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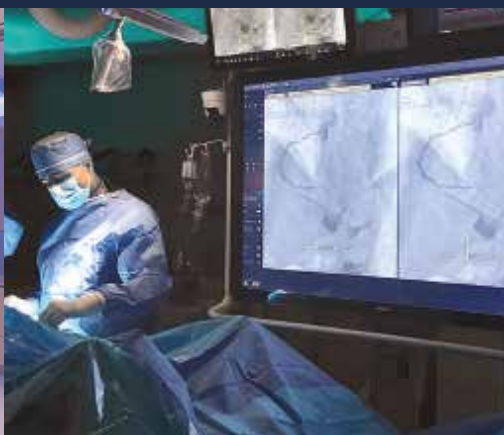
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Cardiac MRI in Argentina: strengths, weaknesses, and the road ahead.

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ABSTRACT

The IMAGGEN AR-CMR Registry provides a comprehensive and representative overview of cardiac magnetic resonance (CMR) utilization in Argentina. With more than 1,000 studies performed between 2018 and 2022 across 15 centers in 9 provinces, it reflects both strengths and weaknesses of national practice. Non-ischemic cardiomyopathy was the leading indication (55.7%), consistent with international registries. However, stress CMR, a Class IB recommendation in clinical practice guidelines for ischemia assessment, was performed in only 0.6% of cases, compared with 16–30% reported in international registries. Similarly, limited use (~6%) of tissue characterization techniques (T1/T2 mapping) was observed. Beyond these differences, the registry confirms the high diagnostic quality, excellent safety profile, and increasing adoption of macrocyclic gadolinium agents. These findings validate the capacity of our centers while underscoring the need to expand the use of stress CMR and advanced sequences such as T1 and T2 mapping to achieve international standards.

In the last decade, cardiac magnetic resonance imaging (MRI) has consolidated as the model technique in multiple clinical scenarios.¹ Its capacity to assess ventricular function, perfusion, tissue and anatomy in a single test yields advantages in comparison with traditional methods like echocardiography or nuclear medicine. However, in Argentina, little is known about the degree of protocol standardization and the level of integration of this tool in clinical practice.

In this scenario, the publication of the IMAGGEN AR-CMR Registry offers a comprehensive view on the use of cardiac MRI in the country. This is the second multicenter registry of this magnitude after the RENAREC, and the first to report on the use of sequences such as T1/T2 mapping and the type of gadolinium used.² Although both registries included a considerable number of provinces, it is important to highlight that distribution was not homogeneous: in the IMAGGEN AR-CMR, 70% of studies were made in the province of Santa Fe; while in the RENAREC, 70% of centers were in the province of Buenos Aires, introducing a bias in representation.

Among the most relevant findings, the main indication of cardiac MRI stands out: nonischemic heart disease, in agreement with international registries, although with differences deserving attention: cardiac MRI of stress, widely recommended for the evaluation of ischemia, is still markedly underused in Argentina.^{3,4,5,6,7,8,9}

The extent of this gap is reflected when comparing international registries. The EuroCMR included more than

27,000 patients in 15 European countries, in which 34% of indications corresponded to risk stratification for CAD, with 30% of stress cardiac MRI.¹⁰ Likewise, in the Global CMR Registry (GCMR), with more than 11,000 patients from 6 continents, stress cardiac MRI represented 16% of indications and showed a significant prognostic impact.¹¹ The SCMR Registry, with more than 150,000 studies, confirmed this tendency (30% of stress cardiac MRI).¹² In contrast, in Argentina, the use of stress cardiac MRI was just 0.6%, reflecting a markedly different reality.

The causes for such discrepancies are probably multifactorial. On the other hand, availability and experience in stress protocols are still limited in comparison with Europe and North America. On the other hand, clinical practice in the country still prioritizes traditional methods such as stress echocardiography or nuclear medicine, partly due to costs, even though stress cardiac MRI has the same level of recommendation (IB) and comparative studies have shown its diagnostic superiority versus SPECT in detecting CAD.^{3,13}

Although in Europe and North America, cardiac MRI has consolidated as a first line tool for the evaluation of ischemia and feasibility, in Argentina there is still uncertainty on its capacity for replacing traditional methods.⁹ Beyond cardiac MRI offering a higher diagnostic accuracy, its implementation should be evaluated according to availability and cost effectiveness, and more evidence is required, showing a real benefit in clinical results for patients.

Another relevant finding of the registry is the pattern of use of sequences. In agreement with international registries and the SCMR recommendations, a wide use of cine (91.7%) and late enhancement (85.6%) sequences was observed.¹⁴ Nonetheless, in spite of nonischemic cardiomyopathy being the most frequent indication (55.7%), the use of tissue characterization sequences, such as T1 and T2 mapping, was surprisingly low (5.8% and 5.6%, respectively). This information is in contrast with what was reported in the GCMR Registry, where nonischemic cardiomyopathy represented 21% of indications and the use of T1 mapping reached 26%, in agreement with the current recommendations.^{8,14}

Beyond these differences, the IMAGEN AR-RMC registry confirms the high diagnostic quality, the excellent safety profile and the tendency to using macrocyclic gadolinium agents, in line with international recommendations.¹⁴ These results validate the technical capacity of the participating centers and locate Argentinian cardiac MRI in a converging trajectory with global standards, although with quite a way to go yet. Overcoming structural obstacles will be essential for cardiac MRI to hold the place that has already reached in other international scenarios, encouraging a greater use of stress cardiac MRI and advanced sequences, such as T1 and T2 mapping.

Just as Everett Rogers described in "Diffusion of innovations", adopting a new technology follows a predictable course, that goes from innovators and early adopters, to an early majority, late majority, and finally, laggards.¹⁵ While in Europe and North America, cardiac MRI seems to have reached the "early majority", consolidating as part of routine clinical practice, Argentina is still in an intermediate stage, with the potential to advance to a wider use if access obstacles are overcome, hindrances that limit its full integration in clinical practice.

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Editorial

Editorials express the opinions of their author(s), not necessarily those of the Editorial Committee of the Revista FAC.

When distance is the enemy: barriers in the treatment of acute myocardial infarction

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ABSTRACT

Atrial fibrillation (AF) is the most prevalent arrhythmia worldwide, associated with a significant increase in major cerebrovascular events and morbidity and mortality. In Latin America, the prevalence of hypertension, obesity, alcohol consumption, and smoking is high, contributing to an increased risk of AF and its associated complications.

The HARMS2-AF score emerges as a simple, clinically applicable model with high predictive performance.

This approach, focused on modifiable factors, reaffirms that AF is not an isolated disease, but rather a reflection of lifestyle choices and poorly controlled comorbidities. This is especially valuable for Latin America, where these risk factors are prevalent and treatable in primary care.

INTRODUCTION

Atrial fibrillation (AF) is the most prevalent arrhythmia at world level, associated with a significant increase in major cerebrovascular events and morbimortality. In Latin America, the prevalence of hypertension, obesity, alcohol consumption and smoking is high, contributing to an increase in the risk of AF and its associated complications. This scenario places it as a problem of public health, transcending frontiers, and raises the need for risk stratification tools adapted to the local population, which would allow an early identification of individuals in risk and the implementation of efficient preventive interventions in primary care. So, this timely study, which evaluated the usefulness of the HARMS2-AF score for a 10-year follow-up, is a valuable contribution for medicine in Latin America. Its main contribution lies in that it integrates modifiable risk factors, positioning prevention as the focus of discussion.

THE HARMS2-AF STUDY

The HARMS2-AF score emerges as a simple model, clinically applicable, and with a high predictive performance (AUC 0.81). Unlike other scores (CHA2DS2-VASc, Framingham, Charge-AF), it grants weight to directly modifiable causes: hypertension, obesity, smoking, alcohol and sleep apnea. This shifts the focus from passive prevention to active intervention, being particularly valuable in primary prevention.

The study analyzed a cohort of 2482 individuals from northwest Colombia for 10 years. Adult patients, with no previous diagnosis of AF, associated to a program of cardiovascular prevention, were monitored and AF incidence was estimated.

The results of the cohort are conclusive:

1. Hypertension emerged as the strongest predictor for AF (HR 4.0).
2. Obesity and sleep apnea showed an independent association, reinforcing the relevance of metabolic syndrome and respiratory disorders of sleep for atrial remodeling.
3. A high consumption of alcohol behaved in a dose-dependent manner, with a higher risk in those ingesting >15 drinks/week.
4. Therapeutic adherence modulated risk, highlighting the significance of early education.

This approach, focused on modifiable factors, reaffirms that AF is not an isolated disease, but a reflection of lifestyles and poorly controlled comorbidities. This is particularly valuable in Latin America, where these risk factors are prevalent and treatable from primary care.

STRENGTHS OF THE STUDY

The HARMS2-AF score has displayed a superior predictive performance in comparison with traditional tools, such as Framingham-AF and CHARGE-AF, where it presented a comparable capacity.

In clinical practice, particularly in Latin America, many patients present to the medical office in advanced stages of AF, when complications have already occurred or there are significant echocardiographic alterations. This scenario underscores the need to implement early prevention strategies; interventions addressed to control modifiable risk factors, which may have a substantial impact on AF incidence decrease.

This study contributes:

1. Regional validation: it provides evidence in a Latin American population, filling a void in knowledge, in a region with an increasing incidence of cardiovascular diseases and AF.

2. Prolonged follow-up: 10 years of monitoring provide statistical strength and allow understanding the natural progression of AF.

3. Clinical applicability: the model is feasible and uses simple, accessible and clinically validated tools, not requiring expensive or specialized tests. This facilitates guiding and educating patients, particularly in populations with obstacles for accessing the health care system.

4. Elevated discrimination capacity: an AUC of 0.81 places HARMS2-AF in a competitive level with the main international scores.

LIMITATIONS AND EXPECTATIONS

In spite of its robustness, the study presents limitations to consider:

1. Its retrospective nature includes self-reporting risks. Many variables were estimated by questionnaires, with a risk of under or overestimation.

2. Exclusion of structural or electrical markers: no measures like atrial dilatation, or electrocardiographic ones (interatrial block) were incorporated, which could lead to enriching the prediction.

3. Underregistration of asymptomatic AF: as it is based on registries and reports, there could have been an underestimation of the real incidence of AF.

4. Limited generalization: although the findings are valuable for Latin America, they require external validation in populations with different ethnical and socioeconomic compositions.

CLINICAL AND PUBLIC HEALTH IMPLICATIONS

This study offers the chance of using simple and inexpensive tools to intervene early in risk populations, which may not only reduce the incidence of AF, but also the economic burden associated to its complications.

Its simplicity in its application and execution turns this tool into an ally for family doctors and primary care, which may work as a bridge between cardiology and public health, with the integration of community programs of control of hypertension, obesity and alcohol consumption.

FUTURE EXPECTATIONS

Multicenter, external validation is necessary to confirm its applicability in different realities of Latin America. Also, the integration of echocardiographic and electrocardiographic parameters could supplement prediction.

Cost-effective studies would be beneficial to evaluate whether the implementation of preventive measures in a large scale, like the HARMS2-AF, reduces major events and hospitalizations in relation to the costs of prevention programs.

CONCLUSION

The HARMS2-AF is a useful and valuable tool, particularly because it is easily available and applied. Its implementation in primary care can optimize the early identification of individuals in risk and facilitate personalized preventive interventions, adapted to the reality of Latin American countries.

Nevertheless, to reach a higher level of accuracy, we consider it essential for future versions of the model to integrate key cardiac structural variables, like left atrial dilatation. Likewise, it is necessary to enhance the study base and validate its use in different populations to facilitate its standardization.

The incorporation of this score into clinical practice may significantly contribute to the support of decision-making and timely interventions. In a context where AF presents an increasing prevalence and is still an important cause of cardiovascular morbidity and mortality, reinforcing prevention strategies can be a priority in all health levels. Its management is clear: AF is not unavoidable, but a condition whose emergence can be delayed or prevented by intensive control and prevention of risk factors.

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Review Article

Cardiogeriatrics: a 21st Century Perspective

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Cardiogeriatrics; frailty; aging; cardiovascular prevention; comprehensive geriatric assessment.

ABSTRACT

Cardiogeriatrics in the 21st century has become a central discipline in the face of accelerated aging in Latin America. This article reviews the historical background, demographic transition, and clinical challenges posed by multimorbidity, frailty, polypharmacy, and healthcare inequities. It examines the evidence gap due to the underrepresentation of older adults in clinical trials and highlights the importance of integrating biological age, functional status, and cognition into risk stratification. Expanded prevention strategies are emphasized—including adapted Life's Essential 8, vaccination, and social determinants of health—along with the partial reversibility of frailty through telerehabilitation and rehabilitation that include gerontology. Finally, the GOAL algorithm is presented as a practical framework for patient-centered decision making in older adults with cardiovascular disease. In cardiogeriatrics, the future is prevention.

HISTORICAL AMERICAN CONTEXT FOR THE 21ST CENTURY

The concept of Geriatric Cardiology has Egyptian roots, by the acknowledgement of the relationship of age with the heart; similarly, indigenous Latin American cultures (with the sonqo for the Incas, the yollotl for the Mexica and py'a in the Guaraní peoples) associated the heart with life, energy and the passing of time. Geriatric cardiology is defined as the adaptation of the principles of geriatrics to the practice with evidence from daily cardiology. Its modern development in America started at the mid-20th century, with studies like Framingham (1948), Baltimore (1958), Bogalusa (1972) and the Cardiovascular Health Study (1989), that defined the relationship between ageing, risk factors, frailty and cardiovascular outcomes in the elderly. In a parallel way, key institutions were created in the United States, such the National Institute on Aging (NIA). In that country, in 1970, the first English-language textbook on the field was written by Dr. Raymond Harris, and in 1985, the Council on Geriatric Cardiology was created, with its own journal, directed by Nanette Wenger, although modern cardiogeriatrics gained momentum with the Editorial by William W. Parmley in 1997 in JACC.¹ Finally, at the begin-

ning of the 21st century, the discipline was integrated to the American College of Cardiology (ACC), consolidating in 2010 with the Geriatric Cardiology Section Leadership Council.¹

In Latin America, in a parallel way with college academic support, Brazil and Mexico were pioneers. Brazil had taken its first steps in 1982, when Prof. Luis Gastão Costa Carvalho do Serro Azul created the Clinical Unit of Cardiogeriatrics of the InCor, and in the 1990s, the Brazilian Society of Cardiology formally acknowledged the field, first as a study group (GEBRAC), and since 2005, as a department (DECAGE), besides starting specific conferences.²

In Mexico, the Instituto Nacional de Cardiología Ignacio Chávez (founded in 1944) had shown interest, at the end of the 20th century, along with the Mexican Society of Cardiology (SMC), founded in 1935, and the Inter-American Society of Cardiology (IASC) founded in 1944, both the result of the work by the master Chávez; however, it was formally at the beginning of the 21st century that Dr. Luis Alberto Lasses y Ojeda created the first Service of Geriatric Cardiology, and the course of High Specialty of the UNAM, integrated to the institute, besides formal sections within the society.³

Since 2017, several Latin American societies have created formal sections, such as the Colombian of Cardiology, the Argentine one (the Argentine Federation of Cardiology and the Argentine Society of Cardiology) and the Interamerican Society of Cardiology, while others (Chile, Uruguay, Ecuador, etc.) included sessions, symposia or consensuses in their academic meetings, generally jointly with societies of geriatrics and gerontology in the region.

In brief, the last 10 years have been witnesses to the emergence of cardiogeriatrics in Latin America: groups were formally created, alliances were created, guides were disseminated, books were written and specific conferences were carried out. This regional effort of the continent aligns with the international tendency of preparing cardiologists and geriatricians for a differentiated care for older patients, and there is a call to build today, as a region, the geriatric cardiology of the 21st century, where the future of cardiogeriatrics is prevention.

DEMOGRAPHIC TRANSITION AND CARDIOVASCULAR LOAD IN THE ELDERLY

Latin America is going through an accelerated demographic transition: ~15% of the population already exceeds 60 years, and by 2050, one in every four Latin Americans will be a senior citizen; the subgroup ≥80 years will triple its size; with the subsequent increase in the demand for health care and pressure on sanitary systems.¹ This outlook turns cardiogeriatrics into a strategic axis, because cardiovascular diseases (CVD) concentrate a great load of disease and disability after the 70 years of age. Beyond mortality, there is a concern about functionality and autonomy: heart failure (HF), ischemic heart disease (IHD), atrial fibrillation and cerebrovascular CVD explain a substantial volume of lost disability-adjusted life years, with a strong social and financial repercussion.²

DEMYSTIFYING CARDIOGERIATRICS: MORE THAN "CARDIOLOGY FOR OLD PEOPLE"

The distinctive clinical feature of this population is multi-morbidity and therapeutic complexity: most senior citizens will combine several chronic conditions, polypharmacy (>5 drugs) and high biological heterogeneity. For this reason, cardiogeriatrics proposes a change in paradigm: to go from protocols focused on a single disease and chronological age, to health care plans focused on the individual with a biological age, prioritizing the results that matter to the patient (function, independence, quality of life), integrating a brief geriatric assessment into cardiovascular practice and preventing "iatrogenesis by omission" (not offering effective therapies due to ageism).² This practical integration requires, at least, a fast screening for frailty, falls, cognition and pharmacological load to decide when to apply the comprehensive geriatric assessment (CGA) in more detail and to adjust goals.

Frailty is a prognostic modulator. As a vulnerability syndrome increased by a lower physiological reserve, it is

associated with a greater risk of events, prolonged hospital stays and worse outcomes after interventions such as TAVI or heart surgery, regardless of chronological age. Prevalence is around ~7-12% in people older than 65 years of age, and it increases with age. Measuring it (for instance, Fried frailty phenotype, gait speed <0.8 m/sec or simple tools such as the FRAIL) enables anticipating complications and planning adjusted prehabilitation, nutrition and rehabilitation.³ It is important to highlight that frailty is not the same as terminality or disability: it could be partially reversible with multimodal interventions.³

Equity by sex and gender adds another layer of complexity. Older women, a demographic majority in advanced ages, are still underrepresented in studies, present different clinical profiles (e.g.: a higher rate of HF with preserved ejection fraction) and suffer more adverse pharmacological effects. Reducing these gaps entail improving their inclusion in evidence and personalizing doses/therapeutic choices, avoiding both overmedicating and undertreating.

In decision-making, two operative concepts guide practice: time to benefit (TTB) and strategic deprescribing (suspending therapies). TTB helps to align preventive interventions (e.g.: statins in primary prevention, blood pressure goals) with life expectancy and goals of the patient; its systematic use prevents treatments with unlikely benefits in the clinical horizon of very fragile senior citizens, and in turn, it supports early benefit therapies (e.g.: anticoagulation in AF). Deprescribing (planned, monitored and shared) reduces the load of medications, interactions and adverse events, and improves adherence, not giving up highly important drugs.^{2,4}

THE FUTURE OF CARDIOGERIATRICS IS PREVENTION

We should control risk factors since middle age, promote healthy ageing and, in elderly people, add vaccination, exercise, nutrition and rehabilitation focused on function. In summary, with a rapidly ageing population and high cardiovascular load, an efficient cardiogeriatrics in Latin America combines evidence-based medicine, geriatric reading of risk (frailty, cognition, function) and decisions guided by TTB, with the aim of extending life and preserving independence, from prevention.^{1,4}

In this line of prevention, we should conduct an active assessment with the practical approach of "2-minute screening", to identify early whether older patients require complete CGA and to prevent events (*Figure 1*).

EVIDENCE GAP AND WHAT WE DO KNOW

Randomized clinical trials (RCTs) are the strongest source to guide medical decisions, but the elderly are still underrepresented. A systematic review showed that 53% of studies explicitly dismissed patients older than 65 years, with just 12.3% of participants being ≥75 years, very far from the real profile of patients cared for in clinical practice.^{5,6} In ischemic heart disease, more than half of trials establis-

Box 1. Ejemplo de 'screening' cardiogeriatrico en 2 minutos



FIGURE 1.

Example of cardiogeriatric screening in 2 minutes. It includes gait speed, falls, FRAIL, Mini-Cog and drug count. If one is positive, specialized support should be requested to perform a comprehensive geriatric assessment.

hed maximum age limits (75-80 years), with a mean age of just 62.7 years.⁶ This bias is concerning, as cardiovascular disease is the main cause of morbidity and mortality in >65 years.

Even in iconic studies, such as the PARADIGM-HF (heart failure) and the SYNTAX (coronary artery disease), patients older than 75 years were barely represented ~20% and ~13% of the sample, respectively. However, post-hoc analyses suggest that the benefits observed also extend to older patients.⁶ In contrast, TAVI (Transcatheter aortic valve implantation) trials (e.g.: PARTNER) achieved a better inclusion, with an average age of ~81 years, although with a bias toward selected patients, without extreme comorbidities or advanced frailty.⁶

A counterintuitive finding is that, between 2006-2015, the rate of trials that exclude elderly people increased, in spite of the recommendations for a greater inclusion.⁶ There are multiple causes: biological heterogeneity, multimorbidity, polypharmacy, functional deterioration, a greater risk of adverse effects and limited life expectancy.

Furthermore, enrollment and retention are complex: elderly patients may leave out of fatigue or disease, compromising external validity.⁷

The result is clear: a good part of cardiovascular guidelines is supported on evidence generated in younger adults, then being applied incompletely or in a risky manner to older patients (Table 1).

In Latin America, the challenges are amplified due to inequality of access to advanced technologies, heterogeneity

in health care systems and a limited capacity to generate robust regional registries.⁷ Overcoming this gap entails encouraging pragmatic trials, designs based on our own registries and metrics relevant to older people, including functional outcomes and quality of life.

BIOLOGICAL AGE VS CHRONOLOGICAL AGE

Chronological age per se does not reflect the heterogeneity of ageing. In practice, patients of the same age may radically differ in physiological reserve and risk. Biological age is defined by the degree of accumulative changes at molecular, cellular and functional level; while the deviation between biological and chronological ages (AgeDev) has been proposed as a marker of accelerated or delayed ageing.⁸

In individuals with normal ageing, both ages coincide, but there are extremes: from premature ageing syndromes to hundred-year old individuals with delayed vascular ageing. With this aim, ageing biomarkers have been explored, which may be better than chronological age to predict morbimortality.⁸

Biomarkers are divided into three categories:

Molecular:

Telomere shortening, associated to cellular senescence and cardiovascular risk, although without clear causality.⁹

Epigenetic clocks (DNAMAge, PhenoAge, GrimAge), based on methylation patterns, that predict with remarkable accuracy outcomes like mortality and diseases related to age.⁸

Omics:

Transcriptomics and miRNA: they reflect the dynamic response of the genome to the environment, linked to ageing and CVD.¹⁰

Proteomics: linked to phenotypes of frailty and cognition, although yet in its initial stages.¹⁰

Inflammaging: characterized by high levels of CRP and IL-6, associated with higher mortality and CVD.^{8,9}

Physiological and functional: they include VO₂max, gait speed, hand grip strength, carotid intima-media thickness and coronary artery calcium.⁸

Digital (imaging): parameters such as BrainAge, retinal or facial age.

The BrainAge gap (difference between brain and chronological ages) correlates with an accelerated ageing, cognitive deterioration and risk of dementia and depression.¹¹

Between the combined tools, the Fragility Index (FI) stands out, which integrates accumulated deficits and predicts mortality, risk of falls and fractures, even being better than some epigenetic clocks in its prognostic capacity, but it includes disabilities.¹⁰

The evidence gap in senior citizens conditions the clinical applicability of a large part of current cardiology Table 2. In a parallel manner, the integration of biological age and cognition opens a new way to individualize attention. Incorporating practical biomarkers, frailty measures and

TABLE 1.

Recent evidence and representation gap of older adults in cardiovascular trials .

Area	Trial (year)	N / Mean age	Participation of older adults	Main findings
Heart failure with preserved EF	EMPEROR-Preserved (2021)	5988 / 72 years	≥75 years ~45%	Empagliflozin reduces CV death and hospitalization due to HF, with consistent benefits in ≥75 years. ⁶
Heart failure with preserved or reduced EF	DELIVER (2022)	6263 / 72 years	≥75 years with similar effects	Dapagliflozin decreases hospitalization due to CVDs and HF, regardless of age. ⁶
Coronary arteries stable with moderate ischemia	ISCHEMIA (2019; subanalysis in older patients)	5179 / 64 years	Subgroup ≥75	Invasive strategy not better to conservative one in death/MI; decisions should be individual, frailty. ⁶
ACS with no ST elevation in ≥70 years	POPular AGE (2020)	1002 / ≥70 years	100% ≥70	Clopidogrel reduces bleeding in comparison with ticagrelor/prasugrel, with no increase in ischemia. ⁶
AF in very old and frail patients	ELDERCARE-AF (2020)	984 / 86 years	Frail, eighty-year old people	Edoxaban 15 mg reduces thromboembolic events; greater bleeding but manageable, low weight. ⁶
TAVI in low risk (5-year follow-up)	PARTNER 3 (2023)	1000 / 73 years	A few ≥80	Within 5 years, TAVI ≈ SAVR in death/stroke/readmission; evidence in eighty-year old people still limited. ⁶
Anticoagulation post-TAVI with AF	ENVISAGE-TAVI AF (2021)	1426 / 82 years	Predominance of eighty-year old patients	Edoxaban not inferior in efficacy vs VKA; more gastrointestinal bleeding. ⁶
Post-AMI multimodal rehabilitation in older patients	NEJM Multidomain Rehabilitation (2025)	1500 / 80 years	100% ≥75	Multicomponent program reduced CV mortality and readmission after AMI in older adults. ¹⁷
Primary prevention in dyslipidemia	ESC/EAS Focused Update (2025, analysis in >75)	Based on large European registries	Subanalysis in older adults	Use of statins and lipid-lowering agents shows benefits, but direct evidence in ≥85 years and frail patients is still limited. ²¹

VKA: vitamin K antagonists; CV: cardiovascular; RCT: randomized controlled trial; EF: ejection fraction; HF: heart failure; AMI: acute myocardial infarction; MI: myocardial infarction; SAVR: surgical aortic valve replacement; ACS: acute coronary syndrome; TAVI: transcatheter aortic valve implantation. The gap persists, even with the partial inclusion of older adults; frail patients are those mostly absent.

functional outcomes will enable the design of interventions aligned with true risks and benefits expected in this population.

Thus, cardiogeriatrics in the 21st century should advance toward:

1. More inclusive and pragmatic trials.
2. Incorporation of accessible and validatable biomarkers.
3. Acknowledgement of frailty and biological age as modulators.
4. Clinical decisions that prioritize quality of life, independence and preferences of patients.

This change in paradigm is essential to construct an equitable and efficient cardiovascular medicine in population ageing in Latin America, besides local studies.

ENHANCED PREVENTION IN THE 21ST CENTURY

Enhanced prevention: from Life's Essential 8 to the 5Ms of geriatrics

Chronological age is still the main risk factor for chronic diseases, including cardiovascular ones. In 2022, the American Heart Association (AHA) updated the classical Life's Essential 7 to the Essential 8, adding sleep as a new pillar along with diet, physical activity, weight control, smoking,

diabetes, cholesterol and blood pressure. These determinants, essential over life, acquire a particular relevance in elderly people, where multimorbidity, frailty, sarcopenia and cognitive deterioration condition cardiovascular prevention.¹²

However, applying the Essential 8 to older adults requires adapting them to a geriatric framework. In this regard, the 5Ms of geriatrics (mind, mobility, medications, multi-complexity and what matters most) constitute a conceptual bridge. This integration allows preventive goals to not only reduce cardiovascular risk, but also preserve quality of life and functional independence, essential goals in modern cardiogeriatrics (Figure 2).¹²

VACCINATION AS CARDIOVASCULAR STRATEGY

Respiratory infections are a well-known trigger for cardiovascular events, for their impact on inflammation. Influenza, pneumococcal pneumonia, SARS-CoV-2, the respiratory syncytial virus (RSV) and recently herpes zoster have proven to be associated to a greater risk of infarction, stroke and heart failure. Recent studies estimate that up to 5% of hospital admissions by influenza in patients with heart failure are directly attributable to the infection.¹³

TABLE 2.

Chronological vs biological ageing: repercussions on cardiogeriatrics.

Dimension	Chronological	Biological	Measurement/ examples	Clinical relevance
Definition	Years since birth	Accumulated molecular, cellular and functional changes. ¹	—	It explains why two 80-year-old patients can present different risks. ¹
Variability	Scant	High (AgeDev: accelerated or delayed) ²	—	It requires personalization of goals and therapies. ⁶
Molecular biomarkers	—	Telomere shortening, epigenetic clocks (DNAmAge, PhenoAge, GrimAge). ¹²	qPCR, DNA panels	They predict mortality, even without consensus for routine use ¹²
Omics and inflammation	—	Transcriptomic/miARN, proteomic, “inflammaging” (CRP, IL-6) ^{3,4}	Molecular profiles	Related to frailty and CV events; still in research ^{3,4}
Physiological biomarkers	—	VO ₂ max, gait speed, hand grip strength, PWV, coronary artery calcium ¹²	Physical tests, CT	Accessible and prognostic; applicable in clinical practice ¹²
Digital biomarkers	—	BrainAge, retinal age, ECG-age ^{4,5}	MRI, PET, AI	BrainAge gap predicts cognitive deterioration and risk of dementia ⁵
Composite tools	—	Fragility index (FI) or multidimensional ^{1,3,4}	Frailty scores	They integrate biology and clinics; key in therapeutic decisions; they may confound with disability. ⁴
Clinical evidence	Based on age	Underrepresentation of ≥75 years and frail patients in CGA ^{6,7}	CGA reviews	It compromises external validity; it is urgent to include frail older patients in trials ^{6,7}

CV = cardiovascular; DNAmAge/PhenoAge/GrimAge = epigenetic clocks; miARN: microARN; PWV: pulse wave velocity; CT: computed tomography; MRI: magnetic resonance imaging; PET: positron emission tomography; FI: fragility index.

The population attributable risk of influenza over CAD has been estimated in 3.9%, and it has been documented that for every 5% increase in monthly activity of influenza, the rate of hospitalizations by heart failure increases by 24%.¹³ Likewise, infections such as RSV, adenovirus and pneumococcal pneumonia display similar effects. In this scenario, vaccination becomes an indirect but critical cardiovascular prevention tool, particularly in frail older adults, in whom infectious and cardiovascular outcomes are usually interlinked.

SOCIAL DETERMINANTS AND SANITARY LITERACY IN THE 21ST CENTURY

Social determinants of health (SDOH) constitute the framework where people are born, grow up and grow old. The WHO differentiates between structural determinants (socioeconomic conditions, gender, education) and intermediate determinants (housing, transportation, employment, support networks).

In Latin America, social inequality is translated to substantial gaps in access to prevention and cardiovascular treatment, with a particularly negative impact on older people in vulnerable situations.¹⁴

We can add to this, the need to strengthen sanitary and digital literacy. In a world with an increasing use of telemedicine and health devices, the senior citizens that have access to these tools show higher rates of adherence and early detection of risks. In a context of frailty, digital health

offers new opportunities for a hybrid follow-up (home and virtual), early identification of complications and promotion of physical activity.

**FIGURE 2.**

Integration of the Essential 8 of cardiovascular prevention with the 5Ms of geriatrics (mind, mobility, medications, multicomplexity and what matters most) as a conceptual bridge in cardiogeriatrics

**FIGURE 3.**

Prevention of delirium in 21st century cardiogeriatrics, a contribution made by the Task Group in Cardiogeriatrics of the Fundación Cardiovascular de Colombia

FRAILITY: MODIFIABLE AND CENTRAL IN 21ST CENTURY CARDIOLOGY

Frailty affects up to 60% of patients with CVD and it constitutes a stronger prognostic determinant than chronological age. Its predictors include: advanced age, multimorbidity, polypharmacy, recent hospitalizations, depression, falls, malnutrition and lack of social support. Evaluating it is crucial, not just to stratify risk, but also to guide preventive and therapeutic interventions.¹⁵

Different publications highlight that frailty should not be considered irreversible. On the contrary, strategies such as cardiac rehabilitation and programs combined with early geriatric rehabilitation have proven to improve strength, mobility and functional performance in older adults with CVDs, discharged after hospitalization.¹⁵ Initiating these programs early allows to partially reverse frailty and improve quality of life. An emergent area is AgeTech: reminders of medication, activity monitors and remote surveillance systems, which favor independence and deterioration detection. Evidence shows that senior citizens that use digital technologies participate more in exercise and prevention programs, key in the fight against frailty.¹⁶

PREVENTION OF PERIOPERATIVE DELIRIUM AND PREHABILITATION

In major cardiovascular interventions, perioperative delirium is a frequent complication, devastating in cardiogeriatrics, particularly in frail patients, so its prevention is imperative in the 21st century, to be implemented in coronary care units and other noncardiological units (Figure 3). Cardiogeriatric prehabilitation strategies, with an approach on multicomponent exercise, nutrition and cognitive stimulation, reduce its incidence (Figure 4).

The WHO recommends for older adults to perform at least 150 minutes of moderate aerobic physical activity or

75 minutes of vigorous activity per week, along with two sessions of strength, resistance and balance exercises. The implementation of personalized programs not only decreases disabilities, but also prepares senior citizens to better tolerate surgeries and hospitalizations.¹⁷

HOW TO MAKE DECISIONS IN CARDIOGERIATRICS

We propose the GOAL algorithm, a clear and shared pathway to provide care for older patients with heart diseases, aligning decisions with the values of patients, their multimorbidity and their biological age (not just chronological age) to maximize functionality, quality of life and neat clinical benefits.

- **G: Goals** (including longevity, function and cognitive independence)
- **O: Organ systems & Overload** (multimorbidity, renal function, cognitive state, polypharmacy).
- **A: Ageing and Ability** (biological age: frailty, performance, biomarkers).
- **L: Likelihood of Benefit and Harm** (real neat clinical benefits, TTB, load of treatment). Integration of shared decisions and deprescribing.

Goals of patients. The first step is to agree on explicit goals: realistic longevity, control of symptoms, preservation of independence and cognition. Decision-making focused on the priorities of patients reduces health care overload and improves results in multimorbidity, by focusing treatments on what matters most, and by dismissing low-performance interventions.^{18,19,20} Simple tools (Katz, Barthel, Lawton; Mini-Cog/MoCA) facilitate translating values into measurable plans (for instance, avoiding readmissions, although this implies deprescribing late-benefit drugs).

Organ systems & Overload (multimorbidity and therapeutic load). Most course with combinations of HTN,

Algoritmo GOAL en Adultos Mayores Cardiopatas



FIGURE 4. GOAL algorithm to know how to act in cardiogeriatrics, based on goals, treatment options, comprehensive assessment and life plans

T2DM, CKD, COPD, depression and cognitive deterioration, with polypharmacy and risk 3-5 times greater of adverse effects. The ESC 2024 Guidelines for chronic coronary syndromes underscore personalizing goals and therapies in the elderly, weighing comorbidities, renal function and frailty.²¹

In the practice, a benefit/risk balance requires: adjustment of dose per estimated GFR (anticoagulation, diuretics), systematic screening of interactions, and planned deprescribing of drugs with no significant benefit for this life horizon (e.g.: aspirin), with reevaluation after each discharge or clinical change (Table 3).^{19,21}

Ageing & Ability (biological age and functional capacity). Therapeutic decisions are nuanced: in severe frailty, control of symptoms and deprescribing are prioritized; in robust older patients, modifier therapies are maintained when they offer concrete gains.

Likelihood of Benefit & Harm (time to benefit [TTB] and treatment load). The real neat clinical benefit should be estimated for each intervention, contrasting TTB with life expectancy and with diet load (monitoring, visits, adverse effects). In stable chronic patients, invasive revascularization is rarely better than optimized pharmacological therapy in hard outcomes (except for severe ischemia or acute syndromes) and its indication in frail patients should

be exceptional and through consensus.²¹ A shared decision (materials, structured conversation) improves adherence and aligns therapies with preferences.²⁰

KEY QUESTIONS

Does the treatment provide a real neat benefit in this patient?

What is the expected TTB (time to benefit) and is it compatible with life expectancy?

Does the load of treatment (adverse effects, controls, impact on quality of life) exceed the benefits?

Other 21st century challenges in cardiogeriatrics are technologies with sense, such as telemonitoring, home cardiac rehabilitation and mHealth, which can decrease readmissions and sustain functionality by allowing an early detection of decompensations, a timely adjustment of drugs and continuous education. The evidence summarized in recent meta-analyses shows significant reductions in admissions due to HF and by all causes, with improvements in functional capacity similar to in-person programs, if patient-carer training is guaranteed, integration with the team and data protection.²² The AgeTech (smart pillboxes, environmental sensors) adds safety at home and favors self-care in frailty scenarios.

TABLE 3. Models of transitional care in older adults with heart diseases^{19,20,22}

Strategy	Impact on readmissions	Impact on patients	Impact on carers
Home visits	↓ readmissions within 30 days	+ adherence, satisfaction	+ safety and support
Case managers	↓ readmissions and costs	+ continuity of care	+ coordination and support
Tele-rehabilitation	Equivalent to rehabilitation in person	+ functional capacity	+ active participation
Multidisciplinary teams	↓ mortality and readmissions	+ comprehensive approach	+ reduction in overload
Education of carers	↓ visits to the ER	+ self-efficacy of patients	+ less emotional overload

Note: adapted from evidence on transitional models in older adults with CVDs.

TABLE 4.
Checklist of Transition of Care in Older Adults with Heart Diseases

Área	Verification items (□)
1. Early contact	☐ Phone call within the first 48 hours after discharge. ☐ Schedule early home visit (first 7 days). ☐ Confirmation of control visit with cardiogeriatrics / cardiology / geriatrics / others.
2. Drug review	☐ Verify updated list of medications. ☐ Identify drugs without benefits on survival for possible deprescribing. ☐ Confirm adherence and understanding by patient / carer. ☐ Coordination with clinical pharmacy for polypharmacy adjustment.
3. Patient and carer education	☐ Explain diagnosis and treatment plan with clear language. ☐ Train in administration of medications. ☐ Teach vital signs monitoring (weight, pressure, heart rate). ☐ Deliver written plan for home management.
4. Review of needs for infrastructure at home	☐ Evaluate home accessibility (stairs, handrails, safe bathroom). ☐ Verify appropriate bed availability and room for medical devices. ☐ Necessary adjustments for mobility and safety.
5. Basic goods and equipment	☐ Sphygmomanometer and scales available at home. ☐ Home oxygen when indicated. ☐ Goods for glycemia control (when applicable). ☐ Basic first aid material (in the case of wounds).
6. Identification of warning signs	☐ Progressive respiratory difficulties. ☐ Sudden weight increase (>2 kg within 3 days). ☐ Limb or abdominal edema. ☐ Persistent chest pain. ☐ Dizziness, syncope or confusion. ☐ Severe hypotension or hypertension.
7. Coordination and continuity of care	☐ Communication with primary care. ☐ Reference to cardiac rehabilitation programs or tele-rehabilitation. ☐ Clear information about how to contact the health care team in case of emergency. ☐ Schedule periodical phone follow-up.

However, preventing the fragmentation of cardiogeriatric care and fighting it with transitional models that work and a checklist may work (*Table 4*). Post-discharge home visits, case management led by nurses/social workers, tele-rehabilitation and multidisciplinary teams (cardiology-geriatrics-pharmacy-physiotherapy-psychology) reduce readmissions and costs, and empower both patients and carers, the operative core of the GOAL.

An efficient 21st century cardiogeriatrics requires prevention, measurement of frailty with no disability, focusing on the priorities of patients, and a practice guided by TTB and neat benefits, supported by useful technology. GOAL offers the structure for wise and humane decision-making, based on evidence in a population that will continue to grow.^{18,22}

Dedicated to the founders of the Latin American geriatric cardiology: Prof. Dr. Luis Gastão Costa Carvalho do Serro Azul and Prof. Dr. Luis Alberto Lasses y Ojeda.

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Review Article

Excessive bleeding in cardiovascular surgery. Usefulness of viscoelastic testing

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ABSTRACT

Excessive bleeding due to coagulation disorders is a well-known complication in cardiovascular surgery. Traditionally, standard coagulation tests have been used for their management, and more recently, viscoelastic testing has gained ground. This is performed using a different methodology and provide information on clot initiation, firmness, and lysis. Viscoelastic testing can diagnose coagulation factor deficiencies, the presence of heparin and protamine, fibrinogen, fibrin or Factor XIII deficiencies, platelet deficiency, and hyperfibrinolysis. The correlation between viscoelastic testing and standard coagulation tests is strong only in a few assays, and they have limitations in detecting the absence of general preconditions for coagulation, platelet aggregation deficiency, von Willebrand factor deficiency, the effect of fractionated heparin, the effect of direct factor Xa inhibitors and low and moderate intensity local or systemic fibrinolysis. To facilitate the treatment of patients with excessive bleeding, algorithms guided by viscoelastic testing have been designed.

INTRODUCTION

1. Introduction

Excessive or severe bleeding is a known complication in cardiothoracic surgery (CTS) that occurs in up to 10% of patients. When present, it increases adjusted mortality in up to 4 times.¹

In spite of some attempts, there is no universally used definition for excessive or severe bleeding in CTS. It could be useful to consider this diagnosis when chest drain output is:

- a. More than 500 ml within 1 hour, with no signs of reducing in the following hour;
- b. More than 300 ml/h during the first 3 hours, with no sign of reducing in the following hour;
- c. More than 200 ml/h for more than 3 hours, with no signs of reducing in the following hour;
- d. More or equal to 1200 ml within the first 12 hours after the surgery.

Another definition that could be valid is the one categorizing bleeding as excessive when drain output exceeds 2 ml/kg/h. Recorded visible excessive bleedings are around 8 ml/kg/h.

When faced with lower volumes of bleeding, but with moderate to severe mediastinal widening in chest X-ray, we should consider that part of the bleeding has remained in

the chest and a diagnosis of excessive bleeding should be contemplated. We should also take into account a diagnosis of excessive bleeding when treatment has been administered for it, even though the previously mentioned values were not reached.

The possible causes for bleeding immediately after cardiothoracic surgery are:²

1. Surgical
2. Coagulopathies
 - 2.1. Hyperfibrinolysis
 - 2.2. Residual heparinemia or heparin rebound
 - 2.3. Platelet dysfunction
 - 2.4. Thrombocytopenia
 - 2.5. Deficiency coagulopathy (hemodilution, insufficient replacement or consumption)
 - 2.6. Excess protamine
 - 2.7. Von Willebrand factor deficiency
 - 2.8. A combination of the above items
 - 2.9. Disseminated intravascular coagulation
3. Mixed (surgical plus coagulopathy).

In the case of bleeding, it is important to diagnose the possible presence of coagulopathy and to characterize it to be able to apply a treatment specifically addressed for it,

as soon as possible. A non-directed therapy for excessive bleeding with blood products, due to the absence of identification of the culprit coagulopathy entails an unnecessary transfusion and it exposes patients to risks such as infections, lung injuries (TRALI), increase in total body water and immunomodulation.^{3,4} All of the above do not include red blood cells replenishment, when considered necessary. Besides clinical history and signs, there are different auxiliary tests by which a diagnosis of coagulopathy can be reached. Traditionally, standard coagulation tests have been used, and more recently, viscoelastic testing (VET).

The benefits described for VET are a fast and full evaluation of coagulation, the identification of specific coagulopathies that are not always detected by standard testing, being useful as guides for the administration of blood products that may reduce excessive transfusion, postoperative monitoring, and a reduction in postoperative complications⁵

For more than two years, VETs have been used in this institution, so it seems timely to carry out an outline focused on their use.

2. TECHNIQUE AND DEVICES TO CARRY OUT VETS

Coagulation viscoelastic testing is based on placing citrated whole blood on a cup with a central pin within it. The cup or the pin (according to the manufacturer) oscillate, while the other element remains fixed. Resistance to movement, as blood coagulates, is measured, yielding the results. Different reagents and chemical products (platelet function inhibitors, antifibrinolytic agents, etc.) are added to the blood in the cup to assess the strength of the clot by different methods.

In *Table 1*, the best known devices and most used assays made by each device are provided.

The ClotPro[®] device, from the Haemonetics[®] company, also performs other analysis such as: RW-test: a test for di-

rect anticoagulation (e.g.: rivaroxaban); ECA-test: a test for direct thrombin inhibitors; and TPA-test that detects anti-fibrinolytic treatments, activating fibrinolysis. The same company has TEG5000[®] and TEG6s[®] devices, which carry out similar assays, and the TEG PlateletMapping[®] assay, which analyzes platelet function.

The Werfer[®] company also produces the ROTEM Sigma device[®] that includes the EXTEM, INTEM, FIBTEM, AP-TEM and HEPTM assays. It also has the ROTEM Platelet[®] device, which has two additional channels to evaluate platelet function through impedance.

3. TYPICAL GRAPH, MAIN PARAMETERS AND NORMAL VALUES

The typical graph generated in viscoelastic testing can be seen in *Fig 1*.

Main parameters and normal values:

The main parameters for VETs can be classified according to the coagulation process characteristics on which they provide information.^{6,7}

I. Clot onset:

- Coagulation time (Werferen) or R time (Haemonetics) (CT). It is the time elapsed from the addition of the reagent to the sample and a width of 2 mm in the produced signal by the onset of clot formation. Its prolongation occurs due to deficit in coagulation factors and by the presence of anticoagulation agents such as heparin, depending on the assay used.
- Clot formation time (CFT) (Werferen) or amplitude time (K) (Haemonetics). It is the time elapsed between CT and a 20 mm amplitude in the signal produced by the clot growth.

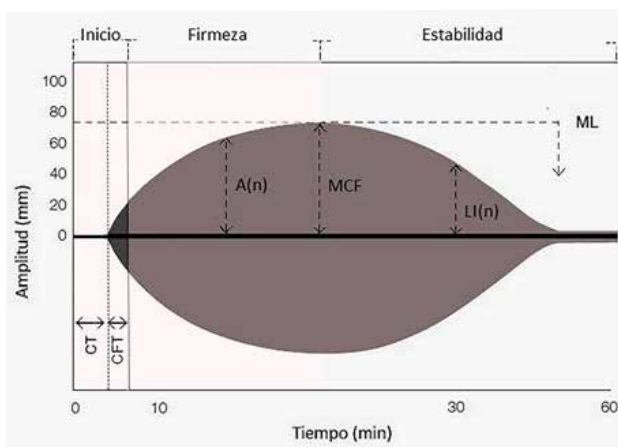


FIGURE 1.

Typical graph generated in a viscoelastic coagulation test
CT: coagulation time (Werferen) or R-time (Haemonetics); CFT: clot formation time (Werferen) or K-time (Haemonetics); A(n): amplitude in n min of CT (e.g.: A5); MCF: maximum clot firmness (Werferen) or maximum amplitude (Haemonetics); LI(n): lysis index in n min of CT (e.g.: LI30); ML: maximum lysis.

TABLE 1.

Viscoelastic coagulation tests. Most disseminated and used devices and assays.

			Purpose
Company	Werferen [®]	Haemonetics [®]	
Model	ROTEM [®]	ClotPro [®] TEG [®]	
Assay	EXTEM	EX-test	It examines the extrinsic pathway of coagulation
	INTEM	IN-test	It analyzes the intrinsic pathway of coagulation
	FIBTEM	FIB-test	It studies fibrinogen and fibrin, blocking platelet contribution
	HEPTM	HI-test	It investigates the intrinsic pathway of coagulation adding a heparin inhibitor
	APTEM	AP-test	It detects hyperfibrinolysis by the addition of an antifibrinolytic agent

TABLE 2.

Normal values of the main parameters of viscoelastic coagulation tests for hypocoagulable conditions.

	EXTEM	INTEM	HEPTEM	FIBTEM	EX-Test	IN-Test	HI-Test	FIB-Test
CT (s)	<80	<240	<240	<600	<65	<185	<185	
A5 (mm)	>35	>30	>30	>8	>39	>32		>6
A10 (mm)	>40	>40	>40	>8	>47	>41		>7
MCF (mm)	>50	>50	>50	>9	>50	>50		>9
LI 30(%)	>85	>85	>85	>85				
ML (%)	<15*	<15*	<15*	<15*				

CT: coagulation time or R-time; A5: amplitude in 5 min of CT; A10: amplitude in 10 min of CT; MCF: maximum clot firmness or maximum amplitude; LI30: lysis index in 30 min of CT; ML: maximum lysis. * reading in 60 min.

II. Clot strength:

- Maximum clot firmness (Werfen) or maximum amplitude (Haemonetics) (MCF). It reports on the input by fibrinogen, fibrin and platelets to clot firmness.
- Amplitude (A5, A10) (amplitude at 5 or 10 minutes of CT or R-time). It reports on the input of fibrinogen, fibrin and platelets to clot firmness and it is used to predict MCF in a shorter time.

III. Clot stability and lysis:

- Lysis index (at n minutes of CT or R-time; for instance, LI30) (LI). It represents the remaining firmness percentage of the clot in relation to MCF. It reports on fibrinolysis or severe Factor XIII deficiency.
- Maximum lysis (ML). It reports on fibrinolysis or severe Factor XIII deficiency.

In [Table 2](#), the normal values of the main VET parameters are shown, to be used in hypocoagulable conditions.^{8,9,10}

4. VET DEVIATIONS FACED WITH BLEEDING-INDUCING CONDITIONS

VETs can be used to diagnose coagulation factors deficiency, presence of heparin and protamine, fibrinogen, fibrin or Factor XIII deficiency, platelet deficiency and hyper-

fibrinolysis.⁶ The deviations that may occur in VETs in these scenarios can be seen in [Table 3](#).

A recent study including 759 patients showed a significant reduction in the use of blood products, infections, intensive care unit stay times and total hospital stay times, and costs using VETs in heart surgery.⁵

5. VET LIMITATIONS

Although VETs may be used to diagnose many coagulation anomalies, not all can be detected by this method. Some alterations, in which VETs are not useful, are: 1) failure in general coagulation preconditions (hypothermia, acidosis, hypocalcemia and anemia); 2) platelet aggregation deficiency (there are special devices for this; e.g.: ROTEM Platelet® or TEG Platelet Mapping®), 3) Von Willebrand factor deficiency; 4) fractionated heparin effect; 5) effect of direct anticoagulants anti-Factor Xa or anti-Factor IIa; 6) local or systemic fibrinolysis of low and moderate intensity.

6. RELATIONSHIP BETWEEN THE DIFFERENT DEVICES AND STANDARD COAGULATION TESTS

Some authors have studied the relationship between the VET results when they are performed with the two most

TABLE 3.

Viscoelastic coagulation testing deviations in the case of conditions producing bleeding.

Prolonged CT	
	Intrinsic pathway factors deficiency
In INTEM or IN-test	Heparin excess (if associated to normal HEPTEM or HI-test)
	Protamine excess (if associated to prolonged HEPTEM or HI-test)
In EXTEM or EX-test	Extrinsic pathway factors deficiency
In FIBTEM or FIB-test	Hyperfibrinolysis
In HEPTEM or HI-test	Intrinsic pathway factors deficiency
	Protamine excess
Decreased A5, A10 and MCF:	
	Fibrinogen/fibrin deficiency (if associated to decreased FIBTEM or Fib-test)
In EXTEM or EX-test	Platelet deficiency (if associated to normal FIBTEM or Fib-test)
	Hyperfibrinolysis
In FIBTEM or Fib-test	Fibrinogen/fibrin deficiency (if associated to decreased EXTEM or EX-test)
Decreased LI and increased ML	
In EXTEM or EX-test	Hyperfibrinolysis (if associated to increased FIBTEM or Fib-test and normal APTTEM or AP-test)

CT: coagulation time or R-time; A5: amplitude in 5 min of CT; A10: amplitude in 10 min of CT; MCF: maximum clot firmness or maximum amplitude; LI: lysis index; ML: maximum lysis.

used devices, and the standard coagulation tests in patients who undergo heart surgery.⁶ The main findings were:

- a. A strong correlation was found between the maximum clot firmness measures, in the tests evaluating the extrinsic and the intrinsic pathway, between ClotPro and ROTEM. The correlation was moderate for the time that points out the onset of coagulation (CT) between ClotPro and ROTEM, and maximum clot firmness in the tests for fibrin (Ex-test and EXTEM).
- b. Prothrombin time strongly correlated with R-time (Ex-test ClotPro); while the correlation was low with coagulation time (EXTEM ROTEM).
- c. Fibrinogen and plasma Factor XIII levels strongly correlated with the maximum clot firmness measure with the FIB-test (ClotPro) and the FIBTEM (ROTEM).
- d. The number of platelets presented a moderate correlation with the difference between coagulation triggered by extrinsic pathway and the fibrin test (EXTEM-FIBTEM, Ex-test FIB-test), both with ROTEM and with ClotPro.

7. EXCESSIVE BLEEDING MANAGEMENT APPROACH

A practical approach to manage excessive bleeding immediately after cardiothoracic surgery should have the basic premise that any medical action should be taken in the shortest time possible, and preventing damage to the patient. The longer they take, the more blood the patient loses, the higher the need for blood products for replenishment, and the higher the risk of morbimortality in patients. The approach may be based on some basic questions:

1) *Is there excessive bleeding or is it usual bleeding?*

- a) Before, it was stated that there is no universal definition for excessive bleeding. As usual bleeding varies with surgical and anesthetic techniques, with extracorporeal perfusion and other scenarios, it would be ideal for each service to analyze which are the volumes considered excessive. Or else, definitions such as the one included at the beginning of this summary can be used.
- b) It is important to highlight that, if there is no excessive bleeding, patients should not be treated even when coagulations tests are altered. This is based on coagulation tests being made in vitro, with variables present in organisms that are not measured. This is expressed in the low positive predictive value of coagulation tests.¹¹
- c) In the case of excessive bleeding, if the systemic blood pressure of a patient is high or within the upper limit of normalcy, the patient should be treated to obtain values according to the situation of the patient (for instance, medium blood pressure of 70 for a previously normotensive patient). For this goal, an IV vasodilation agent is usually used.
- d) In the case of excessive bleeding, and until a specific diagnosis and treatment are realized, the need to replenish red blood cells should be evaluated. In the case of hypotension, and until red blood cells concentrates

arrive, crystalloid replenishment should be started immediately (for instance, saline solution). Five hundred cc should be replenished for every 500 cc of lost blood; however, the loss of the first 500 cc does not require replenishment.

- e) Before excessive bleeding, it is convenient to report it to the surgical team to obtain their opinion, as well as to minimize reintervention times when needed.

2) *Is excessive bleeding due to surgical causes, coagulopathies or both?*

A differential diagnosis of the causes should be established by the history of the patient (e.g.: previous heart surgery, effect of antiplatelet agents), clinical signs (e.g.: bleeding only through drains or universal bleeding) and auxiliary tests (hemostatic values or non-hemostatic values in coagulation tests). A bleeding by surgical cause may be associated to coagulopathy. This happens when a) a bleeding by surgical cause undergoes incomplete blood product replenishment, and b) a bleeding by surgical cause is treated excessively with crystalloid fluids and hemodilution occurs in the patient.

If a patient is a carrier of bleeding by surgical cause, accompanied or not by coagulopathy, the patient should be urgently referred to the OR. Until the patient is moved to the OR, the coagulopathy should be treated.

3) *If it seems there is a coagulopathy, are the general basic conditions for coagulation present?*

For coagulation to work properly in the human body there should be:

- a) Body temperature >35°C
- b) pH >7.2
- c) Hb >8 g/dl (lower levels lead to loss of laminar flow, preventing a proper plasma and platelet contact with the endothelium).¹²
- d) Ionized calcium >1 mmol/l.

4) *If there seems to be a coagulopathy, which is it?*

In [Table 4](#), the main features of VETs and the standard coagulation tests are shown, in some coagulopathies that are usually found during and after heart surgery.

5) *What specific treatment is required for the coagulopathy?*

One of the merits of VET devices has been the dissemination of treatment algorithms by their manufacturers. Thus, they made a contribution to disseminating knowledge on the therapy for coagulopathies. The manufacturer of the ROTEM device has designed an algorithm to manage excessive bleeding, based on the order of treatment: 1st hyperfibrinolysis, 2nd heparinemia, 3rd fibrinogen deficiency, 4th platelet deficiency, and 5th factor deficiency. However, other personalized approaches to treatment can be equally effective.

Next, the most frequent coagulation alterations in the immediate period after cardiothoracic surgery are mentio-

TABLE 4.

Coagulation tests in some coagulopathies associated to heart surgery.

Coagulopathy	Coagulation viscoelastic tests	Standard coagulation tests
Hyperfibrinolysis	ML (in EXTEM or EX-test and FIBTEM or FIB-test) ↑ (in 60 min)	Prothrombin time ↑
	or A5 and A10 (in EXTEM or EX-test) ↓	APTT ↑
	or CT (in FIBTEM or FIB-test) ↑↑ with normal ML (in APTEM or AP-test).	Thrombin time ↑
		Fibrinogen ↓↓ Euglobulin lysis time ↓ Factors V and VIII ↓ D-dimer ↑↑
Heparinemia	CT (in INTEM or IN-test) ↑ with normal CT (in HEPTM or HI-test).	APTT ↑
		Thrombin time ↑
Factor deficiency	CT (in EXTEM or EX-test) ↑ (vitamin K-dependent coagulation factors)	APTT ↑
	CT (in INTEM or IN-test) ↑ with	Prothrombin time ↑ (vitamin K-dependent coagulation factors)
	CT (in HEPTM or HI-test) ↑ (intrinsic pathway factors) with normal FIBTEM or FIB-test.	Normal fibrinogen or ↓
		Normal number of platelets or ↓ (hemodilution)
Protamine excess	CT (in INTEM or IN-test) ↑ with	APTT ↑
	CT (in HEPTM or HI-test) ↑	Thrombin time ↑
	normal CT (in EXTEM or EX-test)	Normal prothrombin time
Platelet deficiency	A5, A10 and MCF (in EXTEM or EX-test) ↓ with	Number of platelets ↓ and/or
	Normal A5, A10 and MCF (in FIBTEM or FIB-test)	Smear with no platelet aggregation
Fibrinogen/ fibrin deficiency	A5, A10 and MCF (in EXTEM or EX-test) ↓ with A5, A10 and MCF (in FIBTEM or FIB-test) ↓	Fibrinogen ↓

CT: coagulation time or R-time; A5: amplitude in 5 min of CT; A10: amplitude in 10 min of CT; MCF: maximum clot firmness or maximum amplitude; ML: maximum lysis; APTT: activated partial thromboplastin time; ↑: prolonged; ↓: reduced or decreased.

ned, along with the most widely used therapeutic resources and their usual doses.

a) Treatment for hyperfibrinolysis:

* *Epsilon aminocaproic acid*:¹³

Presentation: 2 g ampoule (Ipsilon®).

Dose: 4 to 5 g diluted in 250 ml of IV saline solution (SS) or dextrose (D5%) over one hour, followed by continuous infusion of 1 g/h over 8 hours or until bleeding control. Maximum dose 30 g/day.

* *Tranexamic acid*:¹⁴

Presentation: 5 ml ampoule with 500 mg (Arotran®).

Dose: in the postoperative period: 500-1000 mg (if not used during the surgery, a 1 g dose is probably the most appropriate) or 25 mg/kg. This dose can be repeated every 8 h. It can be directly administered by intravenous access slowly, over a time of no less than 1 ml/min, or diluted in SS or D5%.

b) Treatment for heparinemia:

* *Protamine*:¹⁵

Presentation: 5000 U ampoule in 5 ml (protamine 1000 Ri-vero®).

Dose: 2500-5000 U or 30-60 U/kg. Administration: IV access, diluted in 100 ml of SS over 20 minutes.

c) Treatment of fibrinogen deficiency:

* *Cryoprecipitate*:¹⁶

Dose: initially 1 unit/10 kg of weight and later following clinical control.

* *Fibrinogen concentrate*:¹⁶

Presentation: ampoule. One gram of lyophilized powder, reconstituted with sterile water (Haemocomplettan®).

Dose: 1-2 g or 25 mg/kg initially, with successive administration as required.

d) Treatment of platelet deficiency:

* *Desmopresin*:¹⁷

Presentation: ampoule: 1 ml, with 4 µg/kg (maximum 20 µg – 5 amp).

* *Platelet concentrates (individual)*:¹⁸

Presentation: platelets suspended in plasma volume of 50-70 ml.

Dose: 1 individual concentrate per each 10 kg of weight or 1 apheresis.

e) Treatment for factor deficiency:

* *Fresh frozen plasma*:⁵

Dose: 10-15 ml/kg – usually 4 U (increase the coagulation factors of the patient by 10%).

* *Prothrombin complex* (Factor II, factor VII, factor IX and factor X):¹⁹

Protromplex Total Tim 4®: presentation: 600 IU/20 ml, Beriplex P/N®: presentation 500 IU, Octaplex®: presentation 500 IU.

Dose: initial 15-25 IU/kg or desired increase in Quick value (in % of normal) x body weight (Kg) x 1.2

* *Recombinant activated factor VII* (rFVIIa) (Novoseven®)

Presentation: ampoule of 1 mg (50 KIU) and of 5 mg (250 KIU).

Dose: 40-80 µg/kg have been used, or even higher. Recently, using doses less than <20 µg/kg has been proposed, in early and rescue therapy, with no unwanted effects.²⁰ Use is controversial and requires a risk/benefit evaluation of individual patients.

6) Does bleeding require surgical treatment, even in the presence of coagulopathy?

Before, it was mentioned that a bleeding by surgical

cause could be associated to a coagulopathy (bleeding by surgical cause with incomplete replenishment of blood products or excessively treated with crystalloid fluids, producing hemodilution). Furthermore, if pericardial clots appear, producing coagulopathy by factor consumption, the latter will not improve until they are surgically removed.

On the other hand, bleeding by coagulopathy can produce cardiac tamponade, requiring urgent surgical treatment.

8. CONCLUSION

Excessive bleeding by coagulation alterations is still observed in cardiothoracic surgery, and it worsens the outcome. To help with diagnosis, there are standard coagulation tests, and more recently, viscoelastic tests. These two types of tests differ in their methodology and both have advantages and disadvantages. Having both types of tests increases the diagnostic capacity in the perioperative periods of heart surgery patients.

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Original Investigation Reports

Determination of Global Registry of Acute Coronary Events score based on initial symptoms of coronary syndrome using multilayer perceptron

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Acute Coronary Syndrome;
GRACE Scale; Predictive Models;
Cardiovascular Mortality;
Artificial Neural Networks.

ABSTRACT

Introduction: the GRACE scale estimates prognosis and mortality due to acute coronary syndrome.

Objective: to predict the GRACE score according to admission characteristics for acute coronary syndrome in a Peruvian hospital using multilayer perceptron.

Materials and methods: analytical and cross-sectional study of a secondary database of 106 patients from a Peruvian hospital admitted for acute coronary syndrome. The variables were GRACE score, heart rate, systolic blood pressure, left arm pain, neck pain, abdominal pain, age, and ST-segment elevation. Multilayer perceptron-type neural networks were used.

Results: The neural network had a relative error of 0.168 and 0.139 in training and testing, respectively. The scatter plot had a homogeneous distribution, with an R-squared of 0.847, indicating that 85% of the variation in the GRACE score can be explained by the GRACE score predicted by multilayer perceptron. The average GRACE score in patients without ST elevation was 104.74, while with ST elevation it was 142.14, similar to the GRACE score obtained using multilayer perceptron, where the average in the absence of ST elevation was 105.52, while with ST elevation it was 140.36.

Conclusions: the use of neural networks is efficient for the prediction of GRACE score based on symptoms and signs upon admission in patients with acute coronary syndrome.

INTRODUCTION

Cardiovascular diseases are the first cause of death in the world, having increased by 60% in recent decades, representing a significant socioeconomic load in all countries, with indirect costs estimated in 237 billion dollars per year and a projected increase to 368 billion dollars by 2035 at world level.^{1,2} In Peru, more than 4 thousand people die by myocardial infarction.³

Acute coronary syndrome (ACS) is a condition coursing with decrease in coronary artery flow, affecting the function and vitality of the myocardium, causing the death of this tissue. It may course with ST-segment elevation (coronary total occlusion) associated to atherosclerotic plaque rupture, or without ST-segment elevation (coronary partial occlusion) associated to plaque erosion.⁴ The symptoms of both types of ACS are similar, with chest pain standing out, experienced as oppression or sharp pain radiating to or located in the arm, shoulder, neck, back, upper abdomen or jaw, associated to nausea, diaphoresis and dyspnea.⁵

Scores have been developed to estimate prognosis and mortality by coronary syndrome, such as the Thrombolysis In Myocardial Infarction (TIMI), as well as the GRACE score

(Global Register of Acute Coronary Events). In regard to the GRACE score, it assesses the risk of in-hospital mortality and 6 months after discharge, both in patients with and without ST-segment elevation. For this, it uses the markers of age, systolic blood pressure, heart rate, creatinine, elevated biomarkers (such as troponin), ST-segment changes, heart arrest during hospital stay and Killip classification for heart failure.⁶ This score, developed from data from more than 100 countries, is a valuable resource for clinical decision-making in the short and long term.⁷

To obtain accurate estimations with the GRACE score, biochemical, hemodynamic and electrocardiographic markers are required, which are not always available in the short term because of the saturation of hospital services, which could generate a mild but significant time gap until obtaining the required variables to reach predictor results, so having a provisional datum may guide cardiologists or ER doctors to have a view to plan the management to follow (along with their clinical criteria), until the time when enough information is available to make new decisions. Generally, the earliest data available are physical symptoms, blood pressure and electrocardiographic pattern.

In this regard, the development of possible predictor factors may benefit from using deep learning methods, capable of modeling complex relationships, flexible, and with the ability to solve complex problems. For this reason, the aim of this investigation was to predict the GRACE score according to the characteristics of admission due to acute coronary syndrome to a Peruvian hospital by multilayer perceptron.

MATERIALS AND METHODS

Design and population of the study

Analytical and cross-sectional study from a secondary database, belonging to Herrera-Castillo et al, from the article "Performance of the TIMI and GRACE scores in identifying the risk of death from acute coronary ischemic syndrome: a retrospective study in patients with chest pain at a Peruvian Hospital". The article has been added to the F1000research.com platform.⁸ The population was made up by 106 patients admitted to the Regional Hospital José Alfredo Mendoza Olavarría of Tumbes, Peru, due to acute coronary syndrome (ACS), evaluated within 10 minutes of their clinical manifestations, including precordial pain within 48 hours before admission to the ER, being evaluated by the GRACE score. The total of the database population was 106 patients, using the whole population for this investigation. The characteristics of the population studied are included in *Table 1*.

Variables and measurements

The dependent variable was the GRACE score, which is a model applied to all coronary syndromes, estimating in-hospital mortality and within six months, based on the score that considers the following variables: age, heart rate, systolic blood pressure, creatinine in blood, heart arrest upon admission, ST-segment deviation in ECG, abnormal cardiac enzymes (troponin) and Killip classification.⁹ The independent variables included as predictors in the multilayer perceptron neural network were: age (continuous, in years), systolic blood pressure (continuous, in millimeters of mercury), abdominal pain (categorical, yes and no), ST-segment elevation (categorical, yes and no), neck pain (categorical, yes and no), heart rate (continuous) and left arm pain (categorical, yes and no).

Statistical analysis

Multilayer perceptron neural networks were used. They are artificial neural networks constituted by several layers of interconnected neurons, analogous to biological neurons, and organized in three layers: input layer, one or more hidden layers, and an output layer. Each neuron of the hidden and output layers has a nonlinear activation function, enabling the perceptron to model complex relationships. The perceptron has the ability to perform classification, prediction and regression tasks. In a system that can learn by backpropagation from labeled data, adjusting the weights of connections during training. The neural net-

TABLE 1.

Characteristics of the population studied

		Frequency	Percentage
Sex	Male	67	63,20
	Female	39	36,80
Older than 50 years	No	54	50,90
	Yes	52	49,10
ST elevation	No	70	66
	Yes	36	34
Precordial pain	No	3	2,80
	Yes	103	97,20
Left arm pain	No	28	26,40
	Yes	78	73,60
Neck pain	No	83	78,30
	Yes	23	21,70
Diaphoresis	No	63	59,40
	Yes	43	40,60
Abdominal pain	No	92	86,80
	Yes	14	13,20
Dyspnea	No	45	42,50
	Yes	61	57,50
Nausea	No	77	72,60
	Yes	29	27,40
Syncope	No	93	87,70
	Yes	13	12,30
HTN	No	46	43,40
	Yes	60	56,60
Hypercholesterolemia	Yes	44	41,50
	No	62	58,50
Diabetes	Yes	38	35,80
	No	68	64,20
Smoker	Yes	82	77,40
	No	24	22,60
Cardiac arrest	Yes	103	97,20
	No	3	2,80
Elevated biomarkers (troponin)	Yes	22	20,80
	No	84	79,20
Death	Yes	97	91,50
	No	9	8,50

work was trained to predict the GRACE score on the basis of age, systolic blood pressure, abdominal, neck and left arm pain, ST-segment elevation, and heart rate.

After obtaining the quantitative data predicted by the perceptron, a dispersion graph was carried out to determine the degree of linearity of distribution. The graph included the R2 coefficient of determination, which measures the accuracy of a statistical model to predict an outcome; in this case, to what extent the GRACE score variation can be explained by the GRACE score derived from the multilayer perceptron.¹⁰ Finally, to supplement the dispersion graph findings, a table was made, where according to the presence or absence of ST-segment elevation, the GRACE

TABLE 2.

Outline of the neural network model to predict the GRACE score from clinical symptoms upon admission

Training (n=72)	Sum of square error	5.947
	Relative error	0.168
	Stopping rule used	1 consecutive step(s) with no error decrease
	Training time	0:00:00.01
Tests (n=36)	Sum of square error	2.195
	Relative error	0.139

score average obtained in the hospital was compared with the GRACE score predicted by multilayer perceptron. This was done with the aim of observing whether the averages were similar in both types of scores. For the comparison of averages, a Student's t-test was applied. Data processing and analysis, including the neural network modeling, were made by the SPSS statistics 25™ software. The neural network training route was: analyzing → neural networks → multilayer perceptron, including the GRACE score as dependent variable, and age, abdominal, left arm and neck pain, systolic blood pressure, ST-segment elevation and heart rate as covariates.

Ethical considerations

The study was observational and data were taken from a secondary database; therefore, there was no intervention or use or manipulation of biological samples, using only clinical registries and anonymous data, freely provided by the author of the original database, under creative commons license, so that no evaluation was required by a committee on ethics. Supplementary information, including the database where the neural network training was made, was available through the following link: https://figshare.com/articles/dataset/data_csv/23897043/1?file=41896686

RESULTS

The neural network made its training with 72 patients; while the test was with 26. The sum of squares error was 5.947 and 2.195 in the training and the testing, respectively, and the relative error was 0.168 in training and 0.139 in the test (Table 2).

The neural network had 1 input layer with 7 units, 1 hidden layer with 3 units, and one output layer with one unit. The activation function of the hidden layer was by hyperbolic tangent; while the output layer activation function was identity. The variables, in descending error, were age, systolic blood pressure, abdominal pain, ST-segment elevation, neck pain, heart rate and left arm pain (Figure 1).

The dispersion graph between the GRACE score and the predicted value by multilayer perceptron, had a ho-

TABLE 3.

Average of GRACE score based on clinical markers and average of GRACE score predicted by multilayer perceptron according to the presence of ST-segment elevation

ST elevation	GRACE score (p<0,001)		GRACE score predicted by multilayer perceptron (p<0,001)	
	Average	SD	Average	SD
No	104.74	29.593	105.52	26.659
Yes	142.14	37.037	142.36	30.629

SD: standard deviation

mogeneous distribution, with an R2 determination quotient of 0.847, indicating that 85% of the GRACE score variation, can be explained by the GRACE score obtained by symptoms and signs upon admission to the ER by acute coronary syndrome (Figure 2).

The average of the GRACE score in patients with no ST-segment elevation was 104.74; while in those with ST-segment elevation, it was 142.14. In regard to the GRACE score obtained by multilayer perceptron, the average in absence of ST elevation was 105.52; while it was 140.36 in those with ST elevation (Table 3).

DISCUSSION

The neural network model based on age, systolic blood pressure, abdominal pain, ST-segment elevation, neck pain, heart rate and left arm pain had a proper performance to predict the GRACE score. In this neural network,

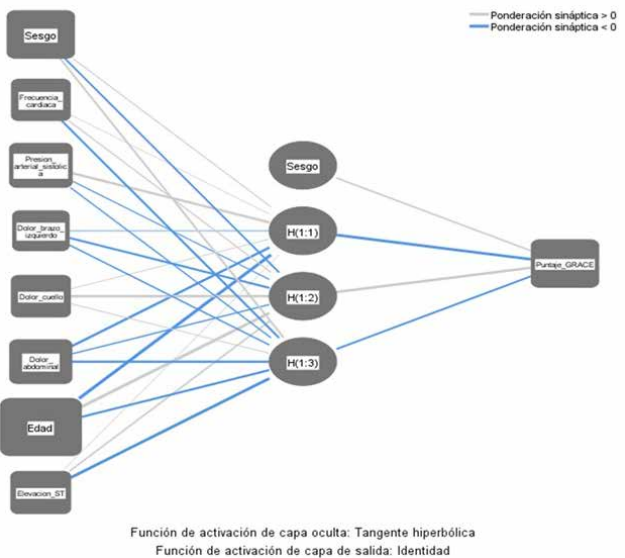
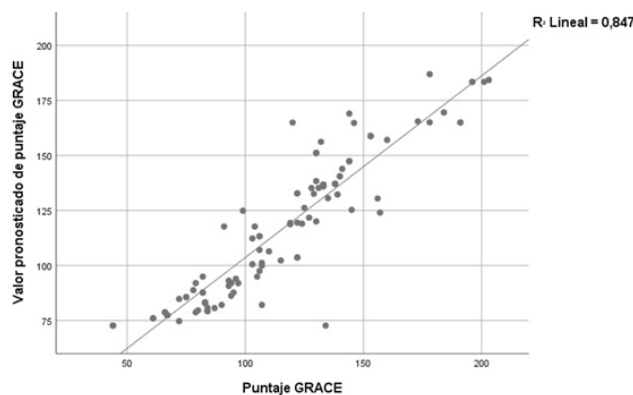


FIGURE 1.

Neural network structure of the multilayer perceptron type for the prediction of GRACE score according to symptoms and signs upon admission of patients with acute coronary syndrome

**FIGURE 2.**

Dispersion between the GRACE score and values predicted with multilayer perceptron for the GRACE score

besides including the parameters proper of the GRACE score, such as age, heart rate, blood pressure and ST-segment elevation, it also included characteristics associated to early symptoms of coronary syndrome, such as abdominal, neck and left arm pain. These symptoms had less weight for the neural network than age and blood pressure, but similar to heart rate and ST-segment elevation, being greater than left arm pain, which is a frequent symptom of acute coronary syndrome.

The contribution to the neural network by abdominal and neck pain suggests that its presence during the first stages of ACS are relevant predictors of severity. In terms of atypical presentations, previous studies have found that some types of pain, like abdominal pain, are associated to higher rates of morbidity and mortality, even when present in outpatients, often being underdiagnosed, as initially they may resemble gastrointestinal or respiratory symptoms, in some cases presenting as severe ear and throat pain.^{11,12,13,14,15}

However, the pathophysiological foundations for a greater severity of atypical symptoms have not yet been clarified completely in medical literature, with risk factors known such as age, smoking history and hypertension.¹⁶ However, it is known that craniofacial pain is a pain radiated from the vagus nerve, afferent from the heart, toward the somatic nerves, efferent to the head and neck, in a similar way to sympathetic and parasympathetic innervation linked to the level of the abdomen.^{17,18} Possibly, the atypical extrathoracic presentation is a manifestation of an early extension of myocardial damage, adjacent to the infarcted area. However, it is necessary to develop studies to explain this phenomenon.

The neural network had an R2 quotient of more than 80%, indicating that the results are close to the GRACE score, which could be verified also when comparing the score averages according to the presence or absence of ST elevation, where the averages were virtually identical

when compared with the GRACE values and when compared with the multilayer perceptron values. These results open a chance to implement artificial neural networks algorithms in emergency services, allowing to obtain fast estimations of the degree of severity of patients with acute coronary syndrome, until being able to have all biochemical and hemodynamic values available, which are part of the GRACE score criteria. In this regards, this trained neural network does not entail a replacement of severity scores validated at international level; however, it can be provisory supplement during the early stages of care of patients with acute coronary syndrome, during the time gap before obtaining all the elements that would allow cardiologists and emergency specialists to opt for TIMI or GRACE scores, mainly considering scenarios where ER services have a high flow of patients and low availability of staff and medical teams.

Between the limitations of this investigation, there were the facts that data was taken from a secondary database, so there could be information and classification biases. Moreover, about the variables related to abdominal and neck pain, there were no specifications available, such as the location of the abdomen or cervical region where pain occurred, or the time elapsed since symptoms appeared. Likewise, although using this neural network may suggest an immediate usefulness, it should be perfected in terms of the sample size of the study, which was 106 patients, so we invite cardiology researchers to develop trained models with a greater number of patients, if possible increasing the data of this trained network, which is made available.

To conclude, the neural network based on age, systolic blood pressure, abdominal pain, ST-segment elevation, neck pain, heart rate and left arm pain had a good performance to predict the GRACE score in patients admitted to a Peruvian hospital due to acute coronary syndrome. Its implementation could orient about severity score until the elements that make up the GRACE score criteria are available, allowing physicians to have a tool to supplement clinical criteria and the management to follow during the early stages of care by acute coronary syndrome. However, studies are required with a higher population number to improve the prediction of the neural network model.

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Original Investigation Reports

IMAGGEN AR-RMC registry: use of cardiac magnetic resonance in Argentina.

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Cardiac magnetic resonance, registry, Argentina, cardiomyopathy, gadolinium.

ABSTRACT

Introduction: cardiac magnetic resonance imaging (CMR) is a fundamental tool in the diagnosis of cardiovascular diseases. The Argentine Registry of Cardiac Magnetic Resonance (IMAGGEN AR-RMC) was designed to obtain information on the use of CMR.

Materials and Methods: A prospective registry of patients undergoing CMR was carried out.

Results: 1006 CMR were included. The most frequent indications were non-ischemic cardiomyopathy (55.7%), ischemic heart disease (14.6%). Macrocytic gadolinium was used in 61.9% of the studies, with an increase from 54.3% in the period 2018-2020 to 83.5% in the period 2021-2022 ($p < 0.001$); 89.7% of the studies had an impact on patient management. The complication rate was 0.5%.

Conclusions: Non-ischemic cardiomyopathy was the main indication. Macrocytic gadolinium utilization increased during registration. CMR was a safe study with an impact on patient management.

INTRODUCTION

In spite of research studies giving rise to magnetic resonance imaging being close to 70 years old, it was during the 1970s that the development of this technique quickened, because of fundamental studies that allowed the definitive placement of this technique as a diagnostic tool in medical practice.^{1,2,3,4} In the last 20 years, cardiac MRI has emerged as a tool for diagnosis, prognosis and management of CAD, pericardial disease, cardiomyopathies, cardiac masses and tumors, and congenital heart diseases, among others.^{5,6,7,8,9}

In spite of having several international registries showing the reality of cardiac MRI, there is no wide-ranging information available about the reality in Argentina, in terms of cardiac MRI indication in medical practice, or about the use of different sequences, techniques or contrast agents used in MRI laboratories in our country.^{10,11,12}

For this reason, we developed from the Committee of Cardiac CT and MRI of the Argentine Federation of Cardiology, a registry (IMAGGEN AR-RMC) that would enable data gathering about the reality of MRI in our country, pro-

viding an informative and conceptual framework to prepare strategies for the improvement and dissemination of this auxiliary method.

MATERIALS AND METHODS

A prospective, cross-sectional registry was designed, along with the medical centers of the country that wished to participate. The patients signed an informed consent and were included consecutively. Data were uploaded to a digital platform anonymously. Information was divided into two periods of time: the 2018-2020 term and the 2021-2022 term, to evaluate the variation in the use of macrocytic contrast agents over time.

Statistical analysis

Continuous variables are presented as mean and standard deviation and median and interquartile range according to them being of Gaussian distribution or not, respectively. Categorical variables are expressed as frequencies and percentages. Student's t-test or Wilcoxon test was per-

formed as it corresponded for quantitative variable comparison. Quantitative variables were compared with Chi-square test or Fisher's exact test, according to the case. A p value <0.05 was considered a statistically significant value.

RESULTS

There were 1006 MRI tests included, from January 2018 to October 2022, in 15 centers from 9 provinces of Argentina. In **Table 1**, we show the percentages corresponding to each of them, with 70.6% of them having been made in the province of Santa Fe. The 1.5 Tesla MRI device was used in 80.2%, and the 3 Tesla was used in the remaining 19.8%. In this sample, the most frequent brand was General Electric, in 61.6% of cases. The median of age was 47 (27-61) years. The most frequent cause for requesting MRI was non-ischemic cardiomyopathy, within which, the most frequent indications were dilated cardiomyopathy (18.9%) and hypertrophic cardiomyopathy (17.8%). In 14.6% of cases, the request was related to ischemic heart disease (**Figure 1**). In 96.9%, the tests were requested with contrast agents. The MRI sequences made in the tests are shown in **Table 2**, with cine (91.7%) and late enhancement (85.6%) being the most used ones.

In 38.1% of tests with contrast agents, linear gadolinium was used. Viewgam® was the most used contrast agent in this group (90.7%), macrocyclic gadolinium in 61.9%, and Gadovist® was the one most used in the latter group (59.7%). During the 2018-2020 period, the percentage of use of macrocyclic contrast agents was 54.3%, and during the 2021-2022 period, 83.5% ($p<0.001$) (**Figure 2**). The median gadolinium dose was 15 ml in the 2018-2020 period, and 14.8 ml in the 2021.2022 period ($p=0.89$).

The test reports were made by cardiologists in 97.2% of cases, in 2.4% they were made jointly with radiologists, and in 0.4% they were made only by radiologists. After the report, it was considered that in 89.7% of cases the report was conclusive with an impact on the management of patients, in 9.8% there was no impact, and in 0.5% the report was not conclusive and/or diagnostic. The rate of complications was very low, presenting in 5 patients (0.5%): two patients with heart failure worsening, one patient with vomits, one patient with a mild allergic reaction, and another one with unspecific discomfort. None of them required suspending the procedure.

DISCUSSION

This study shows a wide information about the reality of using cardiac MRI in Argentina, including 9 provinces and 15 centers. This registry presented a greater use of 3T MRI scanners than in the European cardiac MRI registry, being 19.8% in our registry, and 5.9% in the European one; however, it is less than in the recently published study by the Society for Cardiovascular Magnetic Resonance, where it was 26%.^{11,12} In this registry, the indication by ischemic cause represented almost 15%, with a very low use of stress MRI, a methodology that presents, since 2021, a IB

TABLE 1.

General characteristics of the population

Variable	Datum
Age (mean (SD)) (years)	47 (27-61)
Male gender n (%)	627 (62.3)
Weight (kg mean (SD))	75 (66-88)
Height (cm mean (SD))	168 (160-174)
HTN n (%)	222 (22.1)
Smoking n (%)	73 (7.3)
Diabetes n (%)	50 (5.0)
Dyslipidemia n (%)	98 (9.7)
History of ischemic heart disease n (%)	140 (13.9)
Chronic kidney disease n (%)	10 (1.0)
Province	
Buenos Aires n (%)	73 (7.3)
Chaco n (%)	2 (0.2)
Córdoba n (%)	75 (7.5)
Corrientes n (%)	132 (13.1)
Entre Ríos n (%)	10 (1.0)
La Rioja n (%)	1 (0.1)
Misiones n (%)	2 (0.2)
San Luis n (%)	1 (0.1)
Santa Fe n (%)	710 (70.6)
MRI scanner brand	
General Electric n (%)	620 (61.6)
Philips n (%)	375 (37.3)
Siemens n (%)	11 (1.1)
Contrast agent use n (%)	975 (96.9)
Contrast agent dose	15 (10-20)
Macrocyclic contrast agent n (%)	594 (61.9)
Tesla number	
1.5 T n (%)	807 (80.2)
3 T n (%)	199 (19.8)
Complications	5 (0.5)
Cardiac MRI indication	
Stress test (dipyridamole or adenosine) n (%)	6 (0.6)
Feasibility n (%)	123 (12.2)
Post-infarction complications n (%)	18 (1.8)
Nonischemic cardiomyopathy n (%)	561 (55.7)
Nonischemic dilated cardiomyopathy n (%)	191 (18.9)
Hypertrophic n (%)	180 (17.8)
Arrhythmogenic RV cardiomyopathy n (%)	51 (5.1)
Restrictive n (%)	18 (1.7)
Infiltrative n (%)	31 (3.8)
Noncompaction cardiomyopathy n (%)	60 (5.9)
Takotsubo n (%)	30 (2.9)
Myocarditis n (%)	64 (6.4)
Valve disease n (%)	71 (7.1)
Pericardial disease n (%)	19 (1.9)
Congenital heart disease n (%)	144 (14.3)

level of indication for evaluating precordial pain, and with a marked difference with international registries, showing this methodology being underused in our country.⁵ The most frequent indication in this registry was nonischemic cardiomyopathy, similarly to other international registries.^{10,11,12}

The pharmacological characteristics of the different extracellular gadolinium chelate complexes are very similar. The main difference between the molecules lies in their structure and ion charge, conditioning their capacity to modify tissue signaling. The stability of gadolinium chelates relates to their structure, that could be linear or macrocyclic. Macrocyclic complexes bind the gadolinium ion more strongly than those of linear structure, preventing the release of free gadolinium, remaining trapped within the macrocyclic structure after injection.¹³ The most feared adverse effect with gadolinium infusion is nephrogenic systemic fibrosis, a rare but highly lethal entity. The recorded cases of nephrogenic systemic fibrosis were reported with linear gadolinium agents.¹⁴ On the other hand, patients subjected to several injections (4-5 injections or more) of gadolinium contrast agents have been observed to present a signal increase in some brain areas (dentate nucleus and globus pallidus) due to T1 shortening, displaying gadolinium deposits in the brain. Linear gadolinium contrast agents seem to persist for a longer time than macrocyclic ones, that only show a transient increase in the brain and seem to experiment an early clearance; it is for this reason that macrocyclic gadolinium agents are advised.^{15,16,17} In this registry, the global use of macrocyclic contrast agents was 61.9%, with a statistically significant increase from the 2018-2020 period to the 2021-2022 period, from 54.3% to 83.5%, respectively ($p < 0.001$).

In this study, no severe adverse reactions were observed, and the incidence of mild reactions was higher than those reported previously: 0.5% vs 0.11%.¹⁸

Limitations

The percentage of patients admitted to the participating centers was not uniform, which, in some way, may generate a bias in the global information.

CONCLUSION

The IMAGEN AR-RMC registry is wide, showing the reality of cardiac MRI in Argentina. Cardiac MRI is a safe test, with an impact on the management of patients. Non-ischemic cardiomyopathies was the main indication for cardiac MRI, with a significant increase being observed in the use of macrocyclic gadolinium agents through the registry.

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TABLE 2.

Cardiac MRI sequences used in the tests

Sequence	N (%)
CINE SSFP	923 (91.7)
Fast Spin Echo (FSE)	570 (56.7)
T1-T2 and T2 with fat saturation	549 (54.6)
Flow sequence	410 (40.8)
Perfusion sequence	596 (59.2)
T1 Mapping	58 (5.8)
T2 Mapping	56 (5.6)
Tagging sequence	23 (2.3)
RT sequence	861 (85.6)
MR angiography	40 (4.0)
3D navigator (coronary arteries)	20 (2.0)

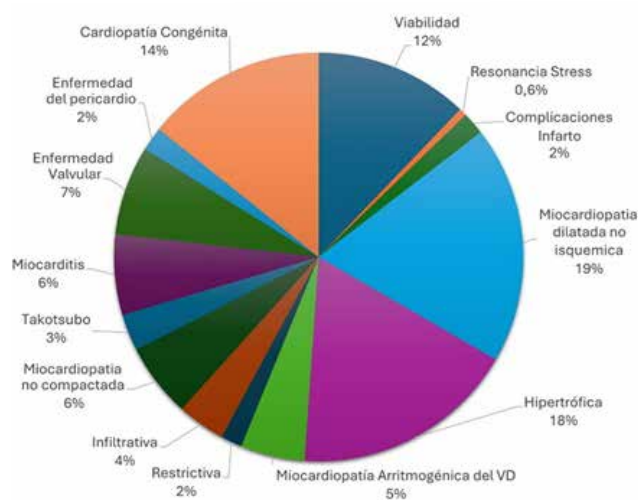


FIGURE 1.

Main cardiac MRI indications

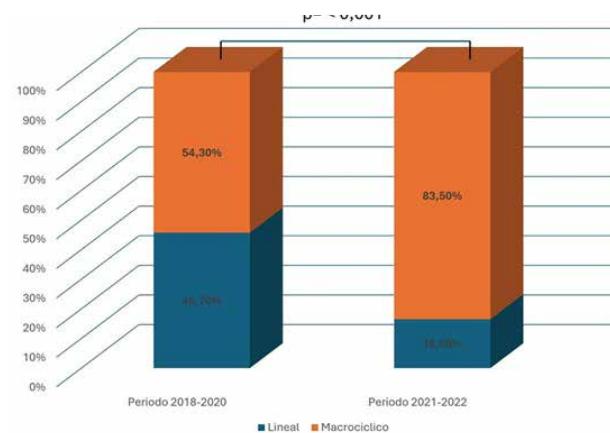


FIGURE 2.

Use of macrocyclic gadolinium contrast in the two periods analyzed.

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Original Investigation Reports

Survey of overweight and hypertension in schoolchildren aged 11 and 12 years in the city of Rosario during the second term of 2023

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ABSTRACT

The main **objective** of this study was to determine the prevalence of overweight and hypertension (HTN) in 11- and 12-year-old schoolchildren in the city of Rosario during the second half of 2023. The study aimed to assess how anthropometric factors such as weight, height, body mass index (BMI), and blood pressure (BP) contribute to cardiovascular risk in this population.

Materials and Methods: an observational, descriptive, cross-sectional study was conducted by convenience sampling. The sample consisted of 337 children from 6th grade in different public and private schools in Rosario. Anthropometric measurements (weight, height, waist circumference, etc.) and blood pressure measurements were taken by trained professionals. Data were analyzed using descriptive and correlational statistics with SPSS 23.0 software.

Results: out of 337 children evaluated, 61.4% were overweight or obese. The average systolic blood pressure (SBP) was 108 mmHg and diastolic blood pressure (DBP) was 68 mmHg, with 17.8% of children showing elevated BP. No significant differences were found in the prevalence of overweight and HTN between genders or types of schools, although some geographic differences were noted.

Conclusions: the study shows a high prevalence of overweight, obesity, and hypertension in schoolchildren. It is urgent to implement preventive programs in schools to promote healthy habits and reduce future cardiovascular risks, especially in vulnerable areas. Public policies should combine efforts in health and education to improve children's well-being.

Keywords:

Hypertension,
Pediatrics,
Obesity.

INTRODUCTION

Chronic noncommunicable diseases, and among them, cardiovascular ones, represent the most common cause of death at world level.¹

Hypertension (HTN) is the main risk factor to experience cardiovascular diseases. Every year, 1.6 millions of deaths occur due to cardiovascular diseases (CVDs) in Latin America. HTN affects 20-40% of the adult population (approximately 250 million people); being a condition that can be reduced or postponed through multiple preventive interventions.¹

Just 57.1% in the adult population estimated to have elevated blood pressure (BP) is aware of having HTN, contributing to the low control level in the population: just 18.8% of hypertensive adults in Argentina, Chile, Colombia and Brazil have their BP controlled. Its measurement constitutes an important preventive practice for an early and timely detection in people who could benefit from effective interventions (like lifestyle or medication changes) and thus reduce the cardiovascular risk associated to HTN.^{2,3,4}

The prevalence of HTN can be assessed in different ways

according to the countries, through population surveys using questionnaires or making physical measurements, just as with the use of clinical or outpatient registries.³

Beyond all of these assertions based on scientific evidence and technological advancements from recent years, there is still a failure both in the detection and in the control of hypertensive patients, whether by essential and secondary etiology, which makes it not to be reduced efficiently even while in treatment for cardiovascular risk.

Cardiovascular evaluation in childhood should unavoidably include the measurement of BP since the third year of age, also with a full physical examination, and the values found should be categorized according to specific tables constructed according to age, gender, weight and height (percentiles).^{5,6,7,8,9,10}

Height and weight are obtained through anthropometry. This tool is used in different areas and disciplines with the aim of contributing useful data for medicine, sports, investigation, and so on.^{5,11,12,13} It provides data that enable evaluating lifestyle and nutrition to optimize competent interventions on them.¹⁴

TABLE 1.
Characteristics of the population studied

	n	%*	p
Total	337		
Female	175	51.9% (46.6-56.8)	>0.05
Male	162	48.1% (43.2-53.4)	
North area	85	25.2 (21.4-29.4)	
Northwest area	34	10.1 (7.1-13.2)	<0.05
West area	46	13.6 (10.1-17.4)	
Central area	51	15.1 (11.6-18.7)	
Southwest area	73	21.7 (17.3-26.1)	
South area	48	14.2 (10.7-17.7)	<0.05
State school	191	56.7% (51.5-62.3)	
Private school	146	43.3% (37.7-48.5)	

*% (95% confidence interval).

Anthropometry comprises a set of standardized procedures that are easy to apply, financially acceptable, reproducible over time, noninvasive, innocuous and reliable, as long as collection techniques are followed. Because of its historical and contextual character, if done properly, it allows to make diagnosis both in individuals and the population, turning it into a widely used tool.¹³

The problem of childhood health during the schooling stage, and mainly its relationship with public policies, usually concern those responsible for decision-making in different areas and levels of the state. This interest on the topic makes them part of the analysis and search for information actively.⁶

From these analysis, a significant aspect emerges, related to the need to learn about the anthropometric measures in this population. These data may be part of the individual medical history of children, but they are not part of an updated profile, available for the Ministry of Education.

For those in charge in governmental areas, this information would be important for the management of measures to implement by different sectors of the state.

OBJECTIVES

Surveying data on overweight and HTN in individuals in school of 11 and 12 years of age, from the city of Rosario, during the second half of 2023.

MATERIALS AND METHODS

An observational, descriptive, cross-sectional investigation was carried out, with convenience sampling according to the available resources. Sixth-grade students of 11 and 12 years of age were evaluated, because in this age group, pubertal development and underlying changes stand out, associated to more freedom of choice in diet patterns and physical activity. In turn, because of the changes in body surface, this stage is characterized by a higher cardiac output, which added to the prevalence of obesity described in previous studies, may increase the risk of hypertension. Two schools were chosen at random, from six districts of the city of Rosario in 2023: north, northwest, west, center, south and southwest. All the chosen schools received breakfast. In every district, a private management school and a public management school were chosen, evaluating 12 institutions in total. The choice of schools was determined by closeness between public and private ones in each district to decrease the difference in geographical determinants between them.

The study was approved by the Committee on Ethics of the School of Medical Sciences of the Universidad Nacional de Rosario, with regulation: 770/2023. The informed consent by parents and the agreement by the children were obtained.

Data were collected between September and November, 2023.

In all selected schools, there was an invitation to participate for 6th grade children, by formal communication

TABLE 2.
Weight, height, waist circumference and hip circumference according to gender, area and type of school

	n	Weight*	Height*	Waist circumference*	Hip circumference*
Total	337	49.97 ± 13.12	150.18 ± 7.27	74.56 ± 12.71	87.68 ± 13.84
Female	175	49.32 ± 11.73	149.98 ± 7.24	74.29 ± 11.61	87.07 ± 12.59
Male	162	50.66 ± 14.48	150.39 ± 7.30	74.85 ± 13.82	88.33 ± 15.08
North area	85	46.81 ± 11.60	148.99 ± 7.62	71.10 ± 13.09	84.28 ± 14.14
Northwest area	34	49.55 ± 11.23	150.97 ± 5.46	72.46 ± 10.62	87.17 ± 8.13
West area	46	51.71 ± 12.54	149.28 ± 5.41	77.22 ± 12.74	89.37 ± 15.69
Central area	51	49.40 ± 14.26	149.58 ± 7.85	73.90 ± 12.31	86.54 ± 9.66
Southwest area	73	51.02 ± 13.66	151.86 ± 7.24	75.63 ± 12.28	89.02 ± 13.89
South area	48	53.18 ± 14.69	150.65 ± 8.36	78.68 ± 13.04	91.61 ± 17.04
State school	191	49.42 ± 13.53	149.70 ± 7.78	74.21 ± 13.51	87.59 ± 15.79
Private school	146	50.69 ± 12.59	150.80 ± 6.51	75.01 ± 11.59	87.80 ± 10.81

*Mean±standard deviation.

TABLE 3.

Body mass index (BMI), waist-to-hip ratio (WHR), waist-to-height ratio (WHtR) according to gender, area and type of school

	n*	BMI*	WHR*	WHtR*
Total	337	21.96 ± 4.76	0.846 ± 0.087	0.496 ± 0.0786
Female	175	21.80 ± 4.56	0.849 ± 0.079	0.495 ± 0.0756
Male	162	22.13 ± 4.97	0.842 ± 0.095	0.497 ± 0.0823
North area	85	20.89 ± 4.13	0.829 ± 0.109	0.476 ± 0.0815
Northwest area	34	21.56 ± 3.84	0.831 ± 0.097	0.480 ± 0.0650
West area	46	23.12 ± 4.95	0.854 ± 0.088	0.518 ± 0.0856
Central area	51	21.85 ± 5.27	0.851 ± 0.071	0.494 ± 0.0760
Southwest area	73	21.90 ± 4.60	0.851 ± 0.066	0.498 ± 0.0706
South area	48	23.24 ± 5.50	0.863 ± 0.079	0.522 ± 0.0807
State school	191	21.79 ± 4.64	0.842 ± 0.095	0.495 ± 0.0810
Private school	146	22.18 ± 4.91	0.849 ± 0.076	0.498 ± 0.0756

*Mean±standard deviation.

through the school authorities. From all the invited subjects, 11 children were excluded as they were older than 12 years, with the sample being constituted by 337 children.

Anthropometric and blood pressure measurements were conducted by specialists in cardiology, investigators with an approach in anthropometry as their study goal and advanced students of medicine, previously trained both in anthropometric measurements and blood pressure collection. No intra- or inter-evaluator measurement error was observed ($p>0.05$).

Weight

Participants were weighed with standardized light clothes, with light gym sweatshirt and t-shirt, with no shoes and no personal ornaments; at the same time, before breakfast. The measurement technique was that advised by the Argentinian Society of Pediatrics.⁵ The reading was carried with the individual standing in the center of the platform of a single scale, with no contact of the rest of the body

with any other structure. In all cases, the same digital scale was used, verifying its calibration with witness weights.

Height

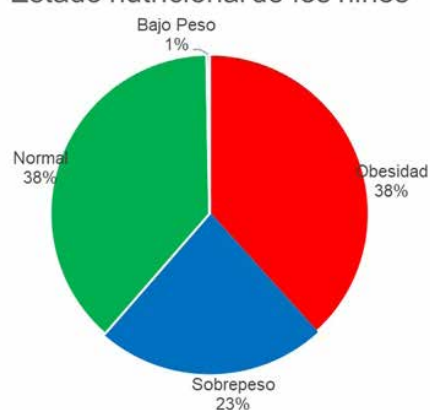
Height was measured with a single stadiometer; individuals were barefoot, with a few clothes to check the position of the body, hair arranged so that it would not obstruct measurement, with no ornaments. Children were standing on a flat surface in a right angle in relation to the vertical section of the stadiometer, with their ankles touching the base of the vertical section of it, shoulder blades, buttocks and back side of the cranium in the same vertical plane, and touching the instrument, and head in Frankfurt plane, arms hanging free at both sides of the body. As with the scales,

TABLE 4.

Systolic blood pressure (SBP) and diastolic blood pressure (DBP) according to gender, area and type of school

	n	SBP*	DBP*
Total	337	108.80 ± 12.29	68.22 ± 10.62
Female	162	109.20 ± 12.58	68.62 ± 9.82
Male	175	108.44 ± 12.04	67.84 ± 11.32
Menarche	98	110.60 ± 12.74	69.20 ± 11.59
No menarche	77	105.69 ± 10.52	66.10 ± 10.78
North area	85	108.49 ± 9.95	67.70 ± 8.93
Northwest area	34	108.79 ± 13.89	69.15 ± 12.26
West area	46	108.74 ± 15.27	70.30 ± 13.33
Central area	51	108.63 ± 11.81	66.18 ± 8.77
Southwest area	73	108.97 ± 12.85	68.34 ± 10.44
South area	48	109.35 ± 11.90	68.44 ± 11.36
State school	191	108.25 ± 13.26	68.62 ± 11.79
Private school	146	109.53 ± 10.89	67.69 ± 8.86

*Mean±standard deviation.

Estado nutricional de los niños**FIGURE 1.**

Nutritional state (BMI) of children with ages 11 and 12 in the city of Rosario

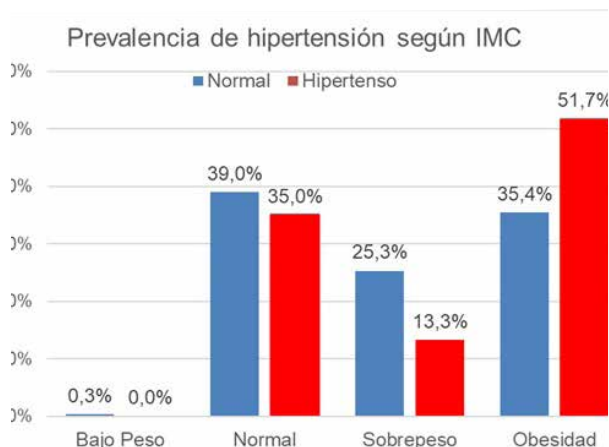


FIGURE 2.

Prevalence of hypertension according to nutritional state (BMI) in children with ages 11 and 12 in the city of Rosario.

for the measurement a single removable stadiometer was used, of graph paper and laminated, on a wall along with a mobile sliding piece in a right angle of 6 cm of width. A plumb was used to properly install it and the position was verified several times before starting the measurements.¹¹

Waist and hip circumferences

Waist circumference measurements were taken at umbilical level, at the end of exhalation and with the abdomen relaxed. Hip circumference measurement was made at the most prominent point of the buttocks. For this, a single flexible retractable measuring tape was used, calibrated in millimeters (1 mm accuracy) with individuals standing and the observer at the right.^{11,12,13}

Based on the abovementioned measurements, body mass index (BMI), waist-to-height ratio (WHtR) and waist-to-hip ratio (WHR) were estimated.^{11,12,13,14}

BMI was estimated using Quetelet's index: weight in kilograms divided by height squared in meters (kg/m^2); WHR as the quotient between waist circumference in centimeters and hip circumference in centimeters, and WHtR as the division of waist circumference in centimeters by height in centimeters.¹¹

Later, with weight and height data, each student was categorized from tables of percentiles of weight/age and gender, and height/age and gender of the Argentinian Society of Pediatrics 2011, into normal percentiles ($P > 3$ - < 97), elevated percentiles ($P < 97$), and low percentiles ($P < 3$).⁵ Also, they were categorized based on percentile tables from the WHO 2007 of BMI for gender and age, into low weight ($P < 3$), normal weight ($P < 3$ - < 85), overweight ($P 85$ - < 95), and obesity ($P < 95$).¹⁴

Blood pressure

To be able to unify data collection, due to the difficulties of collaboration by children, the first BP measurement was analyzed, carried out with aneroid sphygmomanometers,

following the steps indicated for a correct measurement by the Argentinian Society of Pediatrics and the National Program for School Health.^{6,15} Students were evaluated in a sitting position, with the back resting on the back of the chair, in a sound-free environment, at a comfortable temperature, with the right arm resting on the table and the cuff at the level of the heart, with their feet on the floor, not crossing. They followed the indication of resting before the measurement for 2 to 5 minutes. During all measurements, there was always a cardiologist present in charge of overseeing the procedure and its subsequent percentile analysis, as well as some school management members, and on occasions the parents of the students.

According to the recommendation from the last consensus on cardiovascular prevention in children and adolescents, HTN diagnosis was made based on percentiles until the age of 16 years, since from this age the classification proposed for adults is used.¹³

Blood pressure reference tables were used, created by the American Academy of Pediatrics/American Heart Association (AAP/AHA 2017).⁸ Hypertension criteria and its grades were estimated according to the percentiles: HTN stage 1 ($\text{SBP}/\text{DBP} > p95$ and $< p99 + 5$ mmHg) and HTN stage 2 ($> p99 + 5$ mmHg).

Statistical analysis

The data obtained were published on a database in the Repository of Academic Data of the Universidad Nacional de Rosario (RDA-UNR).¹⁶ The results of quantitative variables are expressed as mean $\pm$ standard deviation and the qualitative variables as absolute frequency, relative frequency and 95% CI. Chi-square test was used to evaluate the relationship between qualitative nominal variables and/or ordinal variables, student's t-test and Anova test to compare continuous quantitative variables. Spearman's correlations were conducted. The smallest level of significance used was $p < 0.05$. The statistical program SPSS 23.0 was used.

RESULTS

From the 337 individuals evaluated, 175 (51.9%) were women and 162 (48.1%) were men. There were 12 schools surveyed: 6 private ones and 6 public ones, two by each previously mentioned neighborhood (*Table 1*).

The average weight of all school students was 49.9 ± 13.1 kg. There were no differences observed between sexes ($p = 0.350$), between the types of schools ($p = 0.381$), or between geographical areas ($p = 0.099$) (*Table 2*).

When evaluating by weight percentiles, it was observed that from the 337 students assessed, 28.2% (23.6-33.2%) presented an elevated percentile ($p < 0.05$), 70.9% (66-75.4%) a normal percentile and 0.9% (0.0-2.1%) a low percentile ($p = 0.168$) (*Table 2*). Although there were no significant differences between areas ($p = 0.166$), it was possible to observe that the students from the southwest area were taller than the rest. When dividing students by gender, in girls

there was no significant relationship between height and area ($p=0.993$); unlike boys from the southwest area, who presented a significantly higher height ($p=0.023$) than their counterparts in other areas.

When classifying the height percentiles, it was possible to observe that 0% of children had a low percentile (<3), 87.8% (84.6-91.6%), a normal percentile ($>3<97$) and 12.2% (8.4-15.4%) a high percentile (>97) ($p<0.05$). There was no relationship between percentile and gender ($p=0.667$), or with the type of school ($p=0.797$). Instead, there were indeed differences by area ($p=0.000$), where once again the southwest presented a higher ratio of children with an elevated percentile.

The average of hip circumference in students was 87.6 ± 13.8 cm. There were no significant differences found between boys and girls ($p=0.405$) or between types of schools ($p=0.891$).

During the analysis by area, it was observed that in public school students in the northwest area there was a tendency in the limit of statistical significance to presenting a smaller hip circumference, while those in public schools in the southeast had a higher average.

The average BMI of all students was 21.9 ± 4.7 kg/m². There were no significant differences observed between gender ($p=0.528$), or type of school ($p=0.463$). In regard to areas, although there were no significant differences, there was a small tendency to be higher ($p=0.055$) in the south area (Table 3). When comparing the areas of state schools, it was observed that children in the west area presented a greater BMI in comparison with the north area ($p=0.018$). Between the private schools, the south area presented significantly higher differences of BMI in comparison with those from the southwest area ($p=0.013$) (Table 3).

When classifying BMI in percentiles, a marked excess in weight was observed between students (61.4% adding obesity and overweight). The proportions were the following: 23.1% (18.7-27.6%) overweight ($p\geq85<97$), 38.3% (33.4-43.6%) obesity ($p\geq97$), 38.3% (32.8-43.9%) normal weight ($p\geq3<85$), and a single case of low weight (<3). We should clarify that the student with low weight is under treatment for alterations in growth (Figure 1).

Although there was no relationship with gender ($p=0.801$), there was indeed a significant relationship between overweight and obesity in girls with menarche ($p=0.007$). There was no relationship between the percentile of BMI with the area ($p=0.614$) or the type of school ($p=0.591$). When combining both variables, it was possible to see that in the southwest area, the proportion of students with obesity is significantly higher in the state school in comparison with the private one ($p=0.003$).

The average waist-to-hip ratio (WHR) of all students was 0.84 ± 0.08 . There were no differences observed between sexes ($p=0.500$), type of school ($p=0.439$), and area ($p=0.240$) (Table 3).

The average waist-to-height ratio (WHtR) of all students was 0.49 ± 0.07 . There were no differences observed between

gender ($p=0.902$), or type of school ($p=0.729$). However, there was a significant difference between areas ($p=0.007$), where once again the children of the south area had a higher WHtR greater than in those of the north area ($p=0.017$) (Table 3).

The average SBP and DBP of all students was 108 ± 12 mmHg and 68 ± 10 mmHg, respectively. There was high BP in 17.8% of the population during the school evaluation. There were no significant differences in SBP and DBP according to gender ($p=0.887$) (Table 4).

The presence of menarche correlated significantly with elevated values of SBP ($p=0.018$); not so with DBP values ($p=0.3$).

The correlation between SBP and weight was also significant ($p=0.000$), as well as with BMI ($p=0.004$), WHtR ($p=0.007$), waist circumference ($p=0.035$) and hip circumference ($p=0.049$). There were no significant differences observed with WHR ($p=0.205$) (Figure 2).

In regard to SBP, a significant correlation was found with a greater waist circumference ($p=0.028$). A correlation tendency presented with waist circumference ($p=0.054$), but its relationship with BMI was not significant ($p=0.398$).

When analyzing by area, there were no statistically significant differences observed in regard to SBP ($p=0.999$) and DBP ($p=0.530$); although SBP was observed to be higher in the south and southwest areas and DBP was higher in the west and northwest areas.

Between private and public schools, it was found that DBP was higher in the latter, in a statistically significant manner ($p=0.04$). There were no significant differences observed in regard to SBP ($p=0.1$).

With the data obtained, we created and published a database, available in the free access and free-of-charge digital repository of the UNR.¹⁷

DISCUSSION

Overweight and obesity constitute a severe public health problem, that currently has reached characteristics of a pandemic. In 2022, there were around 390 million children and adolescents with overweight and obesity at world level.⁴

In Argentina, the problem of obesity is also concerning and has presented a sustained increase over years. It is argued that the increase in BMI observed would be the result of an increase in sedentary life associated to dietary patterns characterized by a high consumption of products with low nutritional value, high calorie content, and a habitual ingestion of sugar-sweetened beverages.^{4,14,17,18,19}

Childhood obesity is strongly linked to noncommunicable diseases like diabetes and coronary artery disease in adults.^{20,21,22}

The nutritional situation of the childhood and adolescent population can be characterized from the anthropometric information in relation to age and gender. In this report, the data come from registries of 337 children with ages 11 and 12 who are in 6th grade in public and private schools from different areas of the city of Rosario.

An approach to the problem of malnutrition is visualizing its distribution according to calorie deficit and/or excess, which would have an impact both on weight and height.

When evaluating the expected weight for age and height, 3 in every 10 children presented an elevated percentile; i.e. weight excess; although the remaining population presented normal weight, since the number of children with low weight was less than 1%. The evaluated variable should generate a warning about the possible relationship with malnutrition by excess in the evaluated children.

On the other hand, there were no children found with low height, which is a great advancement in regard to nutritional deficits affecting other provinces in the country.

In the case of the anthropometric variables mentioned previously, it seems that malnutrition in the city of Rosario is not as high in regard to world references. However, when evaluating the combined variables, malnutrition by excess is manifest with another magnitude.

A key result was the BMI obtained in this evaluated group. When adding children with overweight and obesity, weight excess is overwhelming in the evaluated population, where nearly 2 in every 3 children presented elevated BMI, regardless of the gender of the evaluated individuals.

As it was to be expected, due to the relationship described in the literature about weight excess and BP increase, a prevalence of HTN was found in 17.8% in the evaluated cohort. Therefore, 1 in every 5 children of the city of Rosario presented elevated BP at the time of the evaluation.

It is remarkable that only SBP and not DBP significantly correlated with weight, BMI, waist circumference and hip circumference. Although no significant differences were identified by gender; in the female students a positive relationship was found between SBP and menarche.

According to the Second National Survey on Nutrition and Health (Segunda Encuesta Nacional de Nutrición y Salud) from 2019, where children with ages from 5 to 17 years were evaluated, 41.1% of children and teenagers present overweight and obesity in Argentina, a proportion of 20.7% and 20.4%, respectively, with no differences by socioeconomic level.³

The present findings at anthropometric level in the city of Rosario not just coincide with the Argentinian data from 2019, but present an increase in the prevalence of overweight and obesity in regard to the findings from four years ago.

The relationship between obesity and HTN in childhood has been widely documented in previous studies. In particular, the prevalence of HTN in children with overweight or obesity may reach between 27% and 47%, with BMI being considered one of the strongest determinant factors for elevated blood pressure in children and adolescents.^{21,22,23} These findings coincide with the results of this study.

Puberty also plays a role in BP regulation, as shown in this study with the correlation between SBP and girls that had already had their menarche. Changes in hormone regulation influence fat-free mass and sensitivity to insulin,

which may have an impact on BP levels.⁶ These findings coincide with previous studies that suggest that during puberty, the relationship between fat-free mass and blood pressure is altered, contributing to an increase in blood pressure in this stage. It is necessary to analyze whether percentile tables for blood pressure are appropriate for this type of patient, that chronologically is categorized as pediatric, but biologically could be considered closer to adulthood.

The highest prevalence of HTN in the south and southwest areas could be related to socioeconomic factors, which, according to literature, may influence on the development of HTN since an early age.^{24,25,26}

Strengths and limitations

This study has as strength the wide sampling from different areas of the city, which allows obtaining a representative view of the school population. Nonetheless, within the limitations, we find the cross-sectional nature of the study, which prevents establishing causality relationships; the only measurement of blood measurement, which could be biased by hyperreactivity or "white coat" effect, the lack of information on other variables such as family history, diet, level of physical activity and hours in front of screens, which may also influence on results.

Although sampling was by convenience, since only 2 schools were tested in each district, the number of surveyed individuals is very close to the number we should have to get a probabilistic sampling. It is known that in such type of sampling there could be a selection bias, but by having such a high number of patients and as results coincided with literature, these conclusions could be extrapolated to the whole population.

Clinical and public health repercussions

These results highlight the significance of developing health care policies that reinforce education on healthy habits, both nutritional by promoting consumption of food with a low content of ultra-processed food, and physical exercise, particularly during growing and developing in children and teenagers.²⁷

In this regard, the schools that provide food through state programs play a key role in promoting health. Improving the nutritional quality of the food provided and supplementing these initiatives with education in nutrition and physical activity is essential to fight obesity and HTN in this population. Regular monitoring of blood pressure in childhood is crucial, particularly in children with overweight or obesity, due to the high risk of developing HTN and cardiovascular diseases in adulthood. The schools, both public and private ones, should be spaces where self-care should be promoted since an early age, integrating the educational community in this process.

CONCLUSIONS

This study reveals a high prevalence of overweight, obesity and hypertension in children in school age in the city

of Rosario, which displays the need of intervening early to prevent cardiovascular complications in adulthood.

Obesity is one of the main risk factors of HTN in childhood; for this reason, children with overweight and obesity present up to four times more possibilities of developing hypertension in comparison with their counterparts with normal weight.^{20,25,28,29} This fact reinforces the need for preventive interventions addressed to reducing child obesity to decrease the prevalence of HTN and its consequences in the long term, as HTN in childhood is a known predictor of cardiovascular disease in adulthood, particularly when children are found in the highest percentiles of blood pressure.

It is essential for health and education sectors to work coordinately to develop programs promoting healthy life habits and to make regular controls in schools, enabling an early detection of risk factors.

Therefore, public policies combining health and education efforts are essential to generate a positive impact on childhood health, particularly in more vulnerable areas.

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Original Investigation Reports

Precarina: A new app to measure Cardiovascular Health Score in Children

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ABSTRACT

Introduction: in 2010, the American Heart Association (AHA) defined cardiovascular health (CVH) as a lifelong health promotion strategy. Inspired by the AHA's Essential 8th publication and the My Life Check application launched in 2022, our goal was to create an application (app) tailored to pediatric outpatient care aligned with Argentina's CVH consensus and promote cardiovascular prevention in children in Argentina and Latin America.

Materials and Methods: the app analyzes eight CVH components, including healthy behaviors (diet, physical activity, tobacco exposure, sleep) and health factors (body mass index, blood lipids, blood glucose, and blood pressure). Users must accept terms and conditions to download the app, ensuring security standards for iPhone and Android. The estimated CVH score serves as a guide and highlights the importance of regular evaluations.

Results: results show individual metric scores from 0 to 100, allowing focused progress tracking. The overall score, an unweighted average, aids in comprehensive evaluation. The app facilitated the identification of cardiovascular risk factors in children, promoting early and personalized interventions.

Conclusions: this accessible and free app facilitates the long-term evaluation and monitoring of children's CVH. Its widespread use will contribute valuable data and tools to promote healthy behaviors in public health initiatives, improving childhood CVH and preventing future diseases in Argentina and Latin America.

INTRODUCTION

Cardiovascular diseases (CVDs) are still the main cause of mortality and morbidity throughout the world, representing 32% of all deaths.¹ In Argentina, nearly 30% of deaths are related to CVD.²

Figures are still more concerning if the load of the disease is considered in early ages, as many cardiovascular risk factors (CVRF) develop since childhood (obesity, type 2 diabetes, hypertension and dyslipidemias), resulting in CVD in adulthood.³

Health literacy considers that health behaviors sustained at an early age become standard, preventing vascular compromise and its consequences.

It is essential to promote healthy habits from the family environment, such as a balanced diet, regular practice of physical activity and appropriate rest. This also entails educating about the importance of controlling blood pressure,

glucose and cholesterol levels, as well as explaining the need to carry out blood analyses for an initial screening.

Educational interventions are effective to improve health in children and teenagers, as a better communication in health may reduce the risk of CVD in the long run.⁴

Cardiovascular prevention in young adults is essential, as this group faces risks due to unhealthy behaviors (irresponsible alcohol consumption, smoking, sedentary lifestyle, poor diet habits and excessive weight gain). There is a considerable gap in the continuity of preventive strategies during adolescence into adulthood, increasing the risk of developing CVRFs. Closing this gap is essential, particularly promoting prevention practices since childhood and adolescence, which would enable transferring young adults with or without controlled risk factors, thus reducing their vulnerability to CVDs in the long run.^{5,6}

In August 2022, the American Heart Association (AHA) defined cardiovascular health as the promotion of health throughout life. Thus, they have released a free of charge application for adults, My Life Check™, based on the publication Life's Essential 8.^{7,8}

The components of Life's Essential 8 are divided into healthy behaviors (diet, physical activity, exposition to tobacco, and sleep) and health factors (body mass index, cholesterol levels, sugar levels in blood and blood pressure). These eight components are essential to maintain and improve cardiovascular health (CVH).

Mobile health (mHealth) is an emerging field, using mobile devices and apps for health interventions. Among more than 100,000 health apps, near 29,000 are focused on weight loss, offering solutions for obesity in comparison with traditional methods. Although mHealth technologies have shown to be promising in different populations, evidence of their effectiveness to manage obesity and increase physical activity in children and teenagers is variable.⁹

There are different applications focused on CVH in adults, which monitor CVRFs with the aim of helping with self-management.¹⁰ Personalized, educational and technology-based interventions are effective to prevent and manage CVRFs in young adults, in the promotion of healthy lifestyles, particularly in diet and exercise.

In children, the use of apps of physical activity and general wellbeing is promoted, which allows approaching risks before they manifest as diseases.⁹ In contrast, apps for adults seek to control and reduce CVRFs that have already affected CVH, focusing on the management of preexisting CVDs.

This difference in approach is key: while in children the aim is preventing problems from emerging, in adults the focus is on managing conditions already affecting health.

This concept has inspired numerous projects with a common goal: promoting cardiovascular health throughout life, starting since childhood.

PRECARINA, an innovative digital tool to evaluate CVH in children, measures the score facilitating CVRF monitoring and promoting the adoption of healthy habits.

In a context of international efforts to approach cardiovascular health in a comprehensive manner, the PRECARINA app is presented, developed from the definition proposed by the AHA.

GOALS

The AHA article motivated several sectors of the Hospital de Niños Dr. Ricardo Gutiérrez (Buenos Aires - Argentina) to:

1. Design an app for children and teenagers, PRECARINA (PREvención CARDiovascular INfantil Argentina [Cardiovascular Prevention in Children in Argentina]) to estimate the cardiovascular health score, addressed to the health care and educational systems, and the community.¹¹
2. Promoting Cardiovascular Prevention since childhood.

METHODOLOGY

PRECARINA estimates the CVH score according to the AHA guidelines, but adapted to the population of Argentina by local consensus. This estimation is made for individuals from 6 to 17 years, evaluating the established eight components.

Next, we present the components of Life's Essential 8 for children and teenagers. We suggest using it as a guide for patients and the community, promoting family and social health.

A. Healthy behaviors

1. Diet: healthy diet

Currently, the food environment presents a high offer and availability of food with high energy density and poor nutritional quality, with high contents of salt, sugar and fat, that have replaced the consumption of natural food that provides fibers, vitamins, minerals and nutrients beneficial for health. This modification in consumption patterns constitute an important risk for CVH.

The recommendations include daily consumption of: all food groups, 8 glasses of water, 5 portions of fruit and vegetables in a variety of types and colors, raw oil, dairy products (preferably with low fat content), lean meat, increase in the consumption of fish and including eggs, legumes, nuts and/or seeds. Furthermore, limiting the consumption of sugary drinks, salt, food high in sodium, fat and sugar; alcohol consumption. The guidelines that establish these recommendations for individuals and the general population are the GAPA (guías alimentarias para la población argentina [diet guidelines for the Argentinian population]), whose last issue is from 2018, and the DGA (Dietary Guidelines for Americans) 2020-2025.^{8,9}

In terms of diet, the questionnaire on diet habits adjusts the variables to follow according to gender and age group. It is the result of an adjustment of the DGA 2020-2025 publication, evaluating the diet component through scores (Healthy Eating Index - HEI), measuring the cardiovascular health of the pediatric and adult population. The score allows to estimate cardiovascular health in the pediatric population by a method of inquiry. For this reason, to make a more accurate diagnosis, a more detailed evaluation should be conducted on the risks for CVH.

On the other hand, caloric and nutritional needs from the USDA Dietary Guidelines for Americans 2020-2025 were taken as reference, as they are appropriate for the age range and the gender of individuals.^{12,13}

Finally, this task group acknowledges that there is no ideal method to evaluate all the food patterns, individually or in the population. But we emphasize that it is essential for professionals and health care systems to implement a periodical evaluation of dietary patterns, to monitor health in a wider way, and to intervene earlier and more effectively (*Tables 1 and 2*).

TABLE 1

Variables: domain, measurement method, quantifications and cardiovascular health score

DOMAIN	CV METRICS	MEASUREMENT METHOD	QUANTIFICATIONS AND CVH SCORE			
HEALTHY BEHAVIORS	DIET	Daily ingest reported of a healthy diet pattern, adapted to the cultural patterns of the national population (DGA 2020-2025)	Children of 6 to 18 years Score (individual): Points 100 (81-100) 80 (80-51) 50 (50-26) 25 (25-0) 0 See table of food portions by age group and gender (TABLE 2)			
			Diet pattern Healthy diet pattern Moderately healthy diet pattern Diet pattern poor in quality of nutrients Not healthy diet pattern Not healthy diet pattern			
			Points 100 90 80 60 40 20 0			
			Minutes/week ≥ 420 360-419 300-359 240-299 120-239 1-119 0			
	PHYSICAL ACTIVITY	Validated questionnaire of self-report according to WHO metrics criteria: minutes of physical activity per week in ages 6 to 18	Points 100 90 80 60 40 20 0			
			Minutes/week ≥ 420 360-419 300-359 240-299 120-239 1-119 0			
			Points 100 50 25 0 Note: subtract 20 points (unless the score is 0) for living with an active smoker in the house.			
			State Never tried it Tried any product with nicotine more than 30 days ago Habitual use of inhaled NDS Habitual use of combustible tobacco within 30 days			
	HEALTHY SLEEP	Score in hours according to age	Age Appropriate Inappropriate			
			6 to < 13 years 9-12 h <9 to >13 h			
			13-18 years 8-10 h <8 to >10 h			
HEALTHY FACTORS	BMI	Score according to percentile and Z score	NORMAL OVERWEIGHT OBESITY SEVERE OBESITY			
			< percentile 85 > 85th percentile and < 95th percentile > 97th percentile > 99th percentile			
			(Z SCORE <1) (Z SCORE OF 1 AND 2) (Z SCORE ≥2<3) (Z SCORE ≥3)			
	MEASUREMENT OF LIPID LEVELS IN BLOOD	Metrics in mg/dl	ACCEPTABLE LIMIT HIGH			
			Total choles ≥170 170-199 ≥200			
	FASTING BLOOD GLUCOSE AND GLYCOSYLATED HEMOGLOBIN (HbA1c)	Métrica en mg/dl	NORMAL PRE-DIABETES DIABETES			
			Fasting blood glucose HbA1c			
			≤ 100 mg/dl ≤ 5.7%			
			≥ 100 and < 126 mg/dl ≥5.7% to <6.5%			
	BLOOD PRESSURE	SBP and DBP by auscultatory method (mmHg)	According to BP percentiles up to 16 years of age; older than 16 years by fixed values according to the current guidelines in Argentina.			
			LEVEL			
			100 75 50 25 0			
			NORMAL PRESSURE (less than 90th percentile or for teenagers older than 16 years systolic BP < 130 mmHg and diastolic <85 mmHg) HIGH PRESSURE OR PRE-HYPERTENSION (systolic and/or diastolic BP ≥P90 and <P95 for age, gender and height or for teenagers older than 16 years systolic BP between 130-139 mmHg and/or diastolic between 85-89 mmHg) STAGE 1 HYPERTENSION (systolic and/or diastolic BP ≥ P95 and <P95 + 12 mmHg for age, gender and height or for teenagers older than 16 years systolic BP between 140-159 mmHg and/or diastolic 90-99 mmHg) STAGE 2 HYPERTENSION (≥P95 + 12 mmHg for age, gender and height or for teenagers older than 16 years systolic BP 160-179 mmHg and/or diastolic 100-109 mmHg) For adolescents older than 16 years systolic BP ≥180 and/or diastolic ≥110 mmHg.			

2. Physical activity: more participation

An Argentinian study offers a reliable evaluation on the levels of physical activity (minutes per week).¹⁴ PRE-CARINA implements the questionnaire and improves it by adding an additional question on sedentary activities, as an extended time in front of screens (Table 1).

3. Exposition to nicotine: prevent it

Smoking constitutes a preventable pandemic. Infants

and small children are those most affected by the time of involuntary exposition in their homes.¹⁵

Besides cardiovascular consequences, prenatal exposition generates in descendants a decreased pulmonary function, repeated pulmonary infections, bronchial hyperresponsiveness, chronic obstructive pulmonary disease and cancer in adulthood.^{16,17}

Exposition to secondhand smoke (SHS) in childhood is associated to left ventricular diastolic dysfunction, increase

TABLE 2

Combined table with portions of daily and weekly food, by age range for children: score

Food	Girls 1200 kcal (6- 8 years)	Girls 1600 kcal (9-13 years)	Girls 1800 kcal (14-18 years)	Boys 1400 kcal (5-8 years)	Boys 1800 kcal (9-13 years)	Boys 2200 kcal (14-18 years)	Score
Calories	1200 kcal	1600 kcal	1800 kcal	1400 kcal	1800 kcal	2200 kcal	
Green vegetables	1 serving per week	1 and 1/2 serving per week	1 and 1/2 serving per week	1 serving per week	1 and 1/2 serving per week	2 servings per week	2
Green vegetables	1/2 serving per week	1 serving per week	1 serving per week	1/2 serving per week	1 serving per week	1 serving per week	1
Green vegetables	< 1/2 serving per week	< 1 serving per week	< 1 serving per week	< 1/2 serving per week	< 1 serving per week	< 1 serving per week	0
Red/orange vegetables	3 servings per week or 1 small unit per day	4 servings per week	5 servings per week	3 servings per week or 1 small unit per day	5 1/2 servings per week or 1 medium unit per day or 3/4 serving per day	1/2 cooked serving per day or 3/4 raw serving per day or 6 medium units per week	2
Red/orange vegetables	1 serving per week	2 servings per week	3 servings per week	1 and 1/2 servings per week or 1 small unit every other day	3 servings per week or 1 small unit per day or 1/3 serving per day	1/4 cooked serving per day or 1/2 raw serving per day or 3 medium units per week	1
Red/orange vegetables	< 1 serving per week	< 2 servings per week	< 3 servings per week	< 1 and 1/2 serving per week or < 1 small unit every other day	< 3 servings per week or < 1 unit per day or < 1/3 serving per day	< 1/4 cooked serving per day or < 1/2 raw serving per day or < 3 medium units per week	0
Legumes	1/2 serving per week or 2 small patties per week	1 serving per week or 1/2 serving + 1 patty per week	1 1/2 serving per week or 1 serving + 1 patty per week	1/2 serving per week or 1/4 serving + 1 patty per week	1 1/2 serving per week or 1/2 serving 3 times per week or 1 patty per day	2 servings per week or 1 serving + 2 patties per week	2
Legumes	1/4 serving per week or 1 small patty per week	1/2 serving per week or 1/4 serving + 1 patty per week	1 serving per week or 1/2 serving + 1 patty per week	1/4 serving per week or 1 small patty per week	1 serving per week or 1/2 serving per week or 1 patty 3 times per week	1 serving per week or 1/2 serving + 1 patty per week	1
Legumes	< 1/4 serving per week or < 1 small patty per week	< 1/2 serving per week or < 1/4 serving + 1 patty per week	< 1 serving per week or < 1/2 serving + 1 patty per week	< 1/4 serving per week or < 1 small patty per week	< 1 serving per week or < 1/2 serving per week or < 1 patty 3 times per week	< 1 serving per week or < 1/2 serving + 1 patty per week	0
Tubers (potato, sweet potato, cassava)	1/2 small unit per day or 1/4 serving per day or 3 small units per week	1/3 serving per day or up to 3 medium units per week	1/2 serving per day or up to 5 small units per week	1/2 small unit per day or 1/4 serving per day or 3 small units per week	1 small unit per day or 3 medium units per week or 1/3 serving per day	Up to 6 small units per week or 3 large units per week or 1/2 serving per day	2
Tubers (potato, sweet potato, cassava)	1 small unit per day or 1/2 serving per day or 3 medium units per week	1/2 serving or up to 5 small units per week	3/4 serving per day or small unit every day	1 small unit per day or 1/2 serving per day or 3 medium units per week	1 medium unit per day or 3 large units per week or 3/4 serving per day	Up to 9 units per week or 5 large units per week or 1 serving per day	1
Tubers (potato, sweet potato, cassava)	> 1 small unit per day or > 1/2 serving per day or > 3 medium units per week	> 1/2 serving or > 5 small units per week	> 3/4 serving per day or small unit every day	> 1 small unit per day or > 1/2 serving per day or > 3 medium units per week	> 1 medium unit per day or > 3 large units per week or > 3/4 serving per day	> 9 units per week or > 5 large units per week or > 1 serving per day	0
Other vegetables	3 medium units per week or 1/3 raw serving per day or 1/4 cooked serving per day	4 medium units per week or 1/2 raw serving per day or 1/4 cooked serving per day	5 medium units per week or 1/2 raw serving per day or 1/4 cooked serving per day	3 medium units per week or 1/3 raw serving or 1/4 cooked serving	5 medium units per week or 1/2 raw serving per day or 1/4 cooked serving per day	1 medium unit per day or 3/4 raw serving per day or 1/2 cooked serving per day	2
Other vegetables	1 medium unit per week or 1/4 raw serving per day or 1/4 cooked serving 4 times per week	2 medium units per week or 1/4 serving per day	2 1/2 medium units per week or 1/3 raw serving per day or 1/4 cooked serving	1 medium unit per week or 1/4 raw serving per day or 1/4 serving 4 times per week	2 1/2 medium units per week or 1/3 raw serving per day or 1/4 cooked serving	1 small unit per day or 1/2 raw serving per day or 1/4 cooked serving per day	1
Other vegetables	< 1 medium unit per week or < 1/4 raw serving per day or < 1/4 cooked serving 4 times per week	< 2 medium units per week or 1/4 serving per day	< 2 1/2 medium units per week or 1/3 raw serving per day or 1/4 cooked serving	< 1 medium unit per week or 1/4 raw serving per day or 1/4 serving 4 times per week	< 2 1/2 medium units per week or < 1/3 raw serving per day or < 1/4 cooked serving	< 1 small unit per day or 1/2 raw serving per day or 1/4 cooked serving per day	0

Food	Girls 1200 kcal (6- 8 years)	Girls 1600 kcal (9-13 years)	Girls 1800 kcal (14-18 years)	Boys 1400 kcal (5-8 years)	Boys 1800 kcal (9-13 years)	Boys 2200 kcal (14-18 years)	Score
Fruits	1 medium unit per day or 2 small units per day	1 1/2 large unit per day or 2 medium units per day	1 1/2 large unit per day or 2 medium units per day	2 medium units per day	1 1/2 large unit per day or 2 medium units per day or 3 small units	2 large units per day or 4 small units per day	2
Fruits	1 small unit per day	1 medium unit per day	1 medium unit per day	1 medium unit per day	1 medium unit per day or 2 small units	1 large unit per day or 2 small units per day	1
Fruits	< 1 small unit per day	< 1 small unit per day	< 1 medium unit per day	< 1 medium unit per day	< 1 medium unit per day or < 2 small units per day	< 1 large unit per day or 2 small units per day	0
Bread	1 slice of bread or 1 mini bread or 3 crackers	Up to 2 slices of bread per day or 2 mini bread units or 6 crackers	Up to 2 slices of bread per day or 2 mini bread units or 6 crackers	Up to 1 slice of bread per day or 1 mini bread per day	Up to 2 slices of bread per day or 2 mini bread units per day	3 slices per day or 2 mini bread units	2
Bread	2 slices of bread or 2 mini bread units or 6 crackers	3 slices of bread per day or 3 mini bread units or 9 crackers	3 slices of bread per day or 3 mini bread units or 9 crackers	2 slices per day or 2 mini bread units per day	3 slices of bread per day or 3 mini bread units per day	6 slices per day or 4 mini bread units or 2 small baguettes	1
Bread	> 2 slices of bread or > 2 mini bread units or > 6 crackers	> 3 slices of bread per day or > 3 mini bread units or > 9 crackers	> 3 slices of bread per day or > 3 mini bread units or > 9 crackers	> 2 slices per day or > 2 mini bread units per day	> 3 slices of bread per day or > 3 mini bread units per day	> 6 slices per day or > 4 mini bread units or > 2 small baguettes	0
Pasta and whole wheat dough: pizza, savory pie, empanada, cannelloni, tortilla.	1/4 serving per day or 1 portion of dough per day	1/4 serving per day of whole wheat dough or 1 portion of dough	1/2 serving per day of dough or 2 portions of dough per day	1/4 serving per day of whole wheat dough or 1 portion of dough per day	1/4 serving per day of whole wheat dough or 1 portion of dough	1/2 serving per day of whole wheat dough or 1 and 1/2 portions of dough per day	2
Pasta and whole wheat dough: pizza, savory pie, empanada, cannelloni, tortilla.	1/2 serving per day or 2 portions of dough per day	1/2 serving per day or 2 portions of dough	3/4 serving per day or 2 portions of dough per day	1/2 serving per day or 2 portions of dough per day	1/2 serving per day or 2 portions of dough	1 serving per day or 3 portions of dough per day	1
Pasta and whole wheat dough: pizza, savory pie, empanada, cannelloni, tortilla.	> 1/2 serving per day or > 2 portions of dough per day	> 1/2 serving per day or > 2 portions of dough	> 3/4 serving per day or > 2 portions per day	> 1/2 serving per day or > 2 portions per day	> 1/2 serving per day or > 2 portions per day	> 1 serving per day or 3 portions of dough per day	0
Refined doughs (non-whole wheat)	1/4 serving per day or 1 portion of dough per day	1/4 serving per day of whole wheat dough or 1 portion of dough	1/2 serving per day or 2 portions of dough per day	1/4 serving per day of whole wheat dough or 1 portion of dough per day	1/4 serving per day of whole wheat dough or 1 portion of dough	1/2 serving per day of whole wheat dough or 1 y 1/2 portions of dough per day	2
Refined doughs (non-whole wheat)	1/2 serving per day or 2 portions of dough	1/2 serving per day or 2 portions of dough	3/4 serving per day or 3 portions of dough per day	1/2 serving per day or 2 portions of dough per day	1/2 serving per day or 2 portions of dough	1 serving per day or 3 portions of dough per day	1
Refined doughs (non-whole wheat)	> 1/2 serving per day or > 2 portions of dough per day	> 1/2 serving per day or > 2 portions of dough per day	> 3/4 serving per day or > 3 portions of dough per day	> 1/2 serving per day or > 2 portions of dough per day	> 1/2 serving per day or > 2 portions per day	> 1 serving per day or 3 portions of dough per day	0
Dairy products (milk, yogurt) partially skimmed	3/4 mugs per day or 2 teacups per day	2 teacups	2 mugs per day	3/4 mugs per day or 2 teacups per day	2 mugs	2 mugs	2
Dairy products (milk, yogurt) partially skimmed	1/2 mug per day or 1 teacup per day	1 teacup per day	1 mug per day	1/2 mug or 1 teacup per day	1 mug	1 mug	1
Dairy products (milk, yogurt) partially skimmed	< 1/2 mug per day or < 1 teacup per day	< 1 teacup per day	< 1 mug per day	< 1/2 mug or < 1 teacup	> 1 mug	> 1 mug	0
Partly skimmed, spreadable or semi-soft cheese (port salut, mozzarella)	1 portion of the size of a matchbox or the size of 1/2 card or 2 spoons	1 portion of the size of a matchbox or the size of 1/2 card or 2 spoons per day	1 portion of the size of a matchbox or the size of 1/2 card or 2 spoons per day	1 portion of a matchbox or 1/2 card or 2 spoons	1 portion of a matchbox or 1/2 card or 2 spoons per day	1 portion of a matchbox or 1/2 card or 2 spoons	2

[illegible]

in the size of the left atrium, dyslipidemia and thrombosis. These conditions may contribute to the development of atherosclerosis, CAD, heart failure, peripheral artery disease, dementia and stroke, particularly in middle-aged men.^{16,17}

These effects highlight the significance of protecting children from SHS, consumption from an early age and during pregnancy, to prevent cardiovascular complications throughout their lives.^{16,17}

The AHA recommends subtracting 20 points in children and adults exposed to SHS indoors, given its potential effects in the long term on cardiopulmonary health.¹⁸

The score-metrics are related to the following variables:

- Use of combustible smoke or inhaled nicotine-delivery system (NDS): electronic cigarettes or vaping devices.
- Use of NDS at any age (according to the doctor's judgement) (*Table 1*).

4. Healthy sleep

PRECARINA uses the age of patients to generate a score aligned with the last scientific consensus on the optimal durations of sleep according to age. This function ensures for the app to deliver personalized recommendations for the appropriate times of sleep according with the current scientific knowledge (*Table 1*).^{15,16,17,18}

B. Health factors

1. Body mass index: healthy weight

Body mass index (BMI) or the relationship between weight and height is the universally applicable practical indicator, also noninvasive, to identify overweight and obesity. In children and teenagers, percentile tables are used to define overweight (>85th percentile and <95th percentile), obesity (>95th percentile) and severe obesity (>99th percentile). PRECARINA trains an automatic learning model with data from the World Health Organization and the National Health Center to estimate the BMI percentile (*Table 1*).¹⁹

2. Lipid levels in blood-cholesterol: healthy levels

Childhood dyslipidemia is a significant concern, as it persists in adult age and is useful as a risk indicator for the development of atherosclerosis. An accurate evaluation of lipid profiles is essential for an effective management and prevention of CVDs. In obesity, there is an increase in triglycerides levels, low HDL cholesterol and mild increase in LDL cholesterol.²⁰

Unlike what was suggested by the AHA, measurement of non-HDL cholesterol was not included, taking as reference only the value of total cholesterol. However, in the case of detecting a high value, it is necessary to measure all lipid fractions, particularly non-HDL, representing the atherogenic fraction of cholesterol.

For this reason, we highlight the importance of making an initial screening in primary care, supplementing it with a complete lipid profile if there are alterations in the basic tests or family history of dyslipidemias.

All lipid measurements provided by PRECARINA are presented in milligrams by deciliter (mg/dl) (*Table 1*).

3. Glucose in blood-diabetes: healthy levels

Fasting blood glucose and glycosylated hemoglobin measurement should be included in the initial screening to detect alterations that may lead to the development of diabetes. The highest the values, the worse the metabolic control.^{21,22}

All glucose measurements provided by PRECARINA are presented in milligrams per deciliter (mg/dl). Glycosylated hemoglobin measurements are presented in percentages (*Table 1*).

4. Blood pressure: healthy levels

Blood pressure measurements in pediatrics according to the current guidelines in Argentina are considered as values recorded by appropriate technique and size cuffs (inflation bulb covering 2/3 of the arm's diameter and 2/3 of its length). The correct technique is with the patient resting and calm: three measurements should be made and they should be averaged, preferably with the auscultatory technique and aneroid measurement.

For an appropriate use of the app, in the case of having recordings above the 90th percentile, the values to be entered should be 3 averages made in different consultations, with 3 measurements made per consultation.

Metrics:

percentiles of systolic and diastolic pressure (mmHg) for age, gender and size up to 16 years. For an age of more than 16 years, tables with adult values are used.

Variables are based on interpretation guidelines and new reference tables of blood pressure for children and teenagers of the National Program of School Health (PROSANE), on the joint Consensus on cardiovascular prevention in childhood and adolescence of the Argentine Society of Cardiology and the Argentine Society of Pediatrics and on the joint consensus on Hypertension of the Argentine Society of Cardiology, the Argentine Federation of Cardiology and the Argentine Society of Hypertension.^{23,24,25}

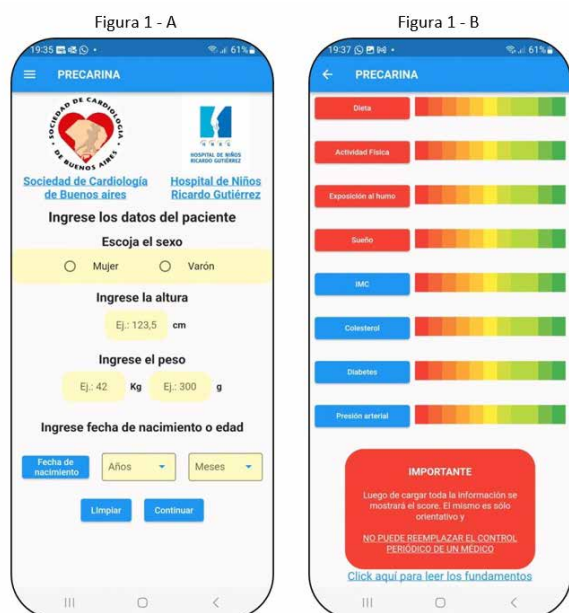
The scores for each variable are made following the opinion of the AHA experts in the article Life's Essential 8.

To simplify the tasks of physicians and reduce potential human error, PRECARINA adds tables of blood pressure directly in its interface, including tables integrated by ages that go from 6 to 17 years, for both genders.

Categories:

Normal, normal high, hypertension stage 1, hypertension stage 2, hypertension stage 3. The scores are adjusted in the case of receiving antihypertensive medication (*Table 1*).

The app estimates and defines by means of Artificial Intelligence trained according to age, gender and height.

**FIGURE 1.**

1A: Load of gender, weight, height and age or date of birth.
1B: Score estimation for healthy factors and behaviors.

RESULTS

PRECARINA can be downloaded for free from the Play Store (Android) and the App Store (iPhone). See link and QR download code at the end of the text.

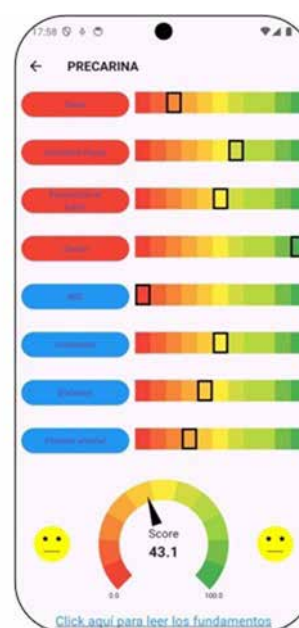
Users should accept the terms and conditions. The app meets the security standards of iPhone/Android.

It is backed by the Hospital de Niños Dr. Ricardo Gutiérrez, Buenos Aires, Argentina, the Society of Cardiology of Buenos Aires and the Argentine Federation of Cardiology.

1. The initial screen is for entering the patient's data, used in several estimations.
 - a. Age: in years and months, or according to birthdate.
 - b. BMI: estimation and percentile by artificial intelligence, trained according to age, gender, and height.
 - c. Blood pressure: according to age, gender and height.
 - d. It has an outline with colors that correlate with the percentiles for each variable in terms of age and gender.
 - e. The CVH score is visualized according to a color metrics that range from 0 (red) to 100 (green). Each metrics maintains a score between 0 and 100, which allows focusing on the time to see a particular progress.
2. The application generates a new score that also ranges from 0 to 100 points, and it is an unweighted average of all metrics (health tank): the general score of CVH.

How to use the app?

1. First screen: enter gender, weight, height and age or date of birth. Anonymous data (Figure 1A).
2. Second screen: each item should be chosen and the questions should be answered (Figure 1B). A score will be pro-

**FIGURE 2.**

CVH score (black rectangle) in the color scale. The addition of the score of the 8 items yields the final score value (tank). This example has a CVH score of 45.9 and is in yellow/red, so it is not good. The individual should improve their diet, sleep, BMI and blood pressure to reach the ideal score and avoid cardiovascular disease in the future.

vided, represented as a black rectangle in the color scale. The score addition of the 8 items yields the final score value (Figure 2).

3. The score ranges from 0 to 100. Green is the healthiest, close to a score of 100, and red represents a very unhealthy scenario, close to a score of 0.

Figure 2 shows an example of how to represent CVH with PRECARINA. The indicator in the inferior part reflects the general cardiovascular health score (general score), from 0 to 100, showing the highest scores in green at the right (a "tank" full of CVH). The general score is estimated as the unweighted average of the scores from the 8 metrics. The situation of an individual in each of the 8 metrics is presented in the upper part as the Individual Score, allowing to identify healthy behaviors and risk factors to focus on.

DISCUSSION

Cardiovascular prevention in childhood is crucial to approach the growing indices of CVD in the adult population. Adopting healthy habits since an early age not just reduces the risk of developing cardiovascular conditions, but also encourages integral wellbeing. It is essential to identify and modify risk factors in children and teenagers, as well as involving families and the community in prevention strategies.

These strategies should be translated to young adults as well. Training pediatricians and specialists on cardiovascular prevention is key to raise awareness in health care teams, teachers, parents and organizations on the importance of

this problem, including teenagers and pregnant adults, given its impact on the cardiovascular health of fetuses.

In this scenario, mobile applications and specific programs play a key role in the early modification of risk behaviors, particularly in childhood and adolescence, where interventions are essential.⁴

There are different projects focused on promoting CVH throughout life, aligned with the definition established by the AHA. The application My Life Check™ is a tool for adults, free of charge, based on the concept of the Essential 8.⁸

The AHA also defines Life's Essential 8 for children and teenagers, promoting healthy habits from the home. This guide offers clear information about eight key elements, facilitating conversations on the health of children, and involving them in decisions that would favor personal and family wellbeing.

The aim of this project was developing a program addressed to children/adolescents and their environments with the aim of improving cardiovascular prevention, in agreement with international initiatives.

It is designed for pediatricians, specialists in adolescent medicine, teachers, parents and the community in general, both in Argentina and Latin America. It is based on the publication Life Essential 8, and on the application My Life Check, adapting these resources to a tool specific for the ambulatory care of children and teenagers, according to the local consensus on CVH.

The app analyzes the eight components, estimating the CVH score with a detailed view of progress, facilitating the identification of improvement areas and the implementation of personalized interventions.

Obtaining a CVH score since childhood is essential to prevent CVD and to facilitate the transition of teenagers with CVRFs to an adult cardiologist. It is crucial to ensure a proper transference, since the age group of young adults with cardiovascular risk often lacks an adequate diagnosis and follow-up. The absence of specialized care in this stage can lead to inefficient control of CVRFs, which increases the risk of developing severe CVDs in the future. This highlights the importance of a continuous approach to cardiovascular health throughout life.²⁶

A prevention app for adults is based on behavior change theories and scientific evidence, increasing awareness on risks and motivating changes in lifestyle. User tests improve the experience by identifying errors and adding functions.¹⁰

This childhood cardiovascular prevention app encourages the active participation of users in the identification and correction of errors in their lifestyle, besides optimizing the platform to promote healthy habits that would prevent diseases and favor a better general health state.

Childhood CVH score is a guide for parents, carers and professionals, allowing a monitoring of progress by metrics from 0 to 100, and a general understandable evaluation.

The My Life Check™ application is a tool for the evaluation of health and wellbeing, based on the concept of the Essential 8. It can be accessed for free, going to: [heart.org/MyLifeCheck](https://www.heart.org/-/media/Healthy-Living-Files/Well-being-Works-Better/my_life_check_brochure.pdf), through the platform Well-being Works Better™ of the AHA (https://www.heart.org/-/media/Healthy-Living-Files/Well-being-Works-Better/my_life_check_brochure.pdf).

Unlike My Life Check, which is focused on adults, this app is adapted to the specific needs of children and teenagers.

Although there are similarities between both applications, there are also noticeable differences that are analyzed below.

Similarities

- Both promote cardiovascular health and offer a comprehensive evaluation.
- They allow for progress monitoring with scores from 0 to 100.
- They are designed to be accessible and easy to use: My Life Check presents a language and design more addressed to adults. PRECARINA has a friendly, colorful and interactive interface to attract and maintain the attention of children and adolescents.

Differences

- Register: My Life Check requires opening a session: PRECARINA doesn't.
- Interface: My Life Check has 4 folders; PRECARINA 8.
- Metrics and evaluation of wellbeing: PRECARINA does not offer this function, but should consider individuals in a family and social environment, if there is discrimination or bullying due to ethnicity or physical condition, empowering to define themselves as healthy or not so, physically and psychologically.
- BMI estimation: different metrics. PRECARINA uses kilos, grams, meters and centimeters, and percentiles by age and gender.
- Score visualization: PRECARINA uses a color system, with emoticons; My Life Check only shows the final score.
- My Life Check offers links to information about CVD, advice on healthy lifestyle and access to support programs. PRECARINA provides guidance to parents or tutors to promote healthy habits, as well as educational resources adapted to childhood understanding and development.

In brief, PRECARINA adapts specifically to children and teenagers, focused on early prevention to improve CVH, while My Life Check is addressed to adults with and without CVH.

Although both apps share the goal of promoting CVH, they have differences in terms of functionality and focus, adapting to the specific needs of their respective users.

Initially, a plan of action was established for the next steps of the PRECARINA app, focusing on ensuring its dis-

semination and effective use. Later, a protocol will be implemented to guarantee anonymous data gathering and the necessary authorization to use them in research and statistical studies. This will enable obtaining valuable information to assess cardiovascular risk at population level.

Additionally, a final report will be generated, which users may save in an appropriate format. This report will include tables with curves that would show the evolution of the cardiovascular health score of each patient over time. This functionality will be useful so that individuals may visualize their progress and perform adjustments to their lifestyle so as to improve their CVH.

Currently, the app has not been validated yet. To carry out this validation, it is necessary to implement a series of stages, including dissemination and use of the app in the target population. Using PRECARINA will allow to detect and correct possible errors in the platform, improving its performance and results. Data gathering from users is a necessity to analyze the effectiveness of the app, and its impact on childhood CVH. This procedure is essential for validation, ensuring that the tool is reliable and useful in cardiovascular risk evaluation in the child and adolescent population.

Although wider studies are required to validate its efficacy, PRECARINA would fulfill its mission by identifying and correcting habits leading to CVD. Its score system enables users to improve their CVH by promoting positive changes in their lifestyle.

The tests on the effectiveness of mobile apps in childhood health are limited, but their accessibility is key in scenarios of low resources and low attendance to health care centers, offering personalized interventions for primordial and primary prevention of cardiovascular diseases.

CONCLUSIONS

The AHA defines CVH as a lifetime approach. PRECARINA estimates the score of cardiovascular health in agreement with international standards and Argentinian consensuses. It differentiates due to its focus on the pediatric and adolescent population, as well as due to its wide accessibility. The application promotes healthy habits and provides guidance, not substituting the professional medical evaluation.

The authors consider that its implementation will be key for cardiovascular prevention in children and teenagers, providing valuable tools and data for public health in Argentina and Latin America.

Link and QR download code of the 2.1.0 version (build 18) for Android and IOS

<https://play.google.com/store/apps/details?id=ar.net.grasso.precarina>



<https://apps.apple.com/us/app/precarina/id6451156229>



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Original Investigation Reports

Assessment of HARMS2-AF for risk stratification: a 10-year follow-up study (2014–2024) in a northwestern Colombian population

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Introduction: Atrial fibrillation (AF) is the most prevalent arrhythmia worldwide and represents a significant public health burden. Several modifiable risk factors (RFs) — such as hypertension, obesity, smoking, alcohol consumption, sleep apnea, and physical inactivity — contribute to its development. However, their combined effect has not been thoroughly assessed in Latin American populations.

Objective: to develop and validate the HARMS2-AF model to predict AF risk based on modifiable RFs, assessing its applicability in primary care settings.

Materials and Methods: an observational retrospective cohort study was conducted with 2,482 participants from Northwestern Colombia, followed over 10 years. RFs evaluated included hypertension, obesity (BMI ≥ 30 kg/m²), smoking, alcohol consumption (≥ 15 standard drinks/week), sleep apnea, physical inactivity, diabetes mellitus, age, and sex. Cox proportional hazards regression models (univariate and multivariate) were used to generate HARMS2-AF scores based on beta coefficients. Model performance was assessed using the area under the receiver operating characteristic curve (AUC) and calibration tests.

Results: hypertension was the most prevalent RF (79.1%) and the strongest predictor of AF (HR 4.0; 95% CI: 3.2–4.8). Obesity, high alcohol intake, smoking, and sleep apnea were also significantly associated with AF. Physical inactivity and diabetes mellitus did not reach statistical significance in multivariate analysis. The HARMS2-AF model showed a two-fold increase in AF risk per 1-point increment (HR 2.38; 95% CI: 2.14–2.62), with an AUC of 0.81.

Conclusion: the HARMS2-AF model is a simple and effective tool for predicting AF risk based on modifiable RFs. Its implementation in primary care could enhance early identification and targeted prevention strategies in Latin American populations.

INTRODUCTION

Atrial fibrillation (AF) is the most prevalent arrhythmia at world level, representing a significant challenge in terms of clinical and economic load.¹ Historically, AF has been closely related with traditional risk factors, many of which are partially modifiable or nonmodifiable, such as hypertension, diabetes mellitus and heart failure. However, advancements in therapeutic strategies, such as catheter ablation and thromboembolic risk prevention with new oral anticoagulants, have substantially improved AF treatment and outcome.

More recently, factors related with lifestyle have been identified as the “fourth pillar” in AF treatment, highlighting their modifiable potential as an opportunity for early directed interventions.² Among the modifiable risk factors of AF we have obesity, sleep apnea, alcohol consumption and smoking. The specific interventions about these factors have shown a significant reduction in the incidence

and recurrence of AF. For instance, a clinical study showed that the reduction or abstinence of alcohol consumption substantially decreased the incidence of AF.³ Moreover, clinics focused on risk factor modification have promoted strategies such as weight loss, increase in physical activity and control of cardiovascular risk factors, with positive effects on the secondary prevention of AF, particularly after ablation.^{4,5}

Nevertheless, it hasn't been determined yet to what extent each lifestyle factor contributes to the individual risk of developing AF, nor how the coexistence of multiple modifiable factors affects this risk.⁶ Although risk prediction models for AF detection in the general population are used increasingly, these are predominantly focused on traditional factors, mainly nonmodifiable ones, leaving a significant gap in the inclusion of lifestyle factors.^{7,8,9,10}

In this study, we aim to evaluate the usefulness of the HARMS2-AF score, a tool previously developed and vali-

dated by Segan et al (2023), integrating modifiable risk factors into AF prediction. Through a retrospective analysis of a north-western cohort of Colombia, we attempted to determine its applicability in a Latin American environment, and to explore its value to identify individuals in higher risk of AF, facilitating personalized interventions for prevention.

MATERIALS AND METHODS

Design of the study and population context

This is a retrospective, observational and cohort study, designed to evaluate the applicability of the HARMS2-AF score in a north-western cohort of Colombia, followed over a period of 10 years (2014-2024). The participants belong to an institutional program of cardiovascular prevention, with regular medical care and digitized clinical records within a network of centers that allow obtaining most clinical events.

Data sources

Data were extracted from institutional electronic clinical histories, including socio-demographic variables, medical history, diagnoses codified by ICD-10, laboratory test results and clinical course documented by family doctors and specialists.

Eligibility criteria

- Inclusion:
 - o Patients ≥18 years at the time of admission.
 - o Members of the cardiovascular prevention program with active follow-up for at least 12 months.
 - o Availability of complete clinical information for the estimation of the HARMS2-AF score.
 - o With no previous diagnosis of atrial fibrillation.
- Exclusion:
 - o Diagnosis of atrial fibrillation before admission.
 - o Incomplete clinical records or essential information missing.
 - o Less than one year of follow-up.

Evaluation of predictors

The risk factors included in the model were: smoking, alcohol consumption, physical inactivity, body mass index (BMI), sleep apnea, type 2 diabetes mellitus, hypertension, age and sex.

- Modifiable factors:
 - o *Smoking*: classified as current, previous or non-smoker.
 - o *Alcohol consumption*: low (≤standard drinks/week), moderate (7-14) and high (≥15).
 - o *Physical inactivity*: defined as <600 MET-min/week, according to IPAQ.
 - o *BMI*: obesity defined as ≥30 kg/m2.
- Non-modifiable factors:
 - o *Age*: <60 years (0 points), 60-64 (1 point), ≥65 (2 points).
 - o *Male gender*: 1 point.

TABLE 1.
HARMS2-AF score criteria.

Criterion	Score
Hypertension	4 points
Age 60–64 years	1 point
Age ≥65 years	2 points
BMI ≥30 kg/m²	1 point
Male gender	1 point
Sleep apnea	1 point
Smoking	1 point
Alcohol consumption (7–14/week)	1 point
alcohol consumption (≥15/week)	2 points

TABLE 2.
Main comorbidities of patients included in the study.

Variable	N values
Hypertension	1963 / 2482
Diabetes mellitus not requiring insulin	751 / 2482
Diabetes mellitus requiring insulin	178 / 2482
Abdominal obesity	458 / 2482
Hypercholesterolemia, low HDL	680 / 2482
Chronic obstructive pulmonary disease	100 / 2482
Hypertriglyceridemia	502 / 2482
Sleep apnea	189 / 2482
Smoking	457 / 2482
Alcohol consumption between 7-14	385 / 2482
Alcohol consumption of more than 15	203 / 2482

- Comorbidities:
 - o *Hypertension, type 2 diabetes and sleep apnea*: diagnosed by clinical history, pharmacological treatment or ICD-10 codes.
 - o *ICD-10 codes used*:
 - AF: I48.x
 - Hypertension: I10–I15
 - Type 2 diabetes: E11.x
 - Sleep apnea: G47.3.

Evaluation of results

The primary outcome was the time until the first diagnosis of atrial fibrillation, defined as:

- Event documented in institutional medical records.
- Codification with ICD-10: I48.x
- Diagnosis confirmed by attending physician or specialist.

Statistical analysis

- Continuous variables are described as mean±standard deviation or median (IQR), according to distribution. Categorical variables are expressed in absolute frequencies and percentages.

- Univariate Cox regression analysis was used to explore individual associations.
- The variables with statistical significance ($p < 0.05$) were included into a multivariate model to assess independent predictors of AF.
- Beta coefficients of the multivariate model were not recalibrated; the original HARMS2-AF structure was used.

Risk stratification

- Low risk: 1-4 points
- Intermediate risk: 5-9 points
- High risk: 10-14 points.

Model validation

The model was evaluated by:

- Area under the ROC curve (AUC) for a 10-year discrimination.
- Calibration curves comparing observed vs expected events.
- Hazard ratio (HR) estimation for each additional point in the score.

Ethical considerations

This study was approved by the Institutional Ethics Committee. It was guaranteed that all principles of the Declaration of Helsinki were met, as well as the national regulations on biomedical investigation.

RESULTS

Sociodemographic characterization

The population studied was made up by 2482 patients, with a predominant distribution of the female gender (1369 patients, 55.2%) in comparison with the male gender (1113 patients, 44.8%). The average age of the participants was 67.9 years, reflecting a mainly adult and advanced age population.

As to access to specialized health services, 5.4% of patients (135/2482) received a psychological assessment, while most, 84.9% (2109/2482) had access to a nutritional evaluation. Besides, 28.3% of patients (702/2482) received odontological care.

The incidence of AF was lower in patients with high therapeutic adherence, with a HR of 1.86 (95% CI: 1.62-2.15) in comparison with those with low adherence.

These data reflect both the sociodemographic characteristics and the pattern of access to health care services of the population included in the study, offering an initial view on the scenario within which the rest of the clinical evaluations were carried out.

In *Table 3*, the data corresponding to adherence, degree of control and means of the values of lipid profile, renal function and glucose of patients are presented.

The mean time until the first event of AF was 4.8 years ($SD \pm 2.1$), with a median of 4.6 years (IQR: 3.2-6.3), displaying a gradual progression of risk in this cohort, showing

TABLE 3.

Adherence, degree of control, means of lipid profile, glucose and renal function of patients.

Variable	Value
Patients with good therapeutic adherence	1205 (48.5%)
Patients with appropriate control	1104 (44.5%)
Total cholesterol (mg/dl)	197.48
HDL (mg/dl)	40.86
LDL (mg/dl)	135.72
TRIGLYCERIDES (MG/DL)	205.85
Fasting glucose (mg/dl)	108.3
HBA1C (%)	6.8
GFR test (ml/min/1.73 m ²)	72.5

a significant increase in risk of AF per each point increase in the general HARMS2-AF score [HR 2.38 (95% CI: 2.14-2.62)]. Furthermore, an incremental risk of AF was observed according to the categories of stratified risk by the score, emphasizing its usefulness as a predictive tool in this population.

DISCUSSION

This study evaluated the impact of modifiable risk factors (RF) on atrial fibrillation (AF) during a 10-year follow-up in a north-western population of Colombia, developing and validating the HARMS2-AF prediction model. The findings reaffirm the clinical relevance of modifiable RFs and underscore the need to incorporate these factors into clinical practice for the prevention and management of AF.^{11,12}

Hypertension emerged as the strongest independent risk factor, with a risk almost four times higher of incident AF; results that coincide with previous studies highlighting the direct association between elevated high pressure and the development of AF. Obesity and sleep apnea also showed a strong relationship with AF. BMI ≥ 30 kg/m² significantly increased risk, while sleep apnea was an independent predictor, even after adjusting for other RFs. These findings reinforce the need for specific strategies to control these conditions in the general population and in primary care.^{13,14}

Alcohol consumption showed a dose-dependent relationship with AF incidence, particularly in those consuming ≥ 15 standard drinks per week. This adverse effect is consistent with studies that have linked the chronic consumption of alcohol with atrial enlargement and low tissue voltage. Although smoking was also associated with a higher risk, data suggest that early interventions in these factors may reduce the incidence of AF.^{15,16}

Physical inactivity and diabetes mellitus, although associated to incident AF in univariate analysis, did not reach significance in multivariate analysis. These could be attributed to biases in the measurement of self-reported physical activity or the lack of detailed information on intolerance to carbohydrates in relation to diabetes.¹⁷

The HARMS2-AF model is the first in Latin America prioritizing modifiable RFs in the prediction of risk of AF. It is a simple tool, that does not depend on complex diagnostic tests and can be used both at the patient's bedside and in population screenings. However, this model requires validation in wider and more diverse populations to confirm its widespread applicability.¹⁸

Adherence to treatment emerged as a significant modulator of AF risk, suggesting that follow-up and therapeutic education strategies may play a key role in the reduction of incident events.

The results suggest that a HARMS2-AF score of ≥ 5 should trigger aggressive interventions to modify RFs and reduce the risk of AF. Besides, the model emphasizes the importance of preventive strategies in primary care, where communication about risks and the prioritization of treatments may play a key role in the prevention of AF and its complications.^{12,19}

Limitations of the study

Self-reported data for some risk factors:

Physical activity and alcohol consumption were based on self-report questionnaires, which may induce memory biases and under or overestimate their impact on the risk of atrial fibrillation (AF).

Lack of electrocardiographic and echocardiographic data:

The HARMS2-AF model does not include parameters such as atrial dilatation or cardiac electrical activity, which may improve accuracy in risk prediction.

Underestimation of asymptomatic AF:

AF detection was based on medical and in-hospital records, which probably excluded asymptomatic or undiagnosed cases, limiting the true incidence reported.

Predominantly Latin American population:

Although this is a strong point for the region, the findings may be not translatable to populations with a different ethnical or socioeconomic composition.

Simplified categories of continuous variables:

Variables such as age, body mass index and alcohol consumption are categorized in clinical thresholds to facilitate the applicability of the model, but this may miss significant details in nonlinear relationships between these factors and AF.

Besides the diagnosis of atrial fibrillation, other major cardiovascular events were documented, such as acute myocardial infarction and ischemic stroke, when such information was available in the institutional records.

It was not possible to systematically capture all major cardiovascular outcomes, which represents a methodological limitation. Their inclusion is advised in future validations, to evaluate the comprehensive impact on risk factors.

Additionally, this study did not include electrocardiographic or echocardiographic variables, widely acknowledged as essential in the evaluation of AF risk. The absence of data on interatrial block, an electrocardiographic finding easy to obtain by 12-lead ECG and related with atrial

remodeling and risk of arrhythmia, is a relevant omission. Likewise, no measurements were added to the size of the left atrium, which reflect chronic structural changes predisposing to the development and perpetuation of AF, and may be easily obtained through transthoracic echocardiography. Numerous studies have shown that interatrial block and left atrial dilatation not only predict the appearance of AF, but are also associated with a worse clinical outcome, including post-ablation relapse and greater risk of embolic events. Their exclusion in the HARMS2-AF model limits the capacity for a comprehensive stratification of risk, by dispensing with anatomical and functional components reflecting the underlying arrhythmogenic substrate. In this regard, although the model is focused on modifiable factors, easily assessed in primary care, the integration of these markers may offer an added value in scenarios where basic diagnostic tools are available, improving the accuracy of the model, not compromising its applicability. We emphatically recommend considering their inclusion in future versions of the score, and in external validation studies that would allow evaluating their impact on the prediction and prevention of AF in a stronger manner.

CONCLUSION

The HARMS2-AF model has proven to be a useful tool to predict the risk of atrial fibrillation based on modifiable lifestyle factors, such as hypertension, obesity, alcohol consumption, smoking and sleep apnea. This study, pioneer in Latin America, highlights the importance of integrating risk scores based on lifestyle in primary care, to identify individuals in high risk and promoting early interventions that may alter the natural history of AF. However, additional studies are required to validate its applicability in different population scenarios and to evaluate the clinical impact of its implementation.

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Position Statement

RNA interference gene therapy for the treatment of cardiovascular disease

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ABSTRACT

The constant progress in molecular biology and genetic engineering technologies within the field of cardiovascular pharmacology, along with the introduction of clinically applied drugs based on these advancements, compels us to reconsider our current understanding in this area. This article aims to provide an update on the underlying mechanisms, pharmacological design, and the clinical applications tested so far, and also to address the safety concerns associated with drugs that utilize RNA interference technology.

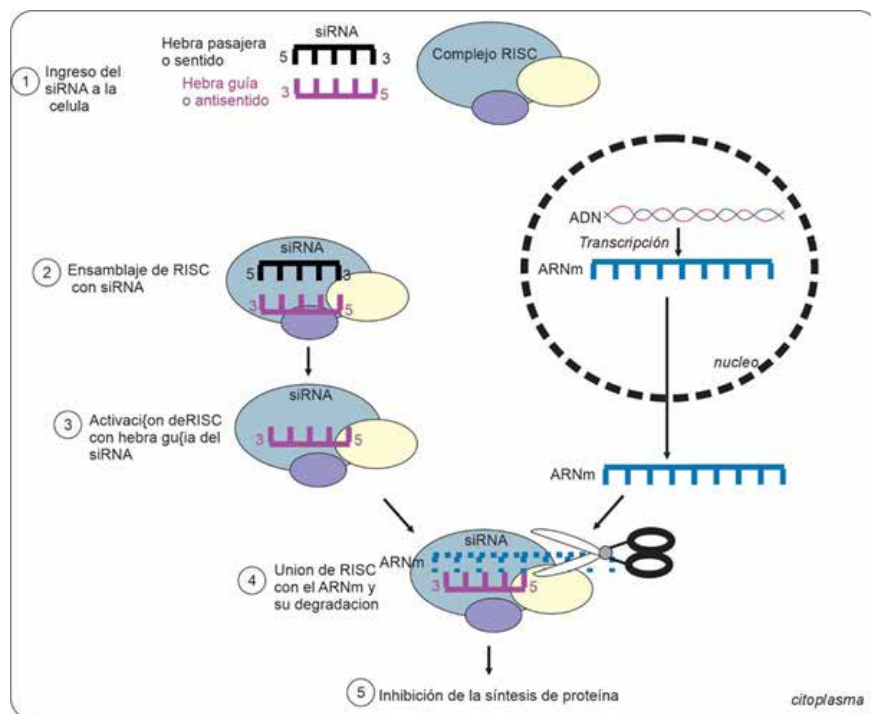
INTRODUCTION

Currently, the pharmaceutical industry is adding advanced technologies derived from molecular biology and genetic engineering, which do not act by physical block of target protein function, but seek to reduce their expression at molecular level. Frequently, terms are found referring to RNA interference (RNAi), with antisense oligonucleotides (ASO), CRISPR/Cas9 modifications. To this date, there are several drugs available, commercially based on RNAi technology that employ the normal cellular mechanism of gene expression regulation. The significance of this mechanism was reflected in the 2006 Nobel Prize awarded to Fire and Mello for the use of double-stranded RNA (dsRNA) as a gene silencing strategy. More recently, the 2024 Nobel Prize in Physiology or Medicine was granted to Ambros and Ruvkun, who discovered micro interfering RNA (miRNA) as a mechanism for gene autoregulation based on a dsRNA encoded in DNA. In brief, the RNAi technology by a small RNA molecule produces messenger RNA (mRNA) degradation in a protein, inhibiting its expression, and consequently, silencing its function.

How is protein expression inhibited? Within the human genome there are DNA regions that enable special encoding for RNAi molecules. The dsRNA synthesized in this manner is cut by the action of an RNase (DICER) into double-stranded fragments of 21-23 nucleotides, called small interference RNA or siRNA/miRNA (*Figure 1*). These fragments are assembled in a protein complex known as

RISC (RNA induced silencing complex), where the two sense and antisense strands of siRNA are decoupled, as shown in *Figure 1*. Next, the antisense strand is complementarily coupled with mRNA in a region determined by the strict order in which the A, U, G, C (adenine, uracil, guanine and cytosine) nucleotides appear. This union will be the more stable the less complementarity errors there are, and vice versa, determining for the target mRNA selection to be extremely specific. The stability of this union provides the necessary time for this RISC protein complex, through an RNase, to cut the mRNA strand, disabling it to translate the protein for which it encodes.¹ This very specific capacity to control protein expression occurs independently from siRNA being generated within the cell or being introduced exogenously, as developed by the RNAi technology.

This technology provides plenty of advantages over conventional pharmacology. Among them, we can mention: 1) high specificity, avoiding the inhibition of similar proteins; 2) high intracellular stability, extending the time of action of a dose for periods from 6 to 12 months; 3) inhibition of therapy targets over which there are no available drugs or that are difficult to implement; 4) improving adherence to treatment. The growth of treatment methodologies based on siRNA as technological platform for development of drugs is reflected on the increase in the number of clinical trials, as well as the approval for commercialization by the Food and Drugs Administration (FDA) in the United States (*Table 1*).

**FIGURE 1.**

Mechanism of action of small-interfering RNA (siRNA) molecules. **1)** siRNA enters cells by endocytosis of lipid nanoparticles or by siRNA interaction, conjugated with N-acetylgalactosamine (GalNAc), which binds to the asialoglycoprotein receptor, expressed in the membrane; **2)** siRNA released in cytosol is associated with proteins to form the RNA-induced silencing complex (RISC), splitting into a single strand and activating; **3)** the strand within the complex works as a guide, so that **4)** the enzyme splits the target region in messenger RNA (mRNA), to then cut it into small fragments, preventing its translation and the encoded protein expression.

It is necessary to mention that the industry has overcome its own limitations associated to these molecules, such as stability and immunogenicity. Naked siRNA molecules in plasma are very labile, have a very low half-life (approximately 5 min), because they are degraded by RNase or because they are filtered in the kidneys. On the other hand, RNAi has to be presented to the organism in a short-strand configuration, because long-strand ones may trigger an immune response. The different chemical modifications of the nucleotide bases of RNAi enabled overcoming these hindrances, reducing toxicity in the administration and assimilation of these drugs.¹

Another limitation has been selectively addressing RNAi toward the target organ, thus preventing its dissemination to other tissues of the body, and the generation of an undesired inhibition. As strategy, the administration of siRNA uses a local application on the desired target tissue, as for instance in the eye through intravitreal injection. For the systemic subcutaneous administration, siRNA is added to a molecule that determines a tropism to the target organ. Thus, the liver as target organ is on the cutting edge of possible targets, as comparatively, access is easier. In this case, siRNA couples with N-acetylgalactosamine (GalNAc), which has a great affinity for the asialoglycoprotein receptor of great expression on the surface of hepatocytes and is mainly absent in other cells.² Another widely used alternative is the association with nanoparticles, as for instance liposomal.² As seen in Table 1, most drugs approved by the FDA have proteins as target, mainly originating in the liver. In the cardiovascular area, there are only 6 treatments with siRNA bases approved by the FDA. However, between the clinical trials of phases I, II and III, more than 50 different products are being evaluat-

ed for the treatment of cardiovascular, metabolic, oncological, endocrine diseases and so on.^{2,3}

In terms of cardiovascular health, the first developments were mainly addressed at the treatment of dyslipidemias. Next, we will mention the most relevant ones:

- **Inclisiran:** addressed at the treatment of homozygous familial hypercholesterolemia with elevated low-density lipoprotein (LDL) in plasma. siRNA inhibits the expression of protease PCSK9, which enables a greater expression of LDL receptors in the liver, favoring a reduction of cholesterol associated to lipoprotein (LDL-C) in plasma. Post-hoc studies in patients with acute myocardial infarction indicated that with the initial injection treatment, in 3 months and then every 6 months, there was an efficient and constant reduction of 40-50% of LDL-C for over a year.⁴ Preliminary studies on cardiovascular risk were not completely conclusive, and encouraged the performance of more trials (ORION-4 and VICTORION-2 PREVENT), whose results on cardiovascular risk are expected for 2026.

- **Olpasiran, leposidaran and zelasiran:** addressed at reducing the levels of lipoprotein (a) or Lp(a), a special type of LDL associated to atherosclerotic cardiovascular diseases (ASCVD) and valve stenosis expressing apolipoprotein A (Apo-A). Hyperlipidemia as a risk factor in ASCVD corresponds to more than 20% of the population in the US, and is primarily determined by genetic alterations of the Apo-A gene, so it does not respond to conventional therapies or changes in lifestyle. Silencing Lp(a) with leposidaran achieved a 90% reduction in up to one year after the last doses. With olpasiran, patients received 4 doses every 3/4 months, achieving reductions in the same range.⁵ There are other drugs based on siRNA against Lp(a) in earlier clinical

TABLE 1.
Outline of approved siRNA-based pharmacological treatments, and/or in different phases in clinical trials.

Name	Protein/gene	Pathology	Formulation	Approval/state
Patisiran	Transthyretin*	Hereditary transthyretin amyloidosis	Lipid nanoparticles	2018
Inclisiran	PCSK9	Heterozygous familial hypercholesterolemia (HeHF)	siRNA-GalNAc	2020-2021
Olpasiran	Lipoprotein A	ASCVD with high Lp(a)	siRNA-GalNAc	2024 Phase III
Lepodisiran	Lipoprotein A	Cardiovascular disease, elevated Lp(a)	siRNA-GalNAc	2024 Phase II/III
Zerlasiran	Lipoprotein A	Cardiovascular disease, elevated Lp(a)	siRNA-GalNAc	2024 Phase II
Zodasiran	ANGPTL3	Mixed hyperlipidemia, elevated LDL	siRNA-GalNAc	2024 Phase II
Plozasiran	APOC3	Mixed hyperlipidemia, elevated TG-VLDL	siRNA-GalNAc	2024 Phase II/III
Zilebesiran	Angiotensinogen	Hypertension	siRNA-GalNAc	2024 Phase II/III
Vutrisiran	Transthyretin	Hereditary transthyretin amyloidosis	siRNA-GalNAc	2022/2025

* Drug studied to evaluate the treatment of amyloidosis in the central nervous system.

cal phases, such as zerlasiran, that tested in patients with ASCVD in 3 and 6 months, according to 2024 June reports, produced a 90% reduction in Lp(a).⁶

- **Zodasiran and solbinsiran:** addressed at favoring plasma clearance of lipoproteins rich in triglycerides (TG) through peptide ANGPTL3 silencing (angiopoietin-like peptide). This peptide inhibits the lipoprotein lipase (LPL), so its inhibition favors lipase action and reduces TG levels in blood. Phase II clinical studies for zodasiran showed, in patients with hyperlipidemia, that with 2 doses, one basal on day 1 and then 3 months later, a 56% reduction was achieved in TG in 6 months. Epidemiological studies with loss of function in this protein show a reduction in cardiovascular disease risk, as well as variable percentages of TG and cholesterol reduction in blood.⁷ This RNAi target is still being researched in other phase II clinical trials (PROLONG-ANG3, NCT05256654). Although the preliminary studies in animals and humans showed efficacy in the management of dyslipidemias also for solbinsiran, its cardiovascular consequences have not yet been studied.⁸

- **Plozasiran:** it is designed to inhibit the liver synthesis of apolipoprotein C3 (APOC3), a protein that acts by decreasing the activity of lipoprotein lipase (LPL), and therefore, by reducing the plasma clearance of lipoproteins rich in triglycerides, thus favoring its accumulation in circulation. In clinical studies made in individuals with dyslipidemias, the administration of this molecule led to a 77% reduction in plasma levels of triglycerides after two doses, an effect that remained in 3 and 9 months of follow-up.⁹ In patients with familial chylomicronemia syndrome, the treatment was associated to an effective control of the disease and a significant decrease in the risk of pancreatitis.¹⁰ Currently, the clinical trials in phase III: SHASTA-3 (NCT06347003) and SHASTA-4 (NCT06347016), with the aim of evaluating

its efficacy and safety in the context of severe hypertriglyceridemia.¹¹ Nevertheless, to this moment no studies have been developed exploring its impact on global cardiovascular risk.

Other clinical trials and treatments are addressed directly to solving cardiovascular disease primarily:

- **Patisiran and vutrisiran:** addressed at treating fatal nerve disease secondary to hereditary transthyretin amyloidosis (ATTR). siRNA inhibits the expression of the transthyretin (TTR) enzyme of liver synthesis, which by being silenced in ATTR, leads to the accumulation of amyloid deposits in key organs, such as the central nervous system, peripheral nervous system, and the heart. Patisiran (Apollo-B study) reduced 81% of TTR in plasma and heart wall thickness, along with contractility improvement in patients.¹² It was the first drug of this nature to be approved by the FDA in 2018. Another medication in the same line, revusiran, was prematurely suspended in phase III.¹³ Recently, in March 2025, the anti-TTR, siRNA-based therapy was approved by the FDA for the treatment of cardiomyopathies. The drug called vitrisiran, tested in the HELIOS-B study, was injected 1 every 3 months during 36 months, achieving reduction in death and recurrence of cardiovascular events among other indices.¹⁴

- **Zilebesiran:** addressed at the reduction of blood pressure by angiotensinogen (AGT) expression inhibition, which prevents the synthesis of angiotensin II and aldosterone in a sustained manner, leading to a sustained decrease in blood pressure. This molecule has been evaluated within the framework of the KARDIA clinical trials program. In individuals with moderate hypertension, zilebesiran achieved a reduction of up to 90% in the plasma levels of AGT, accompanied by a 12-14% decrease in systolic blood pressure.¹⁵ Recent results of the KARDIA-2 study, presented

in the European Meeting on Hypertension and Cardiovascular Protection, showed that in non-controlled hypertensive patients under standard antihypertensive treatment, the administration of a single dose of zilebesiran induced an additional reduction of between 7 and 18 mmHg in systolic blood pressure, an effect that remained for a period of up to 6 months.¹⁶ Currently, there is an ongoing study, the KARDIA-3, with the aim of assessing its efficacy in other hypertensive populations.

The safety and effectiveness at cardiovascular level of RNAi treatments seem to still be an unsolved question. These drugs, strategically addressed to a target only related to the pathology to be treated, present a high index of safety.

In general, phase I and phase II clinical trials showed a good safety profile, and the mass administration of vaccines based on these technologies have proven that the minimization of immunogenicity has been optimized. However, given how recent this development is in the pharmaceutical industry, it is necessary to keep a continuous long-term monitoring. In this regard, some clinical trials with this type of drugs were interrupted, in spite of efficiently achieving target protein silencing, due to the emergence of unexpected adverse effects, such as it occurred with teprasiran and revusiran.^{13,17} The causes included from inappropriate dosing and suboptimal formulations, to using delivery systems (like lipid nanoparticles) that caused inflammatory responses, or the lack of a significant clinical efficacy.

Although currently, most approved or advanced therapies with cardiovascular effects are addressed to rare or hereditary diseases, or with pharmacological vacuums, as a position statement about them it is possible to say that siRNA-based pharmacological therapy offers an optimistic outlook, given the great advantage of specificity and posology. The advantage of being administered spread out over time allows for better adherence, because of the long-duration effect of siRNA. The pharmacological use of RNAi technology is currently a reality of exponential expansion, seeking to reach target organs other than the liver. The growing interest in the translation of experimental results obtained in basic investigation will allow to satisfy vacant pharmacological areas, addressing these technologies directly at the primary causal proteins, linked to the development and progression of cardiovascular diseases.

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Position Statement

Position statement on contraceptives in patients with congenital heart disease

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ABSTRACT

The increase in survival rates among patients with congenital heart disease (CHD) has introduced new challenges that require the involvement of adult cardiologists. Most women of reproductive age with CHD are sexually active, making the evaluation and counseling on contraceptive method (CM) choice an essential practice in cardiology.

Unfortunately, less than half of women with CHD received counseling prior to their first sexual activity. Given the prevalence of sexual activity and the risk of unplanned pregnancy in adolescents and young adults with CHD, contraception and pregnancy counseling should begin during adolescence in consultations with the pediatric cardiologist and continue with the adult cardiologist.

INTRODUCTION

Why is it important to question and educate on contraceptive methods from cardiological consultations?

Unintended pregnancies in women with congenital heart diseases (CHD) could be potentially dangerous and harmful for the health both of mother and fetus.^{1,2,3} Many patients with CHD in a reproductive age are under treatment with potentially teratogenic medication, such as angiotensin-converting enzyme inhibitors, vitamin K antagonists, and so on.^{4,5}

For this reason, we should encourage women to develop reproductive goals with cardiologists, obstetricians and family doctors, to design family planning and reduce as much as possible the risks of morbimortality associated to pregnancy.

Instructing on contraception is extremely important for women classified as mWHO III and IV, as pregnancy entails a very high risk in those with conditions classified as mWHO class III, and it should be avoided in class IV (*Table 1*).^{5,6}

What contraception methods are available?

Contraception eligibility is based on the risk of failure in terms of contraception and the risk of developing secondary effects in women.

Through the medical criteria of eligibility for the use of contraception, the World Health Organization (WHO) proposes categories based on evidence in terms of the conditions in which an individual can use contraception methods safely.^{7,8}

There are 4 categories:

- **Category 1:** a condition where there are no restrictions for contraception.
- **Category 2:** a condition where, in general, the advantages of using the method exceed the theoretical or verified risks.
- **Category 3:** a condition where, in general, the theoretical or verified risks exceed the advantages of using contraception.
- **Category 4:** a condition representing an inadmissible health risk if contraception is used.

The aim of this position statement is selecting the most appropriate contraception method in patients with CHD, mainly in those in categories 3 and 4.

Available contraception currently is:⁷

- Barrier methods
- Combined hormonal contraception (CHC)
- Progestogen-only contraceptives
- Emergency contraception
- Intrauterine devices (IUD) with levonorgestrel or copper
- Diaphragms
- Surgical

These methods according to the rate of failure they present will be divided in different groups: level 1, 2 and 3.

Level 1 are those with less than 1% of failure, including: dermal implants, intrauterine devices and surgical sterilization. Level 2 have 6-12% of failure rate, including:

TABLE 1.

Classification of maternal cardiovascular risk according to the modified World Health Organization (mWHO)

mWHO classification	Diagnosis (when clinical state is stable)	Riesgo asociado al embarazo	Tasa de eventos cardíacos maternos	Recomendación / Asesoramiento
mWHO I	- pulmonary valve stenosis - patent ductus arteriosus - mitral valve prolapse - simple lesions repaired (ASD, VSD, ductus, anomalous pulmonary venous drainage) - isolated ectopic beats	No detectable increase in maternal mortality risk, and no or mild morbidity increase	2.5–5.0%	Indicated advice
mWHO II	- non-operated ASD or VSD - tetralogy of Fallot repaired - supraventricular arrhythmias - Turner syndrome with no aortic dilatation - mild LV dysfunction (EF >45%) - hypertrophic cardiomyopathy - mild or moderate valvulopathy - Marfan or HTAD with no aortic dilatation - aorta < 45 mm (bicuspid valve) - repaired coarctation	Mild to moderate increase in morbidity risk / small increase in risk of mortality	5.7–10.5%	Indicated advice
mWHO II–III	- atrioventricular septum defect - moderate LV dysfunction (EF 30–45%) - previous peripartum cardiomyopathy with no residual dysfunction - mechanical valve prosthesis - systemic right ventricle with normal or mildly depressed function - Fontan circulation with no complications	Intermediate risk of maternal mortality or moderate to severe morbidity	10–19%	Indicated advice
mWHO III	- not repaired cyanotic heart disease - complex congenital heart diseases - moderate mitral valve stenosis - asymptomatic severe aortic valve stenosis - moderate aortic dilatation - ventricular tachycardia	High risk of maternal mortality or severe morbidity	19–27%	Expert advice is required
mWHO IV	- pulmonary hypertension - severe LV dysfunction (EF <30% or NYHA III–IV) - peripartum cardiomyopathy with residual dysfunction - severe mitral valve stenosis - symptomatic severe aortic valve stenosis - systemic right ventricle with moderate or severe dysfunction - severe aortic dilatation - vascular Ehlers-Danlos syndrome - severe recoarctation - complicated Fontan circulation	Extremely high risk of maternal mortality or severe morbidity	40–100%	Contraindicated pregnancy; consider interruption if it occurs

combined estradiol-progestogen pills, progestogen pills, dermal patches, vaginal ring and diaphragms. Level 3 are those with highest rate of failures, represented by barrier methods and spermicides (Figure 1).¹

The choice of contraception should be individual according to the underlying lesion in the patient, risks, efficacy of the method by level and duration.

Barrier methods, coitus interrupts or withdrawal, and the calendar method have a high rate of level 3 failure, so they are not recommended.

In a recent study, carried out by the Hospital Universitario Vall d'Hebron, it was found that at the time of consul-

tation, 25.8% of women with CHD were not using contraception, while 46.4% used level 3 methods, 21.8% level 2 and just 5.8% level 1. After follow-up by a joint consultation with gynecology and cardiology services, distribution was the following: 25% were not using any contraception, 22.8% continued using level 3, 34.6% level 2 and 17.6% level 1. These changes turned out to be statistically significant ($p < 0.001$).⁹

• Combined hormonal contraception

The estrogen component increases the risk of venous thromboembolism (VTE) and it is known that it increases

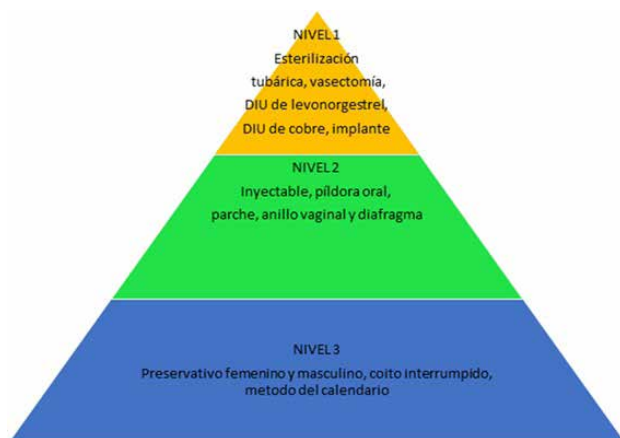


FIGURE 1.

Classification of contraception methods according to the failure rate they present

blood pressure, so it is not advised in patients with preexisting heart disease or hypertension (HTN).³

The absolute risk of TVE in women not using CHC is 0.19 to 0.37 per 1000 women/year; while in those using it is 0.55 to 1.41 per 1000 women/year, with a greater risk among users of third- and fourth-generation progestins (desogestrel and gestodene), in comparison with second-generation ones (levonorgestrel or norgestrel).¹⁰ CHCs are associated to an increase of 2-6 times in risk in comparison with the baseline.¹¹

Evidence showed that CHC with the same dose of estrogen but different progestins were associated to different VTE risks. It was suggested that the progestin component could play a role in the development of thrombosis. However, given that progestogen-only contraception does not interfere with coagulation protein synthesis, the difference in VTE risk specific to each CHC could only be attributed to a distinctive modulation of the procoagulant effect of ethinylestradiol (EE), exercised by progestins.¹²

Paradoxical embolism is a significant entity between patients with VTE and intracardiac shunts such as atrial septal defect (ASD), ventricular septal defect (VSD) and patent foramen ovale (PFO). Although clinical presentation is very diverse, it may endanger life.¹³

The prevalence of stroke in patients with CHD is higher when compared with healthy people with the same age.¹⁴ Patients with transposition of the great arteries (TGA) with atrial switch present a high prevalence of remaining shunts between the new atria; patients with Ebstein anomaly have a prevalence of ASD/PFO of 80-90%; patients with pulmonary and/or tricuspid regurgitation, at least moderate, may manifest the presence of PFO with right-left shunt in exercise, among others.⁵

On the other hand, most patients required at least one catheterization in childhood, so they present a higher likelihood of chronic venous insufficiency and VTE when exposed to CHC.¹⁵

It is important to highlight that heart failure is a frequent complication, present in 20-50% of the population with CHD. History of hospital admission due to heart failure and/or atrial flutter or fibrillation in the last three months presents an odds ratio of more than 10 to predict VTE events.^{5,11}

Because of what has been presented here, this Committee recommends not using CHC in patients with high probabilities of presenting atrial septal defect or patent foramen ovale in any of their forms, even when they are not detected by echocardiogram. Likewise, it is suggested to avoid using them in patients with heart failure or atrial arrhythmias.

Furthermore, we consider that using CHC should be avoided in patients with a higher risk of developing hypertension due to their base pathology, as in the case of coarctation of the aorta.

• What patients with CHD can use CHC?

1. Patients with no intracardiac shunt
2. Patients with no heart failure
3. Patients with no hypertension
4. Patients with no history of embolic events.

• Progestogen-only contraception (POC)

POCs are a more secure option for the previously mentioned patients, as they decrease the risk of complications proper of the estrogen component and maintain a level 1 failure rate.⁷

POCs act by thickening cervical mucus, thus preventing the penetration of sperm and reducing endometrial receptivity, making implantation impossible. The mechanism of action depends on the method used (IUD, contraception pills, implants).^{3,7}

Oral POCs may contain levonorgestrel (LNG), norethisterone acetate or desogestrel, and traditionally, they have been associated to strict timetable rules for their ingestion, particularly for the LNG formulation, whose time variation allowed is 3 hours, and the strict consumption of delayed or forgotten pills demands a high level of discipline by patients.¹⁶

The most common progesterone contraception is the one with the highest dose: desogestrel 75 micrograms, which is more reliable as it inhibits ovulation. Its contraceptive efficacy is similar to that of CHC and is safe for women with congenital heart disease.^{3,8}

The most frequently reported secondary effect by patients in treatment with any of the POCs was irregular bleeding. Considering the high percentage of patients receiving antiplatelet drugs or anticoagulants, this was the main reason for dropping POCs. In most patients, bleeding happens at the onset and then it disappears.⁹

Drospirenone in a 4 mg dose in a 24/4 administration regimen provides an efficient contraception, with a good safety profile and tolerability in a wide range of women, including those with overweight or obesity, and it is an op-

tion for most women, regardless of blood pressure, body mass index or thromboembolic risks. In comparison with desogestrel, it presents a lower rate of bleeding.^{17,18}

Depot medroxyprogesterone acetate can be administered by intramuscular injections every three months.³

Subdermal implants containing levonorgestrel or etonogestrel are another option that maintains contraceptive efficacy for 3 to 5 years, and are efficient and safe reversible contraception methods for women with CHD.¹⁵

Emergency contraception can be used in patients with CHD with no problems, although patients should be trained so that this is not an option due to the risk of unintended pregnancies in classes III and IV of the WHO. They contain LNG in 1.5 milligrams doses.¹⁹

We consider that POCs are a safe option for patients with intracardiac shunt, heart failure and hypertension.

• Intrauterine devices

The two usual types of reversible intrauterine devices are copper IUD, with an average duration of 10 years, and the one that releases LNG, known as intrauterine system (IUS), with an average duration of 5 years.

IUS is one of the most efficient and safe contraception methods. IUS offers other non-contraceptive benefits, such as reduction of heavy menstrual bleeding, iron deficiency anemia, pelvic pain (particularly in women with endometriosis), and prevention of endometrial hyperplasia, in comparison with copper IUS. No prophylaxis is required against infectious endocarditis for the insertion of these devices.^{3,7}

In patients with anemia, reduction of menstrual bleeding could be beneficial, just as in people with valve prosthesis or atrial arrhythmias requiring anticoagulation.

IUS can be inserted in outpatient care with local anesthesia; however, in patients with Eisenmenger syndrome, Fontan-Kreutzer procedure, preexisting arrhythmias or ventricular dysfunction, insertion in a hospital environment is advisable due to the risk of vasovagal reaction during the procedure.^{9,15,19}

Currently, there are two IUS available, the Mirena® and the Kyleena®, which vary in the LNG dose they contain.

A combination of barrier contraceptives for STD prevention and LNG IUS is ideal.

• Surgery

In group IV women with Eisenmenger syndrome or CHD with pulmonary hypertension, laparoscopic or minilaparotomy tubal ligation can be considered as a permanent contraceptive method, assuming the anesthetic risk. As alternative, vasectomy may be considered for the partner.^{3,7,9}

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Clinical Case

Noninfective endocarditis with atypical presentation, resembling infiltrative tumor with coronary vascularization

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coronary vascularization.

ABSTRACT

Noninfective endocarditis is a rare pathologic process, primarily associated with autoimmune diseases and neoplasms. Diagnosis is established by ruling out infective endocarditis and cardiac tumors, such as myxoma or sarcomas. However, it is unusual to find highly vascularized vegetations, and even more unusual for this vascularization to originate from the main coronary arteries. We present the clinical case of a patient with a mass found in the left atrium, which was highly vascularized by the circumflex artery, leading to suspicion of intracardiac tumor. The patient underwent tumor resection, and histopathological analysis revealed findings consistent with endocarditis.

INTRODUCTION

Noninfective endocarditis is a rare pathological process that is mainly associated to autoimmune diseases and neoplasms. Diagnosis is made by ruling out infective endocarditis, and subsequently, cardiac tumors (for instance, myxomas or sarcomas). However, it is rare to find highly vascularized vegetations, and it is even more rare for said vascularization to emerge from the main coronary arteries. Next, we present the clinical case of a female patient with a finding of left atrial mass, that was highly vascularized by the circumflex artery. Because of this, there was suspicion of intracardiac tumor, and tumor resection was conducted. In the histopathological analysis, endocarditis findings were reported.

CLINICAL CASE PRESENTATION

Female, 51-year-old patient, with overweight and dyslipidemia in treatment with non-pharmacological measures and statins. The patient presented at the hospital with clinical symptoms characterized by fever of up to 39°C of afternoon-night predominance, dry cough fits and pleuritic pain in physical exploration with presence of diastolic murmur in mitral focus. As part of the approach, three blood tests were carried out, which were negative. Procalcitonin was within the normal range, and ECG was in sinus rhythm. On the other hand, chest X-rays showed cardiomegaly grade I, with no other significant findings. Transthoracic echocardiogram was also carried out, where left intra-atrial mass

was documented; thus, transesophageal echo was conducted to better identify the lesion (*Figure 1*). In this test, irregular mobile cardiac mass was found, with solid and cystic characteristics and vascularized; likewise, the mass measured 5.1 cm by 9 cm, with an area of 9.2 cm²; adhered from the left atrial appendage to the aortomitral continuity, protruding through the mitral valve, conditioning severe mitral valve stenosis. For this reason, the patient was admitted in the cardiology area, where coronary angiography was performed, with multiple microfistulae being observed with origin in the proximal segment of the circumflex artery draining into the appendage, left atrium and an infiltrative tumor (*Figure 2*). An assessment was requested by the cardiothoracic surgery service, and tumor resection was indicated. The surgical intervention was carried out later, by extracorporeal circulation with aortic cross-clamping for 1 h and 25 min; an irregular tumor was found, of cystic appearance, of 3 cm by 3 cm, vascularized, which was adhered to the left atrial roof, 3 cm from the atrioventricular valve. During the surgery, mesenchymal neoplasm was found; the patient was extubated successfully in the OR, presenting hemodynamic instability, requiring vasopressor and inotropic support, which could be withdrawn immediately after the surgery. Later, the patient was referred to post-surgical care in the Intensive Care Unit, where she coursed favorably, and with no complications associated to the hospital stay. Finally, the patient was discharged 8 days later. The anatomopathological result was collected, with

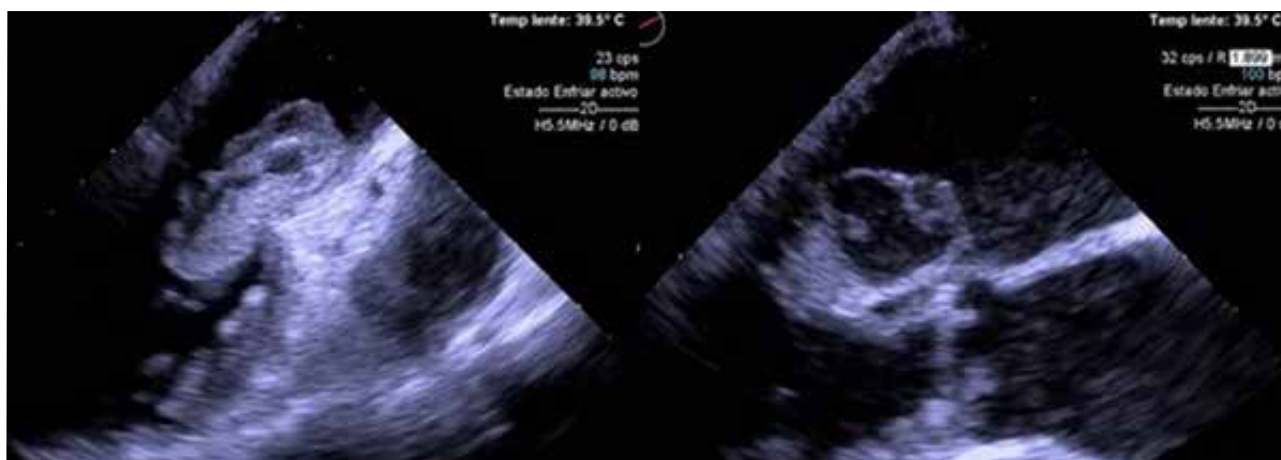


FIGURE 1. Transesophageal echocardiogram: mobile intra-atrial mass, conditioning severe mitral valve stenosis

report of connective tissue with reactive fibroblasts associated to sclerotic areas, with neoformation vessels with fibrin strands deposits, chronic inflammation with lymphocytes, compatible with chronic and acute endocarditis; furthermore, special staining was carried out that led to ruling out neoplastic process (*Figure 3*). Currently, the patient remains asymptomatic and in functional class I of the New York Heart Association.

DISCUSSION

Noninfective endocarditis, also known as nonbacterial thrombotic endocarditis (NBTE) or aseptic endocarditis, refers to a rare condition characterized by the formation of sterile vegetations.

Libman and Sacks published in 1924 a series of cases of four patients in whom these atypical lesions were associated to systemic lupus erythematosus. These vegetations are not associated to inflammatory response or bloodstream in-

fections, and in general occur as a result of fibrin deposition and platelet aggregation.¹

The etiology of NBTE is little known and several interaction mechanisms (including circulating immune complexes, hypercoagulable states and carcinomatosis) may play a role, which in the end, produce endothelial damage and exposition of subendothelial connective tissue to circulating platelets. It is well known that malignant neoplasms have impaired antithrombotic mechanisms, thus increasing the risk of thrombosis and subsequent valve lesions; on the other hand, the NBTE relationship with malignancy is well known.²

Macrophages interact with malignant cells to produce circulating cytokines (such as tumor necrosis factor and interleukin-1) that cause endothelial damage, with the subsequent promotion of sterile thrombi and platelet deposition in the endocardium. These macrophages also stimulate the production of coagulation factors to create a hypercoagulable state.³

It is imperative to differentiate NBTE from infective endocarditis (including culture-negative endocarditis); thus, the diagnostic approach is addressed to ruling out infective endocarditis and assessing the probable cause for NBTE.

Clinically, the patients with NBTE often appear asymptomatic, and occasionally, the only clinical manifestation are thrombotic events, because vegetations are more friable. Rarely, patients present murmurs or signs and symptoms of valve or heart failure. Those who do present them, valve regurgitation is more frequent than stenosis.

Diagnostic tests should be made for infective endocarditis. Equally, three blood tests should be made before starting the therapy with antibiotics, with the aim of differentiating infective endocarditis from culture-negative endocarditis. Also, typical and atypical organisms of infective endocarditis should be sought (including fungi, the HACEK group, *Coxiella burnetii* or chlamydia), using specialized techniques as necessary; furthermore, if there is a clinical suspicion of autoimmune disease, it should be verified: ANA,



FIGURE 2. Coronary angiography: multiple microfistulae are observed, originating in the proximal segment of the circumflex artery, irrigating infiltrative tumor.

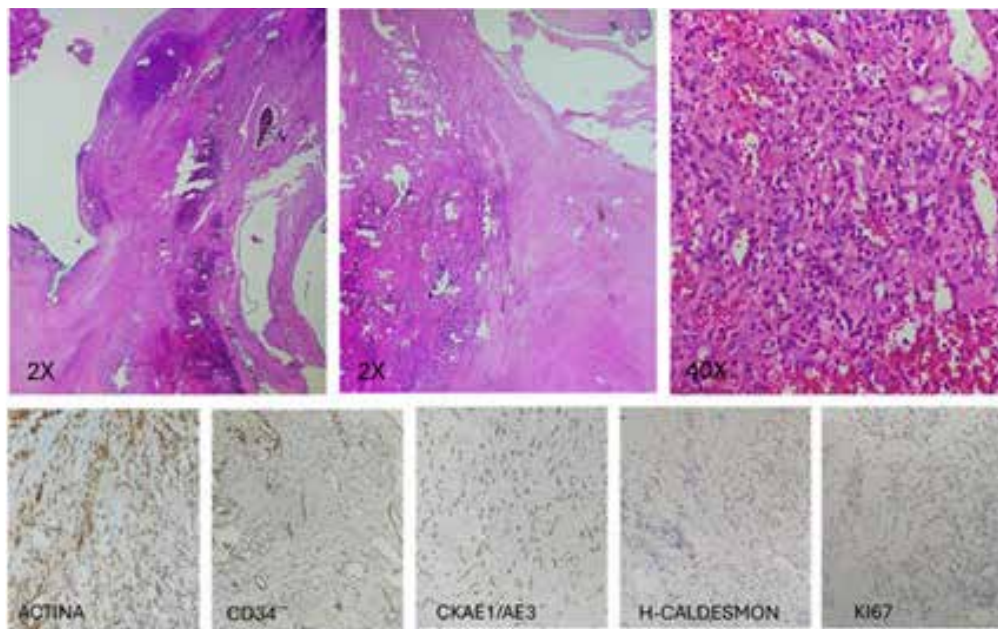


FIGURE 3. Histopathological slice with 10 and 40x images, where findings are observed, compatible with endocarditis. Besides, immunohistochemistry test was performed, where malignant neoplasm was ruled out.

anti-dsDNA, rheumatoid factor, anti-cardiolipin antibodies and anti- β 2-glycoprotein 1 antibodies.⁴

Likewise, transthoracic echocardiogram should be carried out to seek for vegetations in heart valves if NBTE is suspected. It is important to take into account that echocardiogram could be normal if the vegetations are already embolized. Transesophageal echocardiogram is more sensitive in comparison to transthoracic image; mainly in patients with small vegetations (<5 mm), and it should be done in those with normal transthoracic echocardiogram and a strong suspicion of NBTE.⁵ The vegetations of infectious and non-infectious etiology cannot be differentiated in echocardiography. Nevertheless, the vegetations observed in NBTE are usually small (<1 cm), wide-based and irregular.

Diagnosis can only be confirmed in histological evaluation. The vegetations vary in size and are usually located in areas of turbulent flow along the closure lines of the valve or in the valve themselves. Valve lesions present similar histological appearances, regardless of the underlying etiology, consisting of degenerative platelets intertwined with fibrin strands, granulomatous tissue and fibrotic foci. There are no inflammatory cells or infectious microorganisms present.⁶ The histopathology test also enables the diagnosis of primary malignant cardiac neoplasms, such as angiosarcoma and myxoma. In brief, the diagnosis of NBTE can only be confirmed by the demonstration of platelet thrombi in autopsy or in histology tests on surgical samples. Therefore, a high rate of clinical suspicion is required for diagnosis.

CONCLUSIONS

From what has been presented in this text, we can establish that this is a case of atypical presentation of endocarditis (based on histopathological diagnosis); blood tests in the patient were negative, and she had not received antibiotics previously; thus, we could determine that it was not culture-negative endocarditis, but rather noninfective endocarditis. In this regard, an association with autoimmune diseases is very usual; however, the patient did not know about any previous diseases, and had no clinical or biochemical suspicion of autoimmune diseases, so the neoplastic etiology became the second best choice. We suspected a malignant tumor, as during the surgery a neoplastic lesion was reported, together with it being highly visible due to the circumflex artery; however, in the end the lesion was reported as a highly vascularized vegetation, thus being a unique clinical case.

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Clinical Case

Transient left septal fascicular block in acute coronary syndrome. An entity to consider?

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ABSTRACT

The left branch of the conduction system has a complex distribution in the left ventricle, resulting in great anatomical variability. A transient conduction disorder with prominent anterior forces in the right precordial leads has recently been described. This disorder was called left septal fascicular block and occurs when there is an obstruction/occlusion of the anterior descending artery. We present the case of an acute coronary syndrome with ST elevation due to occlusion of the anterior descending artery that was associated with transient left septal fascicular block, which disappeared with percutaneous revascularization. This electrocardiographic finding, which is rarely observed and has limited electrophysiological evidence, should not go unnoticed in the presence and absence of ST elevation, although the presence of ST elevation beyond the conduction disorder always indicates urgent coronary revascularization.

INTRODUCTION

Rosenbaum MB et al, determined more than 50 years ago that the left branch splits into the anterior and posterior fascicles, which can get blocked, and since then the terms anterior hemiblock and left posterior fascicular block are accepted in electrocardiography, determining the trifascicularity of the conduction system.^{1,2} However, anatomical studies suggested that the left branch end is more complex than just a bifurcation. Tawara S. in 1906 pointed out that this branch has fibers coming from it on the surface of the interventricular septum.³ Demoulin and Kulbertus in 1972, in an elegant histological reconstruction of the left conduction system, proved the existence of a third division of the left branch in 20 normal hearts. This structure had a trajectory through the septal region and emerged from the left branch trunk, from the anterior fascicle, posterior fascicle or a complex of ramifications from both fascicles, producing a great anatomical variability as shown in *Figure 1*.^{4,5}

Recently, Perez Riera AR et al, showed a transient conduction disorder by electrocardiogram (ECG) and vectorcardiogram, with prominent anterior forces in precordial leads (V1-V2) in different clinical scenarios, and they called it left septal fascicular block (LSFB).^{6,7} This conduction disorder is rare, hard to identify electrocardiographically due to its transitoriness, and with limited electrophysiological evidence.

CLINICAL CASE

Eighty-three-year old patient, who after moderate effort presented oppressive retrosternal pain, with 8/10 intensity, and no radiation or neurovegetative symptoms. Forty-five minutes after the onset of symptoms, he consulted to the hospital where ECG was performed, showing ST-segment



FIGURE 1.

Outline of the left ventricular conduction system observed in 20 normal hearts. The diagrams show a septal or mid fascicle that emerges from the central area of the left branch trunk (diagrams 1-4), from the left anterior fascicle (diagrams 5-7), the left posterior fascicle (diagrams 8-14) or fibers originating from both fascicles (diagrams 15-20).⁴

elevation acute coronary syndrome (STEACS). He was referred to this hospital, and upon admission we verified ST elevation from V1 through V3, left anterior hemiblock (LAHB) and prominent R waves in right precordial leads. He underwent emergency coronary angiography, showing proximal occlusion of the anterior descending artery (ADA) with TIMI 0 epicardial flow as culprit artery for the acute myocardial infarction (*Figure 2A*). Next, primary percutaneous coronary intervention (PCI) was conducted, with implant of 2 drug-eluting stents of 3.0 x 13 mm, achieving post-PCI TIMI 3 epicardial flow.

The patient had a history of hypertension, treated with losartan 50 mg/day and amlodipine 5 mg/day.

Upon admission to the coronary unit, he presented BP 90/48 mmHg, HR 48 bpm, respiratory rate of 14 bpm, temperature 36°C and oxygen saturation 99%. In physical examination, he had a holosystolic murmur 2/6 in aortic focus. Laboratory tests upon admission showed the following abnormal measures: AST 122 U/L, CPK 520 U/L, LDH 299 U/L, hs-cTnT 959 pg/ml.

ECG upon admission to the coronary unit showed ST-elevation decrease, LAHB and absence of prominent R in V1-V2 (*Figure 2B*).

DISCUSSION

The case presented shows a rare disorder in the conduction system: transient LSFB associated to LAHB during STEACS.

The LSFB is mentioned in literature and is defined as when R wave voltage is observed in V1 ≥ 5 mm, R/S ratio in V1 and V2 ≥ 2 , R width in V2 ≥ 15 mm, S wave ≤ 5 mm and characteristic in crescendo voltage of r/R wave in V1-V3 and decreasing in V5-V6, and absence of q wave in V5, V6 and I.⁶

This electrocardiographic pattern manifests when there is proximal obstruction of the ADA before the septal perforating branches or by subocclusion of the left main coronary artery, leading to ischemia in the upper 2/3 of the interventricular septum and the apical portion of the left ventricle, in the trajectory of the septal fascicle.[8] In this case, early revascularization determined the transitoriness of LSFB, not so of LAHB, which was considered to be chronic due to degenerative phenomenon caused by age and/or hypertension.

This electrocardiographic pattern, appearing transiently or intermittently, is observed more frequently over the course of acute myocardial infarction with occlusion of severe proximal obstruction in the ADA. However, the presence of this conduction disorder over the course of acute ischemic syndrome may resemble two very well established clinical situations; i.e. Wellens syndrome and Winter syndrome, involving coronary angiography and emergency revascularization of ADA.⁹

As in any clinical-electrocardiographic analysis, differential diagnoses have to be made, excluding alterations that may resemble LSFB: for instance, the normal variant,

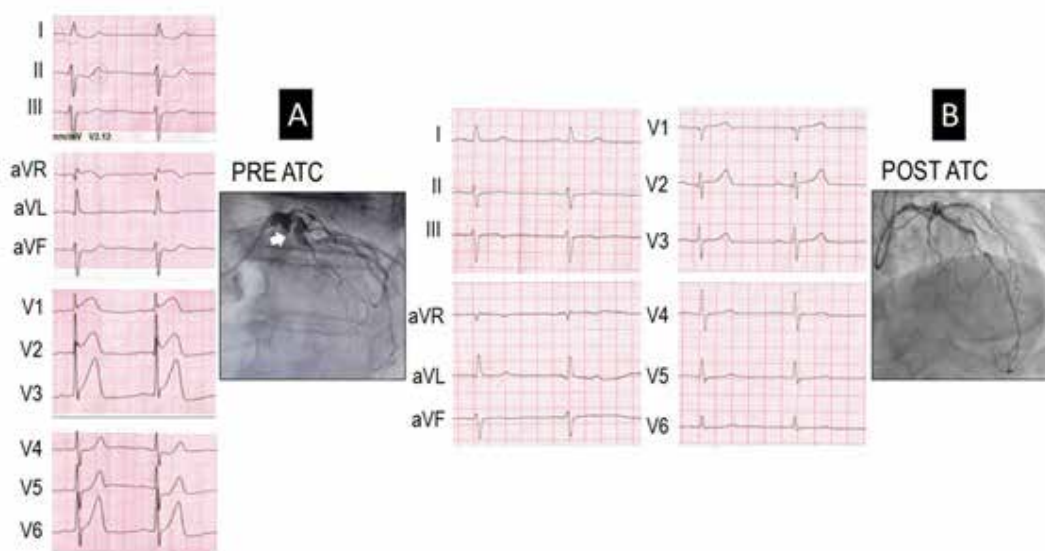


FIGURE 2.

Electrocardiogram with ST elevation in V1-V3, associated to left anterior hemiblock (LAHB) and left septal fascicular block (LSFB) due to proximal occlusion of the anterior descending artery. A. Electrocardiogram during the course of ST-elevation acute coronary syndrome: sinus rhythm, HR 55 bpm, PR 0.20 sec, QRS 100 msec, electrical superior QRS axis (LAHB) associated to LSFB, determined by R wave in V1 of 7 mm, R/S ratio greater than 2, R width in V2 of 14 mm, growth of R from V1 through V3 (prominent anterior forces) and decrease of R from V4 to V5, and absence of Q in V5, V6 and I. Coronary angiography showing proximal occlusion of the anterior descending artery before the septal perforating arteries with TIMI 0 flow in left anterior oblique view. B. Electrocardiogram after revascularization where LAHB persists, with disappearance of ST elevation and prominent right precordial forces, determining transient LSFB. Coronary angiography after stent implant with TIMI 3 flow in the anterior descending artery in cranial front view.

by marked counterclockwise rotation of the heart on its longitudinal axis ($\approx 1\%$ of normal individuals), athlete's heart, error in positioning precordial electrodes, lateral infarction, right ventricular hypertrophy, right bundle branch block, ventricular preexcitation, hypertrophic cardiomyopathy, cardiomyopathy associated to Duchenne muscular dystrophy, and so on.⁶

To conclude, the appearance of prominent R waves in the right precordial leads in acute coronary syndromes may indicate the existence of LSFB, which could be transient, and be determined by ADA obstruction/occlusion. This electrocardiographic finding, rarely observed, of limited electrophysiological evidence, should not go unnoticed, although the existence of ST elevation beyond conduction disorder always requires an emergency coronary revascularization.

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