolidate information on heart transplantation in Colombia, from its first years to date. This effort has allowed the creation of a robust database that documents the evolution and impact of heart transplantation in this country. Despite the advances achieved with these publications, we are currently facing some limitations. The data in this study is reported by each transplant center in the country, which makes it difficult to access and consolidate the information. For example, this registry did not have consolidated 2023 data available from all the institutions that perform heart transplants in Colombia. Despite these limitations, we continue to work on creating a national database (RECOLTRACA) which will provide more reliable and timely information to improve the quality and accuracy of future records.

The goal of this article is to present updated information on heart transplant activity in Colombia. The

Table 3. Heart transplantation up to 2022 and in 2023. Distribution by transplant region and sex

Category	1985-2022 n (%)	2023 n (%)
Adult		
Region 1, n (%)	340 (25)	28 (33)
Males, n (%)	260 (76)	22 (79)
Females, n (%)	80 (24)	6 (21)
Region 2, n (%)	574 (41)	17 (20)
Males, n (%)	495 (86)	15 (88)
Females, n (%)	79 (14)	2 (12)
Region 3, n (%)	311 (22)	13 (45)
Males, n (%)	243 (78)	9 (69)
Females, n (%)	68 (22)	4 (31)
Region 4, n (%)	166 (12)	27 (3)
Males, n (%)	135 (81)	15 (56)
Females, n (%)	31 (19)	12 (44)
Pediátricos		
Regional 1, n (%)	7 (7)	2 (17)
Hombres, n (%)	5 (56)	1 (50)
Mujeres, n (%)	4 (44)	1 (50)
Region 2, n (%)	55 (42)	4 (33)
Males, n (%)	33 (60)	1 (25)
Females, n (%)	22 (40)	3 (75)
Region 3, n (%)	11 (9)	3 (25)
Males, n (%)	7 (64)	3 (100)
Females, n (%)	4 (36)	0
Region 4, n (%)	55 (42)	3 (25)
Males, n (%)	33 (60)	1 (33)
Females, n (%)	22 (40)	2 (67)

Region 1: Cundinamarca, Tolima, Boyacá, Casanare, Meta, Caquetá, Vichada, Vaupés, Guaviare, Guainía, Putumayo, and Amazonas.
Region 2: Antioquia, Caldas, Córdoba, Chocó, and San Andrés y Providencia.
Region 3: Valle del Cauca, Risaralda, Quindío, Cauca, and Nariño.
Region 4: Santander, Norte de Santander, Cesar, and Arauca.

Figure 3. Central figure: most relevant information on heart transplantation in Colombia, 2023.

interinstitutional participation is based on the collaborative effort of the SCC's Heart Failure, Heart Transplant, and Pulmonary Hypertension Chapter, which allows transplant centers, the rest of the nation's institutions, and the medical community to be aware of heart transplant activity at the national level. It also encourages future initiatives to improve the availability of, and access to, information on this population, as well as future descriptions of this group.

Conclusions

Heart transplants have been performed in Colombia for almost four decades. The sustained effort of
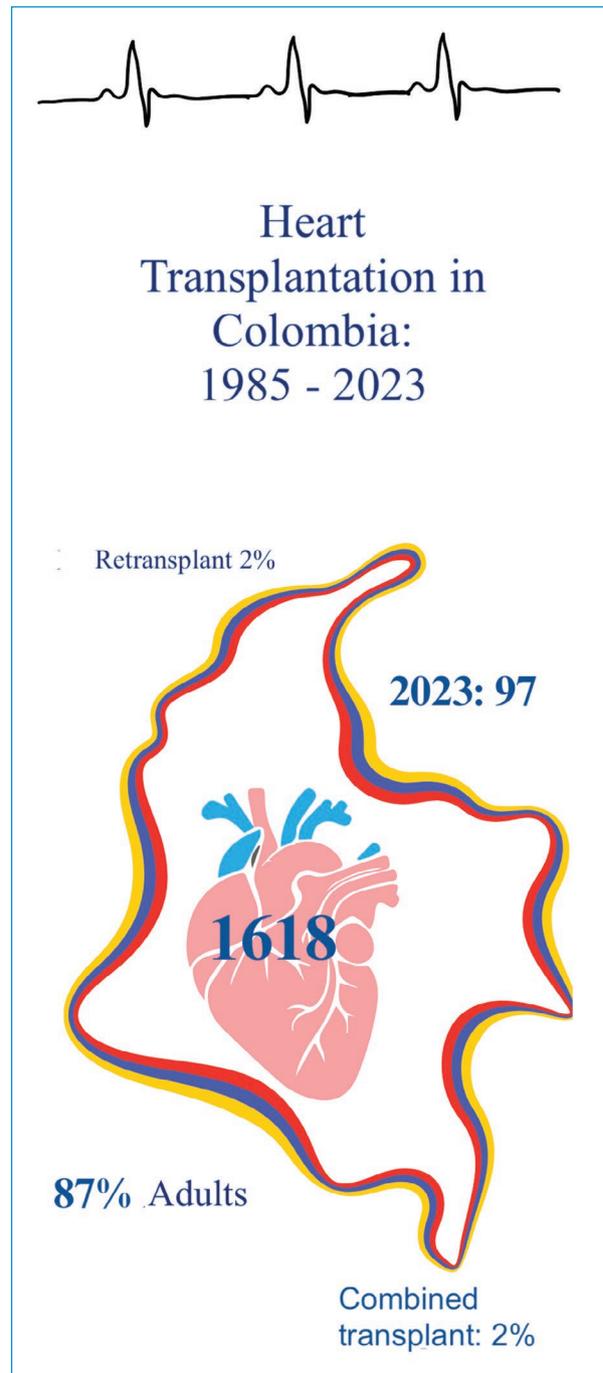
transplant centers and interinstitutional cooperation, together with governmental support, were decisive factors in making this treatment option available to a significant number of patients in 2023.

Transplant centers in Colombia continue to work to overcome the socioeconomic barriers of a low- to

middle-income country, ensuring that patients who need these high-cost procedures receive them.

Funding

The authors declare that they received no funding for this study.

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 in the course of this study.

Confidentiality, informed consent and ethical approval. This study did not involve personal patient data or require ethical approval. The SAGER guidelines did not apply.

Declaration on the use of artificial intelligence. The authors declare that they did not use any type of generative artificial intelligence in writing this article.

References

1. Gómez-Mesa JE, Uribe-Buriticá FL, Galindo-Coral S, Flórez NA, Olaya-Rojas P, Carrillo-Gómez DC, et al. Registro colombiano de trasplante cardíaco: año 1985-2021. Rev Colomb Cardiol. 2023;30(5):243-8.
2. Gómez-Mesa JE, Uribe-Buriticá FL, Galindo-Coral S, Flórez-Alarcón NA, Olaya-Rojas P, Carrillo-Gómez DC, et al. Cronología del trasplante cardíaco: más de tres décadas de historia (1985-2021). Rev Colomb Cardiol. 2023;30(4).180-8.
3. Mehra MR, Canter CE, Hannan MM, Semigran MJ, Uber PA, Baran DA, et al. The 2016 International Society for Heart Lung Transplantation listing criteria for heart transplantation: A 10-year update. J Heart Lung Transplant. 2016;35(1):1-23.
4. Teo K, Chow CK, Vaz M, Rangarajan S, Yusuf S; PURE Investigators-Writing Group. The Prospective Urban Rural Epidemiology (PURE) study: examining the impact of societal influences on chronic noncommunicable diseases in low-, middle-, and high-income countries. Am Heart J. 2009;158(1):1-7.
5. Tsao CW, Aday AW, Almarzooq ZI, Alonso A, Beaton AZ, Bittencourt MS, et al. Heart Disease and Stroke Statistics-2022 Update: A Report from the American Heart Association. Circulation. 2022;145(8), E153-E639.
6. Hsich E, Singh TP, Cherikh WS, Harhay MO, Hayes D, Perch M, et al. The International thoracic organ transplant registry of the international society for heart and lung transplantation: Thirty-ninth adult heart transplantation report—2022; focus on transplant for restrictive heart disease. J Heart Lung Transplant. 2022;41(10):366-75.

Check for updates

Mental health interventions in cardiac rehabilitation programs

Intervenciones en salud mental en los programas de rehabilitación cardiovascular

María C. Tamayo-Mejía*, Johny A. Rentería-Daboin, Jenny García-Valencia, Domingo I. Caraballo-Gracia, Antonio Toro, and Diego A. Espíndola-Fernández

Department of Psychiatry, Universidad de Antioquia, Medellín, Colombia

Abstract

Cardiovascular diseases are frequently associated with psychological symptoms that negatively affect clinical outcomes. Cardiac rehabilitation, traditionally focused on physical recovery, may benefit from incorporating psychosocial interventions that enhance mental health, adherence, and quality of life, leading to improved cardiovascular outcomes. This article synthesizes the available evidence on the effectiveness of mental health interventions within cardiac rehabilitation programs and their impact on clinical, psychological, and functional outcomes. A narrative review of the literature was conducted. Biomedical databases and academic repositories including PubMed, Scopus, EMBASE, Web of Science, Cochrane Library, ClinicalKey, SciELO, LILACS, and PsycINFO were searched for studies published between 2000 and 2024 in English or Spanish. Article selection, critical appraisal, and data extraction were independently performed by psychiatrists and cardiac rehabilitation specialists. The most effective interventions included cognitive behavioral therapy, mindfulness, relaxation techniques, and metacognitive therapy. These approaches were associated with reduced anxiety and depressive symptoms, improved quality of life, and a trend toward a lower incidence of nonfatal cardiovascular events and hospitalizations. Psychological interventions in cardiac rehabilitation, such as cognitive behavioral therapy, mindfulness, relaxation, and yoga, improve mental health and quality of life, with a potential reduction in cardiovascular events. Their structured integration into programs, especially in resource-limited settings, is essential to optimize clinical and psychosocial outcomes.

Keywords: Cardiac rehabilitation. Mental disorders. Psychotherapy. Cardiovascular diseases. Quality of life.

Resumen

Las enfermedades cardiovasculares se asocian con síntomas psicológicos que afectan negativamente el pronóstico clínico. La rehabilitación cardiovascular, tradicionalmente enfocada en la recuperación física, puede beneficiarse de intervenciones psicosociales que impactan la salud mental, la adherencia y la calidad de vida, mejorando así los desenlaces cardiovasculares. Este artículo sintetiza evidencia sobre la eficacia de intervenciones en salud mental, implementadas en programas de rehabilitación cardiovascular para desenlaces clínicos, psicológicos y funcionales. Se realizó una revisión narrativa de la literatura, para lo cual se consultaron bases de datos biomédicas y repositorios académicos como PubMed, Scopus, EMBASE, Web of Science, Cochrane Library, ClinicalKey, SciELO, LILACS y PsycINFO. Se incluyeron estudios publicados entre 2000 y 2024 en inglés o español. Médicos especialistas en psiquiatría y en rehabilitación cardiovascular realizaron la selección, evaluación crítica y extracción de la información de forma independiente. Las intervenciones más efectivas fueron la terapia

cognitivo-conductual, el mindfulness, las técnicas de relajación y la terapia metacognitiva. Estas se asociaron con menor sintomatología ansiosa y depresiva, mejor calidad de vida y tendencia a reducir eventos cardiovasculares no fatales y hospitalizaciones. Las intervenciones psicológicas en rehabilitación cardiovascular, como la terapia cognitivo-conductual, el mindfulness, la relajación y el yoga, mejoran la salud mental y la calidad de vida, y es posible que reduzcan los eventos cardiovasculares. Su integración estructurada en los programas, especialmente en entornos con recursos limitados, es clave para optimizar los desenlaces clínicos y psicosociales.

Palabras clave: Rehabilitación cardíaca. Trastornos mentales, Psicoterapia. Enfermedades cardiovasculares, Calidad de vida.

Introduction

Cardiovascular diseases (CVDs) are one of the main causes of morbidity and mortality worldwide and constitute a public health priority[1]. The current literature suggests that the clinical condition of patients with CVD involves not only physical factors, but also mental health aspects. Understanding this interaction is key, as there is a complex two-way relationship between both dimensions, and its recognition in patient care could affect clinical outcomes.

Studies of patients with CVD have shown that up to one third have psychiatric symptoms or disorders, with anxiety and depression being the most common[2]. These conditions not only reduce the quality of life but are also associated with a higher risk of future cardiovascular events, higher healthcare costs and worse long-term psychological adaptation[3]. Further, anxiety and depressive disorders have been identified as independent risk factors for cardiovascular morbidity and mortality[3].

From another perspective, an examination of the cardiovascular health of people with serious mental illnesses like schizophrenia, bipolar disorder and major depressive disorder reveals an equally concerning situation. Life expectancy in this group of patients is 15-25 years lower than in the general population, with CVD being the main cause of this excess premature death[4]. Although CVD is the main cause of death both for people with serious mental illness and the general population, the rate of cardiovascular mortality in those with serious mental illness more than doubles that of the general population[4].

This higher impact of CVD in people with serious mental illness is supported by a large amount of prospective epidemiological data showing that people with these disorders have a higher risk of developing coronary disease (CD) than those without (hazard ratio [HR] = 1.54; 95% CI: 1.30-1.82)[5]. Likewise, anxiety symptoms or disorders and persistent stress may be independently associated with a higher risk of CVD, with a relative risk (RR) of 1.41 (95% CI: 1.23-1.61) and an HR of 1.27 (95% CI: 1.08-1.49), respectively[5].

Within this context, comprehensive cardiac rehabilitation (CR) emerges as a useful evidence-based multidisciplinary intervention for improving CVD patients' health outcomes and quality of life. It includes physical training, risk factor modification and psychosocial assessment[6]. Its main goal is to help patients achieve the best possible health using a care model in both clinical and nonclinical settings designed to optimize secondary prevention[6]. Cardiac rehabilitation has internationally agreed upon core components: initial patient assessment, risk factor management (diet, smoking, blood pressure, dyslipidemia and hyperglycemia/diabetes mellitus), structured exercise training, education and psychosocial counseling[6].

Despite the recommendation to include mental health interventions in CR programs, few programs have mental health staff[1]. Cardiac rehabilitation is only available in 40% of low and middle-income countries. Most of these programs are led by cardiologists, nurses and physical therapists[1]. Only 25% implement tests for detecting depression, and 45% include smoking treatment interventions, which are much more common in high-income countries[1]. Thus, using a narrative literature review, this article proposes to synthesize the evidence on the use and efficacy of mental health interventions in cardiovascular rehabilitation centers, emphasizing their role in improving cardiovascular, mental and quality of life outcomes.

Methods

A narrative review of the scientific literature was conducted to synthesize the evidence on psychosocial interventions in cardiac rehabilitation programs. The main biomedical databases and academic repositories, including PubMed, Scopus, EMBASE, Web of Science, Cochrane Library, ClinicalKey, SciELO, LILACS, and PsycINFO, were searched, with articles in English and Spanish dealing with psychological or mental health

interventions in patients with cardiovascular disease published between 2000 and 2024 included.

Studies were selected in two phases: first, the titles and abstracts were reviewed to filter relevant articles; then, the full text of the selected articles was read. This process was independently performed by psychiatrists and cardiac rehabilitation specialists, who evaluated the pertinence, currency and methodological quality of each study. The information was organized by topics, following mental and cardiovascular health clinical and impact criteria, according to the methodological guidelines for narrative reviews.

Explanatory models of the relationship between mental illness and cardiovascular health

The relationship between serious mental illness and CVD appears to be bidirectional. Acute cardiovascular events and chronic CVD can trigger mental illnesses or be caused by them, and emerging evidence suggests that they share common pathophysiological mechanisms, including biological, genetic, behavioral and neurohormonal factors[4].

The factors that could explain this relationship include autonomic nervous system dysfunction; these patients have differences in heart rate variability, hypertension and increased QT interval variability, which predisposes them to arrhythmias and cardiovascular events[7].

Furthermore, hypothalamic-pituitary-adrenal (HPA) axis hyperactivity has been described, in which elevated cortisol levels in patients with mental illness contribute to chronic inflammation and insulin resistance, which are key in the development of CVD. Another mechanism that explains the systemic inflammation and platelet activation is the elevation of proinflammatory cytokine levels (for example, IL-6 and TNF alpha) that has been found in patients with mental illness and is related to atherosclerosis and endothelial dysfunction[8].

As far as the contributing genetic mechanisms, previous studies have identified at least 24 genes with possible pleiotropy between mood disorders and cardiometabolic diseases: *MTHFR, CACNA1D, CACNB2, GNAS, ADRB1, NCAN, REST, FTO, POMC, BDNF, CREB, ITIH4, LEP, GSK3B, SLC18A1, TLR4, PPP1R1B, APOE, CRY2, HTR1A, ADRA2A, TCF7L2, MTNR1B* and *IGF1*[9]. An analysis of the side effects of specific pharmacological treatments has also shown an association. For example, the use of some psychiatric medications, like antipsychotics and mood stabilizers, is associated with a higher risk of cardiometabolic disorders, while the medications used to treat cardiac and metabolic diseases could increase the risk of mood disorders[9].

Furthermore, there are psychological factors and personality characteristics. Neuroticism has been associated with a higher risk of myocardial infarction, and extraversion with a higher risk of cerebrovascular accidents[10]. As far as socioeconomic factors, these patients have been found to experience more difficulties in accessing timely medical care[11]. The factors that limit this access include insufficient specialized staff, lack of adequate infrastructure, little training of primary care staff in caring for these patients, and the stigma of this population[11].

The neurocardiac axis has recently been proposed as another important mechanism, representing a core component of the pathophysiological interaction between mental and cardiovascular illness. It is made up of neural circuits that connect the central nervous system (amygdala, hypothalamus, ventrolateral medulla and autonomic nervous system) to the cardiovascular system (heart, blood vessels) and immune system organs (spleen, lymphoid tissue and lymph nodes). Under pathological conditions, both cardiovascular risk and neuropsychiatric vulnerability may be amplified[12]. Sympathetic nervous system hyperactivity, commonly present in chronic stress and mental disorders, can favor atherosclerotic progression through inflammatory pathway activation, hemodynamic disorders and vascular remodeling. In the brain, an association has been found between hyperactivity of the amygdala and arterial inflammation, which suggests a direct link between emotional processing and cardiovascular risk. These findings not only reinforce the two-way nature of the relationship between mental health and CVD but also propose the neurocardiac axis as a promising target for integrated therapeutic interventions[12] (Fig. 1).

The role of cardiac rehabilitation

Cardiac rehabilitation is a comprehensive therapeutic approach aimed at improving the recovery and quality of life of patients with CVD[13]. The American Heart Association and American College of Cardiology recommend CR for patients with stable angina, stable heart failure with reduced ejection fraction, acute coronary syndrome, percutaneous coronary intervention (PCI), coronary artery bypass graft (CABG), and valvular surgery[13]. Patients are referred to the rehabilitation program after an event or diagnosis and, ideally,
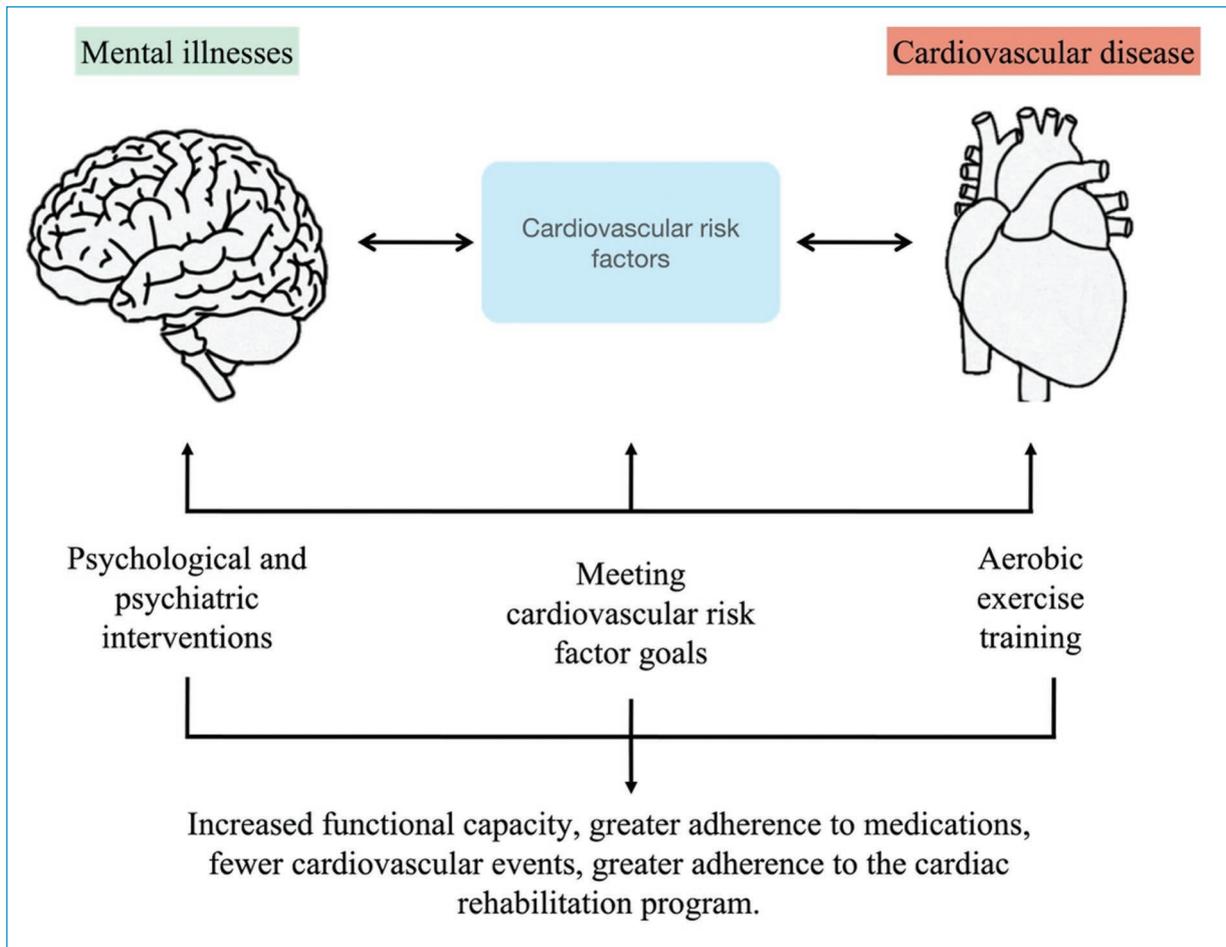
Figure 1. The relationship and possible mental and cardiovascular health effects in cardiac rehabiliation

should begin the program within the next one to two weeks to improve participation and outcomes[14]. Despite the fact that the international guidelines support its use, some studies have reported that only 20% of eligible patients participate in CR[6], which indicates the need for greater dissemination of and accessibility to these programs.

Cardiac rehabilitation has internationally agreed upon core components: initial patient assessment, risk factor management (diet, smoking, hypertension, dyslipidemia and hyperglycemia/diabetes mellitus), structured exercise training, education and psychosocial counseling[6]. Ideally, current and previous cardiovascular diagnoses and medical and surgical procedures should be reviewed during the assessment for program admission, along with symptoms, medications and comorbidities like musculoskeletal, neuromuscular and psychiatric disorders. A complete

physical exam should be performed and paraclinical tests ordered to assess cardiovascular risk. It is also essential for care to be standardized to ensure that all patients receive quality care based on the best available evidence[14].

It is important to highlight that if the patient smokes, a brief motivational message should be provided, along with strategies, education and personalized counseling. Likewise, it is important to identify problematic psychological factors, such as clinically significant depression and anxiety, as these can affect adherence to treatment and patient recovery[14]. To comprehensively address these aspects, mental health specialists must be part of the multidisciplinary CR team, contributing with specialized assessments and appropriate therapeutic strategies to improve the patients' emotional wellbeing and quality of life[3].

Mental health interventions in cardiac rehabilitation

Current scientific evidence suggests that psychological interventions within CR programs can improve both psychological and functional aspects of patients with CVD[15].

A systematic review and meta-analysis published in 2024 evaluated the effectiveness of CR enhanced with psychological interventions in the functional and psychological outcomes of patients with cardiovascular disease[16]. Its findings suggest that integrating psychological strategies into CR provides highly clinically relevant benefits like helping maintain a lower resting blood pressure and improving patients' quality of life, as well as contributing to restored exercise tolerance[17].

Among these reports, the most effective interventions appear to be those in which patients actively participate, like breathing exercise-based relaxation, which has proven to reduce anxiety, improve wellbeing and reduce the resting heart rate[15]. More passive methods, like music therapy or Schultz´s autogenic training, have shown limited results and lower adherence[16].

The literature reports various psychological interventions with promising results. For example, Nagarathna Raghuram et al.[18] conducted a prospective controlled study in India comparing a yoga program to light exercise in postoperative coronary bypass patients. This intervention was structured in three progressive modules distributed over one year. During the first six weeks, the patients engaged in relaxation techniques while lying on their backs (sound meditation and deep guided relaxation), from the sixth week to the six month, gentle physical positions, respiratory exercises, and joint movements were added, and from the sixth to the twelfth month, the intensity of the physical exercises was increased through different positions and dynamic respiration, and relaxation and meditation techniques were reinforced. The results showed that the group that practiced yoga had significant improvements in left ventricular ejection fraction, as well as a notable reduction in stress and anxiety, which suggests a positive impact both physically and psychologically[18]. Other interesting interventions include cognitive behavioral therapy (CBT), which has proven effective in modifying dysfunctional thinking associated with cardiovascular disease. A study performed in Denmark included different cardiology departments in several hospitals. The patients who participated in the study were adults who had been recently diagnosed with coronary disease or heart valve disease, and who also had psychological distress, defined as a score ≥ 8 on the Hospital Anxiety and Depression Scale (HADS). A brief group CBT intervention was carried out in this population, complementary to the usual CR, with five weekly two-hour sessions in groups of three to four people. The intervention was administered by cardiovascular nurses trained in CBT and supervised by a psychologist, according to a standardized manual. The session contents were as follows: introduction to CBT and personal value mapping, anxiety and reduction techniques, behavioral analysis, worries and strategies for dealing with them, and facing the future. The main results showed a significant reduction in the total HADS score in the CBT group (–8.0 points vs. –4.1 in the control group; p < 0.001) after three months; improved heart health-related quality of life (HeartQoL) at six months, especially in the emotional domain; and greater adherence to the CR program in the CBT group and a lower rate of hospital readmission for cardiac reasons at 12 months (25 vs. 49%; HR = 0.43)[19].

Mindfulness-based stress reduction (MBSR) has also been studied, which promotes greater emotional regulation and stress reduction. A study at the University of Minnesota in the United States enrolled 48 patients with recent cardiac events who were eligible for CR[20]. This technique was administered over eight weeks, with two-and-a-half-hour weekly group sessions, plus an intensive six-and-a-half-hour retreat. Formal mindfulness meditation practices were administered throughout the process, along with conscious breathing exercises, light yoga and group discussions on stress management, body awareness and emotions. The results showed a significant reduction in PHQ-9 and GAD 7 in the intervention group. The cardiovascular effects showed a trend toward improvement in several risk factors, although most were not statistically significant (at three months, systolic blood pressure reduced an average of 2.02 mmHg in the MBSR group, while it increased 1.89 mmHg in the control group, with an adjusted difference of –3.84 mmHg [95% CI: –9.57 to 1.90; p = 0.18]). Other parameters, like total cholesterol, LDL, triglycerides, HbA1c and high-sensitivity C-reactive protein (hsCRP), showed slight improvements or less deterioration in the MBSR group, although without statistical significance. At nine months, the difference in systolic pressure between the groups was –1.35 mmHg (95% CI: –9.82 to 7.12), maintaining the trend. In the subgroup with depressive symptoms (PHQ-9 ≥ 5), the improvements were more pronounced, and some achieved significance: total cholesterol reduced –26.60 mg/dl more in the MBSR group compared to

the control (95% CI: –50.74 to –2.46; p = 0.033), while the LDL reduction was –21.95 mg/dl (95% CI: –46.79 to 2.89; p = 0.079) and hsCRP decreased –5.17 mg/L (95% CI: –11.31 to 0.97; p = 0.093). This indicates that MBSR could have a positive effect on cardiovascular risk factors, especially in patients with depressive symptoms[20].

A systematic review and meta-analysis by Albus et al.[21] evaluated the additional effect of specific psychological interventions integrated into exercise-based cardiac rehabilitation (ebCR) in patients with cardiovascular disease. The analysis included 20 studies with a total of 4,450 patients, most with stable coronary disease or acute coronary syndrome and, to a lesser extent, congestive heart failure. All participants carried out CR programs, and a comparison was made between those who also received structured psychosocial interventions and those who only participated in ebCR. The psychosocial interventions were classified into three types: the first was psychological support for lifestyle changes, aimed at fostering healthy habits through motivational education, goal setting and behavioral counseling; the second was management of emotional distress, which included cognitive behavioral therapy, relaxation techniques, psychoeducation and strategies for dealing with anxiety, depression and stress; and the third consisted of a combination of both modalities. The results showed a slight reduction in depressive symptoms (measured with HAD-D, BDI-II, and CES-D, with a standardized mean difference [SMD]: –0.13; 95% CI: –0.30 to 0.05) and a trend toward reduced long-term cardiovascular morbidity (non-fatal clinical events like infarction, revascularization, and hospitalization for cardiac reasons) and hospitalization for cardiovascular events, with a relative risk (RR) of 0.74 (95% CI: 0.51 to 1.07) in the groups with psychological intervention, although these differences did not reach statistical significance. No additional effects on anxiety, quality of life or mortality were found. Despite methodological limitations and heterogeneity between the studies, the findings suggest that psychosocial interventions can provide complementary benefits in the cardiovascular rehabilitation setting[21].

More novel approaches include metacognitive therapy, which is a structured intervention aimed at regulating repetitive negative thinking, like worrying and rumination, rather than the thought content. This therapy seeks to change maladaptive metacognitive beliefs, promoting flexible attention control. This intervention involved six weekly 60-90-minute sessions on the following topics: identifying trigger thoughts, regulating rumination and worry, attention control techniques, and practice sessions (homework), with individual prescriptions for useful behaviors at the end. The addition of group metacognitive therapy (MCT) to CR showed a significant reduction in anxiety and depressive symptoms compared to standard rehabilitation. After four months, the patients in the group with MCT plus CR had a mean reduction of 3.24 points on the total HADS scale, with sustained improvement at 12 months. Reductions were also seen in post-traumatic stress symptoms, repetitive negative thoughts and maladaptive metacognitive beliefs, although there were no significant changes in quality of life. These results suggest that MCT is an effective intervention for improving mental health in patients with heart disease. The additional psychological interventions to change lifestyles or manage stress showed a tendency to reduce depressive symptoms (standardized mean difference –0.13; 95% CI: –0.30 to 0.05). Furthermore, during five years of follow up, stress management was associated with a tendency to reduce cardiac morbidity (HR: 0.74; 95% CI: 0.51 to 1.07)[21].

When considering mental health interventions in CR programs, two key scenarios must be differentiated. On the one hand, there are patients with an established mental health diagnosis, such as depressive or anxiety disorder, who need interventions specifically aimed at their psychiatric condition, along with cardiovascular treatment. On the other hand, there are patients who do not meet the criteria for a formal mental illness diagnosis, but have psychological symptoms associated with their cardiovascular illness, like stress, anxiety or reactive depressive symptoms. This makes it essential for CR care protocols to include specific interventions aimed at a comprehensive mental health assessment for the patients enrolled.

In the first case, comprehensive management of an established mental disorder in patients with CVD has a positive impact on their clinical outcomes. A population-based prospective cohort study was published in 2024, in which 1,563 patients with CVD and anxiety or depression comorbidity were enrolled to compare the cardiovascular outcomes of those who received mental health treatment (either psychotherapy or psychiatric medications) and those who did not[22]. The results showed that the treated patients had a 75% lower risk of readmission, 74% fewer emergency room visits and 66% lower all-cause mortality rates than the untreated group[22]. Furthermore, even approaches focused exclusively on psychological interventions have shown significant benefits. A meta-analysis[23] published in 2024 that

included 32 studies with a total of 15,814 patients evaluated the impact of psychological interventions on patients with CVD. The results showed that these interventions were able to reduce cardiac mortality (RR = 0.81; 95% CI = 0.68-0.96), the incidence of myocardial infarction (RR = 0.79; 95% CI = 0.69-0.89), arrhythmias (RR = 0.61; 95% CI = 0.42-0.89) and angina (RR = 0.92; 95% CI = 0.87-0.97)[23]. A second case represents patients who do not meet the criteria for a formal mental illness diagnosis but have psychological symptoms associated with their CVD, like stress, anxiety or reactive depressive symptoms. A multicenter, prospective randomized clinical trial[19] was conducted in three hospitals in Denmark, with three, six and twelve-month follow up, enrolling 147 patients with CVD and symptoms of anxiety or depression evaluated using the HAD scale. These patients were randomized to two groups; the intervention group received standard CR plus five sessions of group CBT. After three and six months there was a significantly greater reduction in the total HADS score (combined anxiety and depression) in the intervention group (–8.0 points [SD: 5.6 vs. –4.1 points [SD: 7.8) in the control group [p < 0.001]), a significant improvement in quality of life and a lower rate of cardiovascular readmissions[19]. The current evidence increasingly supports the integration of psychological interventions into CR programs because they also have an impact on patients with symptoms of anxiety and depression due to their cardiovascular disease.

The current situation in Colombia

In Colombia, CR programs mostly consist of cardiologists (85%), physical therapists (72%) and nutritionists (72%)[24]. These programs are structured in four phases that go from the inpatient period (Phase I) to long-term maintenance (Phase IV), with Phase II (ambulatory and supervised) being the most common, existing in 92% of the centers. Specific interventions include supervised physical training, nutritional education, cardiovascular risk factor management, clinical and functional assessments and, to a lesser extent, psychological interventions and smoking cessation programs[24].

A wide variety of services are offered, and program content is not standardized. Few programs include mental health interventions. Acording to the study by Cortés-Bergoderi et al.[24], only 68% of the programs offer psychological counseling, and less than 30% screen for depression, despite the fact that this condition is common among patients with cardiovascular disease and is associated with lower adherence to

treatment and worse clinical outcomes. This heterogeneity reflects not only differences in the available resources, but also the lack of national guidelines to unify criteria and minimum standards of care[24].

The strategies used in these programs include relaxation techniques, group therapy, family support programs and recreational activities like yoga, therapeutic dance and tai chi, which seek to improve emotional wellbeing and reduce stress. However, the inclusion of mental health professionals like psychiatrists and psychologists is still limited, with a frequency of 12 and 53%, respectively. In addition, coverage of these interventions varies widely from one center to another[24]. This lack of standardization reflects both the scarcity of specialized human resources as well as the lack of official guidelines to prioritize mental health as a pivotal element of CR. Therefore, strengthening these components is crucial for offering truly comprehensive care to respond to the patients´ biopsychosocial needs.

A quasi-experimental pre-post study with no control group was carried out in CR programs in five countries (Brazil, Canada, Colombia, United States and Venezuela)[25]. In Colombia, the CR program lasted six months, with one-hour sessions two to three times per week, and included structured psychosocial interventions. Weekly educational sessions were offered for both patients and their families, addressing stress management, relaxation techniques and family support strengthening. All participants also filled out a PHQ-9 questionnaire at the beginning of the program; those with high scores were referred to external mental health professionals, and those with moderate symptoms received care from a program nurse. As a result, there was a significant reduction in depressive symptoms, with a mean reduction of 2.33 points on the PHQ-9 (p < 0.001), while the average score of patients with initially high depressive symptoms dropped from 13.90 to 4.67 (p < 0.001), indicating a clinically relevant improvement in the participants´ mental health[25]. A previous study in a CR program in Bogotá, Colombia[26], evaluated quality of life and mental health in program participants before and after rehabilitation. In addition to the supervised exercise component, the interventions included psychoeducation in the emotional response to disease (fear, anxiety and worry). Disease-related beliefs were also evaluated, providing strategies for managing emotions, identifying and strengthening protective psychological factors that contribute to wellbeing and resilience, and identifying and mitigating psychological risk factors. The SF-12 and PHQ-9 questionnaires were measured at the beginning

of the study. Altogether, 44.25% of the patients had some degree of depressive symptoms according to the PHQ-9: mild (31.03%), moderate (8.05%), moderately severe (2.87%) and severe (2.3%). At the end of the program, 44.3% of the patients (n = 77) showed a change in their PHQ-9 scores, mostly positive, as 72.7% (n = 56) improved their depressive symptoms. The specific analysis of the subgroup of patients with coronary disease (n = 147) also indicated a statistically significant improvement in depressive symptoms after rehabilitation. Although the study did not include a structured formal mental health intervention, the results suggest that the CR environment can have an indirect positive effect on emotional wellbeing, probably due to the combination of factors like regular exercise, ongoing clinical support and an educational component[26].

Conclusions

The available evidence shows that psychological interventions incorporated into cardiac rehabilitation programs – including cognitive behavioral therapy, mindfulness, relaxation techniques, yoga and metacognitive therapy – are associated with a significant reduction in symptoms of anxiety and depression, improved quality of life and, in some studies, a lower risk of cardiovascular events and hospitalizations. These benefits are found both in patients with established mental disorders as well as those with reactive psychological symptoms due to their cardiovascular disease. However, there are still significant gaps in standardization, coverage and availability of these components, especially in countries like Colombia, where the inclusion of mental health professionals in rehabilitation programs continues to be limited.

Thus, strengthening the integration of mental health into cardiovascular rehabilitation through structured protocols and trained staff is an opportunity to comprehensively optimize patients' clinical, psychological and functional outcomes.

Acknowledgments

Funding

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 in the course of this study.

Confidentiality, informed consent and ethical approval. The study did not involve patients´ personal information nor did it require ethical approval. The SAGER guidelines did not apply.

Declaration on the use of artificial intelligence. The authors declare that they did not use any type of generative artificial intelligence in writing this article.

References

1. Hughes JW, Serber ER, Kuhn T. Psychosocial management in cardiac rehabilitation: Current practices, recommendations, and opportunities. Prog Cardiovasc Dis. 2022;73:76-83.
2. Wells A, Reeves D, Capobianco L, Heal C, Davies L, Heagerty A, et al. Improving the effectiveness of psychological interventions for depression and anxiety in cardiac rehabilitation: PATHWAY—A single-blind, parallel, randomized, controlled trial of group metacognitive therapy. Circulation. 2021;144(1):23-33.
3. Richards SH, Anderson L, Jenkinson CE, Whalley B, Rees K, Davies P, et al. Psychological interventions for coronary heart disease: Cochrane systematic review and meta-analysis. Eur J Prev Cardiol. 2018;25(3):247-59.
4. Goldfarb M, De Hert M, Detraux J, Di Palo K, Munir H, Music S, et al. Severe mental illness and cardiovascular disease. J Am Coll Cardiol. 2022;80(9):918-33.
5. De Hert M, Detraux J, Vancampfort D. The intriguing relationship between coronary heart disease and mental disorders. Dialogues Clin Neurosci. 2018;20(1):31-40.
6. Ritchey MD, Maresh S, McNeely J, Shaffer T, Jackson SL, Keteyian SJ, et al. Tracking cardiac rehabilitation participation and completion among Medicare beneficiaries to inform the efforts of a national initiative. Circ Cardiovasc Qual Outcomes. 2020;13(1):e005902.
7. Mørch RH, Dieset I, Færden A, Reponen EJ, Hope S, Hoseth EZ, et al. Inflammatory markers are altered in severe mental disorders independent of comorbid cardiometabolic disease risk factors. Psychol Med. 2019;49(10):1749-57.
8. Williams JA, Burgess S, Suckling J, Lalousis PA, Batool F, Griffiths SL, et al. Inflammation and brain structure in schizophrenia and other neuropsychiatric disorders: a mendelian randomization study. JAMA Psychiatry. 2022;79(5):498.
9. Amare AT, Schubert KO, Klingler-Hoffmann M, Cohen-Woods S, Baune BT. The genetic overlap between mood disorders and cardiometabolic diseases: a systematic review of genome wide and candidate gene studies. Transl Psychiatry. 2017;7(1):e1007-e1007.
10. Karlsen HR, Langvik E. Sex-specific psychological risk profiles of CVD in the HUNT study: the role of neuroticism and extraversion. Psychol Health. 2024;39(10):1352-70.

11. Coombs NC, Meriwether WE, Caringi J, Newcomer SR. Barriers to healthcare access among U.S. adults with mental health challenges: A population-based study. SSM - Popul Health. 2021;15:100847.

12. Plott C, Harb T, Arvanitis M, Gerstenblith G, Blumenthal R, Leucker T. Neurocardiac axis physiology and clinical applications. IJC Heart Vasc. 2024;54:101488.

13. Thomas RJ. Cardiac rehabilitation — challenges, advances, and the road ahead. Leopold JA (ed.). N Engl J Med. 2024;390(9):830-41.

14. Balady GJ, Williams MA, Ades PA, Bittner V, Comoss P, Foody JM, et al. Core components of cardiac rehabilitation/secondary prevention programs: 2007 update: a scientific statement from the American Heart Association Exercise, Cardiac Rehabilitation, and Prevention Committee, the Council on Clinical Cardiology; the Councils on Cardiovascular Nursing, Epidemiology and Prevention, and Nutrition, Physical Activity, and Metabolism; and the American Association of Cardiovascular and Pulmonary Rehabilitation. Circulation. 2007;115(20):2675-82.

15. Brown TM, Pack QR, Aberegg E, Brewer LC, Ford YR, Forman DE, et al. Core components of cardiac rehabilitation programs: 2024 update: a scientific statement from the American Heart Association and the American Association of Cardiovascular and Pulmonary Rehabilitation. Circulation [Internet]. 2024 [citado 23 May 2025];150(18). https://www.ahajournals.org/doi/10.1161/CIR.0000000000001289.

16. Wrzeciono A, Mazurek J, Cieślik B, Kiper P, Gajda R, Szczepańska-Gieracha J. Psychologically-enhanced cardiac rehabilitation for psychological and functional improvement in patients with cardiovascular disease: a systematic review with meta-analysis and future research directions. Physiotherapy. 2024;125:101412.

17. Wrzeciono A, Mazurek J, Cieślik B, Kiper P, Gajda R, Szczepańska-Gieracha J. Psychologically-enhanced cardiac rehabilitation for psychological and functional improvement in patients with cardiovascular disease: a systematic review with meta-analysis and future research directions. Physiotherapy. 2024;125:101412.

18. Raghuram N, Parachuri VR, Swarnagowri MV, Babu S, Chaku R, Kulkarni R, et al. Yoga based cardiac rehabilitation after coronary artery bypass surgery: One-year results on LVEF, lipid profile and psychological states – A randomized controlled study. Indian Heart J. 2014;66(5):490-502.

19. Holdgaard A, Eckhardt-Hansen C, Lassen CF, Kjesbu IE, Dall CH, Michaelsen KL, et al. Cognitive-behavioural therapy reduces psychological distress in younger patients with cardiac disease: a randomized trial. Eur Heart J. 2023;44(11):986-96.

20. Nijjar PS, Connett JE, Lindquist R, Brown R, Burt M, Pergolski A, et al. Randomized trial of mindfulness-based stress reduction in cardiac patients eligible for cardiac rehabilitation. Sci Rep [Internet]. 2019 [citado 23 May 2025]; 9(1). https://www.nature.com/articles/s41598-019-54932-2.

21. Albus C, Herrmann-Lingen C, Jensen K, Hackbusch M, Münch N, Kuncewicz C, et al. Additional effects of psychological interventions on subjective and objective outcomes compared with exercise-based cardiac rehabilitation alone in patients with cardiovascular disease: A systematic review and meta-analysis. Eur J Prev Cardiol. 2019;26(10):1035-49.

22. Carmin CN, Ownby RL, Fontanella C, Steelesmith D, Binkley PF. Impact of mental health treatment on outcomes in patients with heart failure and ischemic heart disease. J Am Heart Assoc [Internet]. 2024 [citado 23 May 2025]; 13(7). https://www.ahajournals.org/doi/10.1161/JAHA.123.031117.

23. Nie Y, Wang N, Chi M, Li A, Ji S, Zhu Z, et al. Effects of psychological interventions on clinical outcomes in patients with cardiovascular diseases: A systematic review and meta-analysis. J Psychosom Res. 2024;187:111938.

24. Cortes-Bergoderi M, Lopez-Jimenez F, Herdy AH, Zeballos C, Anchique C, Santibañez C, et al. Availability and characteristics of cardiovascular rehabilitation programs in South America. J Cardiopulm Rehabil Prev. 2013;33(1):33-41.

25. Ghisi GLDM, Santos CVA, Benaim B, Lopez-Jimenez F, Herdy AH, Inojosa JM, et al. Severity of depressive symptoms pre- and postcardiac rehabilitation: a comparison among patients in Brazil, Canada, Colombia, The United States, and Venezuela. J Cardiopulm Rehabil Prev. 2017;37(3):182-90.

26. Rodríguez MJV. Calidad de vida y salud mental en pacientes pre y post rehabilitación cardiovascular en un programa de Bogotá – Colombia.

Check for updates

CASE PRESENTATION

Intraoperative aortic dissection

Disección aórtica intraoperatoria

Yefferson D. Salinas-Herrera[1], Julián. M. Parada-Duarte[1], Jorge A. Marthey-Tello[1],
and Silvia P. Torres-Durán[2]*

[1]Cardiovascular Surgery Service, Hospital Universitario Los Comuneros; [2]Radiology Service, Universidad de Santander (UDES). Bucaramanga,
Colombia

Abstract

Acute aortic dissection is a highly lethal cardiovascular emergency, characterized by the progressive separation of the aortic layers due to a column of blood. Associated cardiac complications, including cardiac tamponade, compression of the coronary ostium by the false lumen, and acute aortic insufficiency, evolve rapidly and can be fatal. Surgical mortality in iatrogenic type A aortic dissection – especially secondary to heart surgery – is estimated to be higher than in non-iatrogenic cases. With this context, we present the case of a 71-year-old patient with severe three-vessel coronary disease who underwent myocardial revascularization surgery, and during cardiopulmonary bypass, a type A aortic dissection was identified and successfully managed.

Keywords: Heart surgery. Acute aortic dissection. Complications. Coronary heart disease.

Resumen

La disección aórtica aguda (DA) es una emergencia cardiovascular letal, que se caracteriza por la separación progresiva de las capas de la aorta debido a la formación de una columna de sangre. Las complicaciones cardíacas asociadas son de rápida evolución y pueden ser fatales; incluyen el taponamiento cardiaco, la compresión del ostium coronario por la falsa luz y la insuficiencia aórtica aguda. Se estima que la mortalidad intrahospitalaria asociada a la disección aórtica de tipo A iatrogénica –particularmente la secundaria a cirugía cardíaca– tiende a ser superior a la observada en los casos de etiología no iatrogénica. En este contexto, se presenta el caso de un paciente de 71 años, con enfermedad coronaria grave de tres vasos, quien fue sometido a cirugía de revascularización miocárdica y en quien, durante la circulación extracorpórea, se identificó una disección aórtica tipo A, la cual fue tratada de manera satisfactoria.

Palabras clave: Cirugía cardíaca. Disección aórtica aguda. Complicaciones. Enfermedad coronaria.

Surgical myocardial revascularization is a common procedure for treating severe coronary disease, in which blood flow is restored to the ischemic myocardium. This procedure entails risks, the most serious being iatrogenic aortic dissection[1], which is a serious heart surgery complication with an incidence ranging from 0.12-0.16%[2]. It consists of an internal aortic layer tear caused by different factors. For example, excessive manipulation of the aorta during the procedure can damage the artery's internal layer and cause a hematoma and/or tearing. Elevated blood pressure during surgery can also increase the risk of aortic dissection[3,4]. It is sometimes difficult to determine the cause of the dissection, as it is an iatrogenic event[5].

Clinical case

This was a 71-year-old patient with a history of hypertension who was admitted with typical chest pain. An electrocardiogram indicated left ventricular hypertrophy and poor R wave progression in the precordial leads, with no ST segment abnormalities or dynamic changes. The chest x-ray showed a typical cardiopulmonary silhouette for the patient's age, and troponins were negative. The patient was therefore considered to have high-risk unstable angina.

Coronary arteriography documented atherosclerotic coronary disease with severe compromise of the left main trunk, anterior descending, first diagonal, ramus intermedius, and circumflex arteries. A transthoracic echocardiogram showed hypokinesia of the basal segment of the inferior septum and inferior wall, and a left ventricular ejection fraction (LVEF) of 58%, with no significant valve disease. Computed tomography of the chest, performed as part of the institution's presurgical protocol, showed aortic arch calcifications, with no contraindication for myocardial revascularization on extracorporeal circulation (Fig. 1). The patient was scheduled for urgent surgical myocardial revascularization. He was monitored with entropy, brain near-infrared spectroscopy, a central venous catheter through the right internal jugular, a left radial arterial line, a rectal probe, and an esophageal and rectal thermometer.

Surgery began with arterial and venous graft harvesting, followed by total systemic heparinization. Arterial cannulation using a 20 Fr EOPA cannula and single venous cannulation established extracorporeal circulation, and a 9 Fr cardioplegia cannula was installed in the ascending aorta. Normothermic extracorporeal circulation was begun with an ACT at 423 seconds, with no pressure gradients in the circuit. The aorta was clamped to perform the end-to-side anastomosis of the saphenous to the first obtuse marginal, first diagonal and posterior descending arteries. An aortotomy was also done with a 4.5 mm Medtronic punch for proximal anastomoses of the aortocoronary saphenous bridges, where the aortic tearing was found and type A aortic dissection was diagnosed. Cooling was begun, with partial clamping of the brachiocephalic trunk for anastomosis of the 8 mm Dacron graft. The aortic cannula was withdrawn, and perfusion continued through the brachiocephalic trunk. The dissected ascending aorta was repaired up to the arch, and the patient was prepared for circulatory arrest with thiopental. At 25°C, extracorporeal circulation was suspended and the aortic clamp was released. Selective cerebral circulation continued through the brachiocephalic trunk, the cerebral perfusion cannula was inserted into the left carotid, and the aortic arch was anastomosed with 30 mm Dacron. The circulatory arrest with cerebral perfusion time was 26 minutes; circulatory arrest was terminated and warming began, along with proximal anastomosis of the Dacron graft and saphenous bridges, as well as anastomosis of the mammary to the anterior descending artery. The patient was taken off extracorporeal circulation, with a total time of 278 minutes. The coagulopathy was corrected with elastography guidance, without adequate bleeding control. The mediastinum was packed, and an intraoperative transesophageal echocardiogram showed left ventricular hypertrophy; global hypokinesia, predominantly in the inferior wall; an LVEF of 50%; preserved global contractility of the right ventricle; normal-sized right and left atria; and a competent trileaflet aortic valve. He was transferred to the intensive care unit, where he progressed favorably and underwent removal of the packs and sternal closure at 48 hours, with no complications. He was on mechanical ventilation for 36 hours, and a total of eight units of blood were transfused. His total intensive care unit stay was six days; he remained hospitalized for another three days and was satisfactorily discharged. Forty days after surgery he developed a left hemothorax that required thoracoscopic lung decortication. He had no complications and was once more discharged satisfactorily.

Discussion

Iatrogenic aortic dissection (IAD) is a rare but potentially fatal complication of cardiac surgery, which has been reported in the literature since 1960[6]. Early diagnosis minimizes complications and improves outcomes,
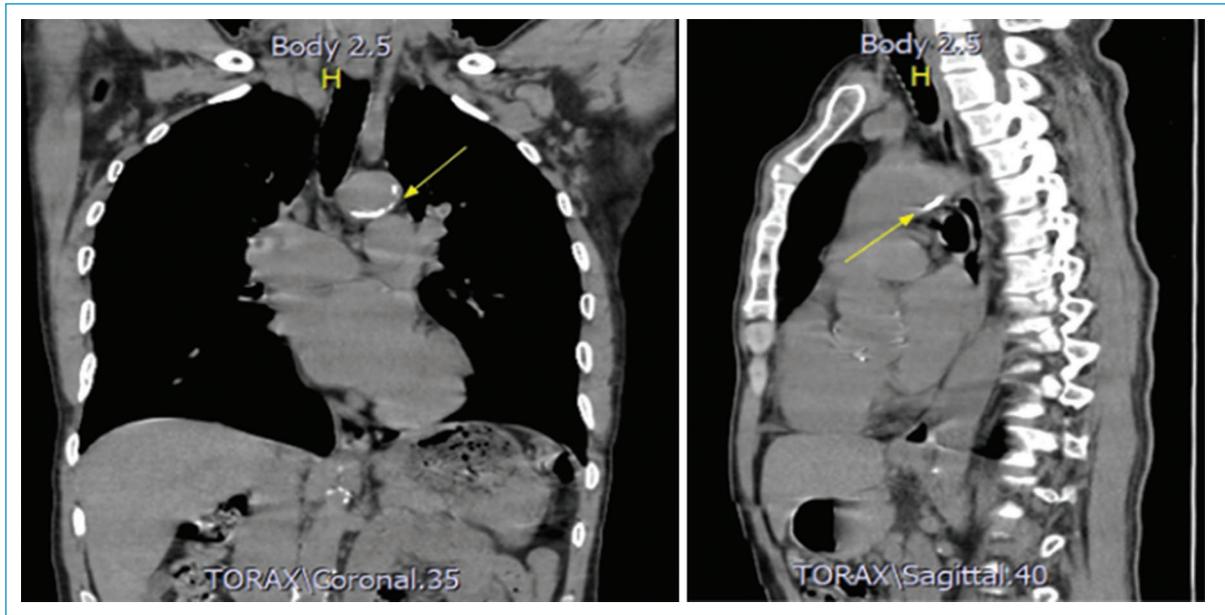
Figure 1. Computed tomography of the chest showing calcification of the aortic arch (arrows) in preoperative testing.

and therefore the entire surgical team must be alert to possible situations associated with this complication. While injury of the intimal layer is secondary to aortic manipulation, there may be predisposing factors like cystic necrosis of the media, uncontrolled hypertension or advanced atherosclerotic disease in the aortic wall. Thus, identification of these conditions can avert complications. Intimal tearing occurs during surgery; however, it is often diagnosed postoperatively, with early diagnosis occurring in the first 30 days and late diagnosis between one month to one year after surgery[6]. The incidence of postoperative IAD is approximately 0.06% when the ascending aorta is the site of arterial cannulation, 0.6% when the femoral or iliac arteries are used, and 0.5% when the axillary or subclavian arteries are used[6].

Murphy presented the first case series in 1983, with a 33% mortality rate[1]. Meanwhile, some authors hypothesize that the number of unknown or undetected cases may be significantly higher since autopsies are not routinely performed for sudden deaths after heart surgery[7].

Due to the rarity of this complication, most data come from the presentation of small case series. This complication was more common in the first decades of cardiac surgery with extracorporeal circulation. At that time, the femoral artery was commonly used for this purpose; today, with the flourishing of minimally invasive surgery, peripheral cannulation has increased, bringing a greater risk of this type of complication.

Iatrogenic dissection accounts for 5% of the globally reported aortic dissections[8]. Other sites where dissection may occur include total or partial aortic clamping sites and the proximal saphenous vein anastomosis site. This complication may also occur during myocardial revascularization surgery without extracorporeal circulation, as well as in valve surgery. Myocardial revascularization has the highest incidence, as it is the most frequent cardiac surgery worldwide.

Iatrogenic aortic dissection's high mortality is estimated to be 30% but may be up to 50% if it is not detected until after surgery[9], which underscores the importance of early detection. Furthermore, IAD has been reported to potentially occur during procedures like coronary catheterization, transcatheter valve replacement (TAVR) and aortic stent placement, with a relatively low but risky incidence, which may range from 0.1 to 0.3%[10]. This case report presents the diagnosis and treatment of a type A aortic dissection during surgical myocardial revascularization.

Treatment of this disease requires adequate true lumen perfusion in the absence of increased pressure (arterial line) or spreading dissection. This is why we performed brachiocephalic trunk cannulation with a Dacron graft. In this case, the extent of the dissection could be directly visualized in the ascending aorta up to but not involving the arch, and complete resection was accomplished with open correction during circulatory arrest. After the distal anastomosis, internal mammary

artery repair and anastomosis to the anterior descending artery were completed during the warming phase.

Conclusion

We have presented an iatrogenic type A aortic dissection case secondary to myocardial revascularization surgery. An early diagnosis was made during extracorporeal circulation. The involved segments were completely resected in the correction, and distal anastomosis was performed in Zone 0 of the aorta, under circulatory arrest. Teamwork between the surgeon, anesthesiologist and perfusionist, with effective communication, is essential for handling emergencies while patients are on extracorporeal circulation. The patient progressed satisfactorily after surgery, and follow-up echocardiograms prior to discharge confirmed proper correction.

Funding

The authors declare that they received no funding for this study.

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 in the course of this study.

Confidentiality, informed consent and ethical approval. The study did not involve personal patient information or require ethical approval. The SAGER guidelines did not apply.

Declaration on the use of artificial intelligence. The authors declare that they did not use any type of generative artificial intelligence in writing this article.

References

1. Murphy D, Craver J, Jones E, Bone D, Guyton R, Hatcher C. Recognition and management of ascending aortic dissection complicating cardiac surgical operations. J Thorac Cardiovasc Surg. 1983 [Internet]; 85(2):247-56. Disponible en: https://doi.org/10.1016/S0022-5223(19)38880-4.
2. Fleck T. Intraoperative iatrogenic type A aortic dissection and perioperative outcome. Interact Cardiovasc Thorac Surg. 2005 [Internet]; 5(1):11-4. Disponible en: https://doi.org/10.1510/icvts.2005.114900.
3. Hiratzka L, Bakris G, Beckman J, Bersin R, Carr V, Casey D, et al. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM Guidelines for the diagnosis and management of patients with thoracic aortic disease. Circulation. 2010 [Internet]; 121(13). Disponible en: https://doi.org/10.1161/CIR.0b013e3181d4739e.
4. Evangelista A, Isselbacher E, Bossone E, Gleason T, Eusanio M, Sechtem U, et al. Insights From the International Registry of Acute Aortic Dissection: A 20-Year Experience of Collaborative Clinical Research. Circulation. 2018 [Internet]; 137(17):1846-60. Disponible en: https://doi.org/10.1161/CIRCULATIONAHA.117.031264.
5. LeMaire S, Russell L. Epidemiology of thoracic aortic dissection. Nat Rev Cardiol [Internet]. 2011;8(2):103-13. Disponible en: https://doi.org/10.1038/nrcardio.2010.187.
6. Ram H, Dwarakanath S, Green A, Steyn J, Hessel E. Iatrogenic aortic dissection associated with cardiac surgery: a narrative review. J Cardiothorac Vasc Anesth [Internet]. 2021;35(10):3050-66. Disponible en: https://doi.org/10.1053/j.jvca.2020.07.084.
7. Tabry I, Costantini E, Reyes E, Tamim W, Habal S, Hughes L. Early postoperative acute aortic dissection, the leading cause of sudden death after cardiac surgery? Critical role of the computed tomography scan. Heart Surg Forum. 2003 [Internet]; 6(5):382-6. Disponible en: https://pubmed.ncbi.nlm.nih.gov/14721815/.
8. Rylski B, Hoffmann I, Beyersdorf F, Suedkamp M, Siepe M, Nitsch B, et al. Acute aortic dissection type A. Ann Surg [Internet]. 2014 [citado 15 Jul 2024]; 259(3):598-604. Disponible en: https://doi.org/10.1097/SLA.0b013e3182902cca.
9. Leontyev S, Borger M, Legare J, Merk D, Hahn J, Seeburger J, et al. Iatrogenic type A aortic dissection during cardiac procedures: early and late outcome in 48 patients. Eur J Cardio-Thorac Surg. 2012. [Internet].;41(3):641-6. Disponible en: https://doi.org/10.1093/ejcts/ezr070.
10. Gómez J, Bárcena A, Caballero F. Disección aórtica aguda, lo fundamental de la historia clínica y la exploración física. SEMERGEN - Medicina de Familia [Internet]. 2014 [citado 15 Jul 2024]; 40(4):228-31. Disponible en: https://doi.org/10.1016/j.semerg.2013.12.011.

Check for updates

LETTER TO THE EDITOR

Impact of risk scores on the clinical evolution of acute coronary syndrome

Impacto de los puntajes de riesgo en la evolución clínica del síndrome coronario agudo

Eros J. Avendaño-Moscaiza

Faculty of Medicine, Universidad Privada San Juan Bautista, Ica, Perú

Dear editors,

I appreciate the opportunity to review this article on "The association between risk scores and clinical outcomes in acute coronary syndrome patients"[1], which, after a detailed review, helps identify the investigation on the correlation between the various risk scoring tools like TIMI, GRACE and PURSUIT and the clinical outcomes of patients with acute coronary syndrome.

On the other hand, I believe it is relevant to point out some observations regarding the follow-up times used, values employed and their possible impact on the validity of the scores for predicting long-term outcomes on the GRACE scale, as its primary objective is to estimate the risk of death or myocardial infarction at six months, thus facilitating stratification of ACS patients[2].

I believe a contribution is relevant at this point, especially regarding the GRACE scale, as there are other studies which, after adjusting for age, indicate that the risk of inpatient mortality increased 3.5% for each year of age[3]. What is more, we must also consider the current status and availability of further tests, as another study on the GRACE scale, modified with the incorporation of hs-cTnT, showed improved yield compared to the original scale and other already established prognostic markers[4]. There is also another study which incorporated triglyceride and glucose indices, thus improving this score's predictive capacity[5]. However, in the study conducted, the "age" factor was used just by adding a general average and the predictive value at three months, without using other possible available tests, which could alter the results. In addition, the scale's updates were not taken into account; a clear example of this is the GRACE 2.0 model[6], or the latest score studied, GRACE 3.0, with sex-specific consideration of each GRACE component, showing excellent discrimination[7].

In conclusion, the article presents a very fundamental analysis of the usefulness of the risk scores for predicting clinical outcomes in patients with acute coronary syndrome, using the TIMI, GRACE and PURSUIT scales. However, future studies must consider including variables, like age, more precisely in risk stratification, along with the sex variable and other possible markers. It would also be useful to conduct more extensive long-term follow-up to evaluate the effectiveness of risk scores in predicting future events. Adapting these tools to diverse populations and continuously adjusting them based on new evidence will allow a more effective and personalized treatment of patients with ACS.

References

1. Farag S, Mostafa S, El-Rabbat K, El-Aziz AA. La asociación entre las puntuaciones de riesgo y el desenlace clínico en pacientes con síndrome coronario agudo. Rev Colomb Cardiol. 2025;32(1):32-8. doi:10.24875/RCCARE.M24000139.
2. Neves VB, Roman RM, Vendruscolo T, Heineck G, de Mattos CAS, de Mattos EI, et al. Validation of the grace risk score to predict in-hospital and 6-month post-discharge mortality in patients with acute coronary syndrome. Int J Cardiovasc Sci. 2022;35(2):174-80. doi:10.36660/ijcs.20200361.
3. Kumar D, Ashok A, Saghir T, Khan N, Solangi BA, Ahmed T, et al. Prognostic value of grace score for in-hospital and 6 months outcomes after non-ST elevation acute coronary syndrome. Egypt Heart J. 2021;73(1):113. doi:10.1186/s43044-021-00227-5.
4. Georgiopoulos G, Kraler S, Mueller-Hennessen M, Delialis D, Mavraganis G, Sopova K, et al. Modification of the grace risk score for risk prediction in patients with acute coronary syndromes. JAMA Cardiol. 2023;8(10):946-56. doi:10.1001/jamacardio.2023.2859.
5. Xiong S, Chen Q, Chen X, Hou J, Chen Y, Long Y, et al. Adjustment of the grace score by the triglyceride glucose index improves the prediction of clinical outcomes in patients with acute coronary syndrome undergoing percutaneous coronary intervention. Cardiovasc Diabetol. 2022;21(1):229. doi:10.1186/s12933-022-01699-z.
6. Bai L, Yang B, Cheng Y, Zhang Y, Liao G. Performance of the risk scores for predicting in-hospital mortality in patients with acute coronary syndrome in a Chinese cohort. Rev Cardiovasc Med. 2023;24(12):385. doi:10.31083/j.rcm.2023.12.385.
7. Wenzl FA, Kraler S, Ambler G, Weston C, Herzog SA, Räber L, et al. Sex-specific evaluation and redevelopment of the grace score in non-ST-segment elevation acute coronary syndromes in populations from the UK and Switzerland: a multinational analysis with external cohort validation. Lancet. 2022;400(10354):744–56. doi:10.1016/S0140-6736(22)01336-6.

Check for updates

Tafamidis in transthyretin amyloid cardiomyopathy

Tafamidis en cardiopatías por amiloidosis transtirretina

Juan D. López-Ponce de León[1,2,3], Germán C. Giraldo-González[4]*, and Enrique Berrios[5]

[1]Fundación Valle del Lili, Centro de Investigaciones Clínicas, Cali, Colombia; [2]Faculty of Health Sciences, Universidad Icesi, Cali, Colombia; [3]Department of Cardiology, Fundación Valle del Lili, Cali, Colombia; [4]Department of Cardiology, Universidad de Caldas, Manizales, Colombia; [5]Cardiology Service, Instituto Nacional de Cardiología Ignacio Chávez, Mexico City, Mexico

Dear editors,

We have carefully reviewed the article titled "Efficacy and cost-effectiveness of tafamidis for managing cardiac transthyretin amyloidosis" by Díaz et al.[1], who published a systematic review with a quantitative analysis to answer four specific questions about the efficacy and cost-effectiveness of tafamidis, the first disease-modifying drug for transthyretin amyloid cardiomyopathy approved in Latin America. We would like to comment on some aspects that, in our view, limit the methodological validity and interpretation of the evidence of the clinical effect and economic profile of the intervention; in particular, in applying its conclusions to the setting of patients with rare or orphan diseases. Below, we describe these aspects and their consequences for the validity and applicability of this systematic review.

Methodological perspective

Preferred Reporting Items for Systematic reviews and Meta-Analyses/A Measurement Tool to Assess Systematic Reviews (PRISMA/AMSTAR) transparency

The article does not mention the protocol being previously registered in the Prospective Register Of Systematic Reviews (PROSPERO) or its publication, which prevents an evaluation of protocol deviations that may have introduced biases. Although the article states adherence to the PRISMA report, we did not find 17 of the applicable items, mainly related to the lack of a detailed report of the article selection strategies and consideration of sources of error (supplementary material 1: PRISMA checklist with highlighted items). A systematic review should make the following explicit: prior protocol/registry, reproducible searches, duplicate selection/extraction and handling of discrepancies, using criteria evaluated by AMSTAR and related guidelines on systematic review quality, which are not in the document. The initial search used basic MeSH terms that only included the study population. It is advisable to use terms related to the intervention, comparison and outcomes of interest; this should preferably be done by an expert in systematic searches, as not following this methodology can result in obtaining limited or biased information. Furthermore, we recommend scoring the certainty of the evidence for each outcome using GRADE and reporting the strength of the conclusions.

Evaluation of the risk of bias in individual studies

A tool other than the one recommended was used to evaluate nonrandomized intervention studies (Downs checklist vs. ROBINS-I). Based on the instrument applied by the authors, two observational studies were reported

to have an intermediate and high risk of bias; however, this did not affect the interpretation of the results of these studies. In addition, there is no mention of publication bias or measures to avoid and evaluate it.

A mix of designs and a narrative summary of effects

The authors conducted a narrative synthesis that combined the results of the randomized clinical trial ATTR-ACT with observational studies using varying designs with different susceptibility to confusion and bias[2]. No quantitative synthesis of the effects of tafamidis was provided through a meta-analysis of primary studies, which is necessary for evaluating the effect of an intervention and the certainty of the evidence that supports it[3]. There are systematic reviews with meta-analyses on this drug in the population of interest that report favorable findings for the intervention. Although most were published after this article's initial submission date, the systematic review by Wang et al.[4] should have been considered, especially given the interest in including financial evidence[4-9].

Although the search results are limited, the information presented is enough for a meta-analysis, with no technical reason for not performing it. We consider this a major limitation in the development of the review to answer the proposed questions. Combining the results of clinical trials, like ATTR-ACT, with the results of observational studies in a meta-analysis is controversial. Therefore, it might be valid to just take the results of the former on their own as better evidence, and this study had a low reported risk of bias. Thus, if only these results are taken as central to the analysis, the conclusions are not concordant, as the study by Maurer et al.[2] presented positive results that support the efficacy and safety of tafamidis in the study population, both in the mortality and hospitalization outcomes, as well as the secondary objectives of quality of life and six-minute walk test.

Certainty of the evidence (GRADE) and statistical report

The certainty and strength of the conclusions need to be scored; the guidelines on the use of the evidence recommend updated systematic reviews and explicit grading before deriving recommendations. It is irregular to report effects with 95% CI, exact p values, and assumptions of methods and power; clinical decisions require reporting of absolute risks, NNT/NNH and natural frequencies along with RR/HR/OR. The systematic review discusses differences by functional class/age, but predetermined criteria and multiplicity control are lacking, along with support from modern subgroup/individualized treatment rules (ITR) and shared decision making (if "respondents" are sought).

Interpretation of economic evidence

Stating that tafamidis is not cost-effective without a local model should be mentioned with its inherent uncertainty (unmodeled Colombian price, costs, profits and outlook). Furthermore, tafamidis is currently the only treatment for transthyretin amyloid cardiomyopathy (ATTR-CM) with evidence of benefit and approval for modifying and controlling the disease, which increases the clinical need for this intervention. As an orphan disease with low prevalence and no alternatives, efficiency and cost must be balanced against equality and distributive justice, seeking to establish a focused access route to ensure that these few affected people have the right to treatment and to justify their coverage through health policies.

Clinical perspective

Transthyretin amyloid cardiomyopathy has been gaining interest in the scientific community due to a rise in cases around the world, more publications on the topic, and the development of specific treatments. Ever since it was first identified, this disease has been included in the group of orphan diseases due to its genetic nature, in most cases, low prevalence compared to other diseases, and low interest of the pharmaceutical industry in researching and developing new technologies. However, orphan diseases have a significant impact on both the patients (who experience diminished quality of life and life expectancy) and their relatives, who are directly affected by the disease, as well as on those indirectly affected (caregivers and social and financial dependents of the patients), healthcare professionals and facilities (who face diagnostic challenges and difficulties in coordinating care), and the pharmaceutical economy.

Minimization of the effect of tafamidis on the frequency and duration of hospitalizations

In their conclusion, the authors mention that the ATTR-ACT study's post-hoc analysis finding on the reduction in annual days of hospitalization provides evidence of clinical benefit, but dismiss it, claiming "clinical irrelevance." The difference reported by the ATTR-ACT

study and cited by the authors comes from a bar graph reporting a reduction of 2.62 day*s per patient-year* in favor of tafamidis. This amounts to 262 inpatient days avoided per 100 patients treated per year, compared to placebo. Furthermore, the analysis of the difference in proportions of the need for any hospitalization was favorable for tafamidis (48 vs. 70%, per year). Therefore, we believe that the drug's effect on the need for hospitalization and number of inpatient days is clinically relevant, as well as statistically significant.

The authors also mention that they did not include the results of a secondary analysis of the ATTR-ACT (CM) study on quality-of-life outcomes because it did not report measures of statistical significance. However, the study reports the quality-of-life outcomes at 30 months that showed a benefit of tafamidis on the EQ-5D-3L, KCCQ-OS and Patient Global Assessment (PGA) scales, reported with confidence intervals and *p* values.

In our view, the difference between the hereditary and wild-type ATTR subgroups should also be considered, since tafamidis's effect differs between these two types of ATTR with regard to efficacy and time to disease progression.

Disease progression

Regarding disease progression, observational studies were reported that included the recently published domains for evaluating the clinical course of ATTR-CM under disease-modifying treatment. All the reported studies show a benefit related to less progression. The authors highlight that none of the studies prove disease regression. In this context, it should be clarified that the domains mentioned have been recently published, and, therefore, relevant clinical information is not yet available in this setting. Also, tafamidis's mechanism is in no way related to disease regression. For this, new Phase 1 technologies are being developed to evaluate the possible elimination of amyloid fibrils from the tissue, which is essential for claiming regression. In the mid-future, we will have scientific evidence available to determine the efficacy of treatments on disease regression. At present, analyzing tafamidis based on this phenomenon is not congruent with its mechanism of action and biology.

Cost-effectiveness analysis of tafamidis

This is only reported in the study by Kazi et al.[10], concluding that when a classic tool (ICER/QALY) is used, tafamidis is not cost-effective unless the price of the drug is substantially reduced. Although this is a valid conclusion for evaluating treatments of prevalent diseases, it involves certain errors of interpretation when applied to orphan diseases. These tools are based on a large group of people receiving a benefit at an acceptable cost. This utopia is impossible in orphan diseases, first because there will never be a large group of people due to the low prevalence of the diseases, and second, because the cost of new technologies will never fall below the evaluation thresholds of these tools. Therefore, using ICER/QALY to evaluate orphan disease drugs will always place them at a disadvantage, and health policy decision-making could be considered discriminatory against orphan diseases. This is why Díaz et al.'s[1] analysis is important in critiquing the method used but is not enough to conclude that the information presented does not justify cost-effectiveness. Probably the greatest harm to be considered with these conclusions is for the patients who are discriminated against due to their condition, justifying not allocating resources to the diagnosis and treatment of their conditions, which would imply an inequitable system for rare diseases.

Conclusions

Funding and access decisions for orphan diseases are limited by evidence and elevated prices. The classic economic methods are applicable but should be adjusted to scenarios with small sample sizes, treatment learning curves and marked heterogeneity. Today, new strategies are being discussed and developed for evaluating the pharmacoeconomic impact of ATTR-CM, and the high cost of treatments like tafamidis undoubtedly need to be discussed and evaluated, but until clear, approved and universal guidelines are available, the available information should be taken with caution, considering the partiular nature of the disease and patient preferences as the core of our decisions.

Funding

Conflicts of interest

E. Berrios received honoraria within the last year from: Bristol (BMS), Pfizer, Takeda, Sanofi, Novartis, BCRI-Brazilian Clinical Research Institute, Servier, Merck, Stendhal, PTC Therapeutics, AstraZeneca and Lilly.

Ethical considerations

Human and animal protection. The authors declare that the procedures followed adhered to the ethical norms of the responsible human experimentation committee and were in accord with the World Medical Association and the Declaration of Helsinki. The procedures were authorized by the institution's ethics committee.

Confidentiality, informed consent, and ethical approval. The authors followed the institution's confidentiality protocols, obtained informed consent from the patients and received approval from the ethics committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that they did not use any type of generative artificial intelligence in writing this article.

Supplementary data

Supplementary data are available at DOI: 10.24875/RCCAR.25000083. These data are provided by the corresponding author and published online for the benefit of the reader. The contents of supplementary data are the sole responsibility of the authors.

References

1. Díaz JC, Aristizábal JM, Bastidas O, Marín JE, Niño CD, Duque M. Eficacia y costo-efectividad de tafamidis para el tratamiento de la cardiopatía por amiloidosis transtirretina. Rev Colomb Cardiol. 2025; 32(3):17033.
2. Maurer MS, Schwartz JH, Gundapaneni B, Elliott PM, Merlini G, Waddington-Cruz M, et al. Tafamidis treatment for patients with transthyretin amyloid cardiomyopathy. N Engl J Med. 2018;379(11):1007-16.
3. Cochrane Handbook for Systematic Reviews of Interventions | Cochrane [Internet]. [cited 15 Aug 2025]. https://www.cochrane.org/authors/handbooks-and-manuals/handbook#how-to-cite.
4. Wang J, Chen H, Tang Z, Zhang J, Xu Y, Wan K, et al. Tafamidis treatment in patients with transthyretin amyloid cardiomyopathy: a systematic review and meta-analysis. eClinicalMedicine. 2023;63:102172.
5. Sukaina M, Rehman S, Waheed M, Shehryar M, Rasool R, Ahmed N, et al. Efficacy of tafamidis in transthyretin amyloid cardiomyopathy: a systematic review and meta-analysis. Ann Med Surg. 2024;86(1):433-8.
6. Hussain B, Duhan S, Patel B, Chang YC, Hamza M, Najam M, et al. Tafamidis: A game changer in transthyretin cardiomyopathy? A systematic review and meta-analysis of safety and efficacy. Curr Probl Cardiol. 2025;50(9):103129.
7. Kato S, Azuma M, Horita N, Utsunomiya D. Monitoring the efficacy of tafamidis in ATTR cardiac amyloidosis by MRI-ECV: A Systematic Review and Meta-Analysis. Tomography. 2024;10(8):1303-11.
8. Prata AA, Katsuyama ES, Scardini PG, Covre AC, Neto WF, Fernandes JM, et al. The efficacy and safety of specific therapies for cardiac Transthyretin-mediated amyloidosis: a systematic review and meta-analysis of randomized trials. BMC Cardiovasc Disord. 2025;25(1):296.
9. Kao TW, Hung YH, Yu AL, Cheng MF, Su MY, Chao CC, et al. Effect of tafamidis on clinical and functional parameters in transthyretin amyloid cardiomyopathy. JACC Adv. 2025;4(2):101511.
10. Kazi DS, Bellows BK, Baron SJ, Shen C, Cohen DJ, Spertus JA, et al. Cost-Effectiveness of Tafamidis Therapy for Transthyretin Amyloid Cardiomyopathy. JAMA. 2019; 322(19):1881–1888.