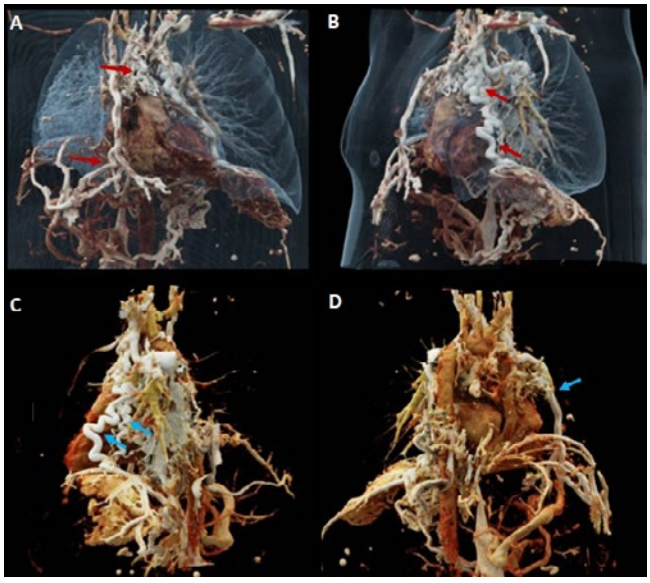
Revista Colombiana de
Cardiología

Volume 31 Number 6 November / December 2024

ISSN: 2938-1525

Indexada en / *Indexed in*: Scopus, DOAJ, EBSCO, EMBASE, MIAR

www.rccardiologia.com
www.revcolcard.org



Chest CT with 3D reconstruction. A-D: mediastinal conglomeradi and collaterals of the azygos vein. J. S. Borges-López, et al. Inferior vena cava agenesis as a cause of pulmonary thromboembolism.

- **Importance and development of cardio-oncology**
- **Standardization of lipid profile reports**
- **Hypertension, neuropsychiatry and CVR**
- **Usefulness of echocardiography in NSTE-ACS**
- **Economic impact of LDL-C control**
- **Echocardiography and mortality in COVID-19**
- **Mortality from Cerebrovascular Disease and Coronary Ischemic Disease**
- **RECCANT/RECCANT-AR: rationale/design**
- **RS with GPT for the diagnosis of infarction**

Órgano oficial de la Asociación

SOCIEDAD COLOMBIANA
DE CARDIOLOGÍA & CIRUGÍA
CARDIOVASCULAR

PERMANYER
www.permanyer.com

10163ACOL246

Revista Colombiana de Cardiología
Órgano oficial de la Asociación Sociedad Colombiana de Cardiología & Cirugía Cardiovascular
Permanyer

Check for updates

EDITORIAL

Importance and development of cardio-oncology in Colombia: present and future

Importancia y desarrollo de la cardio-oncología en Colombia: presente y futuro

Tito Carrera-Rodríguez

Fundación CTIC (Luis Carlos Sarmiento Cancer Treatment and Research Center). Bogotá, Colombia

Cardio-oncology was born approximately 30 years ago with the initial studies documenting increased myocardial injury markers and the onset of heart failure attributable to antineoplastic treatment. Thus, the need to detect, monitor and provide specific follow-up for some cancer patient risk groups was recognized. At that point, the use of anthracyclines was the factor most related to the risk of developing cardiotoxicity.

Since then, this sub-specialty has grown exponentially, and over the last 10 years, its advances have allowed a much better description of patient groups at high risk of developing ventricular dysfunction, as well as the therapies with a greater risk of cardiotoxicity and toxicities other than heart failure, which encompass a broad spectrum of cardiovascular abnormalities (arterial hypertension, pulmonary hypertension, myocarditis, supraventricular and ventricular arrhythmias, and sudden death, among others). These abnormalities may occur both in the short and long term.

According to the Global Cancer Observatory (GLOBOCAN), the incidence and mortality of all types of cancer are expected to progressively increase over the next few years, estimating a growth from 20 million new cases in 2022 to close to 29.9 million in 2040, which is an almost 50% increase in less than two decades. The Colombian estimates also show a growth in both incidence (going from approximately 117,000 new cases in 2022 to more than 190,000 cases by 2040) and mortality (going from 56,000 cases in 2022 to more than 96,000 by 2040)[1], which means an increase in the number of potential cardio-oncology patients.

Thus, improved prognoses for cancer patients due to optimized therapies, progressive population aging and the beneficial impact of more frequent and better cardiovascular interventions have increased the life expectancy of patients in general, which means that it is more common to find patients with cardiovascular comorbidities who develop cancer or cancer patients who develop cardiovascular problems due to aging or anticancer therapies.

Ongoing cancer research has led to the development of new cancer drugs which have drastically improved the prognosis for cancer patients, both for overall survival as well as disease-free survival or a longer time to recurrence. This has allowed an increasingly significant development of precision medicine, individualizing the patients to identify population groups that will respond better to specific drugs, according to their clinical, genetic, molecular and/or mutational profile, thus improving the efficacy and safety of the drugs.

In 2022, cardio-oncology took a big step with the development of the first European Society of Cardiology guidelines[2]. These opened the door to the globalization of the concept of cardiotoxicity, improved identification of patient groups at greater risk of developing it, and the first recommendations (mostly based on expert opinion) for clinical, imaging and biomarker follow-up for early detection of chemotherapy-induced cardiovascular toxicity.

Correspondence:
Tito Carrera-Rodríguez
E-mail: titocarrerar@gmail.com

Date of reception: 26-09-2024
Date of acceptance: 04-10-2024
DOI: 10.24875/RCCARE.M24000131
Available online: 05-02-2025
Rev Colomb Cardiol. 2024;31(6):323-325
www.rccardiologia.com

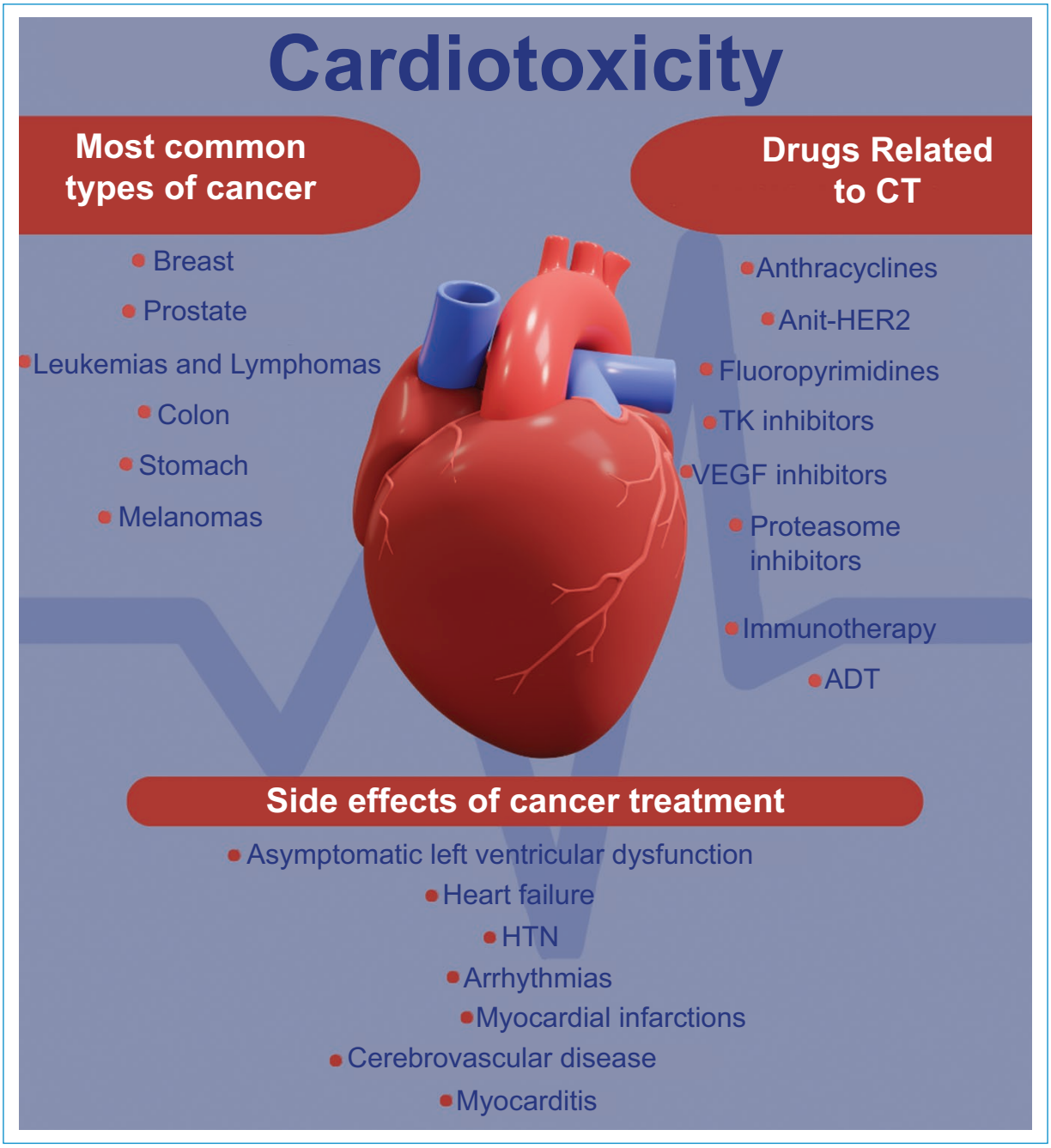


Figure 1. Cancer, therapies and cardiovascular toxicity.

Consequently, it is increasingly important for cardiologists to have a more detailed understanding of the cardiovascular implications of the current cancer treatments. The role of continuing education is to ensure that we, as cardiology specialists, have the necessary capacity and training to face and resolve these new challenges of diseases that are far removed from our daily practice but require us to work together with oncologists, hematologists and surgical oncologists to improve the safety outcomes of these interventions.

In our country, approximately 10 years ago, some interested members of Asociación Sociedad Colombiana de Cardiología y Cirugía Cardiovascular [Colombian Society of Cardiology and Cardiovascular Surgery] started a cardio-oncology chapter. Since then, it has grown progressively in its membership and active participation in national continuing education events.

However, the members' interest has not necessarily gone hand in hand with growth in service provision as, despite the growing number of patients with this

combination of diseases, corresponding cardio-oncology clinics have not been developed. Today, there are few cancer treatment centers with a sub-specialist in cardio-oncology who can provide treatment for these patients according to their specific needs.

Therefore, the creation of cardio-oncology clinics would facilitate cancer patients' access to specialized assessments, favoring a comprehensive and multidisciplinary approach, a proper estimate of the risk of cardiac toxicity due to cancer treatments, the need to adjust treatment according to the estimated cardiovascular risk profile and improved short-, medium- and long-term outcomes. These assessments would be focused mainly on reducing the need to discontinue cancer treatments, favoring the scheduled end of the proposed cancer treatments, extending survival by decreasing treatment interruption and, obviously, improving these patients' cardiovascular morbidity and mortality[3] (using the example of heart failure clinics, which have shown beneficial effects).

Today, risk stratification prior to treatment is the cornerstone for managing patients with potential cardiotoxicity. This is followed by electrocardiographic and echocardiographic assessment of those at high risk or receiving treatment with high cardiotoxicity potential, to determine the early use of drug treatments to modulate the risk of toxicity, as well as stricter follow-up by cardio-oncology[4]. However, it is clear that, in this scenario, the use of new diagnostic techniques that have proven to be more effective in identifying high-risk patients should be generalized, such as a broader use of transthoracic echocardiography with myocardial deformation analysis, or 3D estimation of the LVEF, to reduce the variability of our results. This would also include earlier and routine preventive measurement of troponin and natriuretic peptide levels and more frequent inclusion of cardiac magnetic resonance studies to measure myocardial deformation and provide early measurement of fibrosis, myocardial edema and the risk of arrhythmias[5].

Assessment pathways, risk analysis and early intervention to modulate cardiovascular risk must also be established in each institution with a cardio-oncology clinic, actively involving oncologists and hematologists, to be on the same page[6].

As has occurred in the various cardiology sub-specialties, the care of these patients should ideally be guided by a cardio-oncology specialist, as this person should have targeted training and further knowledge of oncology, hematology and pharmacology. This will help provide an approach that fits better with the objectives of curing and preventing both oncological and cardiovascular complications, together with the oncology support groups.

Training of cardio-oncologists is not yet possible in this country, due to the lack of graduate training programs for cardiologists in this field and formal cardiology programs still not offering a specific training module on this subject. Therefore, in the short-term, training agreements must be sought between oncology and cardiovascular centers of excellence to encourage the training of general cardiologists in cardio-oncology. In the mid-term, the development of university graduate programs in cardio-oncology should be encouraged.

From a research perspective, investigators and drug regulation centers are increasingly considering cardiovascular safety evaluations in the clinical trials of new cancer drugs, focusing on obtaining pharmacological efficacy with adequate safety. This opens the door to the participation of cardio-oncologists in research groups conducting clinical trials of cancer treatment drugs in different disease phases.

We hope that, over the next few years, the Asociación Sociedad Colombiana de Cardiología's cardio-oncology chapter's integration with international societies and, especially, the creation of the Colombian chapter of the International Cardio-Oncology Society (ICOS), will help position us in this increasingly important and necessary field, both in this country and the region, to further the development of this new sub-specialty.

References

1. Ferlay J, Ervik M, Lam F, Laversanne M, Colombet M, Mery L, et al. Global cancer observatory: cancer today. International Agency for Research on Cancer; 2024.
2. Lyon AR, Lopez-Fernandez T, Couch LS, Asteggiano R, Aznar MC, Bergler-Klein J, et al. 2022 Guidelines in Cardio-oncology developed in collaboration with the European Hematology Association, the European Society for Therapeutic Radiology and Oncology and the International Cardio-oncology Society. Eur Heart J. 2022;43:4229-61.
3. Omland T, Lagethon S, Gulati G. The role of cardio protection in Cancer Therapy Cardiotoxicity: JACC: Cardio oncology State of the art Review. J Am Coll Cardiol CardioOnc. 2022;4(1):19-37.
4. Hui-Ming C, Rohit M, Tiziano S, Tochukwu MO. Cardiovascular complications of cancer therapy. Best practices in diagnosis, prevention, and management. JACC. 2017;70(20):2536-51.
5. Contaldi C, Montesarchio V, Catapano D, Falco L, Caputo F, D´Aniello C, et al. Multimodality cardiovascular imaging of cardiotoxicity due to cancer therapy. Life (Basel). 2023;13(10):2103.
6. Lancellotti P, Suter TM, López-Fernández T, Galderisi M, Lyon AR, Van der Meer P, et al. Cardio-Oncology Services: rationale, organization, and implementation. Eur Heart J. 2019;40(22):1756-63. doi: 10.1093/eurheartj/ehy453.

Revista Colombiana de Cardiología
Órgano oficial de la Asociación Sociedad Colombiana de Cardiología & Cirugía Cardiovascular
Permanyer

Check for updates

ORIGINAL ARTICLE

The importance of standardized lipid profile reporting in clinical laboratories

Importancia de la estandarización de los reportes del perfil lipídico en los laboratorios clínicos

Ángel García[1], Javier Arango[2], Javier Cabrera[3], Jaime Melo[4,5], Harold Miranda[6,7], Katherine Restrepo[8,9,10,11], Marlene I. Vélez[12], Iván L. Mojica[13], and Jaime A. Rodríguez[14,15]*

[1]Department of Internal Medicine, Cardiology Unit, Pontificia Universidad Javeriana, Hospital Universitario San Ignacio, Bogotá; [2]Colombian Association of Internal Medicine, Bogotá; [3]Colombian Association of Gerontology and Geriatrics, Bogotá; [4]Scientific Directorate, Keralty Medical Centers, Bogotá; [5]Colombian Society of Family Medicine, Bogotá; [6]Colombian Association of Vascular Medicine (ACMV), Bogotá; [7]Vascular Diagnostics S.A.S., Bogotá; [8]Colombian Association of Endocrinology, Diabetes and Metabolism, Bogotá; [9]Department of Internal Medicine, Universidad Santiago de Cali, Cali; [10]Department of Internal Medicine, Universidad Javeriana, Cali; [11]Department of Internal Medicine, Colsanitas, Cali; [12]National College of Bacteriology, Bogotá; [13]Scientific Direction, SYNLAB, Bogotá; [14]Noninvasive Diagnostic Methods Unit and Heart Failure and Transplant Clinic, Fundación Cardiovascular de Colombia, Floridablanca; [15]Colombian Society of Cardiology and Cardiovascular Surgery, Bogotá. Colombia

Abstract

Introduction: *Abnormal lipid metabolism (dyslipidemia) is the main risk factor for developing cardiovascular diseases, which are the leading cause of death worldwide and in Colombia. They also generate significant resource consumption within the health system. Therefore, strategies must be designed and implemented to ensure early diagnosis and accurate cardiovascular risk assessment, along with standardized guidelines for measuring, reporting, and interpreting lipid profile results. This approach allows preventive measures to be implemented for patients with dyslipidemia or high cardiovascular risk.* **Objective:** *To develop a standardized document emphasizing the importance of lipid measurement in cardiovascular risk assessment, establishing unified criteria for laboratory reports, and defining treatment goals based on risk levels.* **Method:** *A joint initiative and collaborative effort of several scientific societies and other stakeholders involved in lipid reporting in Colombia proposed to develop a document based on available evidence and the expertise of subject matter experts. This document focuses on the importance of blood lipid measurement for cardiovascular risk assessment and the necessity of obtaining standardized reports and defining treatment targets according to the level of risk.* **Results:** *This article is the result of a multi-society effort to provide basic recommendations on the definition of the lipid profile and cardiovascular risk assessment as a necessary step for the prevention, decision-making, treatment, and follow-up of cardiovascular disease in Colombia. The need to unify analysis criteria and guidelines in laboratory lipid profile reports is emphasized to support the patients' cardiovascular risk assessment.* **Conclusions:** *Standardizing lipid profile measurement and reporting is essential to improving cardiovascular risk assessment and optimizing preventive and therapeutic strategies. This consensus represents a key step in aligning national practices with international standards to enhance patient care and reduce the burden of cardiovascular diseases in Colombia.*

Keywords: *Cardiovascular disease. Lipids. Cardiovascular risk. Laboratory reports. Lipid profile.*

***Correspondence:**
Ángel García
E-mail: angelalbertogarcia@hotmail.com

Date of reception: 30-07-2024
Date of acceptance: 29-10-2024
DOI: 10.24875/RCCARE.M24000136
Available online: 05-02-2025
Rev Colomb Cardiol. 2024;31(6):326-332
www.rccardiologia.com

Resumen

Introducción: *Las alteraciones del metabolismo lipídico (dislipidemia) son el principal factor de riesgo para el desarrollo de enfermedades cardiovasculares, que son la más importante causa de muerte en el mundo y en Colombia, y un factor que genera un importante consumo de recursos del sistema de salud. Es entonces necesario diseñar y ejecutar estrategias para asegurar un diagnóstico temprano y una evaluación acertada de riesgo cardiovascular, y contar con lineamientos estandarizados para la medición, reporte en el laboratorio e interpretación de los resultados de los perfiles lipídicos, que permitan instaurar medidas preventivas en pacientes con dislipidemia o con riesgo cardiovascular elevado.* **Objetivo:** *Desarrollar un documento estandarizado que resalte la importancia de la medición de los lípidos para la valoración del riesgo cardiovascular, estableciendo criterios unificados para los reportes de laboratorio y metas de tratamiento basadas en el nivel de riesgo.* **Método:** *Por iniciativa conjunta y esfuerzo colaborativo de varias sociedades científicas y de otros actores implicados en el reporte de los lípidos en Colombia, se propuso elaborar, con base en la evidencia disponible y la experiencia de expertos en el tema, un documento enfocado en la importancia de la medición de los lípidos en sangre para la valoración del riesgo cardiovascular y la necesidad de obtener reportes estandarizados y definir metas de tratamiento según el nivel de riesgo.* **Resultados:** *Este artículo es el resultado de un esfuerzo multisocietario, para dar recomendaciones básicas sobre la definición del perfil lipídico y la evaluación del riesgo cardiovascular como un paso necesario para la prevención, toma de decisiones, tratamiento y seguimiento de la enfermedad cardiovascular en Colombia. Se enfatiza en la necesidad de unificar los criterios de análisis y las pautas en los reportes de los perfiles lipídicos en el laboratorio para apoyar la evaluación del riesgo cardiovascular del paciente.* **Conclusiones:** *La estandarización en la medición y reporte de perfiles lipídicos es clave para mejorar la evaluación del riesgo cardiovascular y optimizar las estrategias preventivas y terapéuticas, alineando las prácticas nacionales con estándares internacionales.*

Palabras clave: *Enfermedad cardiovascular. Lípidos. Riesgo cardiovascular. Reportes laboratorio. Perfil lipídico.*

Introduction

Abnormal lipid metabolism (dyslipidemia) is the main risk factor for cardiovascular diseases (CVDs) which, in turn, are the main cause of death worldwide[1].

In Colombia, according to information from the National Department of Statistics (DANE, in Spanish), CVDs (including cerebrovascular diseases) were the first cause of mortality in 2022 (175.73 per 100,000 inhabitants), mainly due to ischemic heart disease (96.57 per 100,000 inhabitants), cerebrovascular disease (33.53 per 100,000 inhabitants) and hypertensive heart disease (21 per 100,000 inhabitants)[2]. In 2022, 100.5 out of 100,000 people in the country between the ages of 30 and 70 died from CVD (24,395 deaths)[3,4]. In 2023, ischemic heart disease continued to be the main cause of death in Colombia, with 45,465 cases and 17.2% of the total mortality, followed by cerebrovascular disease which totaled 16,946 deaths, equivalent to 6.4% of the total[5].

Furthermore, according to Central Bank of Colombia reports, a 40% increase in care costs for noncommunicable diseases (NCDs) is anticipated between 2022 and 2030, in real terms. Within the NCDs, CVDs have the highest rate of care per 100,000 inhabitants, which leads to a significant outlay of healthcare system resources to manage these diseases[6].

This is a serious public health problem in which all the sector actors (physicians, healthcare institutions, insurers, the Ministry of Health, clinical laboratories, scientific societies and patients) should act in a collaborative and coordinated fashion to prevent CVD, decrease mortality due to this group of diseases and reduce the care and social costs caused by this disease.

Strategies must be designed, executed and implemented to: a) educate the healthcare system actors, including clinical laboratories and the general population, on the risk of and need to treat dyslipidemias; b) inform them regarding the importance of early diagnosis and appropriate cardiovascular risk (CVR) assessment based on validated and standardized laboratory data; c) promote the prevention and prompt treatment of dyslipidemias; and d) have a unified national lipid level reporting model in laboratories throughout the country that reflects the CVR perspective.

Method

The Sociedad Colombiana de Cardiología [Colombian Society of Cardiology] had the initiative to develop a document based on updated evidence and the experience of experts on the topic, focused on the importance of blood lipid measurement as part of CVR

assessment, the need for standardized reporting of lipid measurements in all laboratories throughout the country, and determining treatment goals according to the level of risk. This initiative was discussed and embraced by other scientific societies who were aware of the importance of this project for Colombians' health: Sociedad Colombiana de Medicina Familiar [Colombian Society of Family Medicine] (SOCMEF), Asociación Colombiana de Medicina Interna [Colombian Internal Medicine Association] (ACMI), Asociación Colombiana de Medicina Vascular [Colombian Vascular Medicine Association] (ACMV), Colegio Nacional de Bacteriología [National College of Bacteriologists] (CNB), Asociación Colombiana de Gerontología y Geriatría [Colombian Gerontology and Geriatrics Association] (ACCG) and Asociación Colombiana de Endocrinología, Diabetes y Metabolismo [Colombian Endocrinology, Diabetes and Metabolism Association] (ACE).

Discussion

Reducing LDL-C levels is an effective way to reduce cardiovascular risk

The causal role of low-density lipoprotein cholesterol (LDL-C) in the development of CVD has been proven beyond all doubt through genetic and observational studies and multiple clinical trials[7,8]. Early and prolonged LDL-C reduction has proven to be associated with a lower risk of CVD, which is proportional to the magnitude of LDL-C reduction, regardless of the means or method of reduction[9,10].

The guidelines for managing dyslipidemia in different countries and geographical regions (European Society of Cardiology/European Atherosclerosis Society [ESC/EAS] 2019, American Heart Association/American College of Cardiology [AHA/ACC] 2018, Colombian guidelines and Mexican guidelines, among others) have suggested treatment goals mainly based on LDL-C and non-high-density lipoprotein cholesterol (non-HDL-C) levels, according to the CVR profile, presence of comorbidities or manifest CVD[11-16].

This situation poses interesting challenges. First, challenges derived from the need to use combined and potent interventions to achieve the necessary reductions to ensure achievement of the treatment goals and maximize the benefit of lipid fraction reductions, while trying to maintain high treatment adherence and persistence to minimize the logistical, administrative and economic impact on healthcare systems.

There are also challenges associated with the need to reevaluate how clinical laboratories report to the medical staff, especially in primary care, and the mistaken concept of "normal" population values as well as interpreting them without adjusting for the different CVR profiles. Finally, in Colombia, reporting has often been based on outdated guidelines described more than two decades ago in the ATP III guidelines[17].

The importance of standardized laboratory reporting for appropriate cardiovascular risk assessment

Until the proposed objectives related to the achievement of treatment goals and optimization of the benefit in lipid fraction reduction become a reality, valid and accurate diagnoses of patients with dyslipidemia must be ensured, along with guaranteeing that lipid levels are a true CVR marker. With this aim, clinical biochemistry laboratories should be an important ally for patients, physicians and the healthcare system. This requires implementing changes to assist clinicians in a proper clinical/chemical interpretation of the laboratory reports and, thus, enable them to better estimate the patients' CVR and subsequently determine the treatment they require.

Although there is a consensus on the lipid-lowering treatment objectives according to CVR, laboratory reports often present elevated values (that would be considered to indicate the need for cardiovascular prevention) as normal, and values that would be ideal in terms of cardiovascular prevention as low. This information can cause errors that lead to underestimating the CVR, omitting treatment in patients who need it or reducing treatment in patients who need higher doses to achieve the required levels.

The great advances achieved by clinical biochemistry laboratories in regard to the quality of their analytical processes are evident. However, so far, the comparability and concordance of different clinical laboratories' results cannot be ensured. In this regard, it is important to consider that these analyses have a high rate of biological variability. To have concordant results between different laboratories, the results would have to be compared using the same sample from the same patient and processed with the same technique, since results may vary if different samples are used.

The initiatives aimed at improving harmonization (in techniques, reports and interpretation) of the laboratory results are very important in diagnosing dyslipidemia and predicting CVR, through designing a

Table 1. Lipid measurement as part of CVR assessment

A complete systematic CVR assessment is recommended in people with any major CVR factor (e.g., family history of premature CVD, smoking, hypertension, diabetes mellitus, dyslipidemia, chronic kidney disease, obesity or comorbidities that would increase the risk of CVD)[23,24]
The use of a CVR estimation scale recently validated and adjusted in Colombia (e.g. ASCVD) is recommended for evaluating CVR in adults diagnosed with dyslipidemia in Colombia[25]
Lipid profiles should be ordered as part of the assessment of apparently healthy people, those who are believed to be at risk of CVD (smoking, obesity, familial hypercholesterolemia, sedentarism, hypertension, diabetes), have first-degree relatives with heart disease at an early age, and high-risk patients (with a history of CVD)[23]
Measurement of TC, TG, and HDL-C levels and LDL-C calculation are recommended as a dyslipidemia screening strategy in adults. Lp (a) should be measured in all patients at least once in their lifetime[25] To calculate LDL-C, the TG level should be < 400 mg/dl. An equation like the Friedewald, Sampson or other formulas should be used*. However, if available, direct LDL-C measurement is preferable. It cannot be estimated in patients with TG < 400 mg/dl, and direct LDL-C measurement is required in these cases Lp (a) should preferably be measured in nanomoles/liter (note: there is no conversion formula to mg/dl)
In Colombia, dyslipidemia screening is recommended beginning at 18 years of age[25] Screening should be done every five years. People with special conditions and elevated CVR (clinical evidence of atherosclerosis, abdominal aortic aneurysm, family history of premature CVD [men < 55 years, women < 65 years], a family history of dyslipidemia, clinical signs of familial hypercholesterolemia, adiposity-based chronic disease [BMI ≥ 30], diabetes, hypertension, smoking, CKD [eGFR ≤ 60 ml/min/1.73 m^2], autoimmune inflammatory disease [rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis, psoriatic arthritis, inflammatory bowel disease], HIV infection, erectile dysfunction, preeclampsia) should undergo yearly screening After age 40, screening should be yearly
*Equations: Friedewald equation: LDL-C=TC – HDL-C – (TG/5) Sampson equation: LDL-C=TC/0.948 – HDL-C/0.971 – [TG/0.56 + (TG x non-HDL-C)/2.140 – (TG2/16.100) - 9.44] Martin/Hopkins equation: integrates an individualized factor in the denominator to take heterogeneity of the TG/VLDL-C ratio into account

TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; VLDL-C: very low-density cholesterol; DM: diabetes mellitus; CVD: cardiovascular disease; FH: familial hypercholesterolemia; BMI: body mass index; Lp (a): lipoprotein (a); CVR: cardiovascular risk; eGFR: estimated glomerular filtration rate; TG: triglycerides.

laboratory test profile with standardized and harmonized markers (able to achieve the same result and the same interpretation regardless of the analytical process used, the units, and the reference interval applied). If this were achieved, clinical laboratory results could be compared, regardless of where and when the tests were taken, enabling safe and effective clinical decision-making based on the patients' calculated CVR[18-20].

Blood lipid measurement as part of cardiovascular risk assessment and treatment follow up

Tables 1 and 2 list recommendations for measuring blood lipids as part of the CVR assessment and treatment follow-up. The information has been obtained from different sources that address the topic[21-23] of treatment goals according to CVR level.

These tables were constructed based on information from an article that provides a detailed analysis of these goals: "Documento de consenso para la determinación e informe del perfil lipídico en laboratorios clínicos españoles. ¿Qué parámetros debe incluir un perfil lipídico básico?"[23] [Consensus document for determining and reporting lipid profiles in Spanish clinical laboratories. What parameters should a basic lipid profile include?].

Important factors in determining, reporting and evaluating patients' lipid profiles[23]

- Lipid measurement is not recommended in the midst of an acute non-cardiovascular inflammatory process.
- It is recommended that lipid levels be drawn within 24 hours after an acute arteriosclerotic ischemic process.
- Fasting is not routinely required for determining the lipid profile in the initial risk assessment. A lack of fasting may alter only triglycerides (TGs) by 20%. If the TG concentration is ≥ 4.5 mmol/l (≥ 398 mg/dl), a second, fasting measurement is advisable to confirm.

Table 2. Lipid measurement as part of treatment follow up

Before beginning treatment with lipid-lowering drugs, lipid fractions should be measured at least once, except when a cardiovascular event has occurred, and in patients with very high risk and an indication for immediate treatment[23,24]
For people who begin pharmacological or nonpharmacological treatment, the frequency of follow-up will be determined by the risk profile and treatment goals.
Lipid fraction follow-up is recommended every six weeks until the proposed treatment goals are reached[25]
Annual lipid fraction follow-up is recommended for patients who have reached the treatment goals, or less frequently if the patients have certain conditions (defined in the previous question)
At each office visit, education should be provided on adopting healthy lifestyles, exercise and proper nutrition
The lipid fractions recommended for measurement are TC, HDL-C, TG and direct LDL-C
The proposed treatment goals will be determined according to the patient's risk category

TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol.

Table 3. Recommended lipid levels in adults according to the European Societies of Cardiology, Arteriosclerosis and Laboratory Medicine

Parameter	Recommended level in adults
TC	< 200 mg/dl (5.17 mmol/l)
HDL-C	> 50 mg/dl women (1.29 mmol/l) > 40 mg/dl men (1.03 mmol/l)
Non-HDL-C Secondary prevention and very high CVR High CVR Moderate CVR	Recommended levels according to CVR < 85 mg/dl (< 2.2 mmol/l) < 100 mg/dl (< 2.6 mmol/l) < 130 mg/dl (< 3.4 mmol/l)
LDL-C Secondary prevention and very high CVR High CVR Moderate CVR Low CVR	Recommended levels according to CVR < 55 mg/dl (< 1.4 mmol/l) < 70 mg/dl (< 1.8 mmol/l) < 100 mg/dl (< 2.6 mmol/l) < 116 mg/dl (< 3 mmol/l)
Triglycerides	TG < 150 mg/dl, fasting (< 1.69 mmol/l) TG < 175 mg/dl, non-fasting (< 1.97 mmol/l)
Remnant-like particle cholesterol*	< 30 mg/dl (0.78 mmol/l), fasting < 35 mg/dl (0.91 mmol/l), non-fasting
ApoB Secondary prevention and very high CVR High CVR Moderate CVR	Recommended levels according to CVR < 65 mg/dl (1.27 mol/l) < 80 mg/dl (1.56 mol/l) < 100 mg/dl (1.95 mol/l)
Lp (a)	< 50 mg/dl (< 105 nmol/l)

*Remnant-like particle cholesterol: the cholesterol contained in VLDL, intermediate-density lipoprotein (IDL) and remnant chylomicrons. It can be calculated simply by subtracting LDL-C and HDL-C from total cholesterol.
Apo: apolipoprotein; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; TC: total cholesterol; Lp (a): lipoprotein (a); CVR: cardiovascular risk; VLDL: very low-density lipoprotein.
Adapted from Nordestgaard et al., 2020[28], Wilson et al., 2021[29] and Borén et al., 2020[30].

Table 4. Recommended warnings for the computer system/laboratory report

Parameter	Critical value	Warning
TC	310 mg/dl	High CVR patient
TG	TG > 880 mg/dl	Severe hypertriglyceridemia with a risk for acute pancreatitis
LDL-C adults	> 190 mg/dl	Consider heterozygous familial hypercholesterolemia
LDL-C adults	> 500 mg/dl	Consider homozygous familial hypercholesterolemia
Atherogenic lipid triad	If: TG > 150 mg/dl and HDL-C < 30 mg/dl, LDL-C/Apo B < 1.3 or TG/HDL-C > 2	Lipid triad pointing to atherogenic dyslipidemia with a very high vascular risk
Lp (a)	> 120 mg/dl	Very high risk of atherosclerotic cardiovascular disease and aortic valve stenosis
ApoA-1	< 10 mg/dl	Assess for hypoalphalipoproteinemia
ApoB	< 10 mg/dl	Assess for hypobetalipoproteinemia

Apo: apolipoprotein; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; TC: total cholesterol; Lp (a): lipoprotein (a); CVR: cardiovascular risk; VLDL: very low-density lipoprotein.
The message that should appear on the report when a warning is communicated is directed to the patient: "This value suggests that you have an elevated cardiovascular risk. We recommend that you see your physician."

– The clinical laboratory should report the analytical techniques or unit modifications used, to correctly interpret the results.
– The clinical laboratory is key for estimating the CVR of patients with dyslipidemia.
– It is important to establish differentiated reference values for pediatrics.

Table 5. Lipid targets according to CVR

For very high CVR, a 50% reduction in the baseline level is recommended, with a target LDL-C < 1.4 mmol/l (< 55 mg/dl) For high CVR, a 50% reduction in the baseline level is recommended, with a target LDL-C < 1.8 mmol/l (< 70 mg/dl) For moderate CVR, a target LDL-C < 2.6 mmol/l (< 100 mg/dl) should be established For low CVR, a target LDL-C < 3.0 mmol/l (< 116 mg/dl) can be considered
In whom should familial hypercholesterolemia be suspected? People with very high LDL-C (adults > 5 mmol/l [190 mg/dl]; children > 4 mmol/l [150 mg/dl]) and triglycerides generally within normal limits Atherosclerotic CVD before the age of 55 (men) or 60 (women) Family history: a relative with premature CVD; first-degree relatives with familial hypercholesterolemia The presence of tendinous xanthomas and/or arcus cornealis When HoFH is suspected in children, testing is recommended beginning at age five or younger

LDL-C: low-density lipoprotein cholesterol; CVD: cardiovascular disease; FH: familial hypercholesterolemia; HoFH: homozygous familial hypercholesterolemia; CVR: cardiovascular risk.
Adapted from Visseren et al., 2021[7], Arrobas et al., 2023[23] and Fundación Hipercolesterolemia Familiar[26].

- It is advisable for lipid measurements to be referenced to the desirable values in terms of cardiovascular risk and prevention (Table 3)[7,27].
- Laboratories should have a warning system included in laboratory reports when critical values are reported (Table 4).
- None of the equations perfectly calculates LDL-C levels. Direct measurement is recommended and, when this is not available, calculations using the Friedewald or Sampson formulas, exercising caution in the interpretation and accuracy of the calculation with LDL-C levels < 100 mg/dl or TG levels > 200 mg/dl.

Table 5 contains an example of how a report was previously made with "normal" values and how a report should be made according to this article (with the adjustments mentioned).

Conclusions

Considering the work that has been carried out by the different healthcare system actors (including the Ministry of Health, scientific societies, insurers, healthcare providers, pharmaceutical industry and patients) over the last 30 years to prevent the incidence of CVD in Colombia, and the importance of appropriate reporting and interpretation of the lipid profile in terms of CVR to achieve this goal, the discussion, dissemination and implementation of the recommendations provided in this document are vitally important for the participants in this consensus, whose goal is to have a positive effect on CVDs and their medical and economic consequences.

This document was developed as part of a multi-societal collaborative effort and provides basic recommendations for establishing the lipid profile and assessing CVR in order to guide physicians in CVD prevention, decision-making, treatment and follow-up. We emphasize the need to standardize laboratory analysis criteria and reporting, as well as employ unified standards for evaluating patient risk according to the lipid profiles in laboratory reports.

Funding

This project was funded by Sociedad Colombiana de Cardiología y Cirugía Cardiovascular through a research grant from Novartis.

Conflicts of interest

A. Garcia has provided consulting services, acted as an expert witness, and received compensation for the preparing manuscripts and delivering educational presentations. He has also received stock or stock options, as well as reimbursements for travel expenses, lodging and attendance at meetings not directly related to the activities mentioned. These activities have been conducted for various entities and advisory committees in areas related to the topic addressed in the present document. K. Restrepo has received fees for conferences from Sanofi, AstraZeneca, Merck, Boehringer. J.A. Rodríguez has received compensation for lectures and educational presentations from Novartis and Amgen. I.L. Mojica received support for airline tickets to attend SCC and Novartis academic events (Alianza ATHERO). We also declare that M.I. Vélez, J. Melo, J. Cabrera, J. Arango and H. Miranda have no conflicts of interest with regard to the present article, nor do they have financial relationships to declare.

However, none of the previously mentioned activities directly affects the results of this study or causes a conflict of interest with them.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The study does not involve patient's personal information, nor does it require ethical approval. The SAGER guidelines do not apply.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

References

1. Alloubani A, Nimer R, Samara R. Relationship between hyperlipidemia, cardiovascular disease and stroke: a systematic review. Curr Cardiol Rev. 2021;17(6):e051121189015.
2. Minsalud conmemora el día mundial del corazón [Internet]. Bogotá, Colombia: Ministerio de Salud y Protección Social de Colombia; 2023 [acceso: 9 julio 2024]. Disponible en: https://www.minsalud.gov.co/Paginas/Minsalud-conmemora-el-dia-mundial-del-Corazon.aspx
3. Conozca las 10 causas de muerte más comunes durante 2023 en Colombia [Internet]. Infobae; 24 sept 2023 [acceso: 9 julio 2024]. Disponible en: https://www.infobae.com/colombia/2023/09/24/conozca-las-10-causas-de-muerte-mas-comunes-durante-2023-en-colombia/#:~:text=Enfermedades%20isqu%C3%A9micas%20del%20coraz%C3%B3n%3A%20(16,%2C8%25%20en%20mujeres)
4. DANE. Estadísticas vitales: Informe técnico, primer trimestre de 2023 n.d. https://www.dane.gov.co/files/operaciones/EEVV/pres-EEVV-ITrim2023.pdf (accessed July 17, 2024).
5. DANE. Estadísticas vitales. Nacimientos y defunciones [Internet]. Colombia: DANE; junio de 2023 [acceso: 11 jul 2024]. Disponible en: https://www.dane.gov.co/files/operaciones/EEVV/cp-EEVV-IV-trim2023.pdf
6. Banco de la República de Colombia. Evolución y carga financiera de las enfermedades crónicas no transmisibles en Colombia: 2010-2021 [Internet]. Colombia: Banco de la República [acceso: 15 jul 2024]. Disponible en: https://www.banrep.gov.co/es/evolucion-carga-financiera-enfermedades-cronicas-no-transmisibles-colombia-2010-2021
7. Visseren FLJ, Mach F, Smulders YM, Carballo D, Koskinas KC, Bäck M, et al. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice: Developed by the Task Force for cardiovascular disease prevention in clinical practice with representatives of the European Society of Cardiology and 12 medical societies with the special contribution of the European Association of Preventive Cardiology (EAPC). Rev Esp Cardiol (Engl Ed). 2022;75(5):429.
8. Herink M, Ito MK. Medication induced changes in lipid and lipoproteins. En: Feingold KR, Anawalt B, Blackman MR, Boyce A, Chrousos G, Corpas E, editores. Endotext [Internet]. South Dartmouth (MA): MDText.com; 2000. PMID: 26561699.
9. Bays HE, Jones PH, Orringer CE, Brown WV, Jacobson TA. National Lipid Association annual summary of clinical lipidology 2016. J Clin Lipidol. 2016;10(1 Suppl):S1-S43.
10. Khovidhunkit W, Kim MS, Memon RA, Shigenaga JK, Moser AH, Feingold K. Effects of infection and inflammation on lipid and lipoprotein metabolism: mechanisms and consequences to the host. J Lipid Res. 2004;45:1169-96.
11. Pavía-López AA, Alcocer-Gamba MA, Ruiz-Gastelum ED, Mayorga-Butrón JL, Mehta R, Díaz-Aragón FA. Guía de práctica clínica mexicana para el diagnóstico y tratamiento de las dislipidemias y enfermedad cardiovascular aterosclerótica. Arch Cardiol Mex. 2022;92:1-62.
12. Wilson PWF, Polonsky TS, Miedema MD, Khera A, Kosinski AS, Kuvin JT. Systematic Review for the 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the management of blood cholesterol: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2019;73(24):3210-27.
13. Mach F, Colin B, Alberico LC, Konstantino CK, Manuela C, Lina. Guía ESC/EAS 2019 sobre el tratamiento de las dislipemias: modificación de los lípidos para reducir el riesgo cardiovascular. Rev Esp Cardiol. 2020;73(5):403.e1-403.e70.
14. Barrios V, Escobar C, Gamarra J, Obaya JC, Pallaré V, Barrios V, et al. Comentarios a la guía ESC/EAS 2019 sobre el tratamiento de las dislipemias. Rev Esp Cardiol. 2020;73(5):348-53.
15. Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the management of blood cholesterol: A report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines. Circulation. 2019 Jun 18;139(25):e1182-e1186. doi: 10.1161/CIR.0000000000000698. Erratum in: Circulation. 2023 Aug 15;148(7):e5.16. Vargas-Uricoechea H, Ruiz AJ, Gómez EA, Román-González A, Castillo J, Merchán A, et al. Recomendaciones del panel de expertos sobre la fisiopatología, diagnóstico y tratamiento de las dislipidemias en la población adulta. Rev Colomb Endocrinol Diabetes Metab. 2020;7(Supl 1).
17. Rubio MA, Moreno C, Cabrerizo L. Guías para el tratamiento de las dislipemias en el adulto: Adult Treatment Panel III (ATP-III). Endocrinol Nutr. 2004;51:254-65.
18. López GI, Schreier LE. Armonización del estudio de lípidos en el laboratorio clínico. Acta Bioquim Clin Latinoam. 2019;53:459-68.
19. Plebani M. Quality and future of clinical laboratories: the Vico's whole cyclical theory of the recurring cycles. Clin Chem Lab Med. 2018;56:901-8.
20. Plebani M. Harmonization in laboratory medicine: requests, samples, measurements and reports. Crit Rev Clin Lab Sci. 2016;53:184-96.
21. Visseren FLJ, Mach F, Smulders YM, Carballo D, Koskinas KC, Bäck M, et al. Guía ESC 2021 sobre la prevención de la enfermedad cardiovascular en la práctica clínica, con la contribución especial de la European Association of Preventive Cardiology (EAPC). Rev Esp Cardiol 2022;75.
22. Armario P, Brotons C, Elosua R, Leciñana M, Castro A, Clarà A. Statement of the Spanish Interdisciplinary Vascular Prevention Committee on the updated European Cardiovascular Prevention Guidelines. Clin Investig Arterioscler. 2021;33:85-107.
23. Arrobas VT, Guijarro C, Campuzano RR; en representación del Grupo Multidisciplinar de Trabajo de Lípidos y Riesgo Vascular. Documento de consenso para la determinación e informe del perfil lipídico en laboratorios clínicos españoles. ¿Qué parámetros debe incluir un perfil lipídico básico? Clin Investig Arterioscler. 2023;35:91-100.
24. Wright IS. Correct levels of serum cholesterol: average vs normal vs optimal. JAMA. 1976;236:261-2.
25. Consenso colombiano para el Diagnóstico y tratamiento de dislipidemias en adultos. 2024. Rev Colomb Cardiol. 2024;31(Supl4) 2-66.
26. Fundación Hipercolesterolemia Familiar. Diagnóstico clínico y genético de la HF [Internet]. Fundación Hipercolesterolemia Familiar. Acceso: Junio 2024. Disponible en: https://www.colesterolfamiliar.org/hipercolesterolemia-familiar/diagnostico-clinico-y-genetico-de-la-hf
27. Pedro-Botet J, Rodríguez-Padial L, Brotons C, Esteban-Salán M, García-Lerín A, Pintó X. Homogeneización de los valores del perfil lipídico. Clin Investig Arterioscler. 2018;30:36-48.
28. Nordestgaard BG, Langlois MR, Langsted A, Chapman MJ, Aakre KM, Baum H. Quantifying atherogenic lipoproteins for lipid-lowering strategies: Consensus-based recommendations from EAS and EFLM. Atherosclerosis. 2020;294:46-61.
29. Wilson PWF, Jacobson TA, Martin SS, Jackson EJ, Le NA, Davidson M. Lipid measurements in the management of cardiovascular diseases: Practical recommendations a scientific statement from the national lipid association writing group. J Clin Lipidol. 2021;15:629-48.
30. Borén J, Chapman MJ, Krauss RM, Packard CJ, Bentzon JF, Binder C. Low-density lipoproteins cause atherosclerotic cardiovascular disease: pathophysiological, genetic, and therapeutic insights: A consensus statement from the European Atherosclerosis Society Consensus Panel. Eur Heart J. 2020;41:2313-30.

Revista Colombiana de Cardiología
Órgano oficial de la Asociación Sociedad Colombiana de Cardiología & Cirugía Cardiovascular
Permanyer

Check for updates

ORIGINAL ARTICLE

Cardiovascular risk factors in neuropsychiatric patients with arterial hypertension in the outpatient department of a specialized hospital

Factores de riesgo cardiovascular en pacientes neuropsiquiátricos con hipertensión arterial en un servicio ambulatorio de un hospital especializado

Francisco Barrera-Guarderas[1,2] and Carlos Vásquez-Salgado[1]*

[1]Internal Medicine Service, Hospital Psiquiátrico Julio Endara; [2]Faculty of Medicine, Pontificia Universidad Católica del Ecuador. Quito, Ecuador

Abstract

Introduction: *Psychiatric disorders constitute a group of diseases with high morbidity and mortality that affect the quality of life. Cardiovascular risk is higher in these conditions.* **Objective:** *To associate psychiatric disorders with cardiovascular risk factors in individuals with hypertension being treated as outpatients at a mental health hospital.* **Method:** *An observational study conducted in 2019 among outpatients with hypertension and psychiatric disorders at a specialized hospital in Quito, Ecuador. Measures of central tendency and association tests with a 95% confidence interval (CI) were used.* **Results:** *The average age was 56.48 (± 13.51) years, with a predominance of women. There was a tendency towards obesity (BMI 31.60 ± 5.51), hypertriglyceridemia (183.96 ± 97.63 mg/dl), and decreased high-density lipoprotein cholesterol (HDL-C) (38.4 ± 18.53 mg/dl). Psychiatric diagnoses included mood disorders (44.8%), organic disorders (26.7%), schizophrenia (15.2%), and bipolar disorder (13.3%). Six percent of the patients had high cardiovascular risk, although it was not significant; antipsychotics had no statistical impact.* **Conclusions:** *Comprehensive evaluation and treatment of patients with psychiatric disorders are imperative to reduce cardiovascular risk, even when they cannot be identified using traditional risk scales. Therefore, other approaches considering patient-specific characteristics, such as medication use and additional risk factors, are recommended.*

Keywords: *Hypertension. Cardiovascular risk. Bipolar disorder. Schizophrenia. Emerging risk factors.*

Resumen

Introducción: *Las enfermedades psiquiátricas constituyen un grupo de enfermedades con alta morbimortalidad que afectan a la calidad de vida. El riesgo cardiovascular (RCV) está aumentado en estas.* **Objetivo:** *Asociar enfermedades psiquiátricas con factores y RCV en personas con hipertensión arterial en la consulta ambulatoria de un hospital de salud mental.* **Método:** *Estudio observacional, en pacientes con hipertensión arterial y enfermedad psiquiátrica, ambulatorios, en hospital especializado en Quito (Ecuador) durante el año 2019. Se utilizaron medidas de tendencia central y pruebas de asociación, con IC95%.* **Resultados:** *Edad promedio 56.48 (± 13.51) años, predominan las mujeres, tendencia a obesidad (IMC 31.60 ± 5.51), hipertrigliceridemia (183.96 ± 97.63 mg/dl) y c-HDL disminuido (38.4 ± 18.53 mg/dl). Los diagnósticos psiquiátricos*

***Correspondence:**
Francisco Barrera-Guarderas
E-mail: jfbarrera@puce.edu.ec

Date of reception: 05-03-2024
Date of acceptance: 04-10-2024
DOI: 10.24875/RCCARE.M24000127
Available online: 05-02-2025
Rev Colomb Cardiol. 2024;31(6):333-340
www.rccardiologia.com

son el trastorno del humor (44.8%), trastornos orgánicos (26.7%), esquizofrenia (15.2%) y trastorno bipolar (13.3%). El 6% de los pacientes tienen RCV elevado, no significativo, los antipsicóticos no tuvieron impacto estadístico. **Conclusiones:** *Es imperativa la evaluación y el tratamiento integral de pacientes con enfermedad psiquiátrica para disminuir el RCV aunque no puedan ser identificables con escalas de riesgo clásicas, por lo que se recomendaría otras tomando en cuenta particularidades del paciente, como uso de medicamentos y factores de riesgo adicionales.*

Palabras clave: *Hipertensión. Riesgo cardiovascular. Trastorno bipolar. Esquizofrenia. Factores de riesgo emergentes.*

Introduction

Noncommunicable diseases are global public health problems, and the World Health Organization has prioritized four conditions: chronic obstructive pulmonary disease, diabetes mellitus (DM), hypertension (HTN) and cancer. Hypertension is the main cause of premature death worldwide. In 2020, there were an estimated 1.13 billion hypertensive people, with one in five patients reported to have adequate control[1]. In Ecuador, there was an estimated 19.8% prevalence in 2018, according to the ENSANUT survey[2].

Globally, the approximate prevalence of schizophrenia is 1.5%, with 1% for bipolar disorder and 12.9% for mood disorders (depression, anxiety, etc.)[3,4].

The literature reports several mechanisms through which patients with schizophrenia and bipolar disorder can develop HTN. First, those related to elevated cortisol levels, autonomic dysfunction, nervous system disorders, inflammation, lipid abnormalities, oxidative stress and increased platelet reactivity; and second, those with shared cardiovascular risk (CVR) factors like low birth weight, prematurity and maternal malnutrition, among others[5].

In patients with mental illness, situations like late detection of signs and symptoms of HTN, difficulties in implementing prevention strategies like lifestyle changes, lack of adherence to antihypertensive treatment, associated metabolic comorbidities (DM, obesity, metabolic syndrome, hypothyroidism), a significant social burden and increased healthcare costs are risk factors that determine increased mortality[6-8].

Likewise, HTN, drug interactions and side effects can cause psychiatric disorders and make it harder to manage comorbidities. Furthermore, the sympathetic nervous system is overstimulated, which is a common pathway between HTN and several anxiety spectrum disorders. Finally, psychological stress and diagnosed mental illness serve as predictive factors for HTN[9].

All of the above indicates the two-way relationship between HTN and mental health problems.

The objective of this paper is to identify factors leading to the onset of metabolic diseases and their association with the different diseases treated at a specialized mental health hospital, in a group of patients diagnosed with HTN and followed as outpatients.

Method

Hospital Psiquiátrico Julio Endara is a specialized healthcare facility for mental health illnesses in the metropolitan area of Quito, Ecuador. It is run by the Ecuador Ministry of Public Health and offers laboratory tests, complementary tests and medications free of charge. It offers healthcare services for people who do not have any other way of accessing the healthcare system, predominantly those with limited resources.

Study design

A cross-sectional analytical observational study was carried out in the internal medicine department of a specialized mental health facility that provides medical care for patients with HTN. A statistical analysis of the data was done using the IBM SPSS Statistics (version 23) tool. The characteristics were analyzed using frequency and measures of central tendency and dispersion. The difference in means was determined using Student's t test (for parametric variables), the Mann-Whitney U test (for nonparametric variables) and the χ^2 test (for categorical variables); ANOVA was also run for several groups. A 95% significance level was used.

Procedures

As one of the departments of this mental health hospital, the Internal Medicine Clinic offers comprehensive care focused on the growing number of patients with HTN. In addition, this program incorporates the current national and international clinical practice guidelines for hypertension. The following criteria were used to select the patients: patients over the age of 18, a diagnosis of primary HTN according to the seventh Joint National Committee report (JNC7) criteria, at least two ambulatory visits (including laboratory tests) recorded during

2019, and a definitive diagnosis of concomitant psychiatric illness. The exclusion criteria were as follows: pregnant patients, secondary HTN, chronic corticosteroid use, and no definitive diagnosis of concomitant psychiatric illness.

The individuals in the study had to have an initial visit recorded, consisting of an analysis of the history of the disease, its course, the pillars of treatment to be followed by the patient and the initial recommendations. The patients had to have at least two laboratory reports per year and within the last year after 2020. The laboratory tests included a complete blood count, glucose level, and kidney, liver and lipid panels. These were measured with a KROMA 150 chemistry analyzer. Systolic blood pressure, diastolic blood pressure and body mass index (BMI) were determined based on an average of all the office visits recorded.

Results

There was a predominance of women (56.1%, n = 59). The group of patients was in their fifth decade of life, with anthropometric measurements tending toward class I obesity in the women. The blood counts did not show anemia or a systemic inflammatory response. Mean platelet volume was significantly increased in women. Total cholesterol and high-density lipoprotein cholesterol (HDL-C) were lower in women. Finally, kidney function was not abnormal, but men had a lower filtration rate.

Altogether, 44.8% of the patients had a psychiatric diagnosis classified as a mood disorder, with all types of schizophrenia accounting for 15.2% of the sample and bipolar spectrum disorders for 13.3%. The remaining subjects in the sample (26.7%) had a psychiatric illness which was not classified within the previously mentioned groups (mental illness due to brain injury or dysfunction, cognitive impairment, etc.) (Table 1).

Patients diagnosed with schizophrenia had the highest BMI in the study group. The blood tests are shown for the different psychiatric diagnosis groups; kidney function and blood glucose levels were within normal limits in this sample.

All groups showed some degree of dyslipidemia, which was more pronounced in the mood disorders group, with elevated total cholesterol and low-density lipoprotein cholesterol (LDL-C) levels and lower HDL-C levels than the rest of the groups, which are identified as CVR factors.

The triglyceride level was higher in the group of patients with schizophrenia (Table 2).

The most significant abnormalities in table 2 are the elevated neutrophil-lymphocyte ratio and leukocyte-glucose index in schizophrenia and bipolar disorders, respectively, which were not found in the other study groups. The average total and LDL cholesterol were above normal in the mood disorders group, and the average triglyceride level was above normal in all the study groups.

The average kidney function was not abnormal in any group and, after excluding diabetic patients, the glucose levels were within normal limits (Table 2).

In the study sample, the relationship between the use of antipsychotics (risperidone, quetiapine, haloperidol, clonidine) and CVR was not statistically significant.

When the CVR was calculated according to the American Heart Association (AHA) criteria, 94% of the patients were found to have moderate or low risk. An ANOVA test was run, with no differences between the groups, considering patients between 40 and 70 years old (Table 4 and Fig. 1).

Discussion

Major psychiatric disorders, schizophrenia and bipolar disorder, and organic disorders manifest with abnormal behavior, and therefore are assessed from a mental health perspective. Despite having a low prevalence, the burden of disease, associated HTN and CVR increase their clinical, social and economic complexity.

Life expectancy

More common disorders, such as mood disorders, are much more prevalent and cause high morbidity and mortality. They are sometimes masked by multiple factors, whether patients not seeking care due to the stigma of a psychiatric diagnosis or, on the other hand, associated clinical morbidities not being actively sought in psychiatric assessments without a multidisciplinary focus[10].

Sleep disorders, a prevalent symptom in these diseases, are directly related to intrinsic blood pressure regulation. As reported by Kato et al., sleep deprivation increases resting blood pressure[11]. Circadian rhythm disruptions are found in schizophrenia due to dopaminergic pathway alterations, as well as abnormalities in genes related to the circadian rhythm: *CLOCK* and *ARNTL*, mentioned by Orellana et al., leading to the previously stated effect[10].

This is not the only pathophysiological connection: depression alters sympathetic and parasympathetic tone and heart rate variability[11].

Table 1. Disease and laboratory characteristics, by sex

Characteristics	Total	Female (n = 59)	Male (n = 46)	Student's t/χ^2	p*
	Mean (SD)	Mean (SD)	Mean (SD)		
Age	56.48 (± 13.51)	58.35 (± 11.65)	54.87 (± 15.38)	–1.618	0.109
BMI	31.60 (± 5.51)	33.10 (± 5.15)	29.68 (± 5.42)	–3.301	0.001
Hemoglobin	15.40 (± 1.48)	15.08 (± 1.43)	15.82 (± 1.46)	2.579	0.011
Hematocrit	44.04 (± 5.16)	43.22 (± 5.41)	45.09 (± 4.68)	1.863	0.065
White blood cells	6,876. 28 (± 1,507.22)	6,804.74 (± 1,516.90)	6,968.04 (± 1,506.37)	0.548	0.584
Neutrophils	4,016.63 (± 1,306.03)	3,938.27 (± 1,270.06)	4,115.43 (± 1,357.60)	0.685	0.495
Lymphocytes	2,482.98 (± 671.99)	2,597.41 (± 750.14)	2,338.69 (± 531.67)	–1.977	0.051
Neutrophil-lymphocyte ratio	1.756 (± 0.89)	1.664 (± 0.907)	1.872 (± 0.876)	1.177	0.242
Leukocyte-glucose index	650.67 (± 176.39)	639.395 (± 173.306)	665.14 (± 181.167)	0.740	0.461
Platelets	274.08 (± 79.39)	271.36 (± 66.78)	277.52 (± 93.57)	0.391	0.696
MPV	7.37 (± 1.10)	7.659 (± 1.291)	7.00 (± 0.642)	–3.139	0.002
Total cholesterol	199.63 (± 44.95)	208.49 (± 46.51)	188.26 (± 40.58)	–2.327	0.021
HDL-C	38.40 (± 18.53)	37.81 (± 9.08)	39.15 (± 26.09)	0.3663	0.715
LDL-C	124.39 (± 40.28)	130.53 (± 43.18)	116.65 (± 35.24)	–1.762	0.081
Triglycerides	183.96 (± 97.63)	174.74 (± 74.14)	195.79 (± 121.44)	1.095	0.276
Urea	29.52 (± 8.64)	30.14 (± 8.72)	28.72 (± 8.57)	– 0.829	0.429
Creatinine	0.87 (± 0.17)	0.81 (± 0.15)	0.94 (± 0.16)	4.100	0.0001
Uric acid	5.05 (± 1.29)	4.73 (± 1.11)	5.41 (± 1.40)	2.458	0.016
Schizophrenia	16 (15.2%)	5 (8.5%) (68.8%)	11 (23.9%) (31.3%)	18.319	0.001
Bipolar disorder	14 (13.3%)	10 (16.9%) (71.4%)	4 (8.7%) (28.6%)	-	-
Mood disorder	47 (44.8%)	35 (59.3%) (74.5%)	12 (26.1%) (25.5%)	-	-
Other	28 (26.7%)	9 (15.3%) (32.1%)	19 (41.3%) (67.9%)	-	-

*Statistically significant: $p < 0.05$.
BMI: body mass index; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; MPV: mean platelet volume; SD: standard deviation.

A subclinical inflammatory process with increased proinflammatory cytokines like interleukin (IL)-1, IL-6, tumor necrosis factor alpha and ultrasensitive C-reactive protein serves as a common pathway for developing a major psychiatric disorder, along with insulin resistance and the subsequent onset of metabolic syndrome, with HTN as one of its components. This event occurs even without exposure to antipsychotic treatment[12,13] Our findings note an elevation in the neutrophil-lymphocyte ratio and leukocyte-glucose index (both indirect proinflammatory markers) in patients with schizophrenia and bipolar disorder, respectively. These values cannot be explained by another comorbidity like DM, as this was excluded from the study; however, insulin resistance cannot be ruled out, as serum insulin levels to calculate the homeostatic model assessment (HOMA) index are not routinely ordered in the outpatient laboratory tests.

Medication

Antipsychotics are a group of drugs that have increased CVR as one of their adverse effects, through different mechanisms: weight gain through leptin stimulation, resulting in dyslipidemia and hyperglycemia, which lead to insulin resistance with the subsequent

Table 2. Laboratory characteristics, by disease

Characteristics	Schizophrenia		Bipolar disorder	
	(n = 16)		(n = 14)	
	Mean (SD)	95%CI	Mean (SD)	95%CI
Actual age	50.56 (± 12.37)	43.97-57.15	52.64 (10.69)	46.47-58.81
BMI (kg/m^2)	32.32 (± 4.97)	29.67-34.96	31.56 (± 5.19)	28.57-34.56
Hemoglobin	15.01 (± 1.54)	14.19-15.83	15.34 (± 1.45)	14.50-16.17
Hematocrit	43.12 (± 4.60)	40.67-45.57	44.41 (± 3.87)	42.18-46.65
White blood cells	7.03 (± 1.62)	(6.17-7.89)	7.71 (± 1.74)	(6.70-8.71)
Neutrophils	4.60 (± 1.35)	(3.86-5.35)	4.28 (± 1.59)	(3.36-5.19)
Lymphocytes	2.19 (± 3.41)	(1.99-2.38)	3.05 (± 7.29)	(2.63-3.47)
Neutrophil-lymphocyte ratio	2.13 (± 0.71)	(1.74-2.53)	1.5 (± 0.87)	(0.99-2)
Leukocyte-glucose index	671.66 (± 197.84)	(566.24-777.08)	739.42 (± 241.63)	(599.91-878.93)
Platelets	266.27 (± 52.84)	(237-295.53)	268.57 (± 78.46)	(223.27-313.87)
MPV	7.01 (± 0.42)	(6.79-7.23)	7.7 (± 1.41)	(6.89-8.51)
Glucose	94.89 (± 13.02)	(87.95-101.82)	93.94 (± 13.25)	(86.29-101.59)
Urea	27.79 (± 6.13)	(24.52-31.05)	29.96 (± 8.87)	(22.85-33.08)
Creatinine	0.90 (± 0.16)	(0.81-0.98)	0.84 (± 0.23)	(0.70-0.97)
Uric acid	5.19 (± 1.7)	(3.97-6.40)	5.00 (± 1.44)	(4.08-5.91)
Total cholesterol	193.08 (± 43.85)	(169.71-216.44)	193.50 (± 41.19)	(169.72-217.29)
HDL-C	36.96 (± 8.99)	(32.17-41.75)	38.70 (± 7.83)	(34.18-43.23)
LDL-C	121.63 (± 37.13)	(101.85-141.42)	113.81 (± 41.64)	(89.77-137.86)
Triglycerides	212.85 (± 135.25)	(140.79-284.92)	186.61 (± 68.67)	(146.96-226.26)
Characteristics	**Mood disorder**		**Other**	
	(n = 47)		(n = 28)	
	Mean (SD)	95%CI	Mean (SD)	95%CI
Actual age	58.12 (± 12.38)	(54.49-61.76)	59.03 (± 16.21)	(52.75-65.32)
BMI (kg/m^2)	31.75 (± 5.56)	(30.12-33.38)	30.97 (± 6.10)	(28.61-33.34)
Hemoglobin	15.50 (± 1.37)	(15.09-15.90)	15.52 (± 1.69)	(14.87-16.18)
Hematocrit	44.20 (± 5.77)	(42.50-45.89)	44.13 (± 5.16)	(42.13-46.13)
White blood cells	6.45 (± 1.22)	(6.09-6.83)	7.09 (± 1.60)	(6.47-7.71)
Neutrophils	3.72 (± 1.18)	(3.38-4.07)	4.06 (± 1.27)	(3.57-4.55)
Lymphocytes	2.36 (± 4.98)	(2.21-2.51)	2.56 (± 6.71)	(2.23-2.89)
Neutrophil-lymphocyte ratio	1.72 (± 0.97)	(1.43-2)	1.75 (± 0.85)	(1.42-2.08)
Leukocyte-glucose index	609.76 (± 140.79)	(568.42-651.10)	662.98 (± 169.74)	(597.16-728.80)
Platelets	285.51 (± 94.3)	(257.82-313.20)	261.86 (± 63.65)	(237.17-286.54)
MPV	7.5 (± 1.32)	(7.11-7.89)	7.21 (± 0.41)	(6.93-7.49)
Glucose	94.29 (± 9.63)	(91.46-97.12)	93.37 (± 10.99)	(89.11-97.63)

(Continues)

Table 2. Laboratory characteristics, by disease *(continued)*

Characteristics	Mood disorder		Other	
	(n = 16)		(n = 14)	
	Mean (SD)	95%CI	Mean (SD)	95%CI
Urea	31.28 (± 8.61)	(28.75-33.81)	28.34 (± 9.66)	(27.85-31.20)
Creatinine	0.87 (± 0.17)	(0.82-0.92)	0.90 (± 0.15)	(0.84-0.95)
Uric acid	4.83 (± 1.23)	(4.88-5.83)	5.36 (± 1.16)	(4.88-5.83)
Total cholesterol	210.78 (± 47.82)	(172.26-203.23)	187.74 (± 39.93)	(190.94-208.34)
HDL-C	36.66 (± 9.47)	(33.85-39.47)	41.96 (± 32.68)	(29.29-54.63)
LDL-C	134.96 (± 43.10)	(122.16-147.76)	113.91 (± 33.59)	(100.89-126.94)
Triglycerides	184.26 (± 100.27)	(154.82-213.70)	165.66 (± 80.05)	(134.62-196.70)

BMI: body mass index; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; MPV: mean platelet volume; SD: standard deviation; 95%CI: 95% confidence interval.

Table 3. Characteristics of cardiovascular risk associated with the use of antipsychotics

Use of antipsychotics	Cardiovascular risk		Total
	No (low)	Yes (intermediate, high)	
Yes	20 (51.3%)	28 (48.3%)	48
No	19 (48.7%)	30 (51.7%)	49
Total	39	58	97

Not statistically significant: p = 0.772.

proinflammatory effect previously described[15]. However, this relationship is not found with antidepressants like serotonin reuptake inhibitors[14].

Despite antipsychotics having clear mechanisms that foster greater CVR, there was no statistically significant relationship in the sample collected, probably due to the patients receiving pharmacological and nonpharmacological treatment.

This can help reach conclusions and ultimately recommend intensive treatment of CVR factors as a way of controlling the drug factor in psychiatric patients.

Cardiovascular risk

This interaction of multiple mechanisms in the onset of comorbidities is closely linked to increased CVR factors, and therefore mortality, expressed as a lower survival in this group of patients[16].

However, when a difference is sought between the study groups, the relationship is not statistically significant (ANOVA 0.189). Studies by Salvi et al. in Brazil found no difference in CVR in men with severe psychiatric illness, but it was significant in women[13,17]. Clerici et al. reported a higher prevalence of both obesity and hypertriglyceridemia, but not higher CVR, compared with the general population[18].

These findings, like those of other publications, are noteworthy, considering that while suicide attempts have the highest relative risk of mortality (up to 20 times higher than the general population, depending on the population), 75% of the deaths reported in patients with severe psychiatric illness are caused by cardiovascular disease[19].

Three types of possible explanations are proposed:

The study group had already received treatment, and therefore the group of patients with CVR was smaller than in other studies. However, these findings are not restricted to this sample, as shown in the previous paragraphs.

The screening for CVR in patients with major psychiatric diagnoses is not the same as in the rest of the population. Hardy et al. reported that up to 96% of the general population is screened for CVR in primary care, while 21% of psychiatric patients receive the same screening[20].

Despite international recommendations for intensive monitoring of CVR in patients with severe psychiatric illness, the way to apply risk prediction models in this population is not clearly understood. We suggest that these scales are not accurate for determining long-term risk for several reasons: patients with major psychiatric illness

Table 4. CVR characteristics, by psychiatric illness

Disease	Mean ± SD	95%CI (min.-max.)	Cardiovascular risk			
			High	Intermediate	Low	Total
Schizophrenia (n = 13)	7.04 (± 5.99)	3.41-10.66	1 (25%)	6 (15.8%)	6 (19.4%)	13 (17.8%)
Bipolar disorder (n = 11)	5.20 (± 3.39)	2.92-7.48	0 (0%)	6 (15.8%)	5 (16.1%)	11 (15.1%)
Mood disorder (n = 34)	7.44 (± 5.73)	5.44-9.44	1 (25%)	17 (44.7%)	16 (51.6%)	34 (16.6%)
Neurological disorder (n = 15)	10.26 (± 7.63)	6.03-14.49	2 (50%)	9 (23.7%)	4 (12.9%)	15 (20.5%)
Total	7.61 (± 6.03)		4 (5.48%)	38 (52.05%)	31 (42.47%)	73 (100%)

CVR ANOVA between groups p = 0.189.
95%CI: 95% confidence interval; CVR: cardiovascular risk.

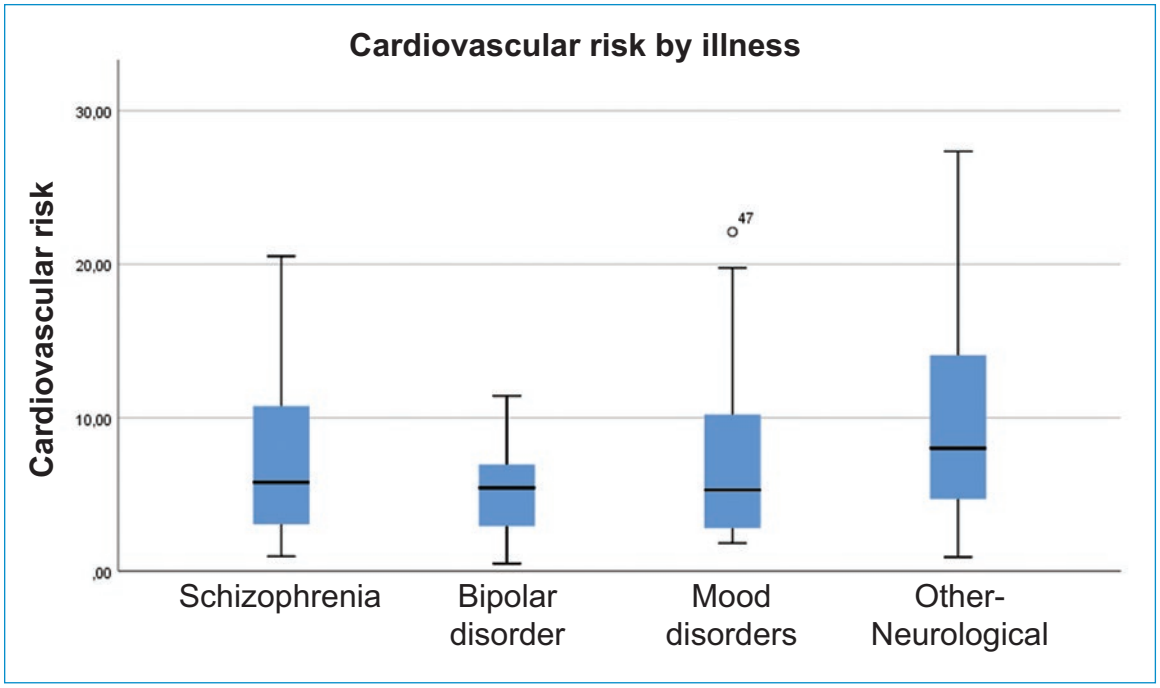


Figure 1. Cardiovascular risk in the different psychiatric disorders.

were excluded from the development of some scales, like the Cox Framingham scale, and prolonged exposure to antipsychotic drugs is not considered, with limited literature available exploring this association; one source proposes the use of other scales, like the Primrose scale[21].

Conclusions

In conclusion, we emphasize first that all CVR factors should be assessed and taken into account in all patients with mental health disorders from the time of diagnosis, with treatment for each one. Second, it would be important to evaluate a CVR scale validated in patients with psychiatric illness. Third, all healthcare staff who handle antipsychotic medications should identify and treat CVR factors to ensure safe use of the medications, and fourth, so-called nontraditional factors like sleep, medication, stress, etc. should be kept in mind.

Acknowledgements

The authors would like to thank the teaching committee and laboratory and nursing staff at Hospital Psiquiátrico Julio Endara for their contributions.

Funding

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

Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. This study was approved by the teaching committee at Hospital Psiquiátrico Julio Endara and used a secondary data source.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

References

1. Organización Panamericana de la Salud. HEARTS: Mejorar el control de la hipertensión en 3 millones de personas. Experiencias de los países sobre la elaboración e implementación de programas [Internet]. Organización Panamericana de la Salud, Institutional Repository for Information Sharing; 2020. Disponible en: https://iris.paho.org/handle/10665.2/53146
2. Ministerio de Salud Pública. Encuesta Steps Ecuador 2018. MSP, INEC, OPS/OMS. Vigilancia de enfermedades no transmisibles y factores de riesgo [Internet]. Quito, Ecuador: Ministerio de Salud Pública; 2018. Disponible en: https://www.salud.gob.ec/wp-content/uploads/2020/10/INFORME-STEPS.pdf
3. Laursen TM, Nordentoft M, Mortensen PB. Excess early mortality in schizophrenia. Annu Rev Clin Psychol. 2014;10:425-48.
4. Lim GY, Tam WW, Lu Y, Ho CS, Zhang MW, Ho RC. Prevalence of depression in the community from 30 countries between 1994 and 2014. Sci Rep. 2018;8(1):2861.
5. Veeneman RR, Vermeulen JM, Abdellaoui A, Sanderson E, Wootton RE, Tadros R, et al. Exploring the relationship between schizophrenia and cardiovascular disease: a genetic correlation and multivariable Mendelian randomization study. Schizophr Bull. 2022;48(2):463-73.
6. Anderson RB, Testa MA. Symptom distress checklists as a component of quality-of-life measurement: Comparing prompted reports by patient and physician with concurrent adverse event reports via the physician. Therapeutic Innovation & Regulatory Science. 1994;28(1):89-114.
7. Briganti EM, Shaw JE, Chadban SJ, Zimmet PZ, Welborn TA, McNeil JJ, et al. Untreated hypertension among Australian adults: The 1999-2000 Australian Diabetes, Obesity and Lifestyle Study (AusDiab). Med J Aust. 2003;179(3):135-9.
8. Murray CJL, Lopez AD. Mortality by cause for eight regions of the world: Global Burden of Disease Study. Lancet. 1997;349(9061):1269-76.
9. Somers VK, Anderson EA, Mark AL. Sympathetic neural mechanisms in human hypertension. Curr Opin Nephrol Hypertens. 1993;2(1):96-105.
10. Ayerbe L, Forgnone I, Addo J, Siguero A, Gelati S, Ayis S. Hypertension risk and clinical care in patients with bipolar disorder or schizophrenia; a systematic review and meta-analysis. J Affect Disord. 2018;225:665-70.
11. Kato M, Phillips BG, Sigurdsson G, Narkiewicz K, Pesek CA, Somers VK. Effects of sleep deprivation on neural circulatory control. Hypertension. 2000;35(5):1173-5.
12. Orellana G, Rodríguez M, González N, Durán E. Esquizofrenia y su asociación con enfermedades médicas crónicas. Rev Med Chile. 2017;145(8):1047-53.
13. Paz-Filho G, Licinio J, Wong ML. Pathophysiological basis of cardiovascular disease and depression: a chicken-and-egg dilemma. Braz J Psychiatry. 2010;32(2):181-91.
14. Kucerova J, Babinska Z, Horska K, Kotolova H. The common pathophysiology underlying the metabolic syndrome, schizophrenia and depression. A review. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2015;159(2):208-14.
15. Henderson DC, Vincenzi B, Andrea NV, Ulloa M, Copeland PM. Pathophysiological mechanisms of increased cardiometabolic risk in people with schizophrenia and other severe mental illnesses. Lancet Psychiatry. 2015;2:452-64.
16. Lawrence D, Hancock KJ, Kisely S. The gap in life expectancy from preventable physical illness in psychiatric patients in Western Australia: retrospective analysis of population based registers. BMJ. 2013;346:f2539.
17. Salvi V, Aguglia A, Barone-Adesi F, Bianchi D, Donfrancesco C, Dragogna F, et al. Cardiovascular risk in patients with severe mental illness in Italy. Eur Psychiatry. 2020;63(1):e96.
18. Clerici M, Bartoli F, Carretta D, Crocamo C, Bebbington P, Carrà G. Cardiovascular risk factors among people with severe mental illness in Italy: A cross-sectional comparative study. Gen Hosp Psychiatry. 2014;36(6):698-702.
19. Holt RI, Peveler RC. Diabetes and cardiovascular risk in severe mental illness. Pract Diab Int. 2010;27(2).
20. Hardy S, Hinks P, Gray R. Screening for cardiovascular risk in patients with severe mental illness in primary care: a comparison with patients with diabetes. J Ment Health. 2013;22(1):42-50.
21. Osborn DP, Hardoon S, Omar RZ, Holt RI, King M, Larsen J, et al. Cardiovascular risk prediction models for people with severe mental illness: results from the prediction and management of cardiovascular risk in people with severe mental illnesses (PRIMROSE) research program. JAMA Psychiatry. 2015;72(2):143-51.

Revista Colombiana de Cardiología
Órgano oficial de la Asociación Sociedad Colombiana de Cardiología & Cirugía Cardiovascular
Permanyer

Check for updates

ORIGINAL ARTICLE

Usefulness of two-dimensional echocardiography in the diagnosis of severe coronary stenosis in patients with non-ST-segment elevation acute coronary syndrome

Utilidad del ecocardiograma bidimensional en el diagnóstico de la estenosis coronaria grave en pacientes con síndrome coronario agudo sin elevación del segmento ST

Liliam G. Cisneros-Sánchez, Geovedy Martínez-García, Lázaro Puig-Benítez, Annia Ma. Carrero-Vázquez, Rosa Ma. Martínez-Peró, and Taimara Pérez-Rivero*

Coronary Care Unit, Hospital General Docente Enrique Cabrera, La Habana, Cuba

Abstract

Introduction: *Echocardiography in patients who suffer from non-ST-segment elevation acute coronary syndrome (NSTE-ACS) can detect the location and extent of wall motion abnormalities and thus infer the severity of coronary lesions.* **Objective:** *To determine the validity of two-dimensional echocardiography in the diagnosis of severe coronary stenosis (SCS) in patients with NSTE-ACS.* **Method:** *This was an observational, analytical, cross-sectional study in 108 patients with NSTE-ACS. An echocardiogram was performed prior to coronary angiography. Subsequently, concordance between both tests was sought and the validity and safety of the echocardiogram in the diagnosis of SCS was determined.* **Results:** *Sensitivity was 61.7%, specificity was 64.29%, the positive predictive value (PPV) was 92.06%, and the negative predictive value was 20%. Sensitivity decreased as the number of severely injured coronary arteries increased, while specificity increased (97.06% in three-vessel disease).* **Conclusions:** *The echocardiogram did not have high sensitivity or specificity for the diagnosis of SCS; however, in the presence of altered regional contractility, the existence of SCS is highly likely, due to a high PPV. Specificity was high for three-vessel disease, so it could help exclude this condition.*

Keywords: *Two-dimensional echocardiography. Non-ST-segment elevation acute coronary syndrome. NSTE-ACS. Coronary stenosis.*

Resumen

Introducción: *El ecocardiograma en pacientes con síndrome coronario agudo (SCA) sin elevación del segmento ST (SCASEST) puede detectar la localización y extensión de las anomalías del movimiento de la pared y así inferir la gravedad de las lesiones coronarias.* **Objetivo:** *Determinar la validez del ecocardiograma bidimensional en el diagnóstico de estenosis coronarias severas (ECS) en pacientes con SCASEST.* **Método:** *Estudio observacional, analítico, transversal, en 108 pacientes con SCASEST, donde se realizó ecocardiograma previo a la coronariografía. Posteriormente se buscó concordancia entre ambas pruebas y se determinó validez y seguridad del ecocardiograma en el diagnóstico de ECS.* **Resultados:** *Sensibilidad del 61.7%, especificidad del 64.29%, valor predictivo positivo (VPP) 92.06% y valor predictivo negativo (VPN) 20%. La sensibilidad disminuyó en la medida que aumentó el número de coronarias con lesiones graves, mientras que la especificidad*

***Correspondence:**
Liliam G. Cisneros-Sánchez
E-mail: liliamgcs@gmail.com

Date of reception: 01-04-2024
Date of acceptance: 25-09-2024
DOI: 10.24875/RCCARE.M24000128
Available online: 05-02-2025
Rev Colomb Cardiol. 2024;31(6):341-347
www.rccardiologia.com

aumentó (97.06% en la enfermedad de tres vasos). **Conclusiones:** *El ecocardiograma no tuvo alta sensibilidad ni especificidad en el diagnóstico de ECS; sin embargo, ante la presencia de alteración de la contractilidad regional es altamente probable la existencia de una ECS por el alto VPP. La especificidad fue alta para la enfermedad de tres vasos, por lo que pudiera ayudar a excluir esta entidad.*

Palabras clave: *Ecocardiografía bidimensional. Síndrome coronario agudo sin elevación del segmento ST. SCASEST. Estenosis coronaria.*

Introduction

Acute coronary syndrome (ACS) is the most dangerous form of coronary artery disease (CAD), involving a significant risk of mortality[1,2].

Although there has been substantial progress in diagnosing and treating acute coronary syndromes, leading to a decreasing mortality trend, mainly in developed countries, cardiovascular disease continues to be the main cause of death worldwide, with almost half of these deaths due to ischemic heart disease, which continues to be a huge public health problem with a global impact[3,4].

In practice, ACS is classified into two groups, according to ST segment abnormalities on the electrocardiogram: those with ST elevation acute myocardial infarction (STEMI), who are candidates for immediate reperfusion, and those without persistent ST elevation, which includes those with non-ST elevation AMI (NSTEMI) and unstable angina (UA)[3-5]. More patients are hospitalized for non-ST-segment elevation ACS (NSTE-ACS) than for persistent ST-segment elevation ACS (STE-ACS)[6].

The most important aspect of this classification is its usefulness for promptly selecting treatment. While reperfusion treatment should be applied immediately in STE-ACS, patients without ST-segment elevation should undergo individual stratification of their degree of risk to determine the type and intensity of treatment[3,7].

The collected evidence has led to clinical practice guidelines unequivocally indicating antithrombotic and anti-ischemic pharmacological treatment for all patients with NSTE-ACS[8,9]. As for invasive treatment, the results of clinical studies and their meta-analyses highlight the role of risk stratification in the decision-making process, supporting routine invasive treatment for patients with very high risk and a selective invasive strategy for the rest. However, the optimal timing for the invasive strategy in this group of patients is still controversial and often, in many countries, an extended revascularization strategy within the first 24 hours is not possible, nor are same-day transfers from a satellite center to a main center[8-11].

Echocardiography is increasingly used in the context of chest pain to complement the diagnosis and stratify the risk of patients with ischemic heart disease, in some cases to order invasive diagnostic tests when coronary disease is suspected[12,13]. This study helps detect segmental contraction abnormalities, indirectly translating the presence of coronary disease. Abnormal contraction in a given territory not only suggests the involvement of a specific coronary artery (anterior descending, circumflex or right coronary), but the extent of this abnormality can indicate whether the proximal, medial or distal third of the artery is affected[12].

The degree and extent of wall motion abnormalities correlate well with the severity and extent of the ischemia. Two-dimensional echocardiography provides an assessment of the location and extent of the acute/chronic stages of coronary heart disease. The main advantage of this technique is the direct clinical use of this method (for instance, as a bedside technology in the emergency room, hospital stations and clinical practice), as well as its accessibility and low cost compared to other echocardiographic and imaging techniques[13].

Patients with UA and NSTEMI are a heterogenous group. Patients with persistent wall motion abnormalities have more severe ischemia and a higher risk of adverse events[14,15]. For these patients, echocardiography could aid the decision-making process, especially if the appropriateness of reperfusion is uncertain, by showing the location and extent of the wall motion abnormalities, which could indicate the severity of the coronary lesions and allow a better stratification of patients hospitalized with NSTE-ACS. This could be especially useful for hospitals without hemodynamics services that must refer patients to other centers for invasive coronary angiography. Therefore, this study was done to determine the validity of two-dimensional echocardiography (2DE) for diagnosing severe coronary stenosis (SCS) in patients with NSTE-ACS.

Method

Methodological design

We conducted a cross-sectional, analytical observational study of patients who were admitted to the

coronary care unit with a diagnosis of NSTE-ACS between September 2018 and September 2021.

Sample

All consecutive patients who were admitted to the coronary care unit and met the following criteria were enrolled.

– Inclusion criteria:
  - Patients admitted for the first time with a diagnosis of NSTE-ACS.
  - Informed consent.
– Exclusion criteria:
  - Prior history of ischemic heart disease.
  - Patients with criteria for a very high risk of ischemic complications.
  - A suboptimal acoustic window.
  - Significant valve disease on echocardiography.
  - Hypertrophic cardiomyopathy or any other type of cardiomyopathy.
  - The presence of a pacemaker, complete left bundle branch block or any other conduction disorder.
  - Cardiac arrhythmias on the electrocardiogram.
  - Autoimmune, infectious, or inflammatory diseases or cancer, as well as recent treatment with immunosuppressants.

Procedures

– Regarding data collection. The information regarding the patients' clinical picture and history was obtained through an interview and data in the medical chart.
– Method used. The patients who met the inclusion criteria underwent a 2DE 48-72 hours after admission, prior to invasive coronary angiography. An ALOKA Alpha 10 echocardiography machine was used, with a 2.5 MHz transducer. To determine abnormalities in regional contractility, we used the 17-segment model related to the area of perfusion of the epicardial coronary arteries which was proposed by the American Society of Echocardiography[16]. The patients were transported to a percutaneous coronary intervention center to undergo coronary angiography. The interventionists were blinded to the results of the previous echocardiogram. Stenosis of the anterior descending (AD), left circumflex (Cx) and right coronary (RC) arteries ≥ 70% was considered SCS. Severe left coronary artery trunk disease was defined as > 50% stenosis[17].
  After invasive coronary angiography, the patients were returned to their hospital of origin, where concordance was sought between the regional contractility abnormalities found on echocardiography and the epicardial arteries affected with severe stenosis. In addition, the validity and safety of echocardiography for diagnosing SCS was determined, taking invasive coronary angiography as the reference method.
– Processing methods, data analysis and techniques to be used. The results were recorded in a data collection template. A database was created in the Microsoft Office 10 Excel program.
  Data processing was done using SPSS version 2.0 and Epidat version 3.1 software programs. The results were presented in statistical tables and figures.
  Cohen's kappa index was used to evaluate the concordance between the affected territories found on echocardiography and the arteries with significant lesions found on coronary angiography. The values shown in table 1 were used as metrics.
  To evaluate diagnostic precision, the sensitivity (probability of correctly classifying a sick person) was established as the basic performance parameter, as long as it was not significantly different from the specificity (probability of correctly classifying a healthy person); positive and negative prediction values were also calculated with the Epidat 3.1 program.

Ethical considerations

This study entailed performing a resting echocardiogram and invasive coronary angiography, with both studies employing perfectly standardized techniques.

Therefore, this study did not involve additional risk for the patients, but rather contributed to a better assessment and treatment of their disease. It adhered to the Declaration of Helsinki. It did not cause any type of social, territorial or environmental impacts.

Results

The sample consisted of 108 patients with NSTE-ACS, 37% of whom were confirmed to have NSTEMI and 63% were diagnosed with UA. Severe stenosis of at least one coronary artery was found in 87% of the cases, as shown in table 2.

Of the total, 74 (68.52%) were males and 34 (31.48%) were females. The age group with the most patients was 50-70-year-olds (72.22%), as seen in table 3.

Table 4 shows the concordance index between the two tests, considering the affected territories on 2DE and the respective coronary arteries with severe lesions

on coronary angiography, which was acceptable for the AD and RC arteries, as was the combination between each of these and the Cx artery, although to a lesser degree. For the diagnosis of the three territories together, the index was low.

The validity and safety of echocardiography for diagnosing SCS in patients with NSTE-ACS is shown in table 5. The sensitivity was 61.7% and the specificity was 64.29%. The positive predictive value (PPV) was 92.06%, and the negative predictive value (NPV) was 20%.

An analysis of the validity and safety of echocardiography for diagnosing SCS in patients with NSTE-ACS, according to the number of coronary arteries affected, found that sensitivity decreased as the number of coronary arteries with severe lesions increased, while specificity increased, reaching 97.06% in three-vessel disease. The PPV was 21.79, 19.0 and 33.33% for one artery, two arteries and three arteries with severe stenosis, respectively, while the NPV was 73.15, 76.85 and 62.96%, in the same order (Table 6).

Table 1. Cohen's kappa index values used as references

Kappa index	Level of agreement
< 0	No agreement (poor)
0 < 0.2	Insignificant (slight)
0.2 < 0.4	Low (acceptable)
0.4 < 0.6	Moderate
0.6 < 0.8	Good (substantial)
0.8-1	Very good (almost perfect)

Table 2. The distribution of patients according to the number of coronary arteries with severe stenosis on coronary angiography

Number of coronary arteries with severe stenosis	Number of patients	%
1	29	30.85
2	25	26.59
3	40	42.56
Total	94	87.04
None	14	12.96
Total	108	100

Discussion

Non-ST segment elevation acute coronary syndrome encompasses a group of patients with marked clinical diversity and multiple pathophysiological phenomena, resulting in a variable prognosis[8]. From this perspective, the effort to stratify patient risk and determine treatment guidelines according to this stratification is justified, with cardiac imaging, especially echocardiography, playing a significant role[13,18].

Generally, the myocardial segments tend to correspond to the three main coronary arteries, although there is some diversity in coronary irrigation[16]. The grouping of segments according to coronary artery irrigation is termed "territories." Some territories are known to be irrigated by either of two coronary arteries, or even have dual irrigation[16,19]. This study had an acceptable concordance between both tests, considering the territories affected by some type of regional motion disorder diagnosed by 2DE and the coronary arteries with significant lesions on coronary angiography, especially for the AD and RC individually (single vessel disease) and, with a lower index, the combination of each of these with the circumflex. Meanwhile, there was slight or insignificant concordance when all three arteries were affected at the same time. A study by Ternera et al.[20] found low concordance between the findings of resting echocardiography and cardiac catheterization in patients with AMI. However, the study by Guaricci et al.[21] found a statistically significant difference between the severity of wall motion abnormalities in patients with NSTE-ACS with severe CAD diagnosed by coronary angiography, compared to no CAD. Most authors agree that, regardless of greater or lesser association, early evaluation of regional contractility disorders in this group of patients is useful for choosing the proper treatment, including the timing of reperfusion therapy[4,21-23].

The sensitivity and specificity of 2DE for diagnosing SCS in this study was 61.70 and 64.29%, respectively, which is considered moderate. However, the positive predictive value was 92%, which shows that there is a high probability of severe stenosis in at least one coronary artery when the test is positive, that is, when regional wall motion abnormalities are detected[24].

The usefulness of the sensitivity and specificity parameters depends largely on the setting in which they are applied; they are important measures of the diagnostic accuracy of a test. Positive and negative predictive values provide estimates of the likelihood of the disease and depend on its prevalence, with considerable inverse variation: as the prevalence increases, the PPV increases and the NPV decreases, and vice versa[24,25]. When a given condition is very prevalent in the study population (as is assumed to occur with SCS

Table 3. The distribution of patients with acute coronary syndrome without ST elevation, by age and sex

Age group	Sex					
	Male	%	Female	%	Total	%
Under 50 years old	8	7.41	3	2.78	11	10.19
Between 50 and 70 years old	56	51.85	22	20.37	78	72.22
Over 70 years old	10	9.26	9	8.33	19	17.59
Total	74	68.52	34	31.48	108	100

Table 4. Concordance between affected territories on two-dimensional echocardiography and arteries with severe stenosis detected by coronary angiography

Arteries and territories	Kappa
AD	0.333
RC	0.341
AD + CX	0.260
RC + CX	0.266
AD + RC	0.233
AD + Cx + RC	0.173

AD: left anterior descending artery; Cx: circumflex artery; RC: right coronary artery.

Table 5. Validity and safety of echocardiography for diagnosing severe coronary stenosis

Operational characteristics	Value	95% confidence interval	
Sensitivity	61.70	51.34	72.06
Specificity	64.29	35.61	92.96
PPV	92.06	84.60	99.53
NPV	20.00	7.20	32.80

PPV: positive predictive value; NPV: negative predictive value.

in patients hospitalized for NSTE-ACS), the test is better at "confirming" and worse at "ruling out" the disease. This is why a high PPV is important[25], as occurred in this study as well as that by Ha et al.[23], who found that regional motion abnormalities had a high PPV along with other variables in diagnosing SCS in patients with NSTEMI.

The NPV in this study was low, at 20%, which is justified by what we explained earlier and indicates that the test does not rule out the disease, even when it is negative[24]. Myocardial blood flow is a complex interplay between epicardial and microvascular patency and myocytic metabolism. Coronary blood flow at maximum vasodilation falls below the ischemic level in 75% or greater stenosis[26]. If the flow interruption is short enough to not cause necrosis, contractions may return to normal immediately once perfusion is restored. Therefore, the echocardiogram may be normal once the acute ischemic phase is over, if a myocardial infarction has not occurred[26,27]. In reversible ischemia, restored myocyte function is determined by factors like early coronary blood flow recovery and ischemic pre- and post-conditioning. Concepts like stunned myocardium (temporary mechanical dysfunction after an ischemic injury, but with normal blood flow and no irreversible damage), and hibernating myocardium (a viable myocardial region without contractility) are quiescent types of heart function and help explain the myocardial capacity to restore normal functioning after an ischemic episode[28].

Some authors associated the presence of wall motion abnormalities on 2DE with other variables, like left ventricular ejection fraction, myocardial deformation, demographic variables, coronary risk factors and abnormal cardiac enzymes, obtaining greater sensitivity, specificity and predictive values for diagnosing severe coronary lesions in patients with NSTE-ACS, even higher than 90%[23,27,29,30].

In this group of patients, an analysis of the validity of 2DE according to the number of coronary arteries with severe stenosis found low sensitivity and high specificity, with the latter increasing as the number of affected coronary arteries increased, reaching 97% with three-vessel disease. As the number of coronary arteries with severe stenosis increases, heart muscle irrigation is more affected, with more extensive damage, and therefore wall contractility abnormalities will be more extensive and easier to see on echocardiography[31], which explains why there is a lower likelihood of false positives (high specificity) with more diseased coronary arteries.

Table 6. Validity and safety of echocardiography for diagnosing severe coronary stenosis according to the number of affected arteries

Number of coronary arteries with severe stenosis	Sensitivity	Specificity	PPV	NPV
1	41.38	77.22	21.79	73.15
2	36.00	81.93	19.05	76.85
3	17.50	97.06	33.33	62.96

PPV: positive predictive value; NPV: negative predictive value.

Conclusions

In patients admitted with NSTE-ACS, 2DE did not have high sensitivity and specificity for diagnosing SCS; however, when there is a regional contractility abnormality, severe stenosis is highly likely, as the test had a high PPV.

The specificity of 2DE for diagnosing severe stenosis according to the number of vessels was high, chiefly for three-vessel disease, and therefore could be used to help rule out this condition.

Funding

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

Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from 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 no generative artificial intelligence was used in writing this manuscript.

References

1. Timmis A, Kazakiewicz D, Townsend N, Huculeci R, Aboyans V, Vardas P. Global epidemiology of acute coronary syndromes. Nat Rev Cardiol. 2023;20:778-88.
2. Bergmark B, Mathenge N, Merlini P, Lawrence M, Giugliano R. Acute coronary syndromes. Lancet. 2022;399:1347-58.
3. Cassiani C, Cabrera A. Síndromes coronarios agudos: epidemiología y diagnóstico. Salud Uninorte. 2009;25(1):118-34.
4. Writing Committee Members; Gulati M, Levy P, Mukherjee D, Amsterdam E, Bhatt D, Birtcher K. 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCRM Guideline for the Evaluation and Diagnosis of Chest Pain. J Am Coll Cardiol. 2021;78(22):2218-61.
5. Viéitez J, García S, Zamorano J. Cardiopatía isquémica: concepto, clasificación, epidemiología, medidas preventivas y tratamiento no farmacológico. Medicine. 2021;13(37):2119-24.
6. Sanchis-Gomar F, Perez-Quilis C, Leischik R, Lucia A. Epidemiology of coronary heart disease and acute coronary syndrome. Ann Transl Med. 2016;4(13):256.
7. Writing Committee Members; Lawton J, Tamis-Holland J, Bangalore S, Bates E, Beckie T, Bischoff J, et al. 2021 +ACC/AHA/SCAI. Guideline for Coronary Artery Revascularization. J Am Coll Cardiol. 2022;79(2):e21-e129.
8. Collet J, Thiele H, Barbato E, Barthélémy O, Bauersachs J, Bhatt D, et al. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J. 2021;42:1289-367.
9. Keykhaei M, Ashraf H, Rashedi S, Farrokhpour H, Heidari B, Zokaei S, et al. Differences in the 2020 ESC versus 2015 ESC and 2014 ACC/AHA Guidelines on the Management of Acute Coronary Syndromes in Patients Presenting Without Persistent ST-Segment Elevation. Curr Atheroscler Rep. 2021;23(12):77.
10. González J, Gutiérrez G, Celis A, Gudiño D. Registro de síndromes coronarios agudos sin elevación del segmento ST en un centro hospitalario de tercer nivel de atención (estudio RESCATA-SEST). Arch Cardiol Mex. 2014;84(2):92-9.
11. Murrone A, Scotto di Uccio F, Amodeo V, Aspromonte N, Caldarola P, Casella G, et al. Timing of coronary angiography in non-ST-segment elevation acute coronary syndromes, Eur Heart J Suppl. 2021;23(Issue Supplement_C).
12. Mahmoud MZ. Echocardiography in the evaluation of chest pain in the emergency department. Pol J Radiol. 2017;82:798-805.
13. Wilben V, Kanchi M, Kumar V, Kumar S. Abstract 10435: A plea for inclusion of surface echocardiography for acute coronary syndrome in the advanced cardiac life support algorithm. Circulation. 2021;144(suppl 1):Abstract 10435.
14. Guaricci AI, Chiarello G, Gherbesi E, Fusini L, Soldato N, Siena P, U et al. Coronary-specific quantification of myocardial deformation by strain echocardiography may disclose the culprit vessel in patients with non-ST-segment elevation acute coronary syndrome. Eur Heart J Open. 2022;2(2):oeac010.
15. Leischik R, Dworrak B, Sanchis F, Lucia A, Buck T, Erbel R. Echocardiographic assessment of myocardial ischemia. Ann Transl Med. 2016;4(13):259.
16. Lang R, Badano L, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recomendation for Cardiac Chamber Quantification by Echocardiographyin Adults: An Update from the American Society of Echocardiographyand the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2015;28:1-39.
17. Yokota S, Ottervanger JP, Mouden M, de Boer MJ, Jager PL, Timmer JR. Predictors of severe stenosis at invasive coronary angio graphy in patients with normal myocardial perfusion imaging. Neth Heart J. 2018;26(4):192-202.
18. Gimenez R, Pöss T. Management des akuten Koronarsyndroms ohne ST-Strecken-Hebung [Management of acute coronary syndrome without ST-segment elevation]. Herz. 2022;47(4):381-92.
19. Cadena A, González, Valdes B, Ruiz F. Concordancia de la motilidad segmentaria evaluada por ecocardiograma transtorácico y resonancia magnética cardiaca en pacientes con infarto agudo de miocardio. Rev Colomb Cardiol. 2018;25(6):366-72.
20. Ternera A, Saavedra M, Sánchez U, Zárate J, Osorio O. Concordancia de los trastornos de contractibilidad en el ecocardiograma con el compromiso del vaso coronado en el cateterismo cardiaco en pacientes con infarto agudo del miocardio. Repert Med Cir. 2018;27(2):100-4.

21. Guaricci A, Chiarello G, Gherbesi E, Fusini L, Soldato N, Siena P, et al. Coronary-specific quantification of myocardial deformation by strain echocardiography may disclose the culprit vessel in patients with non-ST-segment elevation acute coronary syndrome. Eur Heart J Open. 2022;2(2):oeac010.
22. Byrne R, Rossello X, Coughlan J, Barbato E, Berry C, Chieffo A, et al. 2023 ESC Guidelines for the management of acute coronary syndromes: Developed by the task force on the management of acute coronary syndromes of the European Society of Cardiology (ESC). Eur Heart J. 2023;44(38):3720-826.
23. Ha ET, Cohen M, Fields PJ, van Daele J, Gaeta TJ. The utility of echocardiography for non-ST-segment elevation myocardial infarction: a retrospective study. J Diagn Med Sonogr. 2020;36(2):121-9.
24. Pérez I, Taito-Vicenti L, González-Xuriguera C, Carvajal C, Ariel-Franco J, Loézar C. Cómo interpretar las pruebas diagnósticas. Medwave. 2021;21(7):1-12.
25. Shreffler J, Huecker M. Diagnostic testing accuracy: sensitivity, specificity, predictive values and likelihood ratios [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [consultado el 4 de mayo de 2023]. Disponible en: https://www.ncbi.nlm.nih.gov/books/NBK557491
26. Severino P, D'Amato A, Pucci M, Infusino F, Adamo F, Birtolo LI, et al. Ischemic heart disease pathophysiology paradigms overview: from plaque activation to microvascular dysfunction. Int J Mol Sci. 2020; 21(21):8118.
27. Chen M, Liu P, Huang J, Li P, Qin C, Ruan Z, et al. Predictive value of significant coronary stenosis in patiens suspected of non-ST segment elevation acute coronary syndrome by two dimensional speckle tracking imaging combined with real time three dimensional echocardiography. Chinese J Ultrasonography. 2022;12:93-100.
28. Moreno P, del Portillo J. Isquemia miocárdica: conceptos básicos, diagnóstico e implicaciones clínicas. Segunda parte. Rev Colomb Cardiol. 2016;23(6):500-7.
29. Bergmann I, Büttner B, Teut E, Jacobshagen C, Hinz J, Quintel M. Pre-hospital transthoracic echocardiography for early identification of non-ST-elevation myocardial infarction in patients with acute coronary syndrome. Crit Care. 2018;22(1):29.
30. Di Pasquale P, Cannizzaro S, Scalzo S, Maringhini G, Sarullo FM, Cacia A, et al. Sensitivity, specificity and predictive value of the echocardiography and troponin-T test combination in patients with non-ST elevation acute coronary syndromes. Int J Cardiovasc Imaging. 2004;20(1):37-46.
31. Heward S, Widrich J. Coronary perfusion pressure [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [consultado el 13 de mayo de 2023]. Disponible en: https://pubmed.ncbi.nlm.nih.gov/31855375

Revista Colombiana de Cardiología
Órgano oficial de la Asociación Sociedad Colombiana de Cardiología & Cirugía Cardiovascular
Permanyer

Check for updates

ORIGINAL ARTICLE

Health and economic impact of LDL cholesterol control in patients with atherosclerotic cardiovascular disease and high or very high cardiovascular risk: a simulation study for the Colombian context

Impacto clínico y económico del control del colesterol LDL en pacientes con enfermedad cardiovascular aterosclerótica y riesgo cardiovascular alto y muy alto: un estudio de simulación para el contexto colombiano

Mateo Ceballos, Sara Arias, and Carlos Gamboa*

Novartis de Colombia, Bogotá D.C., Colombia

Abstract

Introduction: *Low-density lipoprotein cholesterol (LDL-C) is one of the modifiable risk factors with the greatest impact on atherosclerotic cardiovascular disease (ASCVD).* **Objective:** *To quantify the economic impact of LDL-C control in Colombian patients with ASCVD and high and very high cardiovascular risk.* **Method:** *A Markov model was built from the perspective of the Colombian healthcare system to simulate the impact of a 50% reduction of LDL-C on the occurrence of major adverse cardiovascular events and direct avoided costs, over a time horizon of 5 and 10 years. The number of prevalent and incident patients and cost were quantified from public databases and local literature.* **Results:** *A 50% reduction in LDL-C over 5 years would prevent 105,826 events and reduce the cost for the Colombian healthcare system by 3.4 trillion COP (a 36% decrease) vs. no LDL-c control, while over 10 years these values would rise to 199,583 events and 6 trillion COP, a 34% reduction.* **Conclusions:** *In patients with ASCVD and high and very high cardiovascular risk, a sustained and consistent control of LDL-C prevents major adverse cardiovascular events and generates savings for the Colombian healthcare system.*

Keywords: *LDL cholesterol. Atherosclerotic cardiovascular disease. Costs and cost analysis. Colombia.*

Resumen

Introducción: *El colesterol vinculado a lipoproteínas de baja densidad (c-LDL) es uno de los factores de riesgo modificables con mayor impacto para la enfermedad cardiovascular aterosclerótica (ECVA).* **Objetivo:** *Cuantificar el impacto clínico y económico del control del c-LDL en pacientes con ECVA y riesgo cardiovascular alto y muy alto en Colombia.* **Método:** *Se construyó un modelo de Markov desde la perspectiva del sistema de salud colombiano, para simular el impacto de una reducción del 50% del c-LDL en la ocurrencia de eventos cardiovasculares mayores y costos directos evitados, en un horizonte temporal de 5 y 10 años. Se cuantificó el número de pacientes prevalentes e incidentes y costos a partir de bases de datos públicas y literatura local.* **Resultados:** *Una reducción del 50% del c-LDL durante cinco años evitaría 105,826 eventos y reduciría los costos para el sistema de salud en COP $3.4 billones, una disminución del 36% frente al no control del c-LDL,*

***Correspondence:**
Mateo Ceballos
E-mail: mateo.ceballos@novartis.com

Date of reception: 29-04-2024
Date of acceptance: 03-10-2024
DOI: 10.24875/RCCARE.M24000133

Available online: 05-02-2025
Rev Colomb Cardiol. 2024;31(6):348-355
www.rccardiologia.com

mientras que a 10 años estos valores ascienden a 199,583 eventos y COP $6 billones, una reducción del 34%. **Conclusiones:** *En pacientes con ECVA y riesgo cardiovascular alto y muy alto, el control del c-LDL de manera sostenida y consistente evita eventos cardiovasculares mayores y genera ahorros para el sistema de salud colombiano.*

Palabras clave: *Colesterol LDL. Enfermedad cardiovascular aterosclerótica. Costos y análisis de costos. Colombia.*

Introduction

Cardiovascular diseases are the main cause of death and burden of disease worldwide, taking the life of 18.6 million people and causing 34.4 million years lost due to disability in 2019[1,2]. The Colombian trend is similar, with 94,000 cardiovascular deaths and 1.3 million disability-adjusted life years reported in 2019[3]. In economic terms, cardiovascular diseases were estimated to have caused a loss of 0.3% of the national gross domestic product in 2015[4]. The prevalence is expected to increase to 1.6 million people in 2035, with disease-related costs expected to reach 14 billion USD[5].

Atherosclerotic cardiovascular disease (ASCVD) is defined as the clinical manifestation of atherosclerosis (the pathological process of atherosclerotic plaque formation in the coronary, cerebral, iliac, femoral and aortic arteries) and includes coronary disease, stroke and peripheral artery disease[6,7]. Atherosclerotic cardiovascular disease constitutes the group of diseases with the highest contribution to mortality and burden of disease in Colombia, accounting for 75% of all cardiovascular deaths and 80% of disability-adjusted life years[3].

The control of modifiable risk factors like blood pressure, blood sugar levels, low-density lipoprotein cholesterol (LDL-C), body mass index and diet, among others, has been identified as one of the main pillars for reducing cardiovascular risk and avoiding the exponential growth of cardiovascular disease[1,2]. Of these, LDL-C stands out as one of modifiable risk factors most closely related to ASCVD, with the greatest impact in terms of death and disability[8]. In Colombia, it is estimated that reducing the modifiable risk factors other than LDL-C could save 10.5 billion USD by 2035 and 9.2 billion USD with LDL-C control alone[5].

Consistent, sustained LDL-C reductions are associated with less atherosclerosis and cardiovascular risk and, therefore, less likelihood of major adverse cardiovascular events (MACE) like myocardial infarction, stroke, unstable angina or cardiovascular death[9,10]. A meta-analysis of more than 50 randomized clinical trials found a 20-25% MACE risk reduction for every mmol/l reduction in LDL-C, showing that controlling this component can reduce healthcare costs associated with MACE treatment, which is a significant cost in Colombia[11-13].

The purpose of this study was to measure the clinical and economic impact of LDL-C control in patients with ASCVD outside the target LDL-C, with high and very high cardiovascular risk, using a cohort simulation for the Colombian context.

Methods

To measure the clinical and economic impact of LDL-C control, a Markov model was built with annual cycles and mid-cycle correction, from the perspective of the Colombian healthcare system, considering the clinical effects and direct costs paid by the healthcare system. The population consisted of patients over the age of 18 with ASCVD outside the LDL-C targets, with high and very high cardiovascular risk. This population was used because it has the highest risk of developing a new MACE and requires more intensive treatment[14]. A time horizon of 5 and 10 years was used, where the prevalent population was included as the baseline, as well as entries and exits after the first year along with the population incidence and all-cause mortality, subtracting cardiovascular mortality to avoid double counting, as this is already included in MACE modeling.

The Markov model was built considering prior dyslipidemia cost-effectiveness analyses[15,16]. Major adverse cardiovascular events were defined as acute myocardial infarction, ischemic stroke, unstable angina, coronary revascularization and cardiovascular death. Fifteen discreet and mutually exclusive health states were included in which patients might remain stable, experience a fatal or non-fatal event or enter a post-event state. Tunnel states were included in years 0-1, year 2 and year 2 and following after an event, to consider the differential risk of a new MACE after a prior event. Figure 1 shows the graph of the model used.

It was assumed that patients only progress toward worse states, to avoid illogical outcomes like patients with a history of two types of MACE having a better health-related quality of life than patients with a single event[15,16]. Therefore, states after the event, termed "post-event" in the model, were used to determine the

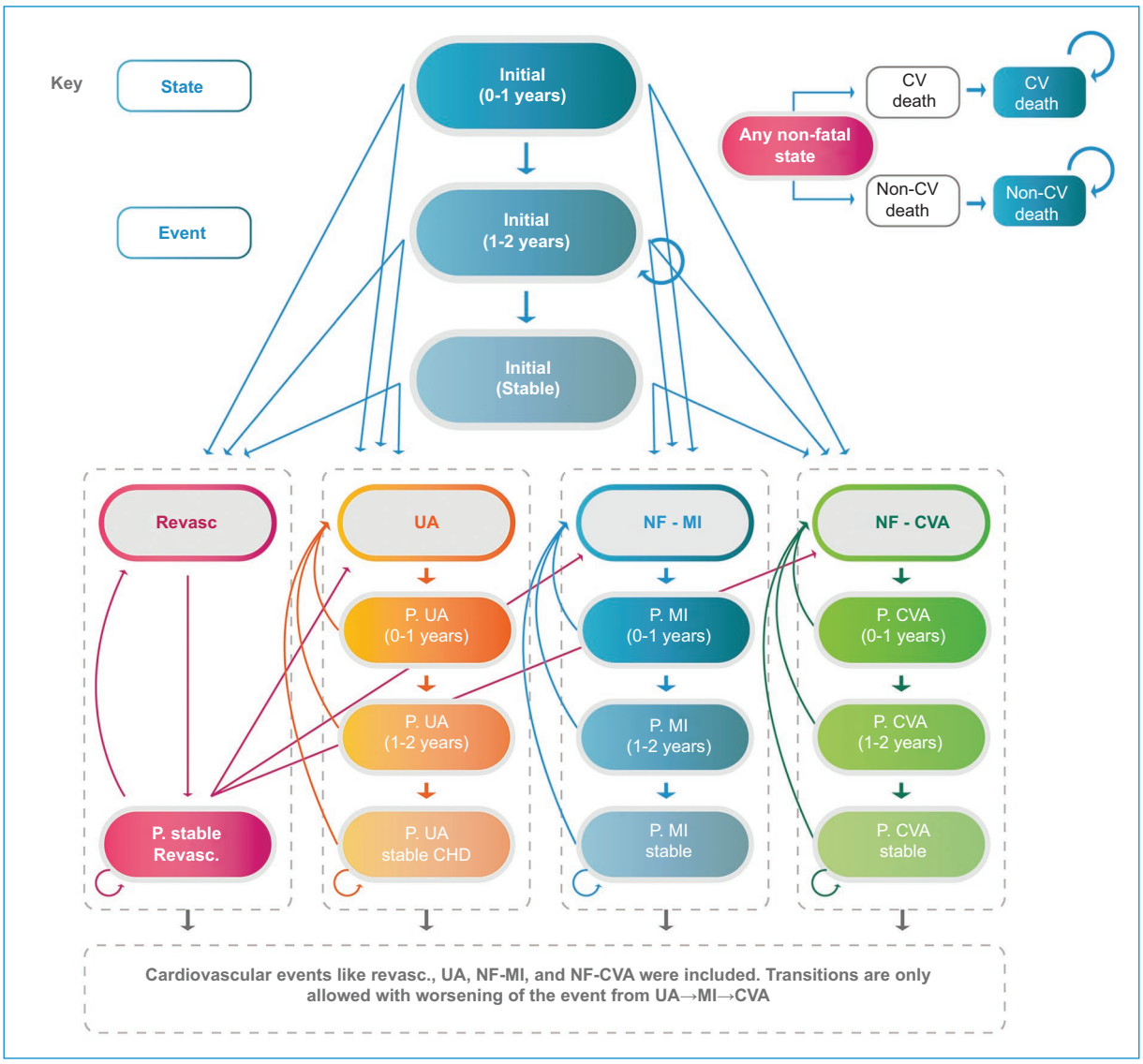


Figure 1. Markov model used to simulate the economic impact of LDL-C in Colombia.
CVA: cerebrovascular accident; NF-CVA: non-fatal cerebrovascular accident; UA: unstable angina; CHD: coronary heart disease; LDL-C: low-density lipoprotein cholesterol; CV: cardiovascular; Revasc: revascularization; MI: myocardial infarction; NF-MI: non-fatal myocardial infarction.

use of resources and subsequent risk of fatal and non-fatal events.

In addition, adjustments were made in the baseline risk of developing a MACE according to age, sex, presence of diabetes mellitus and type and time of occurrence of the previous MACE. For this last point, population sub-groups were built to differentially model the effect of LDL-C control. Specifically, a differentiated baseline risk was considered for patients with a history of acute myocardial infarction or unstable angina in the last 12 months and 12 and 24 months, other coronary diseases, stroke or peripheral artery disease.

The prevalence and incidence of ASCVD in adults (the sum of the data for ischemic heart disease, ischemic stroke and peripheral artery disease) were obtained from the 2019 Global Burden of Disease[3]. Our own national data was used to estimate the number of prevalent patients with out-of-target LDL-C levels and high and very high cardiovascular risk. With these sources, we calculated 570,629 people with ASCVD and an incidence of 8,916 cases per year. The population characteristics of the cohort were taken from local studies described in table 1.

Table 1. Population characteristics of the simulated cohort

Variable	Estimate	Source
Prevalent adult patients with ASCVD Ischemic heart disease Ischemic stroke Peripheral artery disease	2,046,605 1,091,236 365,509 589,860	GBD, 2020[3] GBD, 2020[3] GBD, 2020[3] GBD, 2020[3]
Incident adult patients with ASCVD Ischemic heart disease Ischemic stroke Peripheral artery disease	31,997 17,566 4,560 9,831	GBD, 2020[3] GBD, 2020[3] GBD, 2020[3] GBD, 2020[3]
Percentage of patients outside the LDL-C target	48.49%	CAC, 2020[17]
Percentage of patients with high and very high cardiovascular risk	57.5%	Ruiz, 2020[18]
Baseline LDL-C in the patient population	100 mg/dl	CAC, 202217, Ruiz, 2020[18]
Average age in years	66.4	Ruiz, 2020[18]
Percentage of women	53.4%	Ruiz, 2020[18]
Percentage of patients diagnosed with diabetes	27.5%	Ruiz, 2020[18]
History of acute myocardial infarction<1 year ago	9%	Economic studies[15,16,19]
History of acute myocardial infarction>1 year ago	1%	Economic studies[15,16,19]
History of stroke	19%	Economic studies[15,16,19]
History of peripheral artery disease	9%	Economic studies[15,16,19]
History of other coronary diseases	62%	Economic studies[15,16,19]

CAC: high cost account; LDL-C: low-density lipoprotein cholesterol; ASCVD: atherosclerotic cardiovascular disease; GBD: Global Burden of Disease.

All-cause mortality was calculated from age and sex-adjusted life tables from the National Administrative Department of Statistics for 2022, from which cardiovascular mortality was subtracted to avoid double counting. To estimate the economic impact of LDL-C, a 50% reduction of LDL-C from the baseline was assumed, according to the dyslipidemia treatment guidelines to achieve the proposed goals according to cardiovascular risk in the modeled patient population[14].

The baseline risks were taken from the Clinical Practice Research Datalink database, which links the statistics of hospital episodes and the United Kingdom Office for National Statistics databases[20]. This database was used to quantify the annual risk of cardiovascular events for patients with ASCVD and for patient subgroups according to their history of events and the presence of diabetes. These baseline risks were extrapolated over time, as has been done in other economic studies[15,16,19]. The relationship between LDL-C and cardiovascular events was modeled using the Cholesterol Treatment Trialists program meta-analyses, adjusted by age and sex. Table 2 summarizes the effects of LDL-C reduction on the likelihood of experiencing a MACE[21].

The cost of each acute MACE event was calculated based on information from studies of the sufficiency of the 2021 capitation payment rate using package reimbursement[22]. The average per capita cost of hospitalizations reported with the International Classification of Diseases (ICD)-10 codes was calculated for each MACE up to discharge, including all the resources used during the inpatient process. Since cardiovascular death is not associated with any ICD-10 code, the cost of the acute event was taken to be equal to that of acute myocardial infarction.

In addition, the annual cost of patient follow-up and monitoring after the acute event was included. This was extracted from economic studies in the Colombian context, calculated using a micro-costing method from several sources and clinical expert consultation[23,24]. Table 3 summarizes the costs included for each MACE.

Results

For a five-year time horizon, it is estimated that sustained and consistent LDL-C control in Colombian patients with ASCVD outside of the target LDL-C and

high and very high cardiovascular risk would avoid 105,826 MACEs, which would mean a 36% reduction compared to no LDL-C control. This translates into up to 3.4 trillion COP in avoided costs for the Colombian healthcare system. Figure 2 presents the events and economic impact of each of the MACEs for the five-year time horizon.

On the other hand, for a 10-year time horizon, sustained and consistent LDL-C control would avoid 199,583 MACEs and generate 6 trillion COP in savings for the healthcare system. This represents a 34% reduction compared to no LDL-C control. Figure 3 shows the events and the economic impact of each of the MACEs for the 10-year time horizon.

Table 2. Effects on major adverse cardiovascular events of a 1 mmol/l reduction in LDL-C

Variable	Estimate	Confidence interval
Coronary revascularization	0.75	0.72-0.78
Unstable angina	0.73	0.70-0.76
Acute myocardial infarction	0.73	0.70-0.76
Ischemic stroke	0.79	0.74-0.85
Cardiovascular death	0.84	0.80-0.88
Age adjustment – non-fatal events	1.03	NA
Age adjustment – fatal events	1.05	NA

LDL-C: low-density lipoprotein cholesterol; NA: not available.

Discussion

This study found that a sustained and consistent 50% LDL-C reduction in Colombian patients with ASCVD outside of the target LDL-C with high and very high cardiovascular risk would prevent 105,826 events and reduce healthcare system costs by 3.4 trillion COP, representing a 36% reduction compared with no LDL-C control. On the other hand, over 10 years, the figures rise to 199,583 events and 6 trillion COP, a 34% reduction compared to the no LDL-C control scenario.

To our knowledge, this is the first study to measure the clinical and economic impact of LDL-C control in Colombian patients with ASCVD outside of the target LDL-C and high and very high cardiovascular risk. This measurement was based on data from a simulated cohort using an economic model and considers the events and costs avoided by sustained and consistent LDL-C control over time. The results of this study are in line with Ruiz's (2020) conclusion for the entire spectrum of cardiovascular disease, estimating that LDL-C control could avoid costs of 10.7 billion USD by 2035 in Colombia[18]. Internationally, scientific articles have also calculated substantial savings derived from LDL-C control in direct costs for the healthcare system and indirect costs for patients, their caregivers and society[25-28].

In Colombia, LDL-C control is an integral part of public policies aimed at managing cardiovascular disease, such as the Comprehensive Care Pathway for people at risk for or with manifest cardio-cerebrovascular-metabolic disorders, as well as the dyslipidemia treatment guidelines to reduce cardiovascular risk[14,29]. Low-density lipoprotein cholesterol control is one of the modifiable risk factors that must be reported to the High Cost Account (HCA) for ongoing monitoring of management and risk indicators[30]. However, at the time of this study, the HCA still had an LDL-C target of 100 mg/dl for the entire population, which is not updated according to the international guidelines that recommend different targets according to cardiovascular risk: 100 mg/dl for low and moderate risk, 70 mg/dl for high risk and 55 mg/dl for high and very high risk[14].

According to the HCA, 48.5% of patients with hypertension, diabetes and/or chronic kidney disease do not achieve the 100 mg/dl LDL-C target, and this percentage would be even higher if the figures were updated according to the international guidelines[31]. Other local studies have also found close to 50% of patients in secondary prevention with out-of-target LDL-C levels[18,32,33].

The low percentage of patients who achieve LDL-C control in Colombia may indicate a lack of diagnosis and timely and ongoing access to lipid-lowering treatments[34]. Thus, as far as treatment intensification, there is evidence of the impact of LDL-C control on MACEs with statins, ezetimibe, alirocumab and evolocumab[35-38]. However, further research is needed to show this performance in real life and provide a more in-depth assessment of the population impact in terms of the number of events avoided and their cost.

This study has some limitations. First, some of the simulated cohort data had to be extracted from international evidence, as sufficiently detailed and robust local data is not available. Second, the results are based on a simulation model, which involves the construction of some assumptions, such as sustained and

Table 3. Costs of the acute event and follow-up of major adverse cardiovascular events

MACE	Cost of the acute event	Annual post-event cost	Total	Source
Coronary revascularization	$53,294,253	$5,844,188	$59,138,441	Avila, 2021[24]
Unstable angina	$15,757,288	$1,566,760	$17,324,048	Arango, 2020[23]
Acute myocardial infarction	$21,351,873	$2,722,866	$24,074,739	Avila, 2021[24]
Ischemic stroke	$19,937,397	$2,950,517	$22,887,914	Arango, 2020[23]
Cardiovascular death	$21,351,873*	$0	$21,351,873	Avila, 2021[24]

*Assumed to be the same as acute myocardial infarction.
MACE: major adverse cardiovascular event.

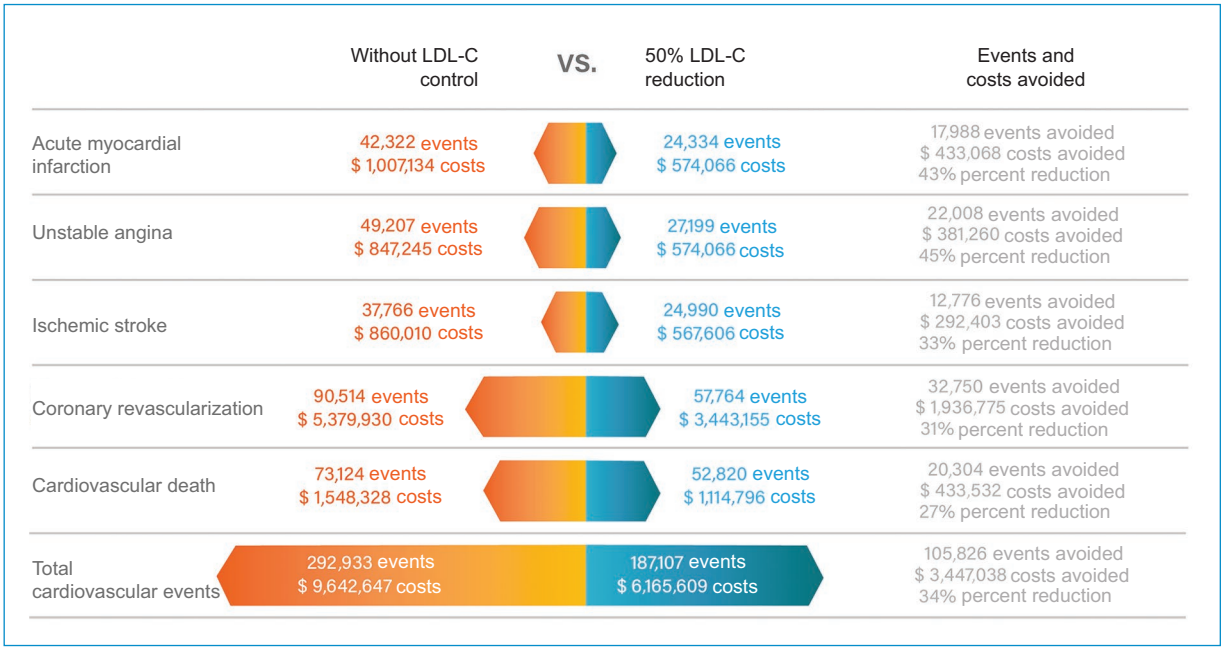


Figure 2. Impact of LDL-C control in patients with out-of-target ASCVD with high and very high cardiovascular risk in Colombia, over a five-year time horizon.
*Costs in millions of pesos.
LDL-C: low-density lipoprotein cholesterol.

consistent LDL-C reduction over time, which may not always be seen in real life cases. This makes a research line to produce real-life evidence of the impact of LDL-C in Colombia essential, to overcome these limitations.

Third, the aggregated costs of the capitation payment unit sufficiency studies, despite aggregating all the healthcare services of the contributive regimen, do not include the reality of the subsidized regimen, which may have different fees[22]. Furthermore, this database is not error-free in the ICD-10 codes used for healthcare services, and therefore a percentage of the MACEs may not be visible due to a lack of reporting and/or inappropriate coding. It is important for the country to advance in the availability of cost information for all the regimens to construct robust evidence of the costs and fees of the healthcare system as a whole.

Finally, this study only includes the economic impact of LDL-C on direct healthcare system costs, and therefore does not consider the indirect costs for the patients, caregivers and society in general. This could be a future research line, inasmuch as international studies have found that LDL-C control can have significant social impacts on patients with ASCVD[28].

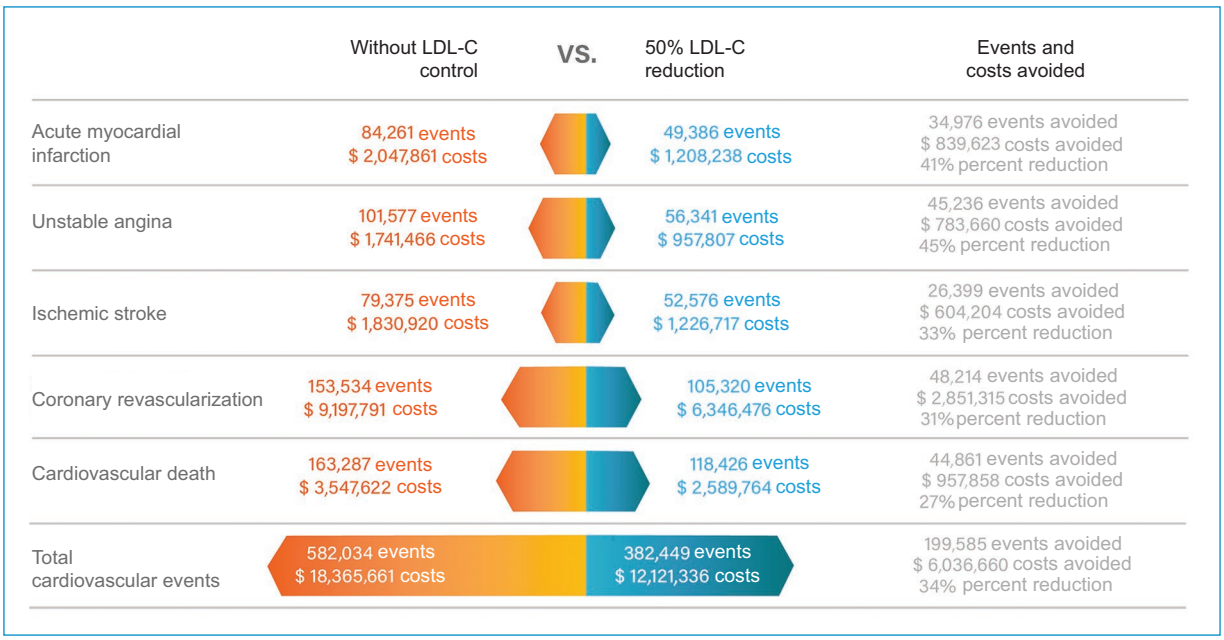


Figure 3. Impact of LDL-C control in Colombian patients with out-of-target ASCVD with high and very high cardiovascular risk, with a 10-year time horizon.
*Costs in millions of pesos.
LDL-C: low-density lipoprotein cholesterol; ASCVD: atherosclerotic cardiovascular disease.

Conclusions

For patients with ASCVD outside the LDL-C target and high and very high cardiovascular risk, sustained and consistent LDL-C control can potentially avoid MACEs and generate substantial savings for the Colombian healthcare system over a 5 and 10-year time horizon.

Acknowledgements

The authors would like to thank B. Dunne, J. Carew and N. Aggarwal for their contributions and suggestions in constructing the mathematical model.

Funding

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

Conflicts of interest

M. Ceballos, S. Arias and C. Gamboa are Novartis de Colombia associates.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

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

Use of artificial intelligence to generate text. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

References

1. Mensah GA, Fuster V, Murray CJL, Roth GA; Global Burden of Cardiovascular Diseases and Risks Collaborators. Global Burden of Cardiovascular Diseases and Risks, 1990-2022. J Am Coll Cardiol. 2023;82(25):2350-473.
2. Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, et al. Global Burden of Cardiovascular Diseases and Risk Factors, 1990-2019: Update From the GBD 2019 Study. J Am Coll Cardiol. 2020;76(25):2982-3021.
3. GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2020;396(10258):1204-22.
4. Stevens B, Verdian L, Tomlinson J, Zegenhagen S, Pezzullo L. PM021 The Economic Burden of Heart Diseases in Colombia. Glob Heart. 2016;11(2):e73-e74.

5. Ruiz-Morales A, Gagnon-Arpin I, Dobrescu A, Sutherland G, Villa G, García-Perlaza J, et al. Modelling the burden of cardiovascular disease in Colombia and the impact of reducing modifiable risk factors. Value Health. 2017;20(9):A918.
6. Libby P, Buring JE, Badimon L, Hansson GK, Deanfield J, Bittencourt MS, et al. Atherosclerosis. Nat Rev Dis Primers. 2019;5(1):56.
7. Herrington W, Lacey B, Sherliker P, Armitage J, Lewington S. Epidemiology of atherosclerosis and the potential to reduce the global burden of atherothrombotic disease. Circ Res. 2016;118(4):535-46.
8. Vaduganathan M, Mensah GA, Turco JV, Fuster V, Roth GA. The global burden of cardiovascular diseases and risk: a compass for future health. J Am Coll Cardiol. 2022;80(25):2361-71.
9. Fulcher J, O'Connell R, Voysey M. Efficacy and safety of LDL-lowering therapy among men and women: meta-analysis of individual data from 174,000 participants in 27 randomised trials. Lancet. 2015;385(9976):1397-405.
10. Cholesterol Treatment Trialists' (CTT) Collaboration; Fulcher J, O'Connell R, Voysey M, Emberson J, Blackwell L, et al. Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel. Eur Heart J. 2017;38(32):2459-72.
11. Silverman MG, Ference BA, Im K, Wiviott SD, Giugliano RP, Grundy SM, et al. Association between lowering LDL-c and cardiovascular risk reduction among different therapeutic interventions: a systematic review and meta-analysis. JAMA. 2016;316(12):1289-97.
12. Romero M, Vásquez E, Acero G, Huérfano L. Estimación de los costos directos de los eventos coronarios en Colombia. Rev Colomb Cardiol. 2018;25(6):373-9.
13. Camacho S, Maldonado N, Bustamante J, Llorente B, Cueto E, Cardona F, et al. How much for a broken heart? Costs of cardiovascular disease in Colombia using a person-based approach. PLoS One. 2018;13(12):e0208513.
14. Mach F, Baigent C, Catapano AL, Koskinas KC, Casula M, Badimon L, et al. 2019 ESC/EAS guidelines for the management of dyslipidaemias: Lipid modification to reduce cardiovascular risk. Atherosclerosis. 2019;290(1):140-205.
15. Abushanab D, Al-Badriyeh D, Marquina C, Bailey C, Jaam M, Liew D, et al. A systematic review of cost-effectiveness of non-statin lipid-lowering drugs for primary and secondary prevention of cardiovascular disease in patients with type 2 diabetes mellitus. Curr Probl Cardiol. 2023;48(8):101211.
16. Husain MJ, Spencer G, Nugent R, Kostova D, Richter P. The cost-effectiveness of hyperlipidemia medication in low- and middle-income countries: a review. Glob Heart 2022;17(1):18.
17. Cuenta de Alto Costo. Magnitud, tendencia y acceso a los servicios de salud en las personas con enfermedad renal crónica en el marco del aseguramiento en Colombia [Internet]. Colombia: Cuenta de Alto Costo; 2022 [consultado: 14 feb 2024]. Disponible en: https://cuentadealtocosto.org/wp-content/uploads/2022/06/mta-15-junio-2022.pdf
18. Ruiz AJ, Vargas-Uricoechea H, Urina M, Román-González A, Isaza D, Etayo E, et al. Las dislipidemias y su tratamiento en centros de alta complejidad en Colombia. Clin Investig Arterioscler. 2020;(3):1-10.
19. National Institute for Health and Care Excellence. Alirocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia [Internet]. UK: National Institute for Health and Care Excellence; 2016 [consultado: 15 mar 2024]. Disponible en: https://www.nice.org.uk/guidance/ta393
20. Clinical Practice Research Datalink. Introduction to CPRD [Internet]. UK: Medicines & Healthcare products Regulatory Agency, Clinical Practice Research Datalink; 2021 [consultado: 15 mar 2024]. Disponible en: https://www.cprd.com/introduction-cprd
21. Wilson PW, D'Agostino R, Bhatt DL, Eagle K, Pencina MJ, Smith SC, et al. An international model to predict recurrent cardiovascular disease. Am J Med. 2012;125(7):695-703.
22. Ministerio de Salud y Protección Social. Cubo de Suficiencia UPC. Consulta para el periodo 2021-2023 [Internet]. Colombia: Ministerio de Salud y Protección Social [consultado: 15 feb 2024]. Disponible en: https://www.SISPRO.gov.co/Pages/Home.aspx
23. Arango J, Ávila D, Benavides J, Betancurt E, Camacho J, Carballo V, et al. Informe técnico de posicionamiento terapéutico para el tratamiento farmacológico de la hipertensión arterial con inhibidores de la enzima convertidora de angiotensina II. Instituto de Evaluación Tecnológica en Salud IETS y Ministerio de Salud y Protección Social; 2020.
24. Ávila D, Barbosa A, Bonilla I, Cortés AJ, Coretes-Palacio KM, Gutiérrez AV, et al. Informe técnico del Posicionamiento Terapéutico para el tratamiento farmacológico (antiagregantes plaquetarios) para prevención primaria de eventos cardiovasculares, prevención secundaria de eventos cardiovasculares, prevención de eventos trombóticos después de la colocación de stent coronarios. Instituto de Evaluación Tecnológica en Salud IETS y Ministerio de Salud y Protección Social; 2021.
25. Journath G, Hambraeus K, Hagström E, Pettersson B, Löthgren M. Predicted impact of lipid lowering therapy on cardiovascular and economic outcomes of Swedish atherosclerotic cardiovascular disease guideline. BMC Cardiovasc Disord. 2017;17(1):224.
26. Jena AB, Blumenthal DM, Stevens W, Chou JW, Ton TG, Goldman DP. Value of improved lipid control in patients at high risk for adverse cardiac events. Am J Manag Care. 2016;22(6):e199-e207.
27. Tran DT, Palfrey D, Lo TKT, Welsh R. Outcome and cost of optimal control of dyslipidemia in adults with high risk for cardiovascular disease. Can J Cardiol. 2021;37(1):66-76.
28. Escobar-Cervantes C, Villa G, Campos-Tapias I, Sorio-Vilela F, Lozano J, Kahangire DA, et al. Achieving lower LDL-c levels after a recent myocardial infarction might be associated with lower healthcare resource use and costs in Spain. Adv Ther. 2022;39(8):3578-88.
29. Ministerio de Salud y Protección Social. Ruta Integral de Atención en Salud para personas con riesgo o presencia de alteraciones cardio-cerebro-vascular-metabólicas manifiestas [Internet]. Colombia: Ministerio de Salud y Protección Social; 2016 [consultado: 15 feb 2024]. Disponible en: https://www.minsalud.gov.co/sites/rid/Lists/BibliotecaDigital/RIDE/DE/COM/enlace-minsalud-81-rias.pdf
30. Ministerio de Salud y Protección Social. Resolución 2463 de 2014, Por la Cual se Modifica la Resolución 4700 de 2008 [Internet]. Colombia: Ministerio de Salud y Protección Social; 2016 [consultado: 15 mar 2024]. Disponible en: https://cuentadealtocosto.org/wp-content/uploads/2019/10/Resolucion-02463-de-2014-ERC.pdf
31. Cuenta de Alto Costo. Situación de la enfermedad renal crónica, la hipertensión arterial y la diabetes mellitus en Colombia 2022 [Internet]. Colombia: Cuenta de Alto Costo; 2023 [consultado: 15 mar 2024]. Disponible en: https://cuentadealtocosto.org/publicaciones/situacion-de-la-enfermedad-renal-cronica-la-hipertension-arterial-y-la-diabetes-mellitus-en-colombia-2022
32. Diaztagle JJ, Chaves WG, Sprockel JJ, Sastoque JA, Nieto JA, Barreto GA, et al. Cumplimiento de metas de lípidos en pacientes de prevención secundaria hospitalizados por medicina interna. Acta Med Colomb. 2013;38(2):54-60.
33. Merchán-Villamizar A, García-Peña AA, Isaza-Restrepo D, Isaza N, Reynales H. Logro de las metas de colesterol LDL en pacientes con enfermedad coronaria aterosclerótica establecida. Rev Colomb Cardiol. 2020;27(6):508-13.
34. Machado-Duque ME, Gaviria-Mendoza A, Machado-Alba JE. Prevalence of lipid-lowering drug use. Rev Colomb Cardiol. 2021;28(1):14-7.
35. Ference BA, Cannon CP, Landmesser U, Lüscher TF, Catapano AL, Ray KK. Reduction of low-density lipoprotein-cholesterol and cardiovascular events with proprotein convertase subtilisin-kexin type 9 (PCSK9) inhibitors and statins: an analysis of FOURIER, SPIRE, and the Cholesterol Treatment Trialists Collaboration. Eur Heart J. 2018;39(27):2540-5.
36. Khan SU, Yedlapati SH, Lone AN, Hao Q, Guyatt G, Delvaux N, et al. PCSK9 inhibitors and ezetimibe with or without statin therapy for cardiovascular risk reduction: a systematic review and network meta-analysis. BMJ. 2022;377:e069116.
37. Cholesterol Treatment Trialists' (CTT) Collaboration; Baigent C, Blackwell L, Emberson J, Holland LE, Reith C, et al. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials. Lancet. 2010;376(9753):1670-81.
38. Boekholdt SM, Arsenault BJ, Mora S, Pedersen TR, LaRosa JC, Nestel PJ, et al. Association of LDL cholesterol, non-HDL cholesterol, and apolipoprotein B levels with risk of cardiovascular events among patients treated with statins: a meta-analysis. JAMA. 2012;307(12):1302-9.

Revista Colombiana de Cardiología
Órgano oficial de la Asociación Sociedad Colombiana de Cardiología & Cirugía Cardiovascular
Permanyer

Check for updates

ORIGINAL ARTICLE

Echocardiographic findings in patients hospitalized for COVID-19 and their relationship to inpatient and one-year mortality

Hallazgos ecocardiográficos en pacientes hospitalizados por COVID-19 y su relación con la mortalidad intrahospitalaria y al año del alta

Jairo A. Rendón-Giraldo[1], Camila Lema-Calidonio[2], and Clara Isaldarriaga-Giraldo[3]*

[1]Cardiology Program, Faculty of Medicine, Universidad CES; [2]Departament of Cardiology, Faculty of Medicine, Universidad CES; [3]Departament of Internal Medicine, Faculty of Medicine, Universidad de Antioquia. Medellín, Colombia

Abstract

Introduction: *In December 2019, the first case of a novel coronavirus infection was reported, and its rapid spread made it a global public health problem. Cardiovascular involvement has been frequently reported.* **Objective:** *In this study, we present the echocardiographic findings of a group of patients hospitalized with COVID-19 and their relationship with inpatient mortality.* **Method:** *This was an observational, cross-sectional study of hospitalized patients diagnosed with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, who had an echocardiogram ordered during hospitalization.* **Results:** *A total of 2,052 patients with a confirmed diagnosis of COVID-19 infection were included, and echocardiograms were performed on 18%. The mean age was 62.9 years, and 37% were female. The inpatient mortality was 36.3%, and the cumulative mortality at one year after discharge was 43%. The most frequent comorbidities were hypertension in 45% of patients and diabetes in 28%. Patients who died in the hospital were significantly older (67 vs. 62 years; p < 0.01) and had right ventricular dilatation (p < 0.01) pulmonary hypertension (p = 0.03), and diastolic dysfunction (p = 0.04). In the 236 patients discharged, the one-year all-cause mortality was 11.9%. Patients who died were older (65.5 vs. 61.5 years) and had a higher percentage of pulmonary hypertension and right ventricular dysfunction, although no statistically significant differences were found between the groups.* **Conclusions:** *This study suggests that in patients hospitalized with severe COVID, clinical and echocardiographic markers such as age over 65, right ventricular dilatation, pulmonary hypertension, and diastolic dysfunction are related to an increased risk of both inpatient and one-year mortality.*

Keywords: *COVID-19. Echocardiogram. Mortality.*

Resumen

Introducción: *En diciembre de 2019 se reportó el primer caso de infección por el nuevo coronavirus. Seha reportado de manera frecuente la presencia de compromiso cardiovascular.* **Objetivo:** *El presente estudio tiene como objetivo presentar los hallazgos ecocardiográficos encontrados en un grupo de pacientes hospitalizados con COVID-19 y su relación con la mortalidad intrahospitalaria y un año posterior al alta.* **Método:** *Se realizó un estudio observacional, de corte transversal, en pacientes hospitalizados con diagnostico de infección por coronavirus 2 del síndrome respiratorio agudo grave (SARS-CoV-2),*

***Correspondence:**
Jairo A. Rendón-Giraldo
E-mail: docjare@hotmail.com

Date of reception: 26-07-2022
Date of acceptance: 27-04-2023
DOI: 10.24875/RCCARE.M23000132
Available online: 05-02-2025
Rev Colomb Cardiol. 2024;31(6):356-362
www.rccardiologia.com

a los cuales se les realizó un ecocardiograma. **Resultados:** *Se incluyeron 2,052 pacientes con diagnóstico confirmado de COVID-19, al 18% de los cuales se les realizó un ecocardiograma. La edad promedio fue de 62.9 años y el 37% fueron de sexo femenino. La mortalidad hospitalaria fue del 36.3% y la acumulada al año del alta del 43%. Las comorbilidades más frecuentes fueron hipertensión arterial en el 45% de los pacientes y la diabetes en el 28%. Los pacientes que fallecieron de manera intrahospitalaria fueron significativamente mayores (67 vs. 62 años; p < 0.01), presentaban dilatación del ventrículo derecho (p < 0.01) hipertensión pulmonar (p = 0.03) y disfunción diastólica (p = 0.04). En los 236 pacientes dados de alta, la mortalidad al año por todas las causas fue del 11.9%. Los pacientes que fallecieron fueron mayores, 65.5 vs. 61.5 años, tenían en un mayor porcentaje hipertensión pulmonar y disfunción ventricular derecha, aunque no se encontraron diferencias estadísticamente significativas entre los grupos.* **Conclusiones:** *Este estudio sugiere que en los pacientes hospitalizados por COVID grave, marcadores clínicos y ecocardiográficos como la edad mayor a 65 años, la dilatación del ventrículo derecho, la hipertensión pulmonar y la disfunción diastólica se relacionan con mayor riesgo de mortalidad intrahospitalaria y al año del alta.*

Palabras clave: *COVID-19. Ecocardiograma. Mortalidad.*

Introduction

The first case of a novel coronavirus infection was reported in China in December 2019, with rapid dissemination that made it a global public health problem[1,2]. Although the symptoms predominantly associated with this infection are respiratory, cardiovascular effects of the virus were increasingly reported. The first reports indicated cardiac involvement in 20 to 25% of the patients, based on clinical signs and elevated troponins[3,4]. Later studies with echocardiography showed myocardial lesions, even without significant respiratory abnormalities[5]. This involvement can include myocarditis, takotsubo cardiomyopathy and heart failure. It can occur as a direct result of the infection or secondary to pulmonary embolism or pneumonia[6-8], and therefore an echocardiogram can help in making treatment decisions for up to a third of the evaluated patients[9]. There is a significant knowledge gap regarding the prognostic value of cardiac involvement in patients with COVID-19.

In this study, we present the echocardiographic findings of a group of patients hospitalized for COVID-19 and their relationship to inpatient mortality and all-cause mortality one year after discharge.

Method

This was an observational cross-sectional study that enrolled patients hospitalized for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection confirmed by a polymerase chain reaction test who had an echocardiogram ordered during hospitalization. Patients on whom a complete echocardiogram could not be performed due to technical limitations were excluded.

Comorbidities were recorded based on the admission history in the medical chart. Kidney failure was defined as having been previously diagnosed with stage 4-5 kidney disease[10], and coronary disease as having a history of surgical or percutaneous revascularization or a history of an old myocardial infarction.

An echocardiogram was considered normal when the morphology of the heart chambers, systolic and diastolic function parameters, and pulmonary pressure were within normal limits, and there was no more than mild valve dysfunction.

Pulmonary hypertension was defined as a calculated systolic pulmonary pressure greater than 35 mmHg. Right ventricular dilatation was defined as a basal diameter greater than 4.1 cm and/or a left-to-right ventricle basal diameter ratio greater than 1.2. The left atrium was considered dilated if the volume index was greater than 34 ml/m^2 bs. Right ventricular dysfunction was defined as < 35% fractional area shortening or < 1.7 cm tricuspid annular plane systolic excursion (TAPSE) with no history of prior cardiac surgery.

Left ventricular ejection fraction (LVEF) was calculated using the modified Simpson method. Right ventricular global systolic function was calculated using tricuspid annular displacement and/or fractional area shortening, and diastolic function was calculated according to the 2016 guidelines[11]. Diastolic function was classified as normal, abnormal or indeterminate for analysis. Pulmonary artery systolic pressure was estimated using tricuspid regurgitation velocity plus calculated central venous pressure or measured directly with a central venous catheter[11].

Mechanical ventilation was recorded in relation to the requirement at the time of the echocardiogram, and the patients' vital status was confirmed by reviewing the chart. The mortality recorded was that which occurred

during hospitalization and one year after discharge, according to the social security registry.

The echocardiographic measurements were taken according to the American Society of Echocardiography guidelines[12].

The statistical analysis was done using SPSS version 23.0. The patients were divided into two groups based on their outcome: recovered and deceased.

Quantitative variables were described with measures of central tendency and measures of dispersion. Qualitative variables were expressed in frequencies and percentages. The differences in quantitative variables were evaluated using the Student´s t or Mann-Whitney U tests, according to their distribution. The differences in qualitative variables were evaluated using Pearson's chi-square test. P values (level of significance) ≤ 0.05 were considered statistically significant.

Results

During the study period, 2,052 patients were hospitalized with a confirmed COVID-19 diagnosis, 376 (18%) of whom had an echocardiogram ordered. Eight patients were excluded because a complete study could not be performed due to an inadequate acoustic window.

The average age was 62.9 years, 37% were females, and the most frequent comorbidities were hypertension in 45% of the patients and diabetes in 28%. Altogether, 77.4% of the patients were overweight and 32.2% were obese, according to their body mass index. A total of 91.3% of the patients were on mechanical ventilation when the echocardiogram was performed.

Sixteen percent of the echocardiograms were reported as normal. The average LVEF was 56.8%, 14.4% had an LVEF less than 50%, and 20.9% had right ventricular dysfunction. Eighteen percent of the population had right ventricular dilatation. The rest of the clinical and echocardiographic characteristics are presented in tables 1 and 2.

Inpatient mortality was 36.3%. The patients who died were significantly older (67 vs. 62 years; $p < 0.01$) and had right ventricular dilatation ($p < 0.01$), pulmonary hypertension ($p = 0.03$) and diastolic dysfunction ($p = 0.04$).

Among the 236 patients who were discharged, one-year all-cause mortality was 11.9%. The patients who died were older (65.5 vs. 61.5 years) and had a higher percentage of pulmonary hypertension and right ventricular dysfunction, although there were no statistically significant differences between the groups (Table 3).

Discussion

This study's results suggest that, in patients with severe COVID, advanced age, right ventricular dilatation, pulmonary hypertension and diastolic dysfunction are associated with a greater risk of death during hospitalization and even a year after discharge.

Our study found a 36.3% mortality rate, similar to what was reported in the Brazilian study by Pimentel et al., which was 34%, but much greater than the Italian study by Silverio, in which it was only 16.1%[13,14]. This is explained by the different characteristics of the populations; both studies enrolled hospitalized patients, regardless of the severity of the disease, while our study only included patients with severe disease. Also, more than 90% of our patients were on mechanical ventilation when the echocardiogram was performed, while the PROVAR-COVID study had 90% ventilated patients only in the group who died, and only 26% of those who recovered were on ventilation[13].

The Italian group reported similar findings, with ventilatory support in 66% of the patients who died and less than 20% of the patients who recovered[11]. The greater need for ventilation in our study could be explained by the type of population at our facility, as only severely ill patients were cared for.

Regarding the relationship between comorbidities and mortality, this study only found a relationship with age over 65; this finding is consistent with what previous studies have reported[15,16]. Underlying diseases like hypertension, diabetes and overweight were not related to mortality, while in studies such as Shi et al.'s[17], diabetes was related to a higher risk of death, and obesity was also a significant risk marker in Gao et al.'s study[18].

In this study, only 16% of the echocardiograms were considered normal, which shows a high prevalence of cardiac involvement in this population. However, due to the nature of the study, we could not determine whether the abnormalities were pre-existent or related to COVID-19.

Right ventricular dilatation was related to increased mortality, while right ventricular dysfunction was not. This finding could be explained by the cut-off points used to determine the latter, as the absolute tricuspid displacement values were significantly different between the groups.

Our study revealed the same findings as those in Ghidini et al.'s systematic review, which showed that right ventricular dilatation was much more frequent than left or right ventricular function deterioration, in patients with more severe disease[19]. Furthermore, these authors

Table 1. Clinical characteristics of patients hospitalized for coronavirus disease 2019 (COVID-19)

	Total n = 369 (100%)	Deceased n = 134 (36.3%)	Recovered n = 235 (63.7%)	p‡
Age years	62.9 (55.0-72.0)	67.2 (61.0-77.0)	62.0 (51.0-71.0)	< 0.01
Male sex	232 (62.9%)	90 (67.2%)	142 (60.4%)	0.24
BMI	29 ± 11.0	28.7 ± 8.8	26.7 ± 2.6	0.56
Mechanical ventilation	337 (91.3%)	122 (91.0%)	215 (91.5%)	< 0.01
Comorbidities				
HTN	168 (45.5%)	65 (48.5%)	103 (43.8%)	0.44
DM	103 (27.9%)	39 (29.1%)	64 (27.2%)	0.71
CD	34 (9.2%)	12 (9.0%)	22 (9.4%)	0.85
BMI > 25	267 (72.4%)	98 (73.1%)	169 (71.9%)	0.72
BMI > 30	119 (32.2%)	49 (36.6%)	70 (29.8%)	0.13
Heart failure	15 (4.1%)	4 (3.0%)	11 (4.7%)	0.58
Pulmonary disease	53 (14.4%)	25 (19.0%)	28 (11.9%)	0.18
CKD	13 (3.5%)	2 (1.5%)	11 (4.7%)	0.15
> 65 years	182 (49.3%)	85 (63.4%)	97 (42.3%)	< 0.01

‡Statistical significance: p < 0.05.
BMI: body mass index; HTN: hypertension; DM: diabetes mellitus; CD: coronary disease; CKD: chronic kidney disease.

Table 2. Echocardiographic findings in patients hospitalized for coronavirus disease 2019 (COVID-2019)

	Total (n = 369)	Deceased (n = 134)	Recovered (n = 235)	p*
Normal echocardiogram	59 (16.0%)	16 (11.90%)	43 (18.30%)	0.14
LVEF %	56.8 ± 10.1	56.7 ± 9.4	56.90 ± 10.6	0.89
LVEF < 50%	53 (14.4%)	23 (17.2%)	30 (12.8%)	0.28
RV dilatation	67 (18.2%)	35 (26.1%)	32 (13.6%)	< 0.01
RA dilatation	70 (19.0%)	32 (23.9%)	38 (16.2%)	0.07
RV dysfunction	77 (20.9%)	32 (23.9%)	45 (19.1%)	2.89
LA dilatation	107 (29.0%)	41 (30.6%)	66 (28.1%)	0.63
PH	266 (72.1%)	106 (79.1%)	160 (68.1%)	0.03
TAPSE cm	2.08 ± 4.7	2.01 ± 4.6	2.12 ± 4.7	0.04
Normal diastolic function	181 (49.1%)	56 (41.8%)	125 (53.2%)	0.04
Diastolic dysfunction	102 (27.6%)	46 (34.3%)	56 (23.8%)	0.04
Indeterminate diastolic dysfunction	86 (23.3%)	32 (23.9%)	54 (23.0%)	0.04

*Statistical significance: p < 0.05.
LVEF: left ventricular ejection fraction; RV: right ventricle; RA: right atrium; LA: left atrium; PH: pulmonary hypertension; TAPSE: tricuspid annular plane systolic excursion; p: level of significance.

suggest that there is a relative preservation of longitudinal shortening, and therefore TAPSE measurement may not be the most appropriate method for evaluating right ventricular function in this group of patients.

Pulmonary hypertension has been reported in different COVID-19 patient populations[20,21]. This occurs due to a convergence of multiple factors: an altered ventilation-perfusion ratio, pulmonary parenchymal abnormalities, increased pulmonary vascular tone due to the inflammatory process and pulmonary thromboembolism[22,23]. Although the current guidelines recommend evaluating other signs in addition to tricuspid regurgitation

Table 3. Clinical and echocardiographic findings in patients with COVID-19 and their relationship to mortality one year after hospital discharge

Characteristics	Total	Alive	Deceased	p*
	n = 236	n = 208 (88.1)	n = 28 (11.9%)	
Age years†	60.7 ± 14.8	61.5 ± 14.9	65.5 ± 13.5	0.18
Male sex‡	143 (60.6%)	127 (61.1%)	16 (57.1%)	0.69
BMI†	28.5 ± 5.9	27.9 ± 5.8	26.8 ± 6.2	0.03
Mechanical ventilation‡	84 (35.6%)	71 (34.1%)	13 (46.0%)	0.21
Comorbidities				
HTA‡	103 (43.6%)	91 (43.8%)	12 (42.9%)	1.0
DM‡	64 (27.1%)	57 (27.4%)	7 (25.0%)	1.0
Coronary disease‡	22 (9.3%)	21 (10.1%)	1 (3.6%)	0.49
BMI > 25‡	168 (71.2%)	151 (72.6%)	17 (60.7%)	0.19
BMI > 30‡	81 (34.3%)	75 (36.1%)	6 (21.4%)	0.14
Heart failure‡	11 (4.7%)	11 (5.3%)	0 (0.0%)	0.37
Pulmonary disease‡	29 (12.3%)	26 (12.5%)	3 (10.7%)	1.0
CKD‡	10 (4.2%)	7 (3.4%)	3 (10.7%)	0.10
> 65 years‡	100 (42.4%)	86 (41.3%)	14 (50.0%)	0.41
#RFs	1.8 ± 1.4	1.8 ± 1.4	1.6 ± 1.2	0.58
Echocardiographic findings				
RV dilatation	33 (14.0%)	27 (12.9%)	6 (21.4%)	0.25
TAPSE, cm†	2.1 ± 0.47	2.1 ± 0.47	2.1 ± 0.47	0.35
RA dilatation‡	39 (16.5%)	32 (15.4%)	7 (25.0%)	0.27
LVEF†	56.8 ± 10.6	60.0 ± 10.9	60.0 ± 7.3	0.13
E/e' †	12.4 ± 6.2	11.4 ± 5.9	12.1 ± 8.1	0.4
PH‡	161 (68.2%)	138 (66.3%)	23 (82.1%)	0.13
E/e' > 14‡	58 (24.6%)	51 (24.50%)	7 (25.00%)	1.0
LVEF < 50%‡	31 (13.1%)	29 (13.9%)	2 (7.1%)	0.55
LA dilatation‡	65 (27.5%)	58 (27.9%)	7 (25.0%)	0.83
TAPSE < 18‡	46 (19.5%)	39 (18.8%)	7 (25.0%)	0.45
Normal echocardiogram‡	43 (18.2%)	41 (19.7%)	2 (7.10%)	0.12
Normal diastolic function‡	125 (53.0%)	112 (53.8%)	13 (46.4%)	0.55
Score†	2.6 ± 1.7	3 ± 1.7	3 ± 1.7	0.06

*Statistical significance: $p < 0.05$.
†mean ± standard deviation.
‡n (%).
BMI: body mass index; HTN: hypertension; DM: diabetes mellitus; CKD: chronic kidney disease; RV: right ventricle; #RFs: number of risk factors identified; TAPSE: tricuspid annular plane systolic excursion; RA: right atrium; LVEF: left ventricular ejection fraction; PH: pulmonary hypertension; LA: left atrium; p: level of significance.

velocity to determine the probability of pulmonary hypertension, many studies have reported that an estimated pulmonary systolic pressure greater than 35 mmHg is a valid parameter for determining the severity of COVID-19[24,25] and an independent predictor of mortality[26].

The study by Pagnesi et al. associated the presence of pulmonary hypertension, but not right ventricular dysfunction, with mortality or the need for intensive care, similar to our study's findings[27].

Left ventricular ejection fraction is a clearly established risk marker for stratifying intensive care patients with other pathologies[28], and some studies suggest a similar behavior in patients with COVID-19. However, our study did not show significant differences between patients who survived and those who did not, possibly due to the low incidence of left ventricular dysfunction in our study.

As far as the association between diastolic dysfunction as an early marker of myocardial involvement and mortality, we found no reports on the measurement of this parameter in echocardiographic studies published up to the time of this writing, but abnormal diastolic function has been associated with a worse prognosis in the outcome of many pathologies[29,30].

The mortality rate after hospital discharge was 11.9%, for a cumulative one-year mortality rate of 43%. This is much higher than what Huang et al. found in their first paper on post-COVID patients, in which there was only 1.5% mortality at six months after discharge[31], and the Ceccato group study[32], with 1% at one year. Maestre's Spanish group was a little closer, with 7.5%[33], which could be explained by the different patient selection criteria, healthcare system differences, and the way in which follow-up was conducted.

Study contributions

During the pandemic, echocardiograms were limited to the most severe cases of the disease to reduce healthcare staff's exposure to the risk of infection. The strict considerations used for ordering an echocardiogram contribute to the high proportion of abnormal echocardiograms in this study and, at the same time, are a significant source of clinical and prognostic information.

Limitations

Echocardiograms were performed on only 18% of the hospitalized patients, and therefore the results cannot be used to infer what occurs in all patients with SARS-CoV-2. However, this reflects the challenges in caring for this disease and adhering to the recommendations for the use of diagnostic imaging in this group of patients.

This was a critically ill and highly selected population, because the hospital where the study was carried out is a referral center for patients with moderate or severe COVID. Echocardiograms were ordered at the attending medical team's discretion and not as a routine test, which may create selection bias.

Conclusion

This study suggests that clinical and echocardiographic markers, like age over 65, right ventricular dilatation, pulmonary hypertension and diastolic dysfunction, can help identify patients with a higher risk of both inpatient and one-year mortality. Post-discharge surveillance programs should be created to reduce the complications and mortality after COVID-19.

Acknowledgements

The authors would like to thank the nurse aides and secretaries, without whose valuable contribution this study could not have been performed.

Funding

The authors declare that they have not received funding.

Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that the procedures followed complied with the ethical standards of the responsible human experimentation committee and adhered to the World Medical Association and the Declaration of Helsinki. The procedures were approved by the institutional Ethics Committee.

Confidentiality, informed consent, and ethical approval. The authors have obtained approval from the Ethics Committee for the analysis of routinely obtained and anonymized clinical data, so informed consent was not necessary. Relevant guidelines were followed.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in writing this manuscript.

References

1. World Health Organization. Pneumonia of unknown cause-China [Internet]. World Health Organization [acceso 5 ene 2021]. Disponible en: https://www.who.int/csr/don/05-january 2021 pneumonia of unkown cause china/en/
2. World Health Organization. Novel coronavirus, China [Internet]. World Health Organization [acceso 12 ene 2021]. Disponible en: https://www.who.int/csr/don/12-january-2021- novel-coronavirus-china/en/
3. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395:1054-62.
4. Guo T, Fan Y, Chen M, Wu X, Zhang L, He T, et al. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). JAMA Cardiol. 2020;5(7):811-8.
5. Inciardi RM, Lupi L, Zaccone G, Italia L, Raffo M, Tomasoni D, et al. Cardiac involvement in a patient with coronavirus disease 2019 (COVID-19). JAMA Cardiol. 2020;5(7):819-24.
6. Hu H, Ma F, Wei X, Fang Y. Coronavirus fulminant myocarditis saved with glucocorticoid and human immunoglobulin. Eur Heart J. 2021;42(2):191.
7. Meyer P, Degrauwe S, Delden CV, Ghadri JR, Templin C. Typical takotsubo syndrome triggered by SARS-CoV-2 infection. Eur Heart J. 2020;41:1860.
8. Chapman AR, Bularga A, Mills NL. High-sensitivity cardiac troponin can be an ally in the fight against COVID-19. Circulation. 2020;141:1733-5.
9. Dweck MR, Bularga A, Hahn RT, Bing R, Lee KK, Chapman AR, et al. Global evaluation of echocardiography in patients with COVID-19. Eur Heart J Cardiovasc Imaging. 2020;21(9):949-58.
10. Levey AS, Eckardt KU, Tsukamoto Y, Levin A, Coresh J, Rossert J, et al. Definition and classification of chronic kidney disease: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). Kidney Int. 2005;67(6):2089-100.
11. Mitchell C, Rahko PS, Blauwet LA, Canaday B, Finstuen JA, Foster MC, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2016;29:277-314.
12. Mitchell C, Rahko PS, Blauwet LA, Canaday B, Finstuen JA, Foster MC, et al. Guidelines for performing a comprehensive transthoracic echocardiographic examination in adults: Recommendations from the American Society of Echocardiography. J Am Soc Echocardiogr. 2019(32):1-64.
13. Pimentel SLG, Nascimento BR, Franco J, Oliveira KKB, Fraga CL, Macedo FVB, et al. Bedside echocardiography to predict mortality of COVID-19 patients beyond clinical data: Data from the PROVAR-COVID study. Rev Soc Bras Med Trop. 2021;54:e03822021.
14. Silverio A, Di Maio M, Scudiero F, Russo V, Esposito L, Attena E, et al. Clinical conditions and echocardiographic parameters associated with mortality in COVID-19. Eur J Clin Invest. 2021;51(12):e13638.
15. Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, et al. Association of cardiac injury with mortality in hospitalized patients with covid-19 in Wuhan, China. JAMA Cardiol. 2020(5):802-10.
16. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with covid-19 in Wuhan, China: A retrospective cohort study. Lancet. 2020(395):1054-62.
17. Shi Q, Zhang X, Jiang F, Zhang X, Hu N, Bimu C, et al. Clinical characteristics and risk factors for mortality of COVID-19 patients with diabetes in Wuhan, China: a two-center, retrospective study. Diabetes Care. 2020;43(7):1382-91.
18. Gao F, Zheng KI, Wang XB, Sun QF, Pan KH, Wang TY, et al. Obesity is a risk factor for greater COVID-19 severity. Diabetes Care. 2020;43(7):e72-e74.
19. Ghidini S, Gasperetti A, Winterton D, Vicenzi M, Busana M, Pedrazzini G, et al. Echocardiographic assessment of the right ventricle in COVID-19: a systematic review. Int J Cardiovasc Imaging. 2021;22:1-14.
20. Mishra A, Lal A, Sahu KK, George AA, Martin K, Sargent J. An update on pulmonary hypertension in coronavirus disease-19 (COVID-19). Acta Biomed. 2020;91(4):e2020155.
21. Wats K, Rodriguez D, Prins KW, Sadiq A, Fogel J, Goldberger M, et al. Association of right ventricular dysfunction and pulmonary hypertension with adverse 30-day outcomes in COVID-19 patients. Pulm Circ. 2021;11(2):20458940211007040.
22. Patel BV, Arachchillage DJ, Ridge CA, Bianchi P, Doyle JF, Garfield B et al. Pulmonary angiopathy in severe COVID-19: physiologic, imaging, and hematologic observations. Am J Respir Crit Care Med. 2020;202(5):690-9.
23. Ackermann M, Verleden SE, Kuehnel M, Haverich A, Welte T, Laenger F, et al. Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in Covid-19. N Engl J Med. 2020;383(2):120-8.
24. Zeng JH, Wu WB, Qu JX, Wang Y, Dong CF, Luo YF, et al. Cardiac manifestations of COVID-19 in Shenzhen, China. Infection. 2020;48(6):861-70.
25. Barman HA, Atici A, Tekin EA, Baycan OF, Alici G, Meric BK, et al. Echocardiographic features of patients with COVID-19 infection: a cross-sectional study. Int J Cardiovasc Imaging. 2021;37(3):825-34.
26. Pagnesi M, Baldetti L, Beneduce A, Calvo F, Gramegna M, Pazzanese V, et al. Integrated clinical role of echocardiography in patients with COVID-19. Heart. 2020;106(23):1864-5.
27. Pagnesi M, Baldetti L, Beneduce A, Calvo F, Gramegna M, Pazzanese V, et al. Pulmonary hypertension and right ventricular involvement in hospitalised patients with covid-19. Heart. 2020(106):1324-31.
28. Inciardi RM, Adamo M, Lupi L, Cani DS, Di Pasquale M, Tomasoni D, et al. Characteristics and outcomes of patients hospitalized for COVID-19 and cardiac disease in Northern Italy. Eur Heart J. 2020;41(19):1821-9. Erratum in: Eur Heart J. 2020;41(48):4591.
29. AlJaroudi WA, Thomas JD, Rodriguez LL, Jaber WA. Prognostic value of diastolic dysfunction: state of the art review. Cardiol Rev. 2014;22(2): 79-90.
30. Lavine SJ, Murtaza G, Rahman ZU, Kelvas D, Paul TK. Diastolic function grading by American Society of Echocardiography guidelines and prediction of heart failure readmission and all-cause mortality in a community-based cohort. Echocardiography. 2021;38(12):1988-98.
31. Huang C, Huang L, Wang Y, Li X, Ren L, Gu X, et al. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. Lancet. 2021;397:220-32.
32. Ceccato A, Pérez-Arnal R, Motos A, Barbé F, Torres A; Ciberes UCICOVID Consortium. One-year mortality after ICU admission due to COVID-19 infection. Intensive Care Med. 2022;48(3):366-8.
33. Maestre-Muñiz MM, Arias A, Mata-Vázquez E, Martín-Toledano M, López-Larramona G, Ruiz-Chicote AM, et al. Long-term outcomes of patients with coronavirus disease 2019 at one year after hospital discharge. J Clin Med. 2021;10(13):2945.

Revista Colombiana de Cardiología
Órgano oficial de la Asociación Sociedad Colombiana de Cardiología & Cirugía Cardiovascular
Permanyer

Check for updates

ORIGINAL ARTICLE

Mortality in Colombia due to cerebrovascular disease versus ischemic heart disease: 1995-2020

Mortalidad en Colombia por enfermedad cerebrovascular en comparación con enfermedad isquémica coronaria: 1995-2020

María C. Valencia-Mendoza[1], Camilo Romero[1], and Nicolás Molano-González[2]*

[1]Departament of Neurology, Universidad del Rosario; [2]Departament of Research, Universidad del Rosario. Bogotá, Colombia

Abstract

Introduction: *In the last decade, due to the demographic transition and growing global population, the number of deaths from ischemic heart disease (IHD) and cerebrovascular disease (CVD) have been on the rise. Ischemic heart disease and CVD are the main causes of mortality in Colombia. However, there is scant information comparing the mortality rates between the two diseases.* **Objective:** *To describe and compare the mortality rates of IHD and CVD in Colombia from 1995 to 2020.* **Method:** *This was a descriptive, longitudinal, retrospective, ecological study using data extracted from the National Administrative Department of Statistics (DANE, in Spanish) on IHD and CVD mortality in adults over the age of 20 from 1995 to 2020. Age- and sex-adjusted mortality rates were calculated. A qualitative comparative analysis was performed.* **Results:** *The Colombian population grew 39% from 1995 to 2020, with those in the over-74 age group increasing by 165% for men and 187% for women. Ischemic heart disease was the leading cause of mortality until 2019, with the highest mortality rate in women over the age of 74. In the study period, mortality rates increased 67% for IHD and decreased 17.5% for CVD, with more pronounced divergence after 2010.* **Conclusion:** *In Colombia, from 1995 to 2020, there was a divergence in the IHD and CVD mortality rates, with an increase in the former and a decrease in the latter. This trend was more notable after 2010. Further studies are required to evaluate determinant factors for this behavior and to be able to create strategies to reduce mortality from vascular disease.*

Keywords: *Ischemic heart disease. Cerebrovascular disease. Mortality.*

Resumen

Introducción: *Con la transición demográfica y el aumento de la población mundial, el número de muertes por enfermedad isquémica cardiaca (EIC) y enfermedad cerebrovascular (ECV) ha ido en aumento en la última década. En Colombia la EIC y la ECV son las primeras causas de mortalidad. Sin embargo hay escasa información que compare las tasas de mortalidad entre las dos enfermedades.* **Objetivo:** *Describir y comparar las tasas de mortalidad por EIC y ECV en Colombia desde 1995 al 2020.* **Método:** *Estudio descriptivo, longitudinal, retrospectivo y ecológico con datos extraídos del Departamento Administrativo Nacional de Estadística (DANE) sobre mortalidad por ECV y EIC en adultos mayores de 20 años entre 1995 y 2020. Se calcularon las tasas de mortalidad ajustadas por edad y sexo. Se realizó un análisis cualitativo comparativo.* **Resultados:** *La poblacional colombiana aumentó un 39% de 1995 al 2020, para el grupo etario mayores de 74 años un*

***Correspondence:**
María C. Valencia-Mendoza
E-mail: mcvm.362@gmail.com

Date of reception: 07-06-2024
Date of acceptance: 25-09-2024
DOI: 10.24875/RCCARE.M24000134

Available online: 05-02-2025
Rev Colomb Cardiol. 2024;31(6):363-372
www.rccardiologia.com

165% en hombres y un 187% en mujeres. La EIC fue la primera causa de mortalidad hasta el 2019, con la tasa de mortalidad más alta para el grupo etario de mujeres mayores de 74 años. En el periodo de estudio, las tasas de mortalidad mostraron un incremento del 67% para EIC y una disminución del 17.5% para ECV, divergencia más pronunciada a partir del 2010. **Conclusión:** *En Colombia, desde 1995 al 2020 se observó una divergencia en las tasas de mortalidad por EIC y ECV, con un incremento en la primera y disminución en la segunda. Tendencia más notable a partir del 2010. Se requieren más estudios para evaluar los determinantes de este comportamiento y para poder generar estrategias que disminuyan la mortalidad por enfermedad vascular.*

Palabras claves: *Enfermedad cerebrovascular. Enfermedad coronaria. Mortalidad.*

Introduction

Increased longevity and a growing global population have led to an increase in the total number of deaths from noncommunicable diseases[1]. In 2000, this group of diseases caused 60.8% of deaths, and 73.6% in 2019. That same year, seven of the ten main causes of death, worldwide, were noncommunicable diseases, and from 2000-2019, they caused 80-90% of deaths in the Americas[2].

Although between 2000 and 2019, deaths from pulmonary diseases decreased by 37%, cardiovascular disease by 27% and cancer by 16%, in 2019, 33.2 million deaths were attributed to cancer, cardiovascular disease, diabetes and chronic respiratory diseases, a 28% increase compared to 2000[2].

Within the group of noncommunicable diseases, vascular disease is the leading cause of death worldwide. The global burden of disease study showed that ischemic heart disease (IHD) and cerebrovascular disease (CVD) were the main causes of death between 1990 and 2010[3]. From 1990 to 2019, deaths from cardiovascular disease increased from 12.1 million (95% confidence interval [95%CI]: 11.4-12.6 million) to 18.6 million (95% CI: 17.1-19.7 million)[4]. In 2019, global mortality from IHD was 9.14 million deaths (95% CI: 8.40-9.74 million), and 6.55 million for CVD (95% CI: 6.00-7.02 million), with the greatest burden in low and middle-income countries[3]. According to figures from the National Administrative Department of Statistics (DANE, in Spanish), of the 242,609 deaths recorded in Colombia in 2019, 38,475 were due to ischemic heart diseases and 15,543 to cerebrovascular diseases[5].

There are very few studies in Colombia comparing IHD and CVD mortality over the last decades. This study aims to evaluate and compare IHD and CVD mortality in Colombia over the last 26 years.

Method

This was a descriptive, longitudinal, retrospective, ecological study. Data was extracted from the official DANE platform (www.dane.gov.co), using the following route: statistics by topic, demographics and population, and births and deaths, accessing data on deaths and non-fetal deaths. Figures were taken from the national total: table of deaths by age group and sex, according to the departments in which the deaths occurred and cause of death, for the total deaths per year; IHD using code 051 and CVD using code 055. Data was extracted from 1995 to 2020 on male and female subjects over the age of 20, according to the five-year groups in the tables.

Deaths were organized by sex and age groups as follows: 20-49 years, 50-74 years and > 74 years.

To calculate the population for all the years in the study period (1995-2020), DANE figures were taken using the following route: statistics by topic, demographics and population, and population projections. This section contains population projections with post-COVID-19 updates, calculated based on the results of the 2018 National Population and Housing Census (CNPV-2018). Figures were obtained from the section on projections and retroprojections of the national population for 1950-2019 and 2020-2070, based on the CNPV-2018, by area, sex and age.

With the data obtained on the national population and IHD and CVD deaths in Colombia by sex and age group (20-49, 50-74 and > 74 years) for each year in the study period (1995-2020), the crude mortality and age-adjusted mortality rates were calculated for IHD and CVD per 100,000 inhabitants, by sex and age group.

The study was conducted according to the current Colombian regulatory guidelines for health research (Resolution Number 8430 of 1993 and Law 23 1981). Since this was a non-intervention and no-risk health study, informed consent was not required (Resolution Number 8430 of 1993). The protocol was approved by the institutional research and ethics committee. The authors certify the authenticity and fidelity of the information presented and report no conflicts of interest[6].

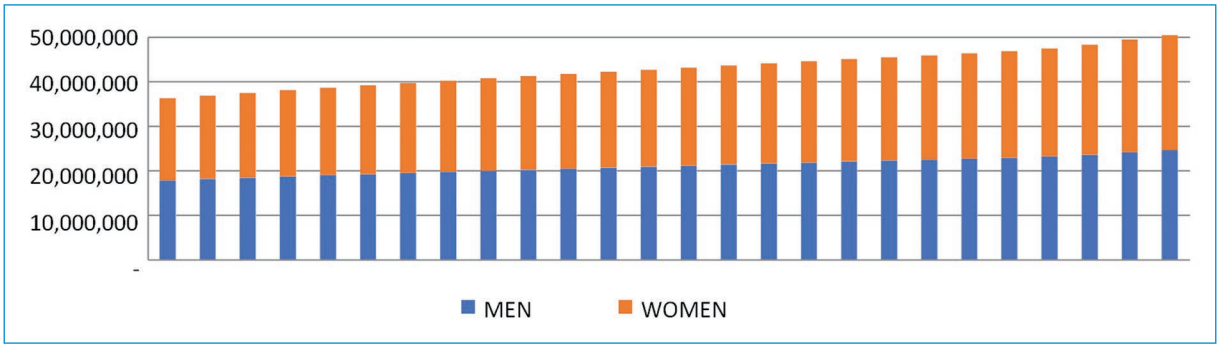


Figure 1. Total population growth in Colombia from 1995 to 2020.

Results

In the adult Colombian population over the age of 20, there was a 39% growth in the population (14,142,594 inhabitants) between 1995 and 2020, from 36,229,830 inhabitants to 50,372,424. The population growth was 37.7% in men and 40.2% in women. The approximately 1:1 male: female ratio was maintained throughout the 26 years of the study (Fig. 1). For our classification by age groups, the population pyramid kept its configuration throughout the 26 years, with the majority of inhabitants being under the age of 50. However, for women beginning in 1995 and men beginning in 2001, the population of the 20-49-year-old age group was slightly larger than that of those under age 20. There was a larger population change in the over-74 age group, with a 165.2% increase in men and 187% in women.

Throughout the 26 years, 5,251,507 deaths were recorded in the country, ranging from 169,896 (1995) to 296,800 (2020). During the study period, IHD was the leading cause of mortality until 2019, exceeded only by COVID-19 in 2020, with 748,594 deaths (14.3%), and IHD deaths ranging from 20,038 (1995) to 43,443 (2020). Cerebrovascular disease was the fourth cause of death in the country in 1995 and 1996, the third cause from 1997 to 2013 (after IHD and assaults/homicides) and the second from 2014 to 2019. A total of 365,617 CVD deaths (6.9%) were recorded, ranging from 12,695 (1998) to 16,090 (2018). For IHD and CVD, the age group with the highest mortality in both men and women was the over-74 group. For men > 74 years old, there were 200,062 IHD deaths recorded (26.7% of the total IHD deaths) over the 26 years, and 82,881 CVD deaths (22.6% of the total CVD deaths). For women > 74 years old, 210,502 IHD deaths were recorded during the same period (28.1% of the total IHD deaths), and 111,199 CVD deaths (30.4% of the total CVD deaths). The highest mortality recorded during the study period was due to IHD in women over the age of 74 (Table 1).

In absolute values, the crude and age-adjusted mortality rates for IHD and CVD throughout the 26 years (1995-2020) increased for those over the age of 74, from 22.7 to 56.3 per 100,000 inhabitants for IHD in men, and from 22.9 to 53.8 per 100,000 inhabitants in women. For CVD in men, they increased from 13.2 (1998) to 16.9 (2018) per 100,000 inhabitants, and for women from 16.4 (2018) to 22.1 (2018) per 100,000 inhabitants. This represents a 2.4 times increase for IHD and 1.3 times for CVD. For the 20-49 and 50-74-year-old age groups, IHD and CVD mortality decreased over the 26 years of the study, except for IHD mortality in 50-74-year-old men. In this group, mortality went from 29.6 (1998) to 38.3 (2018) per 100,000 inhabitants. Over the 26 years, the lowest mortality rate recorded was 1.6 per 100,000 inhabitants, in the IHD group of 20-49-year-old women in 2019. The highest rate was 56.3 per 100,000 inhabitants in the IHD group of men over the age of 74 in 2020 (Tables 2 and 3).

A comparison of the crude mortality rates for IHD and CVD per 100,000 inhabitants in people over the age of 20 from 1995 to 2020 showed increased IHD mortality, with a divergent trend after 2010 (Fig. 2).

The analysis by sex, comparing the IHD and CVD age-adjusted mortality rates per 100,000 inhabitants in people over the age of 20 from 1995 to 2020, showed a parallel trend in the IHD and CVD curves in all age groups (Fig. 3).

For the age group analysis, a comparison of IHD and CVD age-adjusted mortality rates per 100,000 inhabitants over the age of 20 from 1995 to 2020 showed stability for the age groups under 50, a reduction for CVD in those over age 74, and an increase for IHD in those over age 74 (Fig. 4).

Table 1. Mortality for ischemic heart disease (IHD) and cerebrovascular disease (CVD) in Colombia from 1995-2020, by age group and sex

Mortality	Total	Men 20-49 years n (%)	Men 50-74 years n (%)	Men > 74 years n (%)	Women 20-49 years n (%)	Women 50-74 years n (%)	Women > 74 years n (%)
IHD	748,594	26,787 (3.5%)	184,314 (24.6%)	200,062 (26.7%)	12,900 (1.7%)	109,325 (14.6%)	210,502 (28.1%)
CVD	365,617	13,251 (3.6%)	69,655 (19%)	82,881 (22.6%)	14,391 (3.9%)	69,098 (18.8%)	111,199 (30.4%)

Table 2. Age- and sex-adjusted mortality rates per 100,000 inhabitants for ischemic heart disease

Year	Ischemic heart disease					
	Men			Women		
	20-49	50-74	> 75	20-49	50-74	> 74
1995	5.9	32.3	22.7	3.4	21.0	22.9
1996	6.1	33.2	24.9	3.3	21.4	25.6
1997	6.1	30.7	22.7	3.0	20.0	23.4
1998	5.6	29.6	23.0	2.8	19.4	22.6
1999	5.8	31.6	25.6	2.9	20.2	25.6
2000	5.6	32.2	26.3	2.8	19.7	26.5
2001	5.5	32.2	27.4	2.7	20.1	27.6
2002	5.3	31.0	27.1	2.5	19.0	28.3
2003	5.3	30.8	28.3	2.3	19.2	29.0
2004	5.3	32.2	30.4	2.4	19.2	30.2
2005	5.2	34.5	32.4	2.6	19.4	32.1
2006	5.2	33.5	32.9	2.4	19.8	32.9
2007	5.0	33.2	33.5	2.3	18.8	34.1
2008	4.9	33.8	36.2	2.2	19.6	36.3
2009	4.7	32.3	34.2	1.8	18.7	34.3
2010	4.7	33.5	36.9	2.1	18.5	37.5
2011	4.4	32.2	37.5	2.0	17.9	37.8
2012	4.6	34.0	40.7	1.9	18.0	40.2
2013	4.3	34.2	41.5	2.0	18.4	42.1
2014	4.1	34.6	45.3	1.8	18.9	45.7
2015	4.3	35.3	47.0	1.9	19.3	48.6
2016	4.3	37.3	48.3	1.8	19.0	49.5
2017	4.3	36.4	49.8	1.8	19.3	51.5
2018	4.3	38.3	50.8	1.8	19.3	52.4
2019	3.9	35.9	48.1	1.6	18.3	49.5
2020	4.0	37.9	56.3	1.9	19.1	53.8

Table 3. Age- and sex-adjusted mortality rates per 100,000 inhabitants for cerebrovascular disease by sex and age group

Year	Cerebrovascular disease					
	Men			Women		
	20-49	50-74	> 75	20-49	50-74	> 74
1995	3.21	15.12	13.96	3.71	14.75	17.67
1996	3.39	16.31	13.94	3.92	15.22	17.36
1997	3.19	14.15	13.35	3.53	14.97	16.79
1998	2.73	13.55	13.17	3.48	14.16	16.44
1999	3.01	14.43	14.36	3.30	14.67	17.76
2000	3.28	14.67	14.55	3.63	14.77	18.88
2001	2.80	14.15	14.36	3.09	13.93	18.75
2002	2.55	13.63	14.15	2.98	14.20	18.85
2003	2.68	13.43	14.97	2.93	14.86	19.56
2004	2.70	12.92	14.71	2.70	13.09	19.16
2005	2.60	13.25	14.79	2.81	12.16	19.78
2006	2.71	13.21	15.39	2.50	12.81	20.15
2007	2.46	12.59	15.62	2.73	12.23	19.59
2008	2.26	12.26	16.06	2.49	12.62	20.60
2009	2.31	12.03	14.83	2.32	11.34	19.97
2010	1.95	11.68	14.84	2.17	11.16	19.46
2011	2.19	11.33	14.67	2.10	10.32	19.04
2012	2.05	11.63	14.66	1.94	10.43	19.20
2013	1.90	11.65	15.35	1.93	10.64	20.12
2014	2.00	11.56	15.49	1.95	10.30	20.62
2015	1.94	11.54	16.93	1.85	10.50	22.06
2016	2.20	11.57	16.45	1.90	10.77	20.61
2017	1.99	11.83	16.69	1.82	10.07	21.41
2018	2.02	12.31	16.93	2.11	10.70	22.13
2019	1.95	11.85	16.63	1.76	10.18	21.11
2020	1.96	11.47	15.56	1.73	9.53	18.90

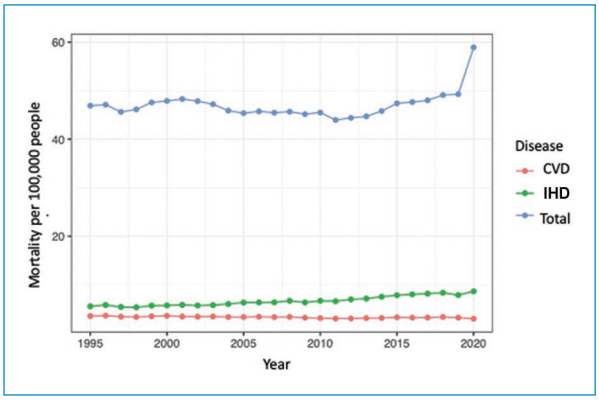


Figure 2. Total, ischemic heart disease (IHD) and cerebrovascular disease (CVD) crude mortality rates per 100,000 inhabitants, 1995-2020.

In the global analysis, a comparison of IHD and CVD age-adjusted mortality rates per 100,000 inhabitants over the age of 20 from 1995 to 2020 showed a greater IHD burden in men over age 74, and stability in IHD and CVD rates for both sexes in the under-50 age groups. Despite a greater number of deaths from CVD in those over age 74, the mortality rates in this age group show a reduction since 1995 and a divergent trend from IHD mortality for both sexes in the study period (Fig. 5).

Regarding CVD crude mortality rates and the introduction of acute treatments for managing ischemic CVD during the study period, mortality decreased after the introduction of hemicraniectomies (2006)[7] and endovascular thrombectomy (2015)[8] (Fig. 6).

Discussion

From 1995 to 2020, the Colombian population grew 39% (14,142,594 inhabitants), with a stable population pyramid, although there was a larger increase in the group of people over age 74. This population change is consistent with the pyramid inversion trends in middle-income countries[9].

During the study period, 5,251,507 deaths were recorded in the country, 14% from IHD and 6.9% from CVD, with IHD being the leading cause of mortality up to 2019 and CVD the second cause from 2014 to 2019. Mortality rates grew approximately 67% for IHD but decreased approximately 17.5% for CVD. The IHD and CVD mortality rates for people under age 50 remained stable during the study period.

Globally, noncommunicable diseases were responsible for 60.8% of deaths in 2000 and 73.6% in 2019[10]. Cardiovascular diseases continue to be the leading cause of disease burden and mortality. Cardiovascular disease mortality increased from 12.1 million (95% CI: 11.4-12.6 million) in 1990 to 18.6 million (95% CI: 17.1-19.7 million) in 2019[11]. Despite efforts to contain this problem, cardiovascular disease mortality continues to increase in low and middle-income countries, as well as some high-income countries[4].

Colombia has not been exempt from the global trends, with growth in the middle-aged and elderly population, increased noncommunicable disease mortality rates, and greater cardiovascular disease mortality. Increased life expectancy, unhealthy lifestyles, environmental contamination and inadequate primary and secondary prevention are probably behind these trends in Colombia and around the world[4].

Cerebrovascular disease

Cerebrovascular disease went from being the fourth cause of death in the country in 1995 to the second after 2014. In the 26 years of our study, the annual mean of CVD deaths was 14,062, with a range from 12,695 in 1998 to 16,090 in 2018. Cerebrovascular disease deaths increased by 3,395 from 1998 to 2018, with an approximately 1.3 times increase in the age-adjusted mortality rate for those over age 74. However, age-and sex-adjusted CVD mortality rates per 100,000 decreased by 16% in men and 19% in women during the study period. This decreasing trend in CVD mortality may be related to better hypertension control, recognition of CVD symptoms among patients and their relatives, and the introduction of intravenous thrombolysis (1996)[12] hemicraniectomy (2006)[7] and endovascular thrombectomy (2015)[8], among other factors.

Our study's findings are in line with a previous study in Colombia by Guerrero et al. [13]. The authors of this study evaluated CVD mortality rate trends in Colombia from 1985 to 2014, adjusted by age and region (department). They found a reduction in global CVD mortality rates, standardized by age and five-year periods, from 40.6 per 100,000 inhabitants between 1985-1989 to 26.3 per 100,000 inhabitants between 2010-2014, and an increase in the number of CVD deaths from 50,588 (1985-1989) to 70,386 (2005-2009).

Around the world, CVD mortality rates and mortality-incidence ratios decreased between 1990 and 2010. However, after 2010, the absolute number of CVD-related deaths increased, with a higher burden for

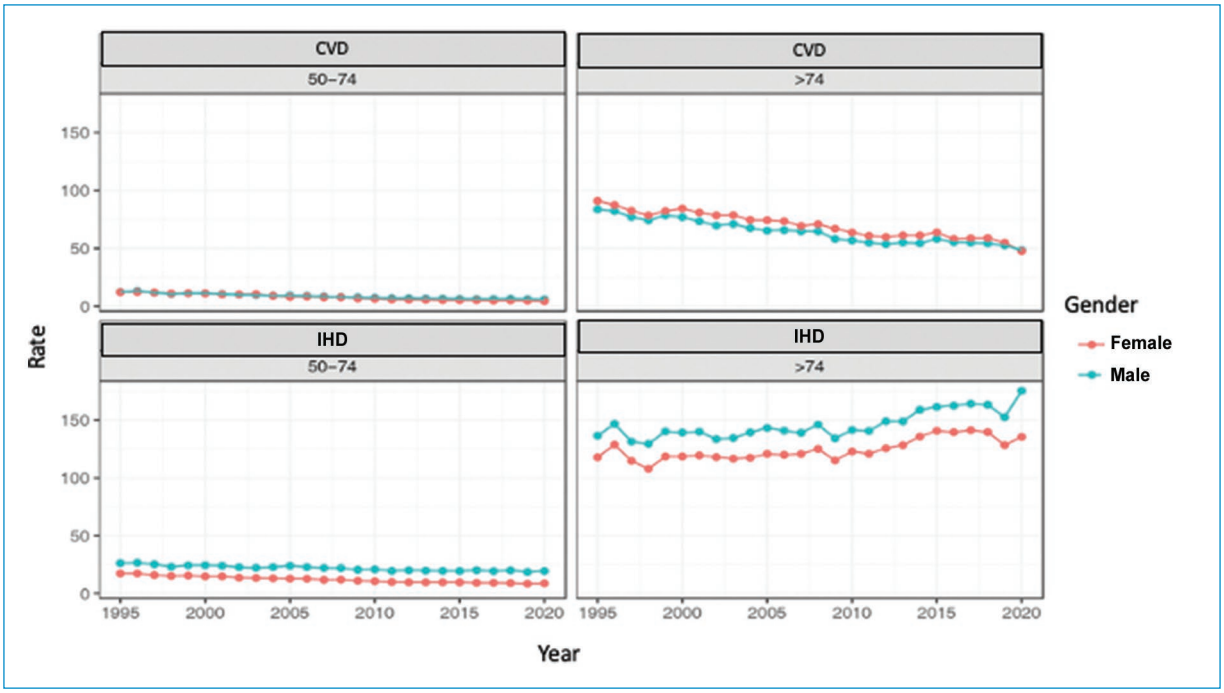


Figure 3. Age-adjusted mortality rates per 100,000 inhabitants in Colombia for ischemic heart disease and cerebrovascular disease, by sex, 1995-2020 (50-74 and > 74-year-old age groups).

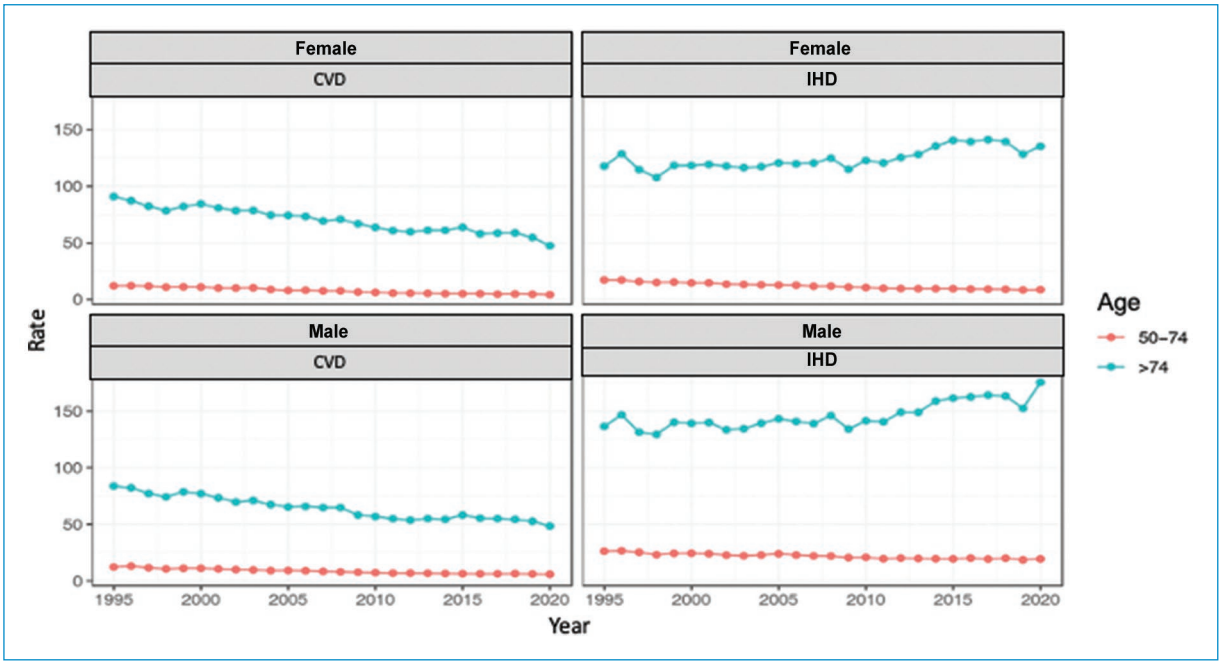


Figure 4. Age-adjusted mortality rates per 100,000 inhabitants in Colombia for ischemic heart disease (IHD) and cerebrovascular disease (CVD) by 50-74 and > 74-year-old age groups, 1995-2020.

middle and low-income countries[3]. In most countries, the age-adjusted CVD mortality rates were higher for men and the older adult and elderly age groups[4].

Although the case fatality rate is higher for hemorrhagic CVD, the incidence of ischemic CVD is much greater. In 2017, the global prevalence of ischemic CVD

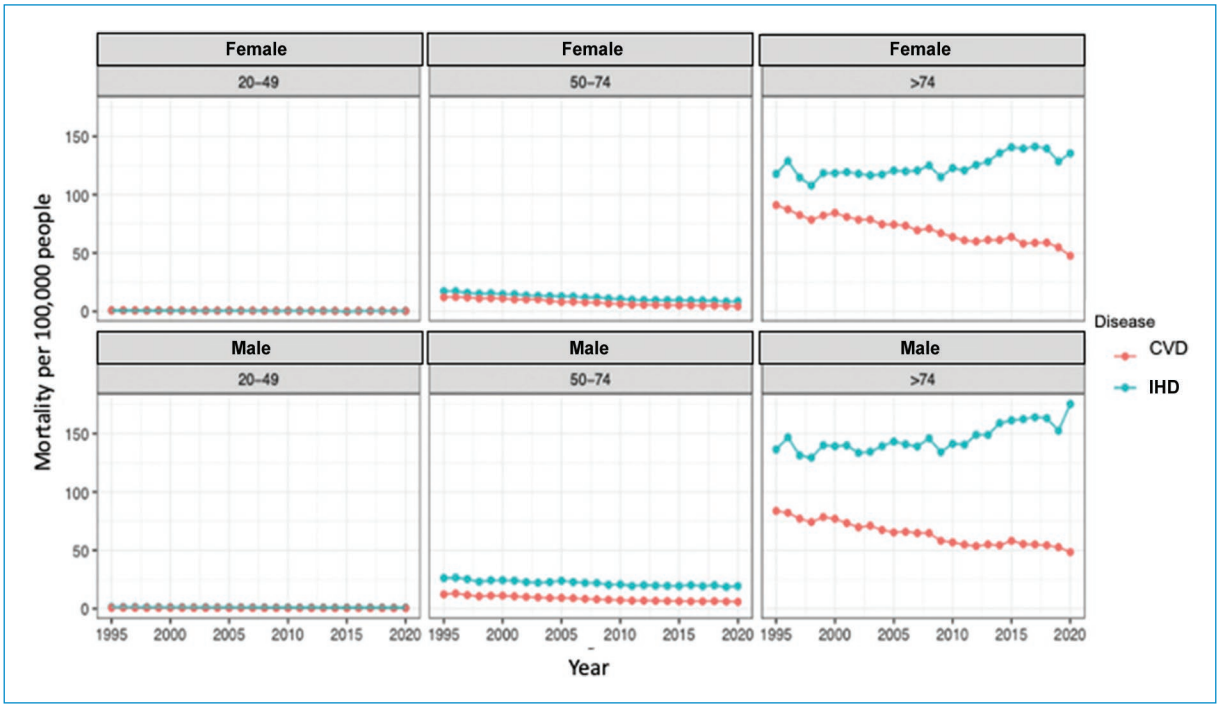


Figure 5. Age-adjusted mortality rates per 100,000 inhabitants in Colombia by sex and age group (20-49, 50-74, > 74 years), for ischemic heart disease (IHD) and cerebrovascular disease (CVD), 1995-2020.

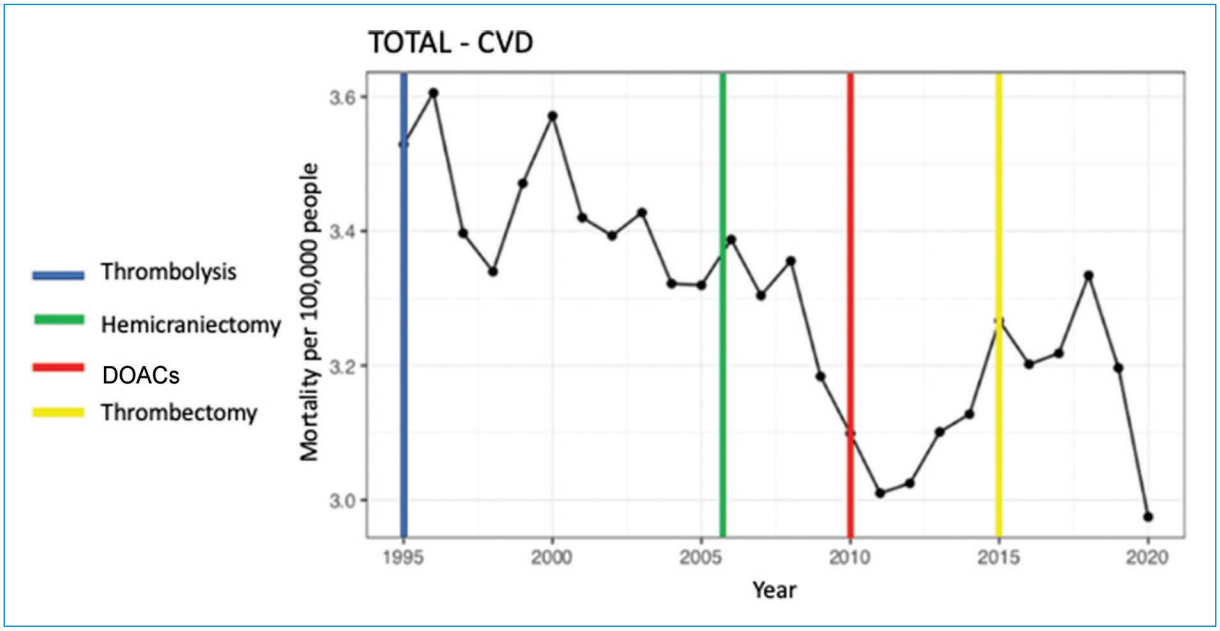


Figure 6. Crude mortality rate per 100,000 inhabitants for cerebrovascular disease (CVD) with regard to treatment innovation. DOACs: direct oral anticoagulants.

was 82.4 million and 27.2 million for hemorrhagic CVD. In that same year, 6.2 million deaths were attributed to CVD, 2.7 million due to ischemic CVD and 3.5 million due to hemorrhagic CVD[14]. Atrial fibrillation (AF) is one of the most important risk factors for, or causes of, CVD. Ischemic CVD may be associated with AF in 20

to 30% of cases. Atrial fibrillation is a public health problem, with evidence suggesting a global rise in its prevalence and incidence. Atrial fibrillation is an arrhythmia that increases with age, with prevalences ranging from 0.1% in adults under the age of 55 up to 9% in those over the age of 80[15]. Oral anticoagulation in patients with AF reduces the risk of CVD and all-cause mortality[16,17]. With the introduction of direct oral anticoagulants in 2010, the safety profile for bleeding improved, and the number of AF patients with thromboembolic prevention increased, as did treatment adherence[15]. This AF treatment revolution may have had an impact on the reduction of CVD mortality rates in Colombia.

In Colombia and around the world, the increased number of CVD deaths with a reduction in CVD mortality rates can be attributed to the demographic transition, population growth, increased healthcare coverage, CVD treatment advances, increased awareness of CVD in the population, and prevention policies.

Ischemic heart disease

The IHD mortality rates worldwide have had a sustained reduction since 1980, especially in high-income countries. For men in Latin America, the age-adjusted IHD mortality rates per 100,000 inhabitants went from 164 in 1990 to 119 in 2005 and 108 in 2010[18]. In 2010, IHD was the leading cause of mortality, globally, with more than seven million deaths, a significant increase compared to 1990 (with 5.2 million deaths) and 2000 (with 6.3 million deaths). In a study on mortality in 16 countries, the crude and adjusted IHD mortality rates showed a decreasing trend between 2005 and 2015. In 2019, global IHD mortality increased, with 9.14 million deaths (95% CI: 8.40-9.74 million). Multiple medical, environmental, social and economic factors contribute to IHD mortality[19].

In Colombia, in a study on mortality from cardiovascular diseases between 1993 and 2017[20], the authors calculated the average number of CVD deaths per year, sex and department. Out of 4,810,907 deaths, 29.2% were from cardiovascular disease, 94% were in people over the age of 45, 47.2% were from IHD, and there was an 18.2% increase in cardiovascular disease mortality between 1993 and 2017. Furthermore, in a descriptive study to describe noncommunicable disease mortality in Colombia between 2008 and 2012 (using data from DANE, and calculating absolute and relative frequencies as well as mortality rates per 100,000 inhabitants and per year), Martínez[21] showed that IHD contributed the largest burden of mortality, with 19% of all deaths in men and 22% in women[22].

During the 26-year period in our study, IHD was the leading cause of mortality until 2019, with a range from 20,038 (1995) to 43,443 (2020). Between 1995 and 2020, the age- and sex-adjusted mortality rates per 100,000 inhabitants for IHD increased by approximately 67% in men and women. The largest growth was seen in both men and women over age 74. However, 50-74-year-old men also showed a 28% increase in the age- and sex-adjusted mortality rate, from 29.6 (1998) per 100,000 inhabitants to 37.9 per 100,000 inhabitants.

Globally, as well as in Colombia, IHD is the leading cause of mortality, exceeded only in 2020 by COVID-19. Although high-income countries have reported a reduction in IHD mortality rates, Colombia has had an increasing trend, as shown by Escobar et al.'s study, with an 18.2% increase from 1993 to 2017[20]. There are many reasons for this phenomenon, possibly related to increased longevity, population growth, unhealthy lifestyles, deficient prevention, not managing risk factors, environmental pollution, social inequalities and deficient healthcare coverage.

Ischemic heart disease and cerebrovascular disease

In a three-decade (1970-2000) study on CVD and IHD mortality trends in America, including 12 countries in the region, Rodríguez et al.[23] found a significant reduction in IHD rates for men and women in Canada, USA and Argentina. The IHD mortality rates during this time also decreased, but not as markedly, in Chile, Puerto Rico, Brazil and Cuba. On the other hand, Venezuela, Costa Rica, Ecuador and Mexico had increased IHD mortality rates over the three decades, with the highest rise in Mexico. For CVD, mortality rates decreased over the three decades of the study, both in men and women, in the 12 countries included. In this study from 1970 to 2000, Colombia showed a reduction in IHD mortality rates of 2% for men and 3% for women, and a reduction in CVD mortality rates of 24% for men and 33% for women.

Pagan et al.[24] compared the mortality trends for IHD and CVD in North and South America from 1980-2013. The male age-adjusted IHD mortality rates per 100,000 inhabitants between 2001-2003 and 2011-2013 decreased for most of the countries except Colombia, Venezuela and Mexico. The largest reductions were

found in Canada, USA, Ecuador, Puerto Rico, Uruguay, Chile and Costa Rica. The male age-adjusted CVD mortality rates per 100,000 inhabitants between 2001-2003 and 2011-2013 decreased for all the countries, with the greatest reduction in Uruguay, Canada, Argentina and USA. In Colombia, the IHD mortality rates decreased by 6% in women, while the CVD rates decreased by 23% in men and 29% in women.

In our study of IHD and CVD mortality in Colombia, the mortality rates for the two etiologies diverged throughout the 26 years (1995 to 2020). The divergence became more evident after 2010. The age- and sex-adjusted IHD mortality rates per 100,000 inhabitants increased by 68% for men and 66% for women. This increase was 148% for men and 138% for women among those over age 74. In the same study period, age- and sex-adjusted CVD mortality rates per 100,000 inhabitants decreased by 16% in men and 19% in women. However, the age- and sex-adjusted mortality rates per 100,000 inhabitants in the over-74 age group increased by 28% in men and 34% in women.

In the age group analysis, the age- and sex-adjusted mortality rates decreased for IHD in 20-49-year-old men, 20-49-year-old women, and 50-74-year-old women. There was also a reduction in CVD in 20-49-year-old men, 50-74-year-old men, 20-49-year-old women and 50-74-year-old women. An increased age- and sex-adjusted IHD mortality rate per 100,000 inhabitants was found in 50-74-year-old men, men over age 74 and women over age 74. For CVD, there was an increase in men and women over age 74.

Although they use different methods, the studies mentioned and our own show the general trend in Colombia of increased IHD mortality, decreased CVD mortality and a higher burden of mortality from vascular disease in older adults and the elderly. These findings are in line with the behavior of vascular disease mortality in the world, and may be related to population growth, demographic transition, greater exposure to vascular risk factors, higher prevalence of vascular risk factors with increased age, social factors and a few other determinants that remain to be studied.

However, regarding the reasons for the divergent IHD and CVD mortality in Colombia and the world, this may be due to the heterogeneity of CVD, the fact that CVD includes hemorrhagic disease, the different weight of vascular risk factors for IHD and CVD, advances in CVD treatment, better control of systemic hypertension in the population, greater awareness of CVD in the population, and as yet undetermined factors[25,26].

The findings of our study and what is described in the literature suggest, among other things, that primary and secondary prevention strategies must be improved, the population must be educated on IHD and CVD, healthcare coverage must be improved, access to acute treatment for IHD and CVD must be broadened, studies on emerging vascular risk factors must be performed, studies on the weight of vascular risk factors by age groups and sex must be deepened, and the socioeconomic determinants of IHD and CVD mortality must be understood[20].

Our study on adult IHD and CVD mortality in Colombia is updated up to the COVID-19 pandemic, covers 26 years, was done in adults over age 20, by sex and age groups, is based on official national mortality statistics and presents information disaggregated by year. However, only three age groups were included, there is no pathological confirmation of the cause of death, CVD is not discriminated by subtypes, the quality control of the official mortality data is unknown, IHD and CVD mortality may be under or overreported, no analysis was done by regions or departments, no analysis was done by ethnic group, computer systems have evolved over the years and, although several years of information were included, the behavior of mortality since the implementation of the national mortality statistics registry in Colombia was not studied.

Vascular disease is the leading cause of death in Colombia, exceeded only by COVID-19 in 2020[5]. With the population changes and current lifestyles, this trend will persist. Individuals, institutions and local, regional and national authorities must make a joint effort to mitigate the burden of IHD and CVD mortality in Colombia.

Conclusion

Ischemic heart disease and CVD are the leading cause of mortality in Colombia, with a growing trend, especially in older adults and the elderly. However, divergence was found in adult IHD and CVD mortality after 2010. To mitigate the burden of IHD and CVD mortality, more studies are needed on their determinants, as well as a joint effort in primary, secondary and tertiary prevention.

Funding

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

Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have obtained approval from the Ethics Committee for the analysis of routinely obtained and anonymized clinical data, so informed consent was not necessary. Relevant guidelines were followed.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

References

1. Campbell BCV, De Silva DA, Macleod MR, Coutts SB, Schwamm LH, Davis SM, et al. Ischaemic stroke. Nat Rev Dis Prim. 2019;5(1):70.
2. Feigin VL, Forouzanfar MH, Krishnamurthi R, Mensah GA, Connor M, Bennett DA, et al. Global and regional burden of stroke during 1990- 2010: findings from the Global Burden of Disease Study 2010. Lancet. 2014;383(9913):245-54.
3. Kim J, Thayabaranathan T, Donnan GA, Howard G, Howard VJ, Rothwell PM, et al. Global Stroke Statistics 2019. Int J stroke. 2020; 15(8):819-38.
4. Vos T, Lim SS, Abbafati C, Abbas KM, Abbasi M, Abbasifard M, et al. Global burden of 369 diseases and injuries in 204 countries and territo- ries, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2020;396(10258):1204-22.
5. Departamento Administrativo Nacional de Estadística. Indicadores basi- cos de salud 2021 Situación de salud en Colombia [Internet]. Colombia: Ministerio de Salud, Departamento Administrativo Nacional de Estadís- tica; 2021. Disponible en: https://www.minsalud.gov.co/sites/rid/Lists/BibliotecaDigital/RIDE/VS/ED/GCFI/indicadores-basicos-salud-2021.pdf
6. Ministerio de Salud de Colombia. Resolución No. 008430 de 1993 (4 de octubre de 1993) [Internet]. Colombia: Universidad del Rosa- rio [consulta: 4 de marzo de 2021]. Disponible en: https://www.urosario. edu.co/Escuela-Medicina/Investigacion/Documentos-de-interes/Files/resolucion_008430_1993.pdf
7. Lin J, Frontera JA. Decompressive hemicraniectomy for large hemisphe- ric strokes. Stroke. 2021;52(4):1500-10.
8. Prabhakaran S, Ruff I, Bernstein RA. Acute stroke intervention: a syste- matic review. JAMA. 2015;313(14):1451-62.
9. Populationpyramid.net. [citado el 26 de octubre de 2024]. Disponible en: https://www.populationpyramid.net/es/españa/2023
10. Feigin VL, Norrving B, Mensah GA. Global burden of stroke. Circ Res. 2017;120(3):439-48.
11. Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, et al. GBD-NHLBI-JACC Global Burden of Cardiovascular Diseases Writing Group. Global Burden of Cardiovascular Diseases and Risk Factors, 1990-2019: Update From the GBD 2019 Study. J Am Coll Cardiol. 2020;76(25):2982-3021. Erratum in: J Am Coll Cardiol. 2021; 77(15):1958-9.
12. Tissue plasminogen activator for acute ischemic stroke. N Engl J Med. 1995 Dec;333(24):1581–7.
13. Guerrero Agámez D, Pestaña Utria G, Díaz Arrieta B, Vargas Moranth R, Alvis Guzmán N. Mortalidad por enfermedades cerebrovasculars en Colombia: 30 años de observación. Acta Neurol Colomb. 2021;37: 173-88.
14. Krishnamurthi RV, Ikeda T, Feigin VL. Global, regional and country-specific burden of ischaemic stroke, intracerebral haemorrhage and subarachnoid haemorrhage: a systematic analysis of the Global Burden of Disease Study 2017. Neuroepidemiology. 2020;54(2):171-9.
15. Chao TF, Potpara TS, Lip GYH. Atrial fibrillation: stroke prevention. Lancet Reg Health Eur. 2024;37:100797.
16. Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. Ann Intern Med. 2007;146(12):857-67.
17. Ruff CT, Giugliano RP, Braunwald E. Comparison of the ef- ficacy and safety of new oral anticoagulants with warfarin in pa- tients with atrial fibrillation: a meta-analysis of randomised trials. Lancet. 2013; 383(9921):955-62.
18. Moran AE, Forouzanfar MH, Roth GA, Mensah GA, Ezzati M, Murray CJL, et al. Temporal trends in ischemic heart disease mortality in 21 world regions, 1980 to 2010: the Global Burden of Disease 2010 study. Circu- lation. 2014;129(14):1483-92.
19. Nowbar AN, Gitto M, Howard JP, Francis DP, Al-Lamee R. Mortality from ischemic heart disease. Circ Cardiovasc Qual Outcomes. 2019; 12(6):e005375.
20. Escobar Díaz GL, Orozco Molina AM, Núñez Montes JR, Muñoz FL. Mortality from cardiovascular diseases in Colombia. An analysis of public policies. Salud Uninorte. 2022;36(3):558-70.
21. Martínez JC. Factores asociados a la mortalidad por enfermedades no transmisibles en Colombia, 2008-2012. Biomédica. 2016;36(4): 535-46.
22. Departamento Administrativo Nacional de Estadística. Defunciones no fetales 2019 [Internet]. Gobierno de Colombia, Departamento Adminis- trativo Nacional de Estadística [citado el 29 de abril de 2023]. Disponible en: https://www.dane.gov.co/index.php/estadisticas-por-tema/salud/naci-mientos-y-defunciones/defunciones-no-fetales/defunciones-no-feta- les-2019
23. Rodríguez T, Malvezzi M, Chatenoud L, Bosetti C, Levi F, Negri E, et al. Trends in mortality from coronary heart and cerebrovascular diseases in the Americas: 1970-2000. Heart. 2006;92(4):453-60.
24. Pagan E, Chatenoud L, Rodriguez T, Bosetti C, Levi F, Malvezzi M, et al. Comparison of trends in mortality from coronary heart and cerebrovas- cular diseases in North and South America: 1980 to 2013. Am J Cardiol. 2017;119(6):862-71.
25. Sacco RL, Kasner SE, Broderick JP, Caplan LR, Connors JJB, Culebras A, et al. An updated definition of stroke for the 21st century: a statement for healthcare professionals from the American Heart Associa- tion/American Stroke Association. Stroke. 2013;44(7):2064-89.
26. O'Donnell MJ, Xavier D, Liu L, Zhang H, Chin SL, Rao-Melacini P, et al. Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): a case-control study. Lancet. 2010;376(9735):112-23.

Revista Colombiana de Cardiología
Órgano oficial de la Asociación Sociedad Colombiana de Cardiología & Cirugía Cardiovascular
Permanyer

ORIGINAL ARTICLE

Colombian registry of anticoagulation clinics (RECCANT) and the use of reversal agents (RECCANT-AR): rationale and design

Registro colombiano de clínicas de anticoagulación (RECCANT) y del uso de agentes reversores (RECCANT-AR): justificación y diseño

*Sebastián Seni-Molina[1], Arturo D. Mora[2], Juliana Gutiérrez-Posso[1], Maribel Ñáñez[2], Juan D. Victoria-Salcedo[3,4], Julio Díez-Sepúlveda[3,4,5], Dora I. Molina[6,7], Ana C. Montenegro[8,9], Kenny M. Gálvez[10], Gilberto A. Castillo[11], Róbinson Sánchez[12], Hoover O. León-Giraldo[1], and Juan E. Gómez-Mesa[1,2,4]**

[1]Centro de Investigaciones Clínicas (CIC), Fundación Valle del Lili, Cali; [2]Cardiology Service, Fundación Valle del Lili, Cali; [3]Departament of Emergency Medicine and Critical Care, Fundación Valle del Lili, Cali; [4]School of Health Sciences, Universidad Icesi, Cali; [5]Semillero de Investigación en Medicina de Emergencias y Reanimación (SIMER), School of Health Sciences, Cali; [6]Centro de Investigación Clínica, Médicos Internistas de Caldas (MIC) IPS, Manizales; [7]School of Health Sciences, Universidad de Caldas, Manizales; [8]Departament of Vascular Medicine, Fundación Santa Fe de Bogotá, Bogotá; [9]Departament of Internal Medicine, Fundación Santa Fe de Bogotá, Bogotá; [10]Cancer Unit, Hospital Pablo Tobón Uribe, Medellín; [11]Cardiology Service, Cardioprevent IPS, Cali; [12]Cardiology Service, Fundación Cardiovascular de Colombia, Bucaramanga. Colombia

Abstract

Introduction: *Anticoagulation is essential for treating thromboembolic diseases and preventing complications associated with pathologies such as atrial fibrillation. However, it carries a significant risk of bleeding, which highlights the importance of reversal agents. In Colombia, scientific evidence regarding these therapies is limited.* **Objective:** *To implement the Colombian Registry of Anticoagulation Clinics (RECCANT) and the Colombian Registry of Anticoagulation Clinics and Reversal Agents (RECCANT-AR), which aim to fill this information gap by providing robust and representative data on these patients.* **Method:** *RECCANT is an observational, analytical, prospective, multicenter study that includes patients over 18 years of age with an indication for at least three months of anticoagulant therapy. RECCANT-AR is an observational, analytical, ambispective, and multicenter study that includes patients over 18 years of age requiring reversal agents due to significant bleeding or the need for priority invasive procedures. Sociodemographic, clinical, and therapeutic data are collected using the Research Electronic Data Capture (REDCap) platform to ensure information security and confidentiality.* **Results:** *RECCANT and RECCANT-AR are established as the first national registries focused on characterizing anticoagulated patients and those requiring reversal agents.* **Conclusions:** *RECCANT and RECCANT-AR are essential for addressing the knowledge gap regarding anticoagulation and the use of reversal agents in Colombia. By providing precise and detailed information, these registries will improve understanding of patient profiles, identify national patterns, and support the development of standardized strategies to enhance care and clinical outcomes in the country.*

Keywords: *Colombia. Anticoagulation. Reversal agents. Clinical registries.*

***Correspondence:**
Juan E. Gómez-Mesa
E-mail: juan.gomez.me@fvl.org.co

Date of reception: 23-09-2024
Date of acceptance: 30-09-2024
DOI: 10.24875/RCCARE.M24000135
Available online: 05-02-2025
Rev Colomb Cardiol. 2024;31(6):373-381
www.rccardiologia.com

Resumen

Introducción: *La anticoagulación es esencial para tratar enfermedades tromboembólicas y prevenir complicaciones asociadas a patologías como la fibrilación auricular. No obstante, conlleva un riesgo significativo de sangrado, lo que destaca la importancia del uso de agentes reversores. En Colombia la evidencia científica sobre estas terapias es limitada.* **Objetivo:** *Implementar el Registro Colombiano de Clínicas de Anticoagulación (RECCANT) y el Registro Colombiano de Clínicas de Anticoagulación y el uso de Agentes Reversores (RECCANT-AR), los cuales buscan llenar esta brecha de información proporcionando datos robustos y representativos sobre estos pacientes.* **Método:** *RECCANT es un estudio observacional, analítico, prospectivo y multicéntrico que incluye pacientes mayores de 18 años con indicación de manejo anticoagulante por al menos tres meses. RECCANT-AR es un estudio observacional, analítico, ambispectivo y multicéntrico que incluye pacientes mayores de 18 años que requieren agentes reversores por sangrado relevante o por necesidad de procedimientos invasivos urgentes o prioritarios. Se recopilan datos sociodemográficos, clínicos y terapéuticos utilizando la plataforma electrónica REDCap (Research Electronic Data Capture) para garantizar la seguridad y confidencialidad de la información.* **Resultados:** *RECCANT y RECCANT-AR se establecen como los primeros registros nacionales enfocados en caracterizar a pacientes anticoagulados y aquellos con requerimiento de agentes reversores.* **Conclusiones:** *RECCANT y RECCANT-AR son esenciales para abordar la brecha de conocimiento sobre anticoagulación y el uso de agentes reversores en Colombia. Al proporcionar información precisa y detallada, estos registros mejorarán la comprensión de los perfiles de los pacientes, identificarán patrones nacionales y apoyarán el desarrollo de estrategias estandarizadas para mejorar la atención y los resultados clínicos en el país.*

Palabras clave: *Colombia. Anticoagulación. Agentes reversores. Registros clínicos.*

Introduction

Anticoagulation is one of the most important treatment strategies in modern medicine. It is the cornerstone of treatment for various conditions characterized by hypercoagulability, venous stasis and endothelial injury, known as Virchow's triad. These conditions can trigger thrombus formation with serious consequences for patients' health[1]. Historically, heparins and vitamin K antagonists (VKAs) have been the most frequently used drugs[2]. However, the advent of direct oral anticoagulants (DOACs) in the last few years has provided a very important alternative, given their high efficacy and greater safety in terms of the risk of bleeding[2-5]. Relevant clinical conditions like atrial fibrillation (AF), venous thromboembolism (VTE), mechanical heart valve replacement and thrombophilia benefit significantly from the use of these anticoagulation therapies[6-8].

Atrial fibrillation is the most common arrhythmia worldwide, with a global prevalence of approximately 60 million cases in 2019[9]. It is also associated with adverse outcomes like the onset of heart failure, chronic kidney disease, stroke and sudden death[10]. Venous thromboembolism affects approximately 10 million people per year around the world and is the third most frequent cause of cardiovascular disease[11]. This condition includes deep vein thrombosis (DVT) and pulmonary thromboembolism (PTE), the latter with a greater than 20% mortality[12]. Valve replacement is also an important indication for extended anticoagulation, as approximately 60% of valve replacement patients receive a mechanical valve, which significantly increases the risk of thrombosis[13]. Thrombophilias, for their part, are associated with a higher risk of VTE[12]. In addition to their clinical impact, thromboembolic diseases generate significant healthcare costs, especially related to anticoagulant prescriptions. The monthly expenditure for anticoagulant prescriptions in Colombia reaches 148,263,960 COP[14].

The clinical impact of these cardiovascular conditions emphasizes the importance of anticoagulant therapy. However, its use entails significant risks, with bleeding being the main complication in anticoagulated patients[15]. Long-term treatment with VKAs has a major bleeding rate ranging from 1.5 to 5.2%[15-17]. In turn, patients treated with DOACs have an up to 3% rate of complications associated with major bleeding[15]. Parenteral anticoagulation has a 2.7% rate of major bleeding for low molecular weight heparins (LMWHs) and 5.5% for unfractionated heparin (UFH)[15]. The literature reports a lethality rate of up to 11.3% from major bleeding in anticoagulated patients[18]. However, a meta-analysis showed that the use of reversal agents has had a 78.5% effectivity in achieving hemostasis, which correlates with a lower relative risk in terms of hemorrhage-related mortality[19]. In these scenarios, early detection and reversal strategies may be crucial for reducing fatal outcomes in these patients[20]. Although the data is more limited, anticoagulation-related

bleeding also causes a significant economic impact. A study in 2019 determined that, for patients on warfarin anticoagulation due to AF, the annual cost of intracranial hemorrhages was 11,875,730,234 COP, while the cost for gastrointestinal bleeding was 19,246,023,614 COP. Retroperitoneal bleeding, espistaxis and urinary tract bleeding cost a total of 735,894,387 COP[21].

Nonetheless, the scientific evidence in Colombia regarding the use of anticoagulants and reversal agents during anticoagulation treatment is limited. Currently, there are no specific registries dealing with these conditions, which highlights the need to obtain detailed information about these patients on a national level. These projects represent a significant effort whose goal is to bridge this knowledge gap by characterizing these patients in our country, seeking to obtain reliable and high-quality information about their sociodemographic, clinical and therapeutic characteristics. Thus, RECCANT and RECCANT-AR are positioned as pioneer projects aimed at generating relevant scientific information to help optimize treatment strategies and improve the clinical outcomes of anticoagulated patients and those who need reversal agents.

Method

Study design

RECCANT is an observational, analytical, prospective, multicenter registry including ambulatory patients on anticoagulants (oral or parenteral), regardless of their indication (Table 1).

RECCANT-AR is an observational, analytical, ambispective, multicenter registry including previously anticoagulated patients who require reversal agents to control bleeding or because they need an urgent/priority diagnostic or invasive procedure during hospitalization or emergency room care (Table 2).

The overall objective of RECCANT is to implement a national registry of patients on anticoagulant therapy. It specifically seeks to provide a sociodemographic and clinical description of patients seen at anticoagulation clinics in Colombia; evaluate the time in therapeutic range (TTR) of patients treated with VKAs, according to their clinical characteristics and medical indications; analyze the relationship between the different anticoagulant treatments and therapy changes, complications and medication adherence; identify factors associated with adverse events like thromboses and bleeds, including mortality; and evaluate how anticoagulant therapy affects the need for urgent medical care or hospitalization.

On the other hand, RECCANT-AR has the overall objective of creating a national registry of patients who need reversal therapy to manage bleeding complications or perform urgent invasive procedures. It seeks to describe the sociodemographic and clinical characteristics of this population at different institutions in Colombia; evaluate the use of reversal therapies and their relationship with the mortality rate in these settings; and identify the factors associated with mortality due to thrombotic or hemorrhagic complications. Finally, the intention is to derive research projects to delve further into the clinical and epidemiological dynamics of patients who receive these treatments, improving the understanding of their management in various institutions throughout the country.

Both registries are implemented collaboratively by the Centro de Investigaciones Clínicas [Clinical Research Center] (CIC) and Cardiology Service at Fundación Valle del Lili (FVL) together with Asociación Colombiana de Antitrombosis, Tromboprofilaxis y Anticoagulación [Colombian Association of Antithrombosis, Thromboprophylaxis and Anticoagulation] (ACATA), the Thrombosis and Anticoagulation Working Group of Asociación Sociedad Colombiana de Cardiología y Cirugía Cardiovascular [Colombian Society of Cardiology and Cardiovascular Surgery] and the Clinical Research Center at IPS Médicos Internistas de Caldas. This agreement seeks to involve different research institutions around the country. The CIC at FVL provides the logistical, technical and epidemiological support needed to implement both projects.

Each registry (RECCANT and RECCANT-AR) has a national coordinator in charge of supervising the interinstitutional agreements and conventions required to link research institutions, supervising data completion, and reporting the weekly progress of both registries. On the other hand, each participating institution in both registries should have a principal investigator (PI) and a sub-investigator (SI), in charge of project supervision and proper data management within their institution.

Data collection

RECCANT is implemented with information obtained from patients who have an indication for anticoagulation therapy (on treatment or about to begin) and are being followed by an outpatient department or anticoagulation program (anticoagulation clinic) at each of the participating institutions. Each participating institution

Table 1. Inclusion and exclusion criteria for the Registro Colombiano de Clínicas de Anticoagulación [Colombian Anticoagulation Clinic Registry] (RECCANT)

Inclusion criteria	Exclusion criteria
Ambulatory patients over 18 years of age Patients with an indication for at least three months of anticoagulation and one of the following: Naive: patients who have an indication for anticoagulant therapy but have not yet started it or started less than seven days ago Recent use: patients who have an indication for anticoagulant therapy and have taken it as outpatients for 7 to 30 days Chronic use: patients who have an indication for anticoagulant therapy and have taken it as outpatients for more than 30 days	Patients on chronic anticoagulants with inadequate adherence to follow-up, defined according to the medication: VKA or LMWH: has not complied with the follow-up program (onsite or telephone follow-up) for the last three months (no follow-up) DOACs: has not complied with the follow-up program (on-site or telephone follow-up) for the last six months (no follow-up) Patients who, according to the principal investigator's opinion, are not adherent to the ambulatory anticoagulant medication or the scheduled follow-up within the study protocol

DOACs: direct oral anticoagulants; VKA: vitamin K antagonist; LMWH: low molecular weight heparin.

Table 2. Inclusion and exclusion criteria for the Registro Colombiano de Clínicas de Anticoagulación y del Uso de Agentes Reversores [Colombian Registry of Anticoagulation Clinics and the Use of Reversal Agents] (RECCANT-AR)

Inclusion criteria	Exclusion criteria
Patients over 18 years of age On ambulatory anticoagulant therapy with warfarin, acenocoumarol, dabigatran, rivaroxaban, apixaban, edoxaban, heparin sodium, nadroparin, enoxaparin, dalteparin, tinzaparin or fondaparinux One of the following conditions: Experiencing an episode of bleeding that requires reversal therapy (vitamin K, tranexamic acid, protamine, factor VIIa, factor VIII, factor VIIIa, idarucizumab, andexanet, octaplex, beriplex, fibrinogen, dialysis, fresh frozen plasma or activated charcoal) to revert the anticoagulant's effect Requires an urgent/emergent/priority invasive procedure and reversal therapy is administered (vitamin K, tranexamic acid, protamine, factor VIIa, factor VIII, factor VIIIa, idarucizumab, andexanet, octaplex, beriplex, fibrinogen, dialysis, fresh frozen plasma or activated charcoal) to revert the effect of the anticoagulant as part of the peri-procedural process	Patients who are scheduled to start anticoagulant therapy but have not started it when the bleeding occurs Patients who have gone more than five days without anticoagulant therapy before the bleeding occurs, according to the information recorded in the medical chart

shall recruit a minimum of 60 patients during the total recruitment period which began on September 1, 2023, and will end December 27, 2024. During this period, each participating institution evaluates the patients that attend their ambulatory care program using the previously described inclusion and exclusion criteria. Those who meet the criteria are enrolled in the registry, which will gather information on their sociodemographic, clinical and therapeutic characteristics. Subsequently, a follow-up phase is implemented, during which information is gathered six months after the registry admission visit (with a maximum window of three months after the scheduled follow-up date). Therefore, the last follow-up visit is expected to be completed in September 2025. This information is taken from the medical records of routine anticoagulation program visits, or if these are not available, through telephone contact, in order to collect the most data possible.

RECCANT-AR gathers information on patients who need reversal agents to manage anticoagulation-related bleeding or who need these interventions in order to undergo urgent, emergent or priority invasive procedures within the hospital wards or emergency rooms of the participating institutions. Patients treated between January 1, 2011, and December 27, 2024 are included, and each participatig institution must recruit at least one patient during the recruitment period. For this registry, data will be collected on demographic and clinical characteristics, prior anticoagulant treatment, the indication for reversal agents, and status at discharge. This registry does not involve ambulatory follow-up of the recruited patients.

All of the information obtained from the patients recruited for both registries is stored on the Research Electronic Data Capture (REDCap) digital platform. Each participating institution receives a unique

username and password to be used by the PI and SI, ensuring the safety and confidentiality of the data recorded. In addition, each research group receives a digital instruction book for filling out the information and managing the database properly.

Data handling and statistical analysis plan

The CIC at FVL provides training in the registries' methodology, how to fill out the database and how to use the platform. To facilitate the identification of the participating institutions and enrolled patients, coding is initially done by cities, using the International Air Transport Association (IATA) nomenclature, which reduces human error, ensuring the accuracy and efficiency of coding. Then, a code is assigned to each institution according to order of enrollment in the registry and, finally, a code is assigned to each patient enrolled in the registry.

A descriptive statistical analysis will be done for all the variables included in the registry. Quantitative variables will first be evaluated for normality using the Kolmogorov-Smirnov or Shapiro-Wilk tests. If normality is present, they will be reported as means and standard deviation; otherwise, medians and interquartile range will be used. Categorical variables will be presented as absolute frequencies and percentages.

For quality control, a random sample of 10% of the data from active institutions will be periodically reviewed (at least every three months), comparing it with the source documents to ensure the registry's quality and consistency. If inconsistencies are found, a systematic process will be used to determine if they are systematic or random errors, ensuring that the integrity of the rest of the database is not affected. If the inconsistencies are not related to the registry methodology, they will be corrected by applying data validation rules, ensuring their completeness and consistency. If the inconsistencies persist, the review will be extended to an additional 20% of the data. If they continue, the entire database will be reviewed, ensuring maximum integrity and accuracy of the data.

Once the recruitment (RECCANT and RECCANT-AR) and follow-up (RECCANT) period concludes, an exhaustive analysis of the databases will be done to determine the prevalence and trends of anticoagulant and reversal agent treatments. In addition, the clinical and epidemiological characteristics of the patients enrolled will be described in detail, enabling a comprehensive analysis of the collected data. Generalized mixed models will be used to handle the additional specific objectives. These models will help capture the intrinsic variability between the participating institutions, adjusting for possible confounding factors and facilitating a robust analysis of the clinical outcomes. This choice of statistical approach ensures greater precision and breadth of the results. Finally, the potential confounding factors which could affect the outcomes, like different clinical practices between institutions and differences in the patients' sociodemographic characteristics, will be considered and adjusted for in the statistical models. The main outcomes of the study will include concrete variables like mortality, hospitalization, and clinical complications. Additional and/or complementary analyses will be done with statistical support from the CIC at FVL.

Ethical considerations

Both registries are implemented in accordance with the Declaration of Helsinki. Their protocol was approved by the Biomedical Research Ethics Committee (CEIB, in Spanish) at FVL (Record of Minutes No. 19, September 26, 2018, Letter No. 283-2018). Each participating institution's ethics committee must approve the protocol.

According to Resolution 8430 of 1993, emitted by the Colombian Ministry of Health, these studies are considered minimal risk studies because the information is gathered from routine medical procedures documented in the medical charts, without involving additional procedures outside of the usual clinical practice. Therefore, the CEIB at FVL, as the coordinating institution, approved the informed consent exemption. However, the application of informed consent at other institutions is left to each institution's discretion.

The PIs and SIs sign a confidentiality agreement, committing to maintain the privacy of the data throughout the entire project. Identity coding is used in the database to ensure the patients' privacy, and data access is restricted by the use of usernames and passwords for data entry and registry analysis purposes.

Discussion

Anticoagulant therapy is essential for managing various conditions with high clinical importance. However, its use entails a variable risk of bleeding and/or major bleeding, which underscores the importance of using reversal therapies in emergency settings. Various studies have researched the specific conditions that require

anticoagulant treatment[22]. Similarly, there is relevant scientific evidence on the use of reversal agents in anticoagulated patients[23,24].

Globally, registries like *Registro Informatizado de Pacientes con Enfermedad TromboEmbólica* [Digitalized Registry of Patients with ThromboEmbolic Disease] (RIETE) or the Global Registry on Long-Term Oral Antithrombotic Treatment in Patients with Atrial Fibrillation (GLORIA-AF) have allowed a detailed description of the diseases that give rise to anticoagulant treatment in different settings and populations worldwide[25,26]. Registries like Global Anticoagulant Registry in the FIELD□AF (GARFIELD-AF) have even described these patients in different countries within Latin America[27]. In contrast, information regarding anticoagulated patients in Colombia is derived from the data in these global registries, along with isolated institutional reports and efforts. These, while valuable, are insufficient for providing a comprehensive and representative view of the practice of anticoagulation in Colombia.

In 2004, a cohort of 139 patients on warfarin anticoagulation at Hospital San Vicente de Paul in Medellín, Colombia was described, highlighting a TTR of less than 50% and a high prevalence of AF as the main indication for anticoagulation[28]. Later, Taboada et al. described the behavior of the first 153 patients on VKA anticoagulation at Hospital Universitario Fundación Santa Fe de Bogotá (HUFSFB) in Bogotá, Colombia, finding a TTR of 53.7% and VTE as the main indication for anticoagulation[29]. Years later, another study with 257 patients at the same institution reported a 71% rate of warfarin use with a TTR of 53.5% for an International Normalized Ratio (INR) between 2 and 3. That study found VTE and AF to be the main reasons for anticoagulation[30]. In 2020, a study with 306 participants revealed a high prevalence of nonvalvular AF as the main indication for anticoagulation, followed by mechanical valve replacement. The predominance of VKAs versus other anticoagulants was another relevant finding[31]. Years later, another national study reported a higher prevalence of DOACs (rivaroxaban) in 146 patients diagnosed with nonvalvular AF[32].

The largest study to date in Colombia was performed in 2021, enrolling 502 patients at HUFSFB and Hospital Universitario San Vicente Fundación de Medellín (HUSVF). This study showed relevant differences between these institutions. The main indication for anticoagulation at HUSVF was AF (46.5%), while at HUFSFB it was VTE (69.7%). One hundred percent of the patients at HUSVF were treated with warfarin, compared to 23% at HUFSFB. Lastly, the TTR was 69% at HUFSFB versus 55% at HUSVF[33].

The above information shows notable diversity in the anticoagulated population in Colombia, even between institutions. There are differences in the indication for anticoagulation, the treatment regimens and the clinical outcomes. The high use of VKAs is notable, even in recent studies with indications like AF and VTE, where, according to the current guidelines, patients would mostly benefit from DOACs[20,34]. This phenomenon could be related to the lower relative cost of warfarin[14]. While one study showed that DOACs are cost-effective, most exceed the thresholds proposed for the Colombian population[35]. This trend relates to the regional analyses of international registries, which indicate a later introduction of DOACs in Latin America[25].

At the same time, relatively low TTRs are notable among patients on warfarin in the studies in Colombian populations, with high variability also noted between institutions. This could suggest differences in clinical management, including different treatment protocols, medical staff training and experience and access to INR monitoring services, as well as sociodemographic and clinical differences among the patients. This underscores the need to establish a national registry to monitor and improve anticoagulation management in different clinical settings around the country.

In light of this, RECCANT incorporates sociodemographic variables like the place of residence (urban or rural), healthcare regimen, socioeconomic status and educational level of the participants. This approach helps evaluate the impact of these social determinants of health on patients' management and prognosis. Other national registries have evaluated this relationship in other diseases of public health significance, like heart failure[36].

The available scientific evidence regarding the anticoagulated population in Colombia continues to be limited, as it comes from isolated studies performed at a small number of institutions. This fragmentation makes it difficult to identify patterns and dynamics between anticoagulation clinics on a national level, which prevents the implementation of standardized strategies to improve the quality of care. RECCANT is positioned as the first national registry of anticoagulated patients, designed to obtain robust and representative data from the Colombian population, enabling a better description and optimization of their health outcomes. Furthermore, its implementation allows possible comparisons with international studies, which will strengthen the scientific evidence and provide a broader context for the findings.

Regarding the use of reversal agents, there are large studies and registries at a global level that have described the population requiring a variety of reversal agents. The RE-VERSE AD study, a prospective cohort that enrolled 90 patients, established the safety and effectiveness of idarucizumab in patients with severe bleeding. Colombia contributed to the recruitment for this study, although the specific number of patients contributed by each country is not available[37]. The START-Event multicenter registry, with a total of 117 patients on DOACs, provided data on the use of idarucizumab and prothrombin complex concentrate (PCC) in patients with major bleeding[38]. Finally, the RADOA multicenter prospective registry enrolled 78 patients being treated with DOACs and VKAs, evaluating the efficacy and safety of agents like idarucizumab and PCC[39].

Various registries in other countries have described their populations. The SOAR registry, implemented in 31 hospitals in the United States, contributed data from 1,513 subjects. The anticoagulants associated with bleeding were warfarin (37.3%), dabigatran (13.3%) and factor Xa inhibitors (49.4%), and 60% of these patients were treated with factor replacement or specific reversal agents. These patients had a longer hospital stay. The results showed that these patients have a variety of presentations, and the acute approach to bleeding is not standardized[40]. In France, the GIHP-NACO registry showed a low rate of excessive bleeding in patients on DOAC treatment undergoing urgent invasive procedures. Hemostatic agents were required for 16% of the 418 patients[41].

In Latin America, evidence regarding reversal agents is much scarcer. So far, we highlight one of the first reports on the use of idarucizumab in a patient on dabigatran anticoagulation who developed an expanding subdural hematoma secondary to trauma that required an urgent surgical procedure[42]. In Colombia, despite bleeding rates of 2.9 and 11% in samples of patients treated with rivaroxaban and warfarin, respectively, the information is also very scarce[43]. At a national level, we highlight a case report from 2011 of a patient on warfarin and LMWH anticoagulation who developed gastrointestinal bleeding and was adequately reverted with vitamin K[44].

The global information on the use of reversal agents is extensive, allowing a description of the population in different countries and providing information such as sociodemographic and clinical characteristics, main indication for reversal, main sites of bleeding and the effectiveness and safety of various reversal agents. However, in Latin America, and specifically Colombia, there is no regional data and most of the results come from the contribution of a small number of patients to international studies, or case reports. This constitutes a situation to be improved at a national and continental level.

In our country, low standardization of hemostatic tests makes it difficult to effectively handle cases of severe bleeding. In addition, the limited availability of reversal agents can make this situation even more difficult. RECCANT-AR will be the first national multicenter registry of reversal agent use in anticoagulated patients. This data will provide information on the availability of reversal agents and a description of these patients. The comparison between our findings and those of other regional or intercontinental reports will better describe this population worldwide, helping to standardize the approach to and treatment of bleeding cases, nationally.

Considering the relevance of the information presented above, we highlight the RECCANT and RECCANT-AR registries as the first national, multicenter projects aiming to describe the sociodemographic and clinical characteristics of anticoagulated patients and those who require reversal agents, in order to address this significant knowledge gap in our country.

Strengths and limitations

The RECCANT and RECCANT-AR registries have methodological strengths that support their impact on the current scientific evidence. Their multicenter design allows greater generalization of the results by including a more diverse and representative population sample. This increases the robustness of the data and external validity of the study. The use of standardized platforms like REDCap for data collection optimizes data management, monitoring and safety, facilitating the replicability of the studies.

Both registries provide a comprehensive view of anticoagulated patients and those who require reversal treatment in Colombia. The detailed collection of sociodemographic, clinical and treatment information allows a multidimensional description of the patients, providing a richer understanding of their profiles and facilitating the identification of patterns and risk factors, which are crucial for developing effective treatment strategies. In addition, the implementation of these registries establishes a solid foundation for future research in larger populations at a regional and international level, obtaining more generalizable and relevant results.

The design of both registries has limitations inherent to this type of study. The potential loss of patients during follow-up in RECCANT can affect the validity of the results by introducing bias. However, this is inevitable in prospective registries. Likewise, the lack of ambulatory follow-up in RECCANT-AR precludes assessment of the long-term progress of patients who require reversal agents, inhibiting a full understanding of the long-term efficacy of these interventions. Furthermore, relying on the quality of the existent medical records can affect the integrity of the data due to variations in their completeness and accuracy.

Taking into account the strengths and limitations described, the RECCANT and RECCANT-AR registries aim to significantly strengthen national and regional scientific evidence. Their implementation not only seeks to enrich the understanding of the profiles of anticoagulated patients and those who require reversal therapy in Colombia, but also to establish a solid foundation for future research in larger populations, both regionally and internationally, providing more generalizable and relevant results.

Conclusions

Anticoagulant therapy is crucial for managing various clinical conditions, and reversal agents, in turn, are essential in cases of bleeding or urgent procedures, to revert the anticoagulant effect.

In Colombia, there is limited scientific evidence regarding these populations, which creates a significant knowledge gap in the practice and outcomes of anticoagulation and management of bleeding complications in this country. The goal of the RECCANT and RECCANT-AR registries is to fill this knowledge gap by providing representative information about anticoagulated patients and reversal agent use.

The implementation of these registries will allow a better description of the population, identification of national patterns and the development of standardized strategies for improving the quality of care and clinical outcomes of Colombian patients.

Funding

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

Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

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

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

References

1. Malone PC, Agutter PS. The aetiology of deep venous thrombosis. QJM. 2006;99(9):581-93.
2. Heestermans M, Poenou G, Hamzeh-Cognasse H, Cognasse F, Bertoletti L. Anticoagulants: a short history, their mechanism of action, pharmacology, and indications. Cells. 2022;11(20):3214.
3. Liu F, Wang Y, Luo J, Huang L, Zhu W, Yin K, et al. Direct oral anticoagulants vs. warfarin in Latin American patients with atrial fibrillation: evidence from four post-hoc analyses of randomized clinical trials. Front Cardiovasc Med. 2022;9:841341.
4. Makani A, Saba S, Jain SK, Bhonsale A, Sharbaugh MS, Thoma F, et al. Safety and efficacy of direct oral anticoagulants versus warfarin in patients with chronic kidney disease and atrial fibrillation. Am J Cardiol. 2020;125(2):210-4.
5. Durand M, Schnitzer ME, Pang M, Carney G, Eltonsy S, Filion KB, et al. Comparative effectiveness and safety of direct oral anticoagulants versus vitamin K antagonists in nonvalvular atrial fibrillation: a Canadian multicentre observational cohort study. CMAJ Open. 2020;8(4).
6. You JJ, Singer DE, Howard PA, Lane DA, Eckman MH, Fang MC, et al. Antithrombotic therapy for atrial fibrillation: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2012;141(2 Suppl.):e531S-e575S.
7. Kearon C, Akl EA, Comerota AJ, Prandoni P, Bounameaux H, Goldhaber SZ, et al. Antithrombotic therapy for VTE disease: Antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2012;141(2 suppl.):e419S-e496S.
8. Whitlock RP, Sun JC, Fremes SE, Rubens FD, Teoh KH. Antithrombotic and thrombolytic therapy for valvular disease: Antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2012;141(2 Suppl):e576S-e600S.
9. Li H, Song X, Liang Y, Bai X, Liu-Huo WS, Tang C, et al. Global, regional, and national burden of disease study of atrial fibrillation/flutter, 1990-2019: results from a global burden of disease study, 2019. BMC Public Health. 2022;22(1):2015.
10. Joglar JA, Chung MK, Armbruster AL, Benjamin EJ, Chyou JY, Cronin EM, et al. 2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2024;149(1):e1-e156.
11. Tran HA, Gibbs H, Merriman E, Curnow JL, Young L, Bennett A, et al. New guidelines from the Thrombosis and Haemostasis Society of Australia and New Zealand for the diagnosis and management of venous thromboembolism. Med J Aust. 2019;210(5):227-35.
12. Wong P, Baglin T. Epidemiology, risk factors and sequelae of venous thromboembolism. Phlebology. 2012:27 Suppl 2:2-11.
13. Salmane C, Pandya B, Lafferty K, Patel NJ, McCord D. Longest event-free survival without anticoagulation in a mechanical aortic valve replacement. Clin Med Insights Cardiol. 2016;10:47-50.
14. Machado-Alba JE, García-Betancur S, Villegas-Cardona F, Medina-Morales DA. Patrones de prescripción de los nuevos anticoagulantes orales y sus costos económicos en Colombia. Rev Colomb Cardiol. 2016;23(4):277-85.
15. Dhakal P, Rayamajhi S, Verma V, Gundabolu K, Bhatt VR. Reversal of anticoagulation and management of bleeding in patients on anticoagulants. Clin Appl Thromb Hemost. 2017;23(5):410-5.
16. Chai-Adisaksopha C, Crowther M, Isayama T, Lim W. The impact of bleeding complications in patients receiving target-specific oral anticoagulants: A systematic review and meta-analysis. Blood. 2014;124(15):2450-8.

17. Konieczyńska M, Kupis RW, Bijak P, Malinowski KP, Undas A. Acceptance of a potential major bleeding among patients with venous thromboembolism on long-term oral anticoagulation: the knowledge of the disease and therapy matters. Thromb Res. 2020;193:116-21.
18. Carrier M, Le Gal G, Wells PS, Rodger MA. Systematic review: Case-fatality rates of recurrent venous thromboembolism and major bleeding events among patients treated for venous thromboembolism. Ann Intern Med. 2010;152(9):578-89.
19. Gómez-Outes A, Alcubilla P, Calvo-Rojas G, Terleira-Fernández AI, Suárez-Gea ML, Lecumberri R, et al. Meta-analysis of reversal agents for severe bleeding associated with direct oral anticoagulants. J Am Coll Cardiol. 2021;77(24):2987-3001.
20. Chaudhary R, Sharma T, Garg J, Sukhi A, Bliden K, Tantry U, et al. Direct oral anticoagulants: a review on the current role and scope of reversal agents. J Thromb Thrombolysis. 2020;49(2):271-86.
21. Mendoza-Sánchez JA, Silva FA, Rangel-Celis LM, Arias JE, Zuñiga-Sierra EA. Modelo de costos asociados al ataque cerebrovascular y los eventos adversos en pacientes con fibrilación auricular no valvular tratados con warfarina. Rev Colomb Cardiol. 2019;26(3):125-32.
22. Holbrook A, Schulman S, Witt DM, Vandvik PO, Fish J, Kovacs MJ, et al. Evidence-based management of anticoagulant therapy. Antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2012;141(2 Suppl.):e152S-e184S.
23. Tornkvist M, Smith JG, Labaf A. Current evidence of oral anticoagulant reversal: a systematic review. Thromb Res. 2018;162:22-31.
24. Milling TJ, Ziebell CM. A review of oral anticoagulants, old and new, in major bleeding and the need for urgent surgery. Trends Cardiovasc Med. 2020;30(2):86-90.
25. Bayer V, Kotalczyk A, Kea B, Teutsch C, Larsen P, Button D, et al. Global oral anticoagulation use varies by region in patients with recent diagnosis of atrial fibrillation: The GLORIA-AF Phase III Registry. J Am Heart Assoc. 2022;11(6):e023907.
26. Monreal M, Jiménez D, Bikdeli B. RIETE Registry: past, present and future. Arch Bronconeumol. 2022;58(3):205-7.
27. Dubner S, Saraiva JFK, Fragoso JCN, Barón-Esquivias G, Teutsch C, Gurusamy VK, et al. Effectiveness and safety of dabigatran in Latin American patients with atrial fibrillation: two years follow up results from GLORIA-AF registry. Int J Cardiol Heart Vasc. 2020;31:100666.
28. Ocampo Kohn C, Hernández Ortiz O, Velásquez Franco CJ, Tobón Acosta I, Mejía Restrepo FA. La clínica de anticoagulación del Hospital Universitario San Vicente de Paúl: Demografía, efectividad y complicaciones. Iatreia. 2004;17(2).
29. Gaviria Jaramillo LM. Beneficios de la clínica de anticoagulación. Acta Med Colomb. 2013;38(4):203.
30. Laverde LP, Gómez SE, Montenegro AC, Lineros A, Wills B, Buitrago AF. Experiencia de una clínica de anticoagulación. Rev Colomb Cardiol. 2015;22(5):224-30.
31. Sáenz M O, Sanabria F, Rubio AM, González A F, Gamba N. Clínica de anticoagulación de la Subred Centro Oriente, en Bogotá. Revi Colomb Neumol. 2021;32(2):37-45.
32. Gil Aldana VJ, Jiménez Lizcano AM, Suárez Ramírez OF, Vera Léon CC, Torres-Dimas AE. Fibrilación auricular no valvular en pacientes anticoagulados. Acta Med Colomb. 2022;47(3).
33. Montenegro A, Plaza M, Álvarez R, Pinto A, Gómez L, Castaño J, et al. Características de pacientes atendidos en dos clínicas de anticoagulación de Colombia. Rev Colomb Cardiol. 2022;28(4):353-9.
34. Ballestri S, Romagnoli E, Arioli D, Coluccio V, Marrazzo A, Athanasiou A, et al. Risk and management of bleeding complications with direct oral anticoagulants in patients with atrial fibrillation and venous thromboembolism: a narrative review. Adv Ther. 2023;40(1):41-66.
35. García-Peña AA. Evaluación de costo-efectividad de los nuevos anticoagulantes orales en pacientes con fibrilación auricular no valvular. Rev Colomb Cardiol. 2017;24(2):87-95.
36. Gómez-Mesa JE, Saldarriaga CI, Echeverría LE, Luna P. Colombian heart failure registry (RECOLFACA): methodology and preliminary data. Rev Colomb Cardiol. 2021;28(3):217-30.
37. Pollack CV, Reilly PA, van Ryn J, Eikelboom JW, Glund S, Bernstein RA, et al. Idarucizumab for dabigatran reversal - Full cohort analysis. N Engl J Med. 2017;377(5):431-41.
38. Testa S, Ageno W, Antonucci E, Morandini R, Beyer-Westendorf J, Paciaroni M, et al. Management of major bleeding and outcomes in patients treated with direct oral anticoagulants: results from the START-Event registry. Intern Emerg Med. 2018;13(7):1051-8.
39. Last J, Herrmann E, Birschmann I, Lindau S, Konstantinides S, Grottke O, et al. Clinical Course and Management of Patients with Emergency Surgery Treated with Direct Oral Anticoagulants or Vitamin K Antagonists-Results of the German Prospective RADOA-Registry. J Clin Med. 2024;13(1):272.
40. Pollack CV, Peacock WF, Bernstein RA, Clark CL, Douketis J, Fermann GJ, et al. The safety of oral anticoagulants registry (SOAR): A national, ED-based study of the evaluation and management of bleeding and bleeding concerns due to the use of oral anticoagulants. Am J Emerg Med. 2020;38(6):1163-70.
41. Godon A, Gabin M, Levy JH, Huet O, Chapalain X, David JS, et al. Management of urgent invasive procedures in patients treated with direct oral anticoagulants: An observational registry analysis. Thromb Res. 2022;216:106-12.
42. Ávila RI, López JEB, De La Rosa EC, Márquez MAH. Idarucizumab to revert the anticoagulant effect of dabigatran in traumatic acute subdural haematoma: A case report of first use in Latin America. Eur Heart J Case Rep. 2019;3(2):ytz098.
43. Ramos-Isaza E, Tuta-Quintero E, Bastidas-Goyes A, Diaz-Quijano D, Aponte-Murcia C, Espitia-Angel J, et al. Long-term survival in venous thromboembolic disease: rivaroxaban vs. warfarin - propensity score matching study. BMC Pharmacol Toxicol. 2023;24(1):77.
44. Varón AR, Cáceres-Méndez EA. Hemorragia de vías digestivas en el paciente anticoagulado. Rev Colomb Gastroenterol. 2011;26(1):39-42.

Revista Colombiana de Cardiología
Órgano oficial de la Asociación Sociedad Colombiana de Cardiología & Cirugía Cardiovascular
Permanyer

Check for updates

ORIGINAL ARTICLE

Systematic review of high-sensitivity troponin based protocols for rule-out and rule-in acute myocardial infarction: a comparison of traditional and Generative Pre-trained Transformer (GPT)-assisted approaches

Revisión sistemática de protocolos basados en troponina de alta sensibilidad para confirmar y descartar el infarto agudo de miocardio: una comparación de enfoques tradicionales y asistidos por transformadores generativos preentrenados (GPT)

John J. Sprockel-Díaz[1,2,3]* *and Juan J. Diaztagle-Fernández*[1,4]

[1]*Faculty of Medicinead de Medicina de la, Fundación Universitaria de Ciencias de la Salud, Internal Medicine Serviceio de Medicina Interna, Hospital de San José de Bogotá;* [2]*Instituto de investigaciones de la Fundación Universitaria de Ciencias de la Salud;* [3]*UIntensive Care Unit,nidad de Cuidados Intensivos de la Subred integrada de Servicios de Salud del Sur, Hospital El Tunal;* [4]*Departament of Physiological Sciences de Ciencias Fisiológicas, Faculty of Medicinead de Medicina, Universidad Nacional de Colombia, Sede Bogotá Campus. Bogotá, Colombia*

Abstract

Introduction: *Chest pain patients' risk is classified using a focused history and cardiovascular risk assessment, and clinical decision pathways are protocols used to define their risk. Natural language processing (NLP) is a field of computer science that enables computers to understand, interpret, and generate human language. ChatGPT is a new network architecture based on attention mechanisms.* **Objective:** *The objective of the study is to investigate the potential of ChatGPT for NLP by selecting articles within a systematic review and utilizing ChatGPT to assist in writing a paper.* **Methods:** *Our group conducted a systematic review of the literature to evaluate the diagnostic accuracy of troponin testing for early discharge of patients with suspected acute coronary syndrome. ChatGPT was tasked with selecting articles by screening their titles, abstracts, and full texts. The results obtained were compared with those of the original search. Reference documents were entered into the chatpdf.com platform under strict supervision.* **Results:** *The initial screening identified 3509 studies, of which three articles were selected for inclusion in the systematic review by ChatGTP: the HEART Pathway randomized trial, a comparison of the 2-h ADAPT versus HEART Pathway, and the RAPID-TnT. These three articles represented 60% of the five articles identified in the original review.* **Conclusion:** *The present paper shows the potential value of ChatGPT in aiding the article selection process for systematic reviews and assist in writing the paper. Nonetheless, further investigation and validation are required to confirm the effectiveness of this technology.*

Keywords: *ChatGPT. Natural language processing. Artificial intelligence. Chest pain. Systematic review. Clinical decision pathways.*

Correspondence:
John J. Sprockel Díaz
E-mail: jjsprockel@fucsalud.edu.co

Date of reception: 28-08-2023
Date of acceptance: 28-08-2024
DOI: 10.24875/RCCARE.M24000121
Available online: 05-02-2025
Rev Colomb Cardiol. 2024;31(6):382-389
www.rccardiologia.com

Resumen

Introducción: *El riesgo en pacientes con dolor torácico se clasifica utilizando una historia clínica enfocada y una evaluación del riesgo, las vías clínicas de decisión son protocolos para definir riesgo. El procesamiento de lenguaje natural (PLN) permite a las computadoras comprender, interpretar y generar lenguaje humano. ChatGPT es una nueva arquitectura de red basada en mecanismos de atención.* **Objetivo:** *Investigar el potencial de ChatGPT para el procesamiento de lenguaje natural seleccionando artículos dentro de una revisión sistemática y utilizando ChatGPT para asistir en la escritura de un artículo.* **Método:** *Sobre una revisión sistemática de la literatura previa para evaluar la precisión diagnóstica de protocolos basados en troponina para el alta temprana de pacientes con sospecha de infarto, se le encomendó a ChatGPT la tarea de seleccionar artículos mediante la revisión de sus títulos, resúmenes y textos completos. Los resultados se compararon con los de la búsqueda original. Los documentos se ingresaron en la plataforma chatpdf.com bajo estricta supervisión.* **Resultados:** *De 3.509 estudios identificados, tres artículos se seleccionaron para su inclusión en la revisión sistemática por ChatGTP: el HEART Pathway, una comparación del ADAPT de 2 horas vs. el HEART Pathway, y el RAPID-TnT. Representaron el 60% de los cinco artículos identificados en la revisión original.* **Conclusión:** *El presente trabajo muestra el potencial valor de ChatGPT en la ayuda al proceso de selección de artículos para revisiones sistemáticas y para ayudar en la escritura del artículo. No obstante, se requiere una investigación y validación adicionales para confirmar la efectividad de esta tecnología.*

Palabras clave: *ChatGPT. Procesamiento de lenguaje natural. Inteligencia artificial. Dolor torácico. Revisión sistemática. Vías clínicas de decisión.*

Introduction

To classify chest pain patients' risk, the American College of Cardiology/American Heart Association (ACC/AHA) guidelines recommend obtaining a focused history that includes the characteristics and duration of the presenting symptoms, as well as associated features and a cardiovascular risk factor assessment[1]. Clinical Decision Pathways are a set of protocols used to define the risk of patients presenting with chest pain; and these pathways are designed to help health-care providers make informed decisions about patient care based on evidence-based diagnostic protocols. Some examples include the HEART Pathway[2], EDACS[3], mADAPT[4], NOTR[5], 2020 ESC/hs-cTn[6], and 2016 ESC/GRACE[7]. The guidelines emphasize the importance of using a validated pathway to identify low-risk patients who can be safely discharged from the emergency department without further testing, and health-care providers should use their clinical judgment and follow established guidelines to determine the most appropriate pathway for each patient[1].

Natural language processing (NLP) is a field of computer science and artificial intelligence (AI) that focuses on the interaction between computers and humans in natural language. It involves developing algorithms and models that enable computers to understand, interpret, and generate human language. The generative pre-trained transformer is a new network architecture based solely on attention mechanisms, completely dispensing with recurrence and convolutions[8]. It relies entirely on an attention mechanism to draw global dependencies between input and output, allowing for significantly more parallelization and achieving state-of-the-art results in machine translation tasks.

ChatGPT was launched on November 30, 2022, based on Generative Pre-trained Transformer 3 (GPT-3), an autoregressive language model that uses deep learning to produce texts that simulate human writing[9]; it was created by OpenAI, a San Francisco-based AI research laboratory. The excitement that followed its launch quickly transferred to medicine. Notably, by January 2023, four papers had already included it as a co-author[10-13] which started an intense debate[14] that led to the retraction of two of the documents under the argument that "ChatGPT" did not qualify for authorship according to the journal's guide for authors and the publishre's ethics policies[15,16].

This article seeks to investigate ChatGPT's potential for NLP by selecting articles within a systematic review and utilizing ChatGPT to assist in writing a paper. The article will present a comprehensive overview of the methodology used, including details on how ChatGPT was integrated into the writing process, and discuss the implications or future directions for research in this area.

Methods

In the original paper[17], our group conducted a systematic review of the literature to evaluate the diagnostic accuracy of troponin testing for early discharge of patients with suspected acute coronary syndrome. To

be eligible for inclusion in this review, studies had to be randomized controlled trials that evaluated the diagnosis of chest pain in the emergency room using high-sensitivity troponin-based protocols and measured early discharge (before 4-6 h) as an outcome. Meanwhile, the exclusion criteria included studies that did not have early discharge as their objective, studies that evaluated troponin in combination with other biomarkers, studies that evaluated troponin at a single time point, and studies that were only published as posters or abstracts.

To identify relevant studies, the authors conducted a literature search on May 17, 2021, using three databases: MEDLINE, Cochrane, and EMBASE. They used search terms such as chest pain, acute coronary syndrome, accelerated diagnostic protocols, high sensitivity troponin, emergency department, risk stratification, and rapid ruling out and ruling in.

ChatGPT was requested to review the titles identified in the initial search to select those that met the inclusion criteria. Afterward, the abstracts of the selected papers were extracted by re-evaluating the inclusion criteria and considering elements for exclusion. Finally, ChatGPT reviewed the full-text articles from the previous selection to determine which articles would be included in the systematic review. The results obtained were then compared with those of the original search, evaluating whether new previously unselected studies were identified or there were errors in ruling out any of the five papers included in the original review.

Researchers utilized the chatpdf.com platform[18] to generate the different sections of the English document with rigorous oversight before the launch of GPT-4 on March 14, 2023. The process entailed uploading chosen reference documents and requesting a summary, followed by crafting key components for presentation or discussion, informed by the reference material. At times, multiple phrasing options were requested for a sentence or paragraph based on diverse concepts. Ultimately, the full text was processed to derive conclusions, and each document section was analyzed to produce a structured summary. Researchers either chose from the provided options or requested new versions based on promising selections. Moreover, they introduced their own ideas or adjustments on several occasions. The platform's pre-established parameters were followed without any modifications to temperature or penalties.

The original systematic review was approved by the ethics and research committee at University Foundation of Health Sciences and was registered in PROSPERO under the code CRD42021255495.

Results

The initial screening identified 3,509 studies, five of which met the inclusion criteria in the original study[19-23]. The title review carried out by ChatGTP identified 25 articles related to the diagnosis of chest pain, diagnostic protocols for acute coronary syndromes, or acute myocardial infarction using troponin. After reviewing the summaries, another 14 studies were eliminated, leaving 11 to be reviewed in full text. Of these, ChatGPT ultimately selected six. The evaluation conducted by the researchers indicated that the HEART Pathway Randomized Trial at 1 year[24] and an assessment of adherence to the same work[25] were excluded, as they were considered to duplicates. Another article was also excluded because it was a presentation at a congress[26].

Finally, three articles were selected inclusion in the systematic review: the HEART Pathway[20] randomized trial[2], a Comparison of the 2-h ADAPT versus HEART Pathway[21], and the RAPID-TnT[23], which were also identified by the original search. The study selection process is depicted in the PRISMA diagram in figure 1.

Table 1 provides an overview of the methodology followed in the three included studies and the two studies that were not identified. Table 2 summarizes the main results obtained in the different studies, highlighting that among the 4,130 patients included in the three clinical trials, 2,985 (72.3%) were discharged early, with the highest rates observed in the 0/3 h ESC (91.0%) and 0/1 h ESC (72.0%) groups, followed by the EDACS (41.6%), HEART (39.7%), and ADAPT (30.5%) groups, and the lowest rates in the usual care groups (18.4%).

The supplementary material includes several sessions that were conducted with ChatGPT, which gathered responses obtained in the review process from the titles to the full text, as well as the article writing process. Figure 2 provides an example of one of these sessions.

Discussion

In this study, we present the results of using an NLP tool based on GPT in the article selection process for a systematic review. At its current stage of development, we consider ChatGPT insufficient as a standalone tool for identifying articles in a systematic review. Nonetheless, we acknowledge its potential as a valuable supplement to existing strategies. While it is evident that identifying the study by Body et al.[22] based solely on the title is challenging ("Feasibility of the

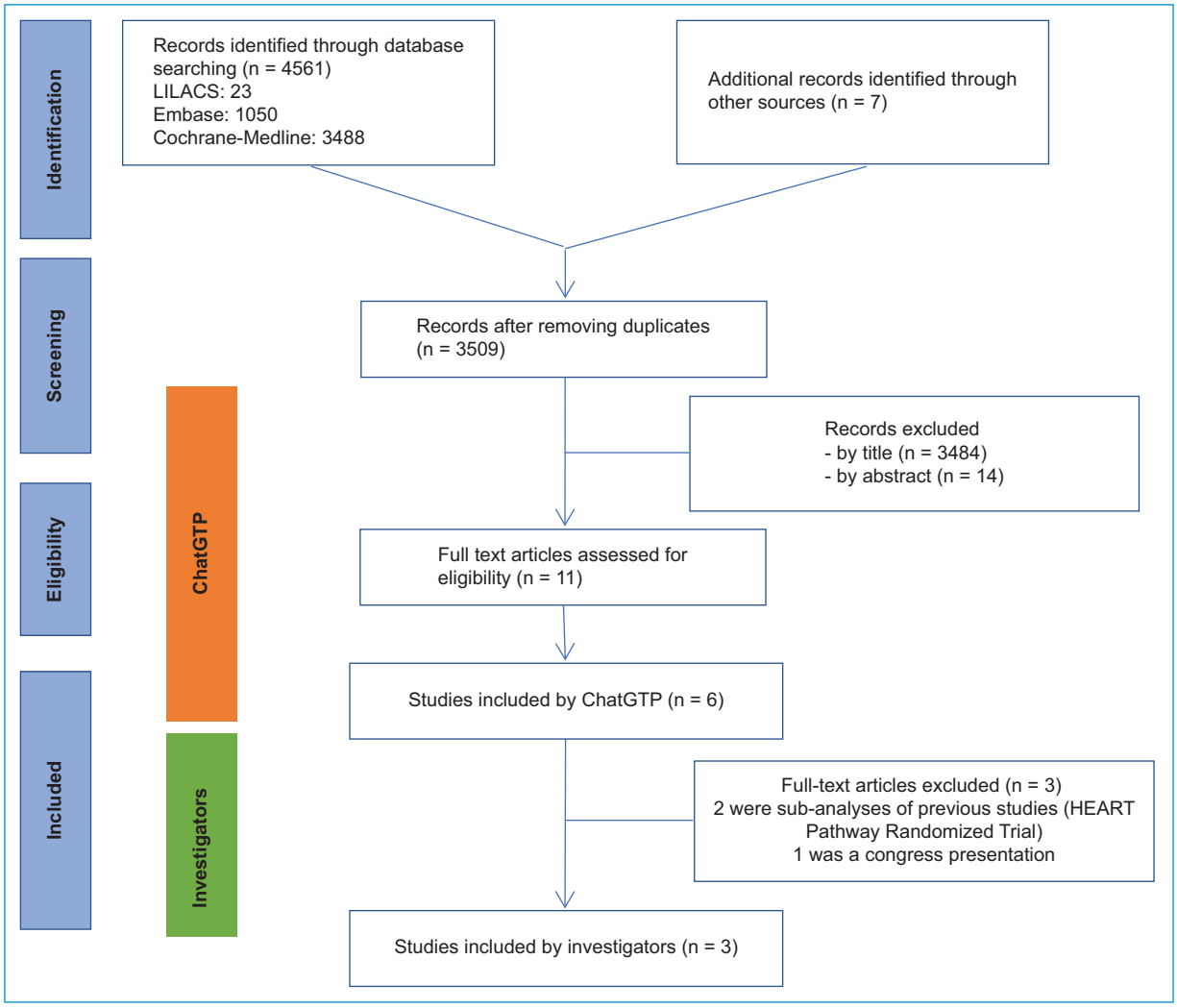


Figure 1. PRISMA diagram.

Manchester Acute Coronary Syndromes decision rule to safely reduce unnecessary hospital admissions: a pilot randomized controlled trial"), this is not the case for the study by Than et al.[19] ("A 2-h diagnostic protocol for possible cardiac chest pain in the emergency department: a randomized clinical trial"). We were unable to find any similar works in our literature search.

ChatGPT has been suggested as a potential tool for various clinical and research scenarios, including supporting clinical practice, facilitating scientific production, identifying potential misuse in medicine and research, and aiding in reasoning about public health topics.[26] In scientific writing, ChatGPT can assist researchers and scientists in organizing material, generating an initial draft, and proofreading. By providing raw information, ChatGPT can also help compose the section on the methods used in the study, justify the sample size, and describe data analysis techniques. When the manuscript has been finalized, ChatGPT is extremely effective for the editing process; formatting and language editing, rewriting a particularly complex sentence in a clearer way, and even summarizing the entire text to compose a suitable abstract are feasible using this approach[27]. In the present paper, we have been able to verify many of these functionalities.

Cascella et al.[27] evaluated ChatGPT's ability to understand and summarize information and draw conclusions based on the text from the Background, Methods, and Results sections of an abstract; GPT was able to correctly indicate the setting and summarize the results of the primary outcome of each study. However, it was more likely to highlight secondary findings while

Table 1. Characteristics of included studies

Study	CLINICAL DECISION Pathways	Type of study	Number of patients	Used troponin	Primary outcome
Studies identified by GTP					
Mahler et al., 2015[2]	HEART	Single-center	282	ADVIA Centaur platform TnI-Ultra™ assay (Siemens)	30 days objective cardiac testing (stress testing or angiography)
	Usual care				
Than et al., 2016[20]	EDACS	Pragmatic single-center	560	Abbott Architect high-sensitivity troponin I (hs-cTnI)	Successful discharge (6 h)
	ADAPT				
Chew et al., 2019[22]	0/1-h Protocol	Non-inferiority multicenter	3288	hs-cTnT; Roche Diagnostics Elecsys 5th generation	30-day MACE
	ESC 0/3-h Protocol				
Studies Non-Identified by GTP					
Than et al., 2014[19]	ADAPT	Single-center	544	Abbott Architect high-sensitivity troponin I (hs-cTnI)	Successful discharge (6 h)
	Usual care				
Body et al., 2017[21]	MACS	Single-center	60	hs-cTnT; Roche Diagnostics Elecsys	Successful discharge (4 h)
	Usual care				

ADAPT: accelerated diagnostic protocol to assess chest pain using troponins; HEART: history, ECG, age, risk factors, troponin; EDACS: emergency department acute coronary syndrome; MASC: Manchester Acute Coronary Syndrome Scale; MACE: major cardiovascular events.

Table 2. Effectiveness of the applied protocols

Study	Clinical decision pathways	Early discharge (%)	30-day MACE	Sensibility (%)	NPV (%)	Length of stay
Studies identified by GTP						
Mahler, 2015[2]	HEART	56 (39.7)	0	9.3	100.0	9.9 h
	Usual care	26 (18.4)	0	8.2	100.0	21.9 h
Than et al., 2016[20]	EDACS	133 (41.6)	0	22.1	99.1	6 h
	ADAPT	90 (30.5)	0	14.9	100.0	6 h
Chew et al., 2019[22]	0/1-h protocol	Effective: 748 (45) Expected: 1187 (72)	17 (1.0%)	88.1*	99.6**	4.6 h
	ESC 0/3-h protocol	Effective: 545 (33) Expected: 1493 (91)	16 (1.0%)	NA	99.4**	5.6 h
Studies Non-Identified by GTP						
Than et al., 2014[19]	ADAPT	52 (19.3)	1	97.9	98.1	6 h
	Usual care	30 (11.0)	0	100.0	100.0	20 h
Body et al., 2017[21]	MACS	17 (26)	3	100.0	100.0	1 day
	Usual care	5 (8)	3	100.0	100.0	1 day

*For rule in, **For rule out, NPV: negative predictive value; NA: not available; MACE: major cardiovascular events; ADAPT: accelerated diagnostic protocol to assess chest pain using troponins; HEART: history, ECG, age, risk factors, troponin; EDACS: emergency department acute coronary syndrome; MASC: Manchester Acute Coronary Syndrome Scale.

not strictly following the text length constraint, in favor of a meaningful message. An experiment conducted by Gao et al. tested ChatGPT's ability to generate abstracts based on 50 titles, which were then reviewed by plagiarism detectors, AI detectors, and blinded human reviewers. The results showed that while some abstracts

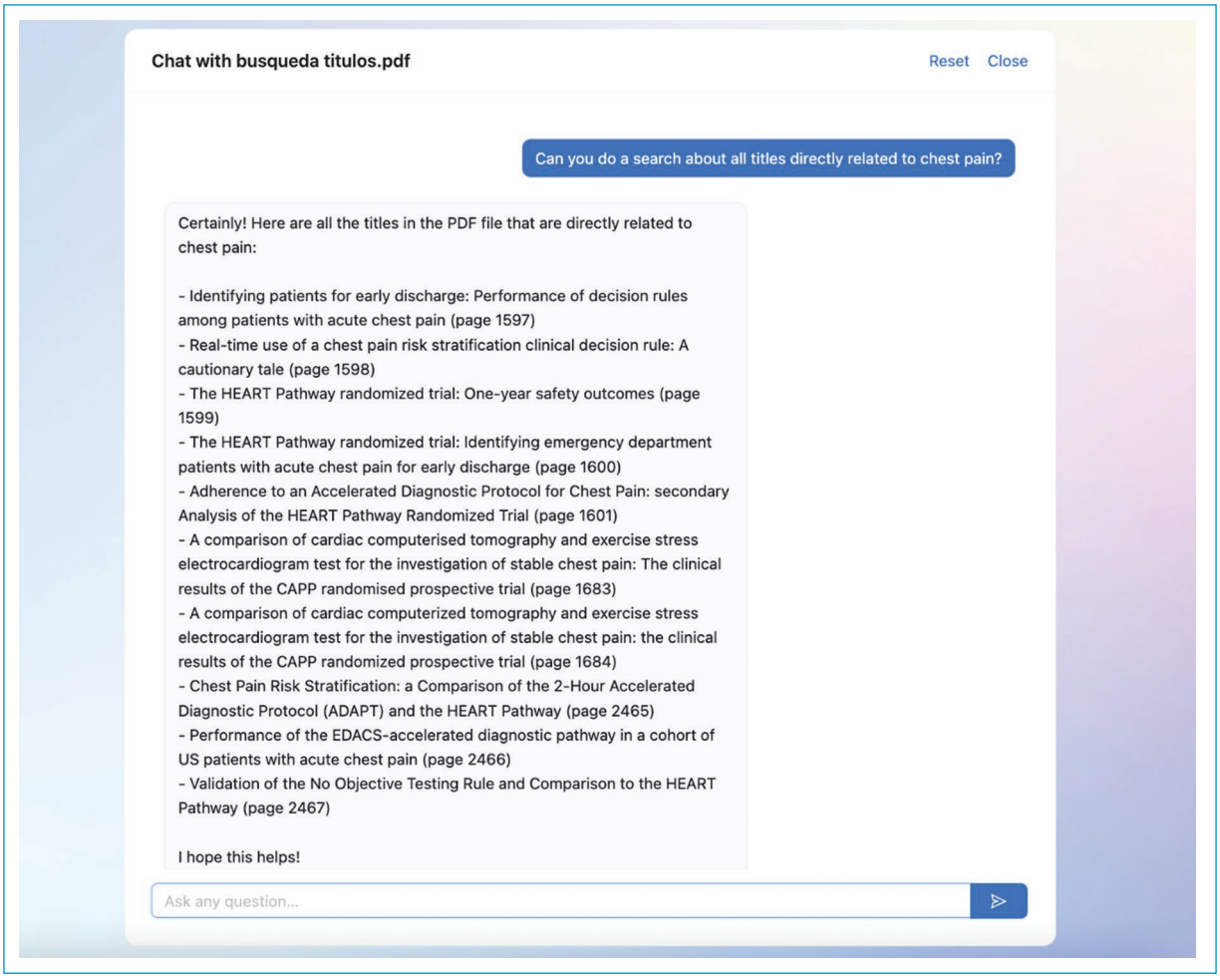


Figure 2. Screenshot of a session with ChatGPT conducted through the website.

generated by ChatGPT were correctly identified as such, human reviewers found it difficult to distinguish between abstracts written by a human author and those generated by ChatGPT[28].

As pointed out in recent papers[29,30], the current version of ChatGPT has the potential to generate false information what is known in AI as a *hallucination* or *artificial hallucination* (a response generated by AI that appears to be confident but lacks justification from its training data[31]); therefore, it is crucial for human authors to thoroughly scrutinize and validate any information generated by ChatGPT before incorporating it into their articles. The use of ChatGPT in scientific writing raises concerns about the accuracy and integrity of the data it generates; therefore, the policy and practice for evaluating scientific manuscripts should be modified to maintain rigorous scientific standards[30].

The use of AI chatbots like ChatGPT in scientific writing raises some ethical concerns and should therefore be regulated. The incredible development of AI tools can lead to a significant increase in the number of publications by some researchers, without a real increase in their experience in that field. Ethical issues can therefore arise regarding academmic institutions hiring professionals based on the number of publications rather than on their quality. It is important to note that while ChatGPT can assist in scientific writing, it should not be used as a replacement for human judgment, and the output should always be reviewed by experts before being used[27]. In addition, any assistance provided by AI should be disclosed in the article[29]. Moreover, it is crucial to recognize that ChatGPT and similar AI tools are not yet adequate replacements for traditional literature search methods grounded in robust methodological guidelines and established databases. These AI tools lack specificity in validating the statistical significance and overall quality of information, making them insufficient as standalone resources for academic research.

The findings of a recent study[32] indicate that the introduction of GPTs could potentially affect approximately 80% of the U.S. workforce, with at least 10% of their work tasks being impacted. In addition, around 19% of workers could see at least 50% of their tasks affected. There is concern about the possible misuse of GPT in medicine and research, such as fabricating research data or results to meet funding or publication requirements, using the model to make diagnoses or treatment recommendations without proper validation or oversight, and generating fake news or misinformation[27]. Health researchers have a responsibility to establish guidelines for the appropriate use of new technologies like ChatGPT, while also exploring their benefits, limitations, and risks. As advancements in this field continue to emerge, it is crucial to adapt quickly in order to maximize their potential.

Conclusion

The integration of ChatGPT in NLP shows promise as an aid in scientific paper writing, although the generated text must be critically evaluated to ensure accuracy and validity. Despite the uncertainty surrounding its current effectiveness, our study demonstrated that ChatGPT can be used to screen articles for a systematic review; additional examinations will be required as technology advances or GPT systems are customized for medical purposes. In addition, the use of clinical decision pathways is recommended to accurately identify the risk in chest pain patients and guide health-care providers in making informed decisions about patient care based on evidence-based diagnostic protocols.

Funding

The authors declare that they have not received funding.

Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The study does not involve patient personal data nor requires ethical approval. The SAGER guidelines do not apply. The original systematic review was approved by the ethics and research committee at Fundación Universitaria de Ciencias de la Salud and was registered in PROSPERO under code CRD42021255495.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

References

1. Gulati M, Levy PD, Mukherjee D, Amsterdam E, Bhatt DL, Birtcher KK, et al. 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR guideline for the evaluation and diagnosis of chest pain: executive summary: a report of the American college of cardiology/American heart association joint committee on clinical practice guidelines. Circulation. 2021;144:e368-454.
2. Mahler SA, Riley RF, Hiestand BC, Russell GB, Hoekstra JW, Lefebvre CW, et al. The HEART Pathway randomized trial: identifying emergency department patients with acute chest pain for early discharge. Circ Cardiovasc Qual Outcomes. 2015;8:195-203.
3. Than M, Cullen L, Reid CM, Lim SH, Aldous S, Ardagh MW, et al. A 2-h diagnostic protocol to assess patients with chest pain symptoms in the Asia-Pacific region (ASPECT): a prospective observational validation study. Lancet Glob Health. 2014;2:e284-91.
4. Carlton EW, Khattab A, Greaves K. Identifying patients suitable for discharge after a single-presentation high-sensitivity troponin result: a comparison of five established risk scores and two high-sensitivity assays. Ann Emerg Med. 2015;66:635-45.e3.
5. Stopyra JP, Miller CD, Hiestand BC, Lefebvre CW, Nicks BA, Cline DM, et al. Validation of the no objective testing rule and comparison to the HEART Pathway. Acad Emerg Med. 2017;24:1165-8.
6. Collet JP, Thiele H, Barbato E, Barthélémy O, Bauersachs J, Bhatt DL, et al. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation [published online ahead of print August 29, 2020]. Eur Heart J. 2021;42:1289-367.
7. Roffi M, Patrono C, Collet JP, Mueller C, Valgimigli M, Andreotti F, et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: task force for the management of acute coronary syndromes in patients presenting without Persistent ST-Segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2016;37:267-315.
8. Vaswani A, Shazeer N, Parmar N, Uszkoreit J, Jones L, Gomez AN, et al. Attention is all you need. In: Guyon I, Luxburg UV, Bengio S, Wallach H, Fergus R, Vishwanathan S, et al., editores. Advances in Neural Information Processing Systems. Curran Associates, Inc.; 2017. Available from: https://proceedings.neurips.cc/paper/2017/file/3f5ee-243547dee91fbd053c1c4a845aa-Paper.pdf
9. OpenAI. Introducing ChatGPT. Available from: https://openai.com/blog/chatgpt [Last accessed on 2023 Mar 09].
10. Transformer GG, Thunström AO, Steingrimsson S. Can GPT-3 write an Academic Paper on Itself, with Minimal Human Input?; 2022. Available from: https://hal.science/hal-03701250 [Last accessed on 2023 Mar 09].
11. ChatGPT Generative Pre-trained Transformer, Zhavoronkov A. Rapamycin in the context of Pascal's Wager: generative pre-trained transformer perspective. Oncoscience. 2022;9:82-4.
12. O'Connor S. Open artificial intelligence platforms in nursing education: tools for academic progress or abuse? Nurse Educ Pract. 2023;66:103537.
13. Kung TH, Cheatham M, Medenilla A, Sillos C, Leon LD, Elepaño C, et al. Performance of ChatGPT on USMLE: Potential for AI-Assisted Medical Education Using Large Language Models. medRxiv; 2022. p. 2022.12.19.22283643. Available from: https://www.medrxiv.org/content/10.1101/2022.12.19.22283643v2 [Last accessed on 2023 Mar 09].
14. Stokel-Walker C. ChatGPT listed as author on research papers: many scientists disapprove. Nature. 2023;613:620-1.
15. O'Connor S. Corrigendum to Open artificial intelligence platforms in nursing education: tools for academic progress or abuse? Nurse Educ Pract. 2023;66:103537.
16. Kung TH, Cheatham M, Medenilla A, Sillos C, Leon LD, Elepaño C, et al. Performance of ChatGPT on USMLE: potential for AI-assisted medical education using large language models. PLoS Digit Health. 2023;2:e0000198.
17. Sprockel J. Protocolos de diagnóstico acelerado basados en troponina de alta sensibilidad en el diagnóstico del dolor torácico: una revisión sistemática. Rev Arg Cardiol. 2023;91:290-7.
18. OpenAI. Chat with any PDF using the new ChatGPT API. OpenAI API Community Forum; 2023. Available from: https://community.openai.com/t/chatpdf-com-chat-with-any-pdf-using-the-new-chatgpt-api/81446 [Last accessed on 2023 Mar 09].

19. Than M, Aldous S, Lord SJ, Goodacre S, Frampton CM, Troughton R, et al. A 2-hour diagnostic protocol for possible cardiac chest pain in the emergency department: a randomized clinical trial. JAMA Intern Med. 2014;174:51-8.
20. Than MP, Pickering JW, Aldous SJ, Cullen L, Frampton CM, Peacock WF, et al. Effectiveness of EDACS versus ADAPT accelerated diagnostic pathways for chest pain: a pragmatic randomized controlled trial embedded within practice. Ann Emerg Med. 2016;68:93-102.e1.
21. Body R, Boachie C, McConnachie A, Carley S, Van Den Berg P, Lecky FE. Feasibility of the Manchester acute coronary syndromes (MACS) decision rule to safely reduce unnecessary hospital admissions: a pilot randomised controlled trial. Emerg Med J. 2017;34: 586-92.
22. Chew DP, Lambrakis K, Blyth A, Seshadri A, Edmonds MJ, Briffa T, et al. A randomized trial of a 1-hour troponin t protocol in suspected acute coronary syndromes: the rapid assessment of possible acute coronary syndrome in the emergency department with high-sensitivity troponin T study (RAPID-TnT). Circulation. 2019;140:1543-56.
23. Stopyra JP, Riley RF, Hiestand BC, Russell GB, Hoekstra JW, Lefebvre CW, et al. The HEART pathway randomized controlled trial one-year outcomes. Acad Emerg Med. 2019;26:41-50.
24. Mahler SA, Riley RF, Russell GB, Hiestand BC, Hoekstra JW, Lefebvre CW, et al. Adherence to an accelerated diagnostic protocol for chest pain: secondary analysis of the HEART pathway randomized trial. Acad Emerg Med. 2016;23:70-7.
25. Mahler SA, Riley RF, Burke GL, Hiestand BC, Miller CD. Real-time use of a chest pain risk stratification clinical decision rule: a cautionary tale. Ann Emerg Med. 2013;62:S112.
26. Cascella M, Montomoli J, Bellini V, Bignami E. Evaluating the feasibility of ChatGPT in healthcare: an analysis of multiple clinical and research scenarios. J Med Syst. 2023;47:33.
27. Salvagno M, Taccone FS, Gerli AG. Can artificial intelligence help for scientific writing? Crit Care. 2023;27:75.
28. Gao CA, Howard FM, Markov NS, Dyer EC, Ramesh S, Luo Y, et al. Comparing Scientific Abstracts Generated by ChatGPT to Original Abstracts using an Artificial Intelligence Output Detector, Plagiarism Detector, and Blinded Human Reviewers. bioRxiv; 2022. p. 2022.12.23.521610. Available from: https://www.biorxiv.org/content/10.1101/2022.12.23.521610v1 [Last accessed on 2023 Mar 09].
29. Kim SG. Using ChatGPT for language editing in scientific articles. Maxillofac Plast Reconstr Surg. 2023;45:13.
30. Alkaissi H, McFarlane SI. Artificial hallucinations in ChatGPT: implications in scientific writing. Cureus. 2023;15:e35179.
31. Ji Z, Lee N, Frieske R, Yu T, Su D, Xu Y, et al. Survey of hallucination in natural language generation. ACM Comput Surv. 2023;55:248.
32. Eloundou T, Manning S, Mishkin P, Rock D. GPTs are GPTs: An Early Look at the Labor Market Impact Potential of Large Language Models. arXiv; 2023. Available from: https://arxiv.org/abs/2303.10130 [Last accessed on 2023 Mar 09].

Revista Colombiana de Cardiología
Órgano oficial de la Asociación Sociedad Colombiana de Cardiología & Cirugía Cardiovascular
Permanyer

Check for updates

CARDIOLOGY IMAGES

Inferior vena cava agenesis as a cause of pulmonary thromboembolism

Agenesia de vena cava inferior como causa de tromboembolia pulmonar

Jesús S. Borges-López, Erlan E. Rosas-Munive, and Axel Cuevas-Campillo*

Echocardiography Service, Hospital General de México Dr. Eduardo Liceaga, Ciudad de México, México

This was a 29-year-old woman with a history of cholecystectomy and hepatectomy secondary to Mirizzi syndrome three years ago. Six months ago, she began to experience increased abdominal girth, facial and lower extremity edema, nausea and dyspnea; she was seen in the emergency room and was admitted by the gastroenterology service. On physical exam, she had jugular distention, bilateral basal rales, grade II ascites, and an abdominal collateral venous network. She underwent paracentesis with negative culture, GenXpert, cytology and cytochemical tests of the ascitic fluid, and well as a negative cytopathology for malignant cells. She was seen by angiology who found bilateral venous stasis in both legs on Doppler ultrasound. Thoracoabdominal computed tomography with contrast reported inferior vena cava (IVC) agenesis with multiple collaterals that drained into the azygous vein, pulmonary thromboembolism (Fig. 1 A and B) and a mediastinal mass (Fig. 2 A-D). A transthoracic echocardiogram reported normal parameters, and hematological, oncological and rheumatological pathologies were also ruled out. She was started on anticoagulants while waiting for corrective surgery to be scheduled.

Inferior vena cava agenesis is a rare congenital vascular malformation that leads to anomalous venous drainage of the lower limbs, increasing the risk of deep vein thrombosis, pulmonary thromboembolism and thromboses in other organs. It is usually an incidental finding in asymptomatic patients; however, it should be suspected in young patients with venous thrombi with no other risk factors.

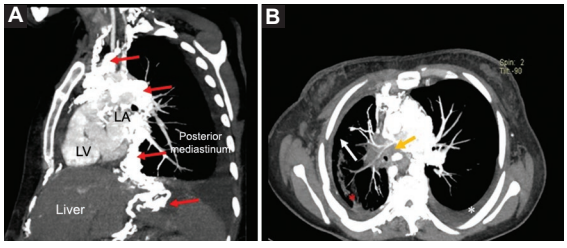


Figure 1. Computed tomography (CT) scan of the chest with contrast. **A:** sagittal view showing mediastinal conglomerate mass and collaterals of the azygos vein (red arrows). **B:** axial view showing a right pulmonary artery branch filling defect compatible with pulmonary thromboembolism (yellow arrow), pleural thickening (white arrow) and evidence of consolidation of the pulmonary parenchyma (asterisk).

Acknowledgements

The authors would like to thank the Cardiology and Echocardiography Service at Hospital General de México Dr. Eduardo Liceaga.

Funding

The authors declare that they did not receive funding for this study.

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

Date of reception: 14-09-2022
Date of acceptance: 13-06-2023
DOI: 10.24875/RCCARE.M22000130
Available online: 05-02-2025
Rev Colomb Cardiol. 2024;31(6):390-391
www.rccardiologia.com

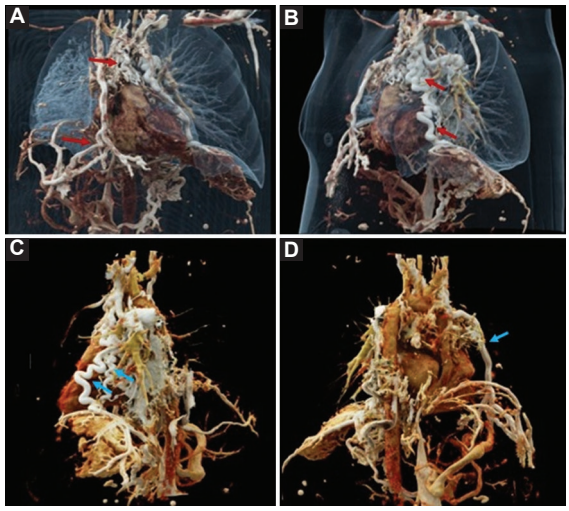


Figure 2. Chest CT with 3D reconstruction. **A-D:** mediastinal conglomerate mass and collaterals of the azygos vein.

Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have obtained approval from the Ethics Committee for the analysis of routinely obtained and anonymized clinical data, so informed consent was not necessary. Relevant guidelines were followed.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in writing this manuscript.

Revista Colombiana de Cardiología
Órgano oficial de la Asociación Sociedad Colombiana de Cardiología & Cirugía Cardiovascular
Permanyer

Check for updates

LETTER TO THE EDITOR

Use of diagnostic methods in pre-participation assessment for physical activity in asymptomatic patients. Is it possible to detect cardiovascular disease and prevent sudden death?

Uso de métodos diagnósticos en la evaluación reparticipativa para la práctica de actividad física en asintomáticos. ¿Es posible detectar la enfermedad cardiovascular y prevenir la muerte súbita?

Jaime A. Gallo-Villegas[1,2]* *and Dagnóvar Aristizábal-Ocampo*[2]

[1]*Graduate Program in Applied Physical Activity and Sports Medicine, Faculty of Medicine, Universidad de Antioquia;* [2]*Knowledge Management Unit, Sicor Clinical and Research Center, Antioquía. Medellín, Colombia*

Dear Editor,

We read the article *A proposal for preparticipation evaluation and follow up in the prescription of exercise and sports for resistance training* by Botia-Osorio et al.[1] in detail and with great interest. We believe some observations should be made regarding the diagnostic methods selected in the preparticipation assessment for physical activity of asymptomatic people to detect cardiovascular disease and prevent sudden cardiac death.

In the article, the authors propose different diagnostic methods according to age group and the goals of the activity. However, some of the proposed methods lack scientific evidence for their use in the Colombian context, and the authors leave out certain screening, diagnostic and prognostic principles.

The World Health Organization (WHO) published the principles and practices of disease detection through screening programs[2]. This organization recommends using screening tests when the following conditions are met: a) the disease being tested for is common; b) the screening test is valid and reproducible; c) there are resources available for prompt diagnosis and treatment; and d) the cost of detection is balanced with the healthcare cost. Failure to meet any of the criteria would cause more harm than good.

Under the first criterion, the main causes of death in children and adolescents are violence, motor vehicle accidents, drowning and suicide[3]. While sudden death occurs in this age group, and the familial and social impact caused by the death of a young person during exercise must be recognized, its occurrence is rare[3].

As far as the screening test (the second criterion), the use of electrocardiography in children/adolescents and young adults is not a standard global practice in preparticipation assessment[4-7]. The choice of a diagnostic method should not only consider the operating characteristics of the test (sensitivity and specificity), but also the frequency of the disease to be detected in the setting where the test will be applied (prevalence). Although the operating characteristics of electrocardiography have recently improved with the incorporation of specific abnormality criteria in physically active people[8,9] and artificial intelligence[10], its interpretation requires trained staff who are not always available. Also, the low frequency of cardiovascular disease in children and young people (0.3%)[11] limits its use, due to its low positive predictive value (3.9%) (Fig. 1). In this scenario, a negative result possibly rules out the disease, but a positive result causes uncertainty. According to the third criterion, if a complete screening program with standardized processes that respond

***Correspondence:**
Jaime A. Gallo-Villegas
E-mail: jaime.gallo@udea.edu.co

Date of reception: 18-04-2024
Date of acceptance: 25-09-2024
DOI: 10.24875/RCCARE.M24000129
Available online: 05-02-2025
Rev Colomb Cardiol. 2024;31(6):392-394
www.rccardiologia.com

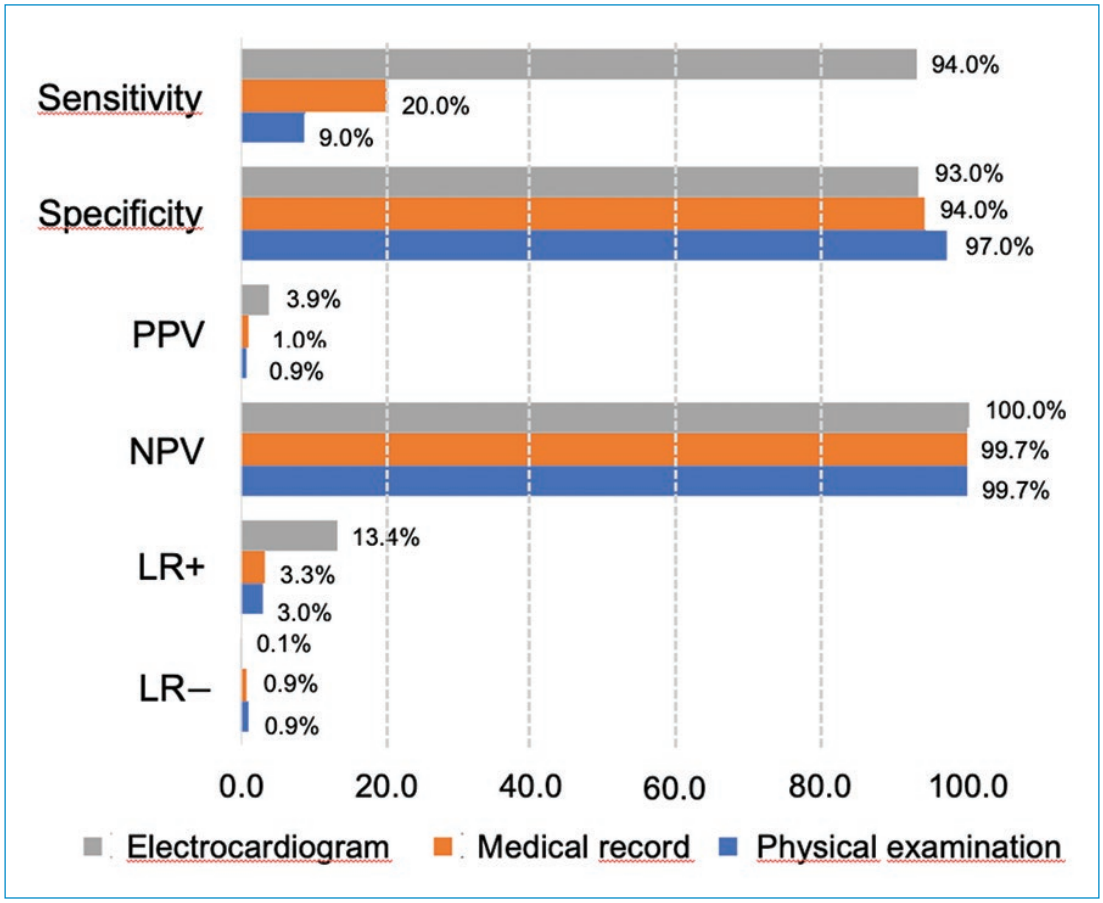


Figure 1. A comparison of the operating characteristics of electrocardiograms, the medical history and physical exam in the preparticipation assessment of asymptomatic children, adolescents and young people. According to Bayes' Theorem, when there is a low disease prevalence (0.3%), even a diagnostic method with good operating characteristics (electrocardiogram: 94% sensitivity and 93% specificity) has a low post-test probability of the disease with a positive result (3.9% PPV). A low PPV and high NPV are also found in the medical history and physical exam, despite having worse operating characteristics than the electrocardiogram. These findings show the importance of the pre-test probability (disease prevalence) in the setting in which the diagnostic test will be used *(operating characteristics of the three diagnostic methods taken from: Harmon et al., 2015[11]).*
PPV: positive predictive value; NPV: negative predictive value; LR+: positive likelihood ratio LR–: negative likelihood ratio.

promptly to the need to confirm the diagnosis is not available, a positive result could have an emotional impact on the individual and his/her family.

On the other hand, cost-effectiveness studies (the fourth criterion) in the United States have shown a high cost (up to 14.4 million dollars) per life saved when an electrocardiogram is added to the medical history and physical exam in the preparticipation assessment of adolescents and young people[12]. A screening program that includes an electrocardiogram would not be financially sustainable in Colombia. Due to the reasons described, we should be critical of the routine use of electrocardiography in this age group as part of the assessment for engaging in physical activity. According to the available evidence, preparticipation assessment and follow up of physical activity in amateur children and young people should focus on the medical history and physical exam (the American Heart Association's 14 elements)[7]; however, we recognize the limitations of their operating characteristics[11] (Fig. 1).

Since coronary disease is the main cause of sudden cardiac death in those over the age of 35[13], the medical history and physical exam should always be accompanied by cardiovascular risk stratification using the available predictive models[14,15]. Nonetheless, the main limitation of these models is their lack of validation in the Colombian population. There is evidence today for the use of stress electrocardiography, due to the incorporation of additional information and the

potential for reclassifying the cardiovascular risk stratification[16,17]. On the other hand, according to Bayes' Theorem, imaging methods like stress echocardiography and computed tomography of the coronary arteries should only be considered in scenarios with greater uncertainty, with intermediate cardiovascular risk[14], or when symptoms are present, with a high pre-test probability of coronary disease, to confirm the diagnosis[18,19]. The tests should be done serially to increase specificity.

For competitive/professional athletes, the decision to use diagnostic methods in preparticipation assessment should consider aspects related to the individual's training and characteristics. Keeping in mind that this activity could lead to the phenotypic expression of genetic abnormalities, short maximum effort tests with electrocardiography could be useful, in addition to the proposed diagnostic methods, as recommended by the Italians[20]. Although ergospirometry could contribute to early detection of cardiopulmonary disorders and help in planning training[21], laboratory tests cannot always be extrapolated to the field. There is also insufficient evidence regarding the frequency of imaging tests in follow up to detect cardiovascular disease and prevent sudden cardiac death.

Finally, we believe that the medical history and complete physical exam should be the cornerstone of preparticipation assessment and physical activity follow up, as recommended by some associations[7]. There is no evidence that mass cardiac screening reduces sudden death events; in addition, there is the potential for false positives with emotional effects and unnecessary consequent disqualification, and screening does not prevent all cardiac deaths in young athletes[4]. Remember that 72% of the children and adolescents with sudden cardiac death had signs or symptoms prior to the fatal outcome[22]. In mass events (marathons), self-administered questionnaires, with education of the trainers and participants, reduced the occurrence of life-threatening events by more than half[23]. Likewise, for secondary prevention, the availability of an automated external defibrillator in sports settings and at races, basic cardiopulmonary resuscitation training for coaches, and cardioverter-defibrillator implantation in athletes with known heart disease, contribute to the reduction of sudden cardiac death[4]. Normal test results in asymptomatic people could produce a false belief that all is well; however, this finding does not guarantee the absence of disease, although some of the proposed methods have prognostic value. The most important thing is to provide follow-up and constant accompaniment for these people, always alert to any warning sign or symptom, regardless of how small it may seem, especially when it occurs during physical activity.

References

1. Botia-Osorio MM, Fernández K, Dueñas R. Propuesta para evaluación preparticipativa y seguimiento en la prescripción del ejercicio y el deporte en el entrenamiento de resistencia. Rev Colomb Cardiol. 2023;30:15-22.
2. Wilson JM, Jungner YG. [Principles and practice of mass screening for disease]. Bol Oficina Sanit Panam. 1968;65:281-393.
3. GBD 2017 Child and Adolescent Health Collaborators; Reiner RC Jr, Olsen HE, Ikeda CT, Echko MM, Ballestreros KE, Manguerra H, et al. Diseases, injuries, and risk factors in child and adolescent health, 1990 to 2017: findings from the Global Burden of Diseases, Injuries, and Risk Factors 2017 Study. JAMA Pediatr. 2019;173:e190337.
4. Finocchiaro G, Westaby J, Sheppard MN, Papadakis M, Sharma S. Sudden cardiac death in young athletes: JACC State-of-the-Art Review. J Am Coll Cardiol. 2024;83:350-70.
5. Sarto P, Zorzi A, Merlo L, Vessella T, Pegoraro C, Giorgiano F, et al. Value of screening for the risk of sudden cardiac death in young competitive athletes. Eur Heart J. 2023;44:1084-92.
6. Risgaard B, Tfelt-Hansen J, Winkel BG. Sports-related sudden cardiac death: How to prove an effect of preparticipation screening? Heart Rhythm. 2016;13:1560-2.
7. Maron BJ, Friedman RA, Kligfield P, Levine BD, Viskin S, Chaitman BR, et al. Assessment of the 12-lead electrocardiogram as a screening test for detection of cardiovascular disease in healthy general populations of young people (12-25 years of age): a scientific statement from the American Heart Association and the American College of Cardiology. J Am Coll Cardiol. 2014;64:1479-514.
8. Drezner JA, Sharma S, Baggish A, Papadakis M, Wilson MG, Prutkin JM, et al. International criteria for electrocardiographic interpretation in athletes: Consensus statement. Br J Sports Med. 2017;51:704-31.
9. Schmehil C, Malhotra D, Patel DR. Cardiac screening to prevent sudden death in young athletes. Transl Pediatr. 2017;6:199-206.
10. Siontis KC, Liu K, Bos JM, Attia ZI, Cohen-Shelly M, Arruda-Olson AM, et al. Detection of hypertrophic cardiomyopathy by an artificial intelligence electrocardiogram in children and adolescents. Int J Cardiol. 2021;340:42-7.
11. Harmon KG, Zigman M, Drezner JA. The effectiveness of screening history, physical exam, and ECG to detect potentially lethal cardiac disorders in athletes: a systematic review/meta-analysis. J Electrocardiol. 2015;48:329-38.
12. Halkin A, Steinvil A, Rosso R, Adler A, Rozovski U, Viskin S. Preventing sudden death of athletes with electrocardiographic screening: what is the absolute benefit and how much will it cost? J Am Coll Cardiol. 2012;60:2271-6.
13. Han J, Lalario A, Merro E, Sinagra G, Sharma S, Papadakis M, et al. Sudden cardiac death in athletes: facts and fallacies. J Cardiovasc Dev Dis. 2023;10(2):68.
14. Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, et al. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2019;140:e596-e646.
15. Khan SS, Coresh J, Pencina MJ, Ndumele CE, Rangaswami J, Chow SL, et al. Novel prediction equations for absolute risk assessment of total cardiovascular disease incorporating cardiovascular-kidney-metabolic health: a scientific statement from the American Heart Association. Circulation. 2023;148:1982-2004.
16. Mora S, Redberg RF, Sharrett AR, Blumenthal RS. Enhanced risk assessment in asymptomatic individuals with exercise testing and Framingham risk scores. Circulation. 2005;112:1566-72.
17. Gallo-Villegas JA, Calderon JC. Epidemiological, mechanistic, and practical bases for assessment of cardiorespiratory fitness and muscle status in adults in healthcare settings. Eur J Appl Physiol. 2023;123:945-64.
18. Saraste A, Knuuti J. ESC 2019 guidelines for the diagnosis and management of chronic coronary syndromes: Recommendations for cardiovascular imaging. Herz. 2020;45:409-20.
19. Gallo-Villegas J, Aristizábal-Ocampo D. La prueba de esfuerzo electrocardiográfica: utilidad en el diagnóstico y pronóstico de la enfermedad coronaria. Med Lab. 2015;21:63-84.
20. Vessella T, Zorzi A, Merlo L, Pegoraro C, Giorgiano F, Trevisanato M, et al. The Italian preparticipation evaluation programme: diagnostic yield, rate of disqualification and cost analysis. Br J Sports Med. 2020;54:231-7.
21. Balady GJ, Arena R, Sietsema K, Myers J, Coke L, Fletcher GF, et al. Clinician's Guide to cardiopulmonary exercise testing in adults: a scientific statement from the American Heart Association. Circulation. 2010;122:191-225.
22. Drezner JA, Fudge J, Harmon KG, Berger S, Campbell RM, Vetter VL. Warning symptoms and family history in children and young adults with sudden cardiac arrest. J Am Board Fam Med. 2012;25:408-15.
23. Schwellnus M, Swanevelder S, Derman W, Borjesson M, Schwabe K, Jordaan E. Prerace medical screening and education reduce medical encounters in distance road races: SAFER VIII study in 153 208 race starters. Br J Sports Med. 2019;53:634-9.