

CARDIOVASCULAR AND METABOLIC SCIENCE

Continuation of the Revista Mexicana de Cardiología

2025



PREVENIR ES NUESTRA META



- **MACARENHA connection in arterial hypertension**
- **Gym benefits?**
- **Atherogenic and cardiovascular risk factors in hospitalized patients with type 2 diabetes**
- **Perception among family members and physicians about cardiovascular resuscitation**
- **Cardiac myeloid sarcoma in acute myeloid leukemia**
- **Coiling gone wrong!**

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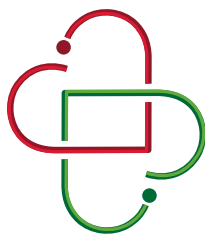
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Metabolic-Adipose-Cardio-Arterial-Renal-Enterohepatic-Neurological connection in arterial hypertension (MACARENHA): positioning for the new approach to prevention, diagnosis, treatment, and follow-up of patients living with arterial hypertension in Mexico

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Gym benefits?

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Metabolic-Adipose-Cardio-Arterial-Renal-Enterohepatic-Neurological connection in arterial hypertension (MACARENHA): positioning for the new approach to prevention, diagnosis, treatment, and follow-up of patients living with arterial hypertension in Mexico

Conexión Metabólica-Adiposa-Cardio-Arterial-Renal-Enterohepática-Neurológica en hipertensión arterial (MACARENHA): posicionamiento para el nuevo enfoque de prevención, diagnóstico, tratamiento y seguimiento de los pacientes que viven con hipertensión arterial en México

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Abbreviations:

ACEi = Angiotensin-Converting Enzyme Inhibitors
 ARBs = Angiotensin Receptor Blockers
 BBs = Beta-Blockers
 BMI = Body Mass Index
 CCBs = Calcium Channel Blockers
 CETP = Cholesteryl Ester Transfer Protein
 CKM = Cardiovascular-Kidney-Metabolic
 CVD = cardiovascular disease
 CVR = Cardiovascular Risk
 DBP = Diastolic BP
 GIP = Glucose-Dependent Insulinotropic Polypeptide
 GLP-1 = Glucagon-Like Peptide-1
 GREHTA = *GRupo de Expertos en HiperTensión Arterial* (Group of Experts on Arterial Hypertension)
 HBP = High Blood Pressure
 HDL = High-Density Lipoprotein
 HMOD = Hypertension-Mediated Organ Damage
 LVEF = Left Ventricular Ejection Fraction
 MACAREHNA = Metabolic-Adipose-Cardio-Arterial-Renal-Entero-Hepatic-Neurological/Behavioral Connection
 MASH = Metabolic Dysfunction-Associated Steatohepatitis
 MASLD = Metabolic Dysfunction-Associated Steatotic Liver Disease
 MRAs = Mineralocorticoid Receptor Antagonists
 NAFLD = Nonalcoholic Fatty Liver Disease
 POMC = Pro-opiomelanocortin
 RSAHT = Randomized Sequence Antihypertensive Escalation
 RSD = Renal Sympathetic Denervation
 SBP = Systolic BP
 T2DM = Type 2 Diabetes
 TNF- α = Tumor Necrosis Factor-Alpha
 TOD = Target Organ Damage

INTRODUCTION

High blood pressure (HBP) is one of the most common cardiovascular risk factors and a primary contributor to the development of cardiovascular complications, which are the leading cause of death in Mexico and around the world. Systemic HBP is a nosological entity resulting from multiple pathophysiological mechanisms. Its onset, development, progression, damage, and systemic complications define the need to study it with a holistic approach. While HBP per se generates structural and functional damage in the micro and macrocirculation, its damage to various target organs in turn triggers feedback mechanisms that perpetuate or accelerate the

harmful behavior of increased pressure values themselves.^{1,2}

For this reason, the GREHTA group, a consortium of experts in arterial hypertension, convened to develop a position on the diagnosis, prevention, treatment, and follow-up of patients with HBP in the context of the metabolic-adipose-cardio-arterial-renal-enterohepatic-neurological/behavioral connection (MACAREHNA) that arises in these patients.

Why a Mexican position on the role of HBP in the MACARENHA connection?

Along with HBP, other significant conditions such as dyslipidemia, dysglycemia, kidney damage, cerebrovascular disease, dementia, and liver disease, among others, frequently occur in the same patient, and the relationship between them is a synchronous interaction effect between separate entities, which nevertheless share common pathophysiological roots. The first attempt to evaluate these entities as distinct components of the same process, was the development of the concept of Metabolic Syndrome coined in 1977 by Herman Haller, and later popularized in 1988 by Gerald M. Reaven, who used the term about to signal the association between obesity, diabetes mellitus, elevated blood lipids, high uric acid levels, and hepatic steatosis as a result primarily of insulin resistance and described how the combined presence of these factors increases the risk for atherosclerosis. The pathological interrelationship between the kidney and the heart was named «Cardiorenal Syndrome» in 2004.³ In 2023, the American Heart Association proposed a broader, multidirectional concept that encompasses the connection between the heart, kidney, and metabolic syndrome, known as Cardiovascular-Kidney-Metabolic (CKM) syndrome.

Key messages

1. The importance of CKM syndrome is evident when analyzing mortality in Mexico in 2023. According to INEGI, there were 799,868 deaths that year, of which 399,667, practically half (48.7%), were due to CKM.

- In the FRIMEX-III study, conducted with 297,370 Mexican participants, 27% had HBP, 50% had hypercholesterolemia, 40% were overweight, and 30% were obese. In these participants, the Body Mass Index (BMI) was found to be linearly correlated with blood pressure, blood glucose, and total cholesterol.⁴
- The results of the RIHTA Registry published in 2023 by our group, showed in 5590 Mexican patients living with HBP, that the average BMI was 28.8 kg/m², waist circumference was 95 cm, fasting glucose was 100 mg/dL, HbA1c was 7.10%, LDL-cholesterol was 110 mg/dL. All these indices exceed the values considered acceptable or desirable. In addition, it was found that 54% of the study subjects were sedentary, and 53% reported anxiety during the previous month. On the other hand, 39% of the participants had diabetes, 83.4% had abdominal obesity, 59.8% had LDL cholesterol levels above 100 mg/dL, 42% had hypoalphalipoproteinemia (low serum HDL-cholesterol), 56.2% had high triglyceride concentrations, and 57.9% were classified as having a high cardiovascular risk.⁵
- These data suggest a relationship far beyond a coincidence by chance, and allow us to affirm that the problem of arterial hypertension is part of a much broader connection than that described as CKM, so we propose the term

- MACARENHA Connection to describe this relationship, in a more didactic way, in which we include a greater number of components: Metabolic-Adipose-Cardio-Arterial-Renal-Entero/hepatic-Neurological, in the context of AH (Arterial Hypertension) (*Figure 1*).
- Comprehensive diagnosis and management of the MACARENHA Connection are crucial for improving population health and reducing the healthcare burden in Mexico resulting from its outcomes. Moving beyond the simple diagnosis of hypertension to a holistic approach that addresses the interconnected nature of MACARENHA has paramount importance for effective prevention and treatment. Public health initiatives and policy changes aimed at addressing the socioeconomic and environmental determinants of health are necessary to mitigate the impact of the MACARENHA Connection on the population.

How to address cut-off points in the diagnosis of MACARENHA?

The pathophysiological mechanisms underlying the MACAREHNA Connection are multiple and closely interconnected. Thus, the activation of one neurohormonal system leads to the activation of another and sometimes potentiates its harmful effect. Therefore, although the parameter used to define high blood pressure is based on a continuous variable (blood pressure) for which a cut-off point is determined, and a similar approach applies to diabetes and dyslipidemia (glucose and lipid concentrations), they must certainly be analyzed in a broader context.

- Treating a patient with a blood pressure of 138/86 mmHg in the absence of other factors will not be the same as treating another one with the same blood pressure level but with dysglycemia or hypercholesterolemia. In the former, their cardiovascular risk may be low, and they may not require pharmacological treatment. However, suppose the patient is at high or very high risk due to the presence of other comorbidities (diabetes and/or

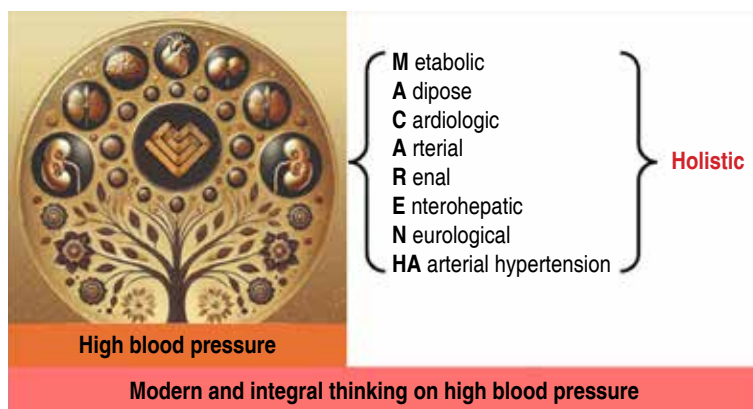


Figure 1: What is MACARENHA? The explanation of the acronym MACARENHA (see text).

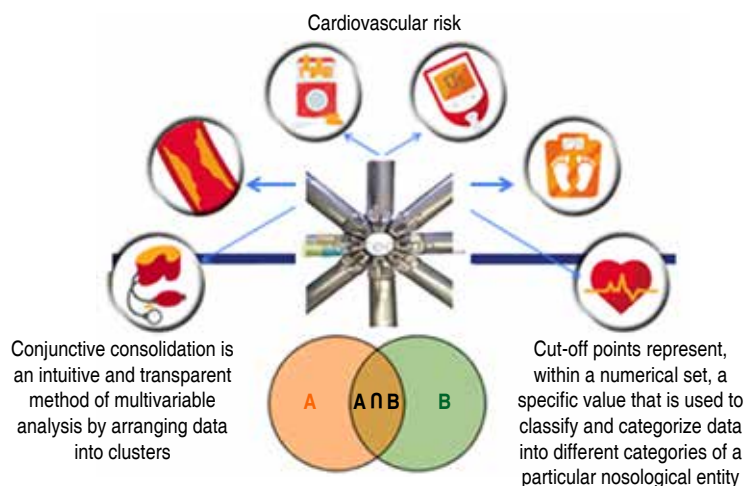


Figure 2: Conjunctive consolidation model. A conjunctive consolidation model emphasizes the importance of analyzing diagnostic cut-off points within the broader context of the patient and their comorbidities.

dyslipidemia, for example) or target organ damage. In that case, they will undoubtedly require pharmacological treatment.^{6,7}

2. This cutoff point situation also applies to the goals to be achieved. For example, in dyslipidemia, the target LDL-C value is 100 mg/dL for very low-risk patients, 70 mg/dL for intermediate-risk subjects, and 55 mg/dL or less for high- and very high-risk individuals. Generally, it can be said that the higher the risk, the stricter the control of risk factors becomes (Figure 2).⁸

What is the pathophysiological connection in MACARENHA?

Pathophysiology of aggregated cardiometabolic risk factors. In the context of the Mexican population, the aggregation of these cardiometabolic conditions is a consequence of abdominal obesity, which affects most of the adult population and a considerable segment of adolescents and school- and preschool-aged children. The imbalance between caloric intake and energy expenditure causes the expansion of fatty tissue beyond its physiological storage capacity. This has two consequences: On the one hand, fat is deposited in other types of tissues (for example, the myocardium, skeletal muscle, and kidney), a phenomenon we have termed lipotthesaurosis (excessive lipid storage),

which causes lipotoxicity and damage to the areas where it occurs.⁹

Key messages

1. These structural pathological changes in adipose tissue establish the insulin resistance syndrome associated with reactive hyperinsulinism as long as pancreatic β cells remain capable of secreting insulin. Although the main cardiovascular and cardiometabolic syndromes, such as hypertension, dyslipidemia, and dysglycemia (diabetes and prediabetes), can be caused by many other factors, including inherited pathogenetic phenotypes, obesity itself, directly or in conjunction with genetic traits, is the central etiopathogenic phenomenon in most cases.^{10,11}
2. Abdominal obesity, alone or accompanied by a hypertensive heritage, can be the origin of hypertension through intra- and extrarenal compression. Intraparenchymal fat compressing the vasa recta causes increased sodium reabsorption in the loop of Henle. Thus, the *macula densa* detects low fluid osmolality in the distal convoluted tubule and sends a signal to the juxtaglomerular cells, activating the renin-angiotensin-aldosterone axis.¹²
3. Angiotensin II is a potent vasoconstrictor and inducer of arteriolar hypertrophy, effects that increase peripheral arterial resistance and blood pressure. On the other hand, leptin, an adipohormone generated primarily in adipose tissue whose plasma concentration increases in obese individuals, among numerous different effects, acts on the arcuate nucleus of the hypothalamus and activates neurons of the pro-opiomelanocortin (POMC) system, which in turn stimulates the action of the sympathetic nervous system, some of whose adrenergic mediators are also potent vasoconstrictors and inducers of cardiovascular hypertrophy. Furthermore, the binomial insulin resistance/hyperinsulinism is the cause of a profound disorder of lipid metabolism. As a result of insulin resistance, stored fat is mobilized to the liver, and the capacity

- of several insulin-sensitive lipolytic enzymes decreases.¹³
4. Macrophages remove cholesterol from tissues, depositing it on immature HDL until they mature, thereby storing lipids through a process known as lipidation. Once engorged, liver scavenger receptors remove mature HDL from the circulation, eliminating or reprocessing their contents. A serum cholesteryl ester transfer protein (CETP) provides an indirect pathway, serving as a bridge for triglyceride-rich lipoproteins to exchange this lipid for cholesterol with high-density lipoprotein (HDL) particles. Vascular and hepatic lipases rapidly attack these cholesterol-poor, TG-rich HDL, which are structurally unstable and easily lose their apolipoprotein Apo A-I.¹⁴
 5. Dysglycemia, the other major atherogenic risk factor, is also a consequence of the insulin resistance/hyperinsulinism complex. Between 85 and 90% of patients with type 2 diabetes (T2DM) are overweight or obese. However, only about 30% of people who are obese or overweight have diabetes, indicating that, in addition to obesity, other, predominantly hereditary, factors are responsible for the development of diabetes.
 6. The two entities, obesity and diabetes, are so closely related that the term «diabesity» was coined to highlight the clinical, epidemiological, and pathophysiological shared complexity of both conditions. The mechanisms of insulin resistance secondary to obesity are numerous, including systemic inflammation and nitroxidation of biomolecules, the effect of adipocytokines such as tumor necrosis factor- α (TNF- α), which impair insulin receptor signaling, and dysfunction of both the endoplasmic reticulum and mitochondria, among others.¹⁵
 7. One consequence of the insulin resistance/hyperinsulinism binomial is a condition formerly known as nonalcoholic fatty liver disease (NAFLD), and recently renamed as metabolic dysfunction-associated steatotic liver disease (MASLD), which includes a broad spectrum of conditions ranging from a relatively benign and even hepatoprotective condition, steatosis, to increasingly severe conditions such as metabolic dysfunction-associated steatohepatitis (MASH), with or without fibrosis, to irreversible and fatal conditions such as cirrhosis and hepatoma.¹³
 8. A final player in this mosaic of pathophysiologically intertwined metabolic and cardiovascular conditions is the intestine, which involves two leading actors: the gastrointestinal hormones and the gut microbiota. Among the former, glucagon-like peptide-1 (GLP-1), a so-called incretin hormone, is secreted by L cells in the intestine in response to the ingestion of food. The hormone intervenes in the energetic and carbohydrate metabolism, inhibiting the pancreatic secretion of glucagon, which promotes glycogenolysis and gluconeogenesis. Another gastrointestinal hormone, the glucose-dependent insulinotropic polypeptide (GIP), increases the release of glucagon and promotes the storage of fat. The «incretin effect» (which refers to the release of two to three times more insulin when a dose of glucose is ingested compared to when the same amount is infused parenterally) is primarily caused by the insulinotropic peptides. Furthermore, GLP-1 regulates appetite, reduces gastrointestinal motility, and enhances myocardial function, as well as various neuronal processes, including neuroprotection, among other effects.^{15,16}
 9. The other intestinal agent is microbiota, the community formed by the conglomerate of bacteria, viruses, fungi, and archaea in the intestinal tract. It is estimated that there are between 500 and 1,000 different bacterial species in the intestine, resulting in a total population of approximately 10^{14} organisms. Therefore, 1-3% of body weight is contributed by the mass of microorganisms, mainly anaerobic bacteria. The microbiota contributes to overall and metabolic health when there is a virtuous balance between various species, primarily grouped into the Gram-negative *Bacteroidetes* and Gram-positive *Firmicutes* (Table 1).¹⁷⁻¹⁹

How to estimate cardiovascular risk in hypertensive patients with MACARENHA?

Cardiovascular risk (CVR) represents the calculated probability that a patient will

Table 1: Predictive algorithms to specific features of MACARENHA.

Factor to evaluate	Algorithm	Construct variables	Description
Visceral adiposity and incidence of T2DM	METS-IR	Serum glucose, HDL-c, BMI, Triglycerides	Non-insulin-based fasting scale for assessing insulin sensitivity validated against the euglycemic-hyperinsulinemic clamp (EHC)
VAT	METS-VF	METS-IR, gender, waist circumference, height, age	Scale in patients with Metabolic Syndrome predicting the incidence of T2DM and HBP, independently of BMI, in primary care
MASLD	FLI, MRE, or THE	GGT, BMI, waist circumference, and triglycerides	Requires validation
Mood	Beck Depression Questionnaire	Symptoms and signs of depression and anxiety	A simplified, self-applied, 21-item scale with four response options that considers the patient's condition over the past two weeks

BMI = body mass index. FLI = fatty liver index. GGT = gamma-glutamyl transferase. HBP = high blood pressure. HDL = high-density lipoprotein. MASLD = metabolic dysfunction-associated steatotic liver disease. METS-IR = metabolic score for insulin resistance. METS-VF = metabolic score for visceral fat. MRE = magnetic resonance elastography. T2DM = type 2 diabetes mellitus. THE = transient hepatic elastography. VAT = visceral adipose tissue.

experience a cardiovascular (CV) event that causes disability or death. This probability is based on the evaluation of factors and/or health conditions that independently contribute a value to this mathematical calculation; these algorithms have been validated in large patient cohorts.

Key messages

1. Real-life epidemiological studies, such as those from the National Registry of Arterial Hypertension (RIHTA) in Mexico, have shown that more than 40% of patients with HBP had an average of 5-6 traditional risk factors, which promote target organ damage (TOD) and cardiovascular disease, with increased frequency in younger adults. Using traditional CV risk calculators such as SCORE 2 and Globorisk, RIHTA showed that 57.9% (95% CI: 56.6-59.2) of patients were at high CV risk. Furthermore, more than half had a high prevalence of cardiometabolic risk factors, whose negative contribution to CV health is well documented.^{5,20}
2. Promote and maintain political will to make CVR assessment mandatory in the context of the MACARENHA acronym at all levels of healthcare. To this end, GREHTA

presents the proposal in this document and undertakes to disseminate it continuously.

3. Promote and maintain political willingness to make CVR assessment mandatory in the context of the MACARENHA acronym at all levels of healthcare. To this end, GREHTA presents the proposal in this document and undertakes to divulge it permanently.

What is the role of clinical judgment in the risk stratification of MACARENHA?

1. Clinical judgment refers to a healthcare professional's ability to integrate information obtained from the medical history, physical examination, and the results of paraclinical studies, enabling them to establish a diagnostic probability and prescribe appropriate treatment. In other words, it is the whole exercise of the scientific method applied to clinical practice. In the context of MACARENHA, the external habitus, targeted questioning, and a comprehensive physical examination enable the use of logic and reasoning to resolve in favor of the patient.
2. All physicians need to exercise clinical judgment, but this requires the following: 1) Being familiar with the constant advances in

- knowledge; 2) To have the time and space to analyze the problem; 3) Having access to equipment and auxiliary studies for precise diagnosis; 4) Being able to seek guidance from a colleague with greater experience and clinical practice. In our setting, several of these premises are limited. The acronym MACARENHA describes the general concept of the problem and provides a clinical guideline helpful for consultation at any level of medical care.²¹
3. Continuing medical education is crucial for enhancing the quality of outpatient care. Although in Mexico and many regions of the world this activity is an individual responsibility, access to the academic environment through medical societies, academies, and colleges is partially accessible and not mandatory in our country. Furthermore, the unfortunate phenomenon of a lack of therapeutic resources undermines physicians' motivation and initiative in learning about and implementing therapeutic advances. GREHTA has the academic structure to support this initiative, which aims to raise awareness and provide training.
 4. MACARENHA is an acronym developed by GREHTA that is added to the approved cardiovascular risk stratification. In addition to the contribution of traditional factors, the presence of established cardiovascular disease (CVD), as well as patient characteristics, there are also metabolic, liver, and mood alterations whose contribution to cardiovascular risk is recognized but not integrated into the mathematical algorithms that determine the probability of experiencing a fatal cardiovascular event. In our environment, evaluating these additional aspects in a systematic, clinical, and accessible manner represents an opportunity for early therapeutic intervention.

How to use the therapeutic approach in MACARENHA?

The goal of hypertension treatment is not only to reduce blood pressure levels, but also to prevent or delay organ damage caused by

hypertension and the complex of metabolic, inflammatory, hemodynamic, and structural alterations that damage vital organs and are the cause of cardiovascular morbidity and mortality.¹⁻³

1. Non-pharmacological treatment, promoting lifestyle changes, diet, exercise, and optimizing body weight, should be established for all patients living with hypertension.
2. In modern hypertension treatment, the use of drugs that only lower blood pressure cannot be conceived without offering additional benefits of organ protection and improvement of at least one of the most common comorbidities.
3. We must seek beneficial effects in reducing ventricular hypertrophy, preserving vascular and renal function, and improving the metabolic and liver profile.
4. Taking this into account, we agree with the recommendations of most international guidelines. It is essential to initiate antihypertensive treatment with at least two different antihypertensive medications. If control is not achieved, it is recommended to add a third antihypertensive, ideally in a single tablet. If adequate control is not achieved, a fourth antihypertensive should be added. However, it is essential to consider the patient's comorbidities and the specific characteristics of the various antihypertensives when selecting the most suitable ones for each case.
5. Most antihypertensive medications are effective for patients with type 2 diabetes mellitus (T2DM). However, it is worth mentioning that both angiotensin-converting enzyme inhibitors (ACEi) and angiotensin receptor blockers (ARBs) have a particular benefit in patients with albuminuria. In this regard, ACEi are considered to have more evidence demonstrating a reduction in cardiovascular morbidity and mortality. Similarly, the recently published FIDELIO DKD and FIGARO DKD studies showed the benefits of finerenone on kidney function and the reduction of cardiovascular events in diabetic patients with nephropathy, suggesting that this could be another

- medication with added benefits in patients with diabetes. It's worth noting that the use of SGLT2i (sodium-glucose cotransporter-2 inhibitors) has been associated with a modest decrease in blood pressure and a significant reduction in cardiovascular events in this patient group; therefore, their use should also be considered.^{1-3,22}
6. Controlling high blood pressure is particularly beneficial in patients with chronic kidney disease, as it reduces both cardiovascular events and mortality. Both ACE inhibitors and ARBs are effective in reducing cardiovascular morbidity and mortality in these patients. Still, the use of ACE inhibitors has been shown to reduce events at a greater rate. Combination therapy with at least two antihypertensives is recommended from the outset in this group of patients: ACE inhibitors or ARBs + BC or diuretics. The use of loop diuretics is often necessary for patients with a glomerular filtration rate of less than 30 mL/min/1.73 m². Thiazide-type diuretics such as indapamide and chlorthalidone may be considered for filtration rates up to 15 ml/min/1.73 m². In patients with T2DM and kidney disease, finerenone has been shown to reduce cardiovascular morbidity and mortality and the progression of kidney disease and should therefore be considered a therapeutic option. The use of SGLT2i has been linked to a modest reduction in blood pressure; however, it is also associated with a significant decrease in cardiovascular events and the progression of kidney disease in this patient group, making its use a consideration.²³
 7. In patients with a history of ischemic heart disease, the use of a combination of ACEIs/ARBs and beta-blockers is especially beneficial. If patients present with angina, both beta-blockers (BBs) and calcium channel blockers (CCBs) can be considered as treatment options. Therefore, the initial combination for hypertension and ischemic heart disease includes the use of ACEIs/ARBs + BBs. If blood pressure is not controlled, adding beta blockers (BCs) is considered, followed by the use of a thiazide-type diuretic.²³
 8. In patients with heart failure and reduced left ventricular ejection fraction (LVEF), it is considered a priority to initiate antihypertensive treatment with agents that have been shown to improve the prognosis in this group of patients. Therefore, initial therapy for hypertension is considered to include a combination of four blood pressure-lowering medications: ARNi (angiotensin receptor-neprilysin inhibitor), beta blockers (BBs), mineralocorticoid receptor antagonists (MRAs), and SGLT2 inhibitors. In cases of ARNi intolerance, the use of ACEIs is recommended, and if they are intolerant, the use of ARBs is considered.²⁴
 9. In this condition, adequate blood pressure control is a priority, and it is recommended as in any case of hypertension. However, as with other conditions, it is essential to include drugs in the treatment that have been shown to reduce cardiovascular events and mortality. Therefore, SGLT2 inhibitors and finerenone should be used in conjunction, considering that both have an antihypertensive effect.²⁵
 10. Benefits of statins: the comprehensive management of hypertensive patients with metabolic and cardiovascular disorders such as diabetes, obesity, dyslipidemia, kidney disease, and fatty liver disease is crucial to reducing cardiovascular risk and improving quality of life. This multidisciplinary approach allows for the treatment of not only hypertension but also comorbidities, thus optimizing the patient's overall health. The use of statins in hypertensive patients with intermediate and high cardiovascular risk has consistently been shown to reduce the incidence of major cardiovascular events and mortality. In this pathology, adequate blood pressure control is a priority, and monitoring is recommended as in any case of hypertension. However, as in all other pathologies, it is essential to incorporate drugs that have been shown to reduce cardiovascular events and mortality in the treatment. Therefore, iSGLT2 and finerenone should be included in parallel with antihypertensive treatment, considering that both have an antihypertensive effect.²⁶

11. This clear benefit of statin use in hypertensive patients at intermediate and high risk leads us to recommend their use in most hypertensive patients, except those who should not use statins.

Conclusion. The main objective of pharmacological treatment for hypertension is to reduce the morbidity and mortality associated with it and its related conditions. Therefore, the use of antihypertensive drugs that have demonstrated this benefit is recommended for both hypertension and the conditions that commonly accompany it. Based on the significant evidence available, it is considered that statins should be used concomitantly in most patients with hypertension who also have one or more of the different conditions included in MACAREHNA.

What to do with patients with resistant hypertension?

Use of invasive devices in patients with resistant hypertension (RH)

1. Hypertension is the leading cause of death from ischemic heart disease, cerebrovascular events (both ischemic and hemorrhagic), chronic kidney disease, and others. Despite efforts to detect and control hypertension, less than half of patients diagnosed with hypertension are on treatment goals. Those with RH are among the group of patients with difficulty controlling their hypertension. RH is defined as blood pressure above the target level despite the use of at least three antihypertensive drugs from different classes of substances, including a diuretic in appropriate doses and combinations. Given the significant problem posed by this disease and its difficult control, non-pharmacological therapies have been developed as adjuvants to current treatment to increase control rates and reduce the morbidity and mortality of HBP. Among them, the most studied in the last decade is renal sympathetic denervation. This interventional treatment aims to reduce the sympathetic overstimulation

that has been shown to occur in patients with difficult-to-control hypertension.²⁷

Is renal sympathetic denervation (RSD) an effective and safe therapy for improving blood pressure in patients with resistant and difficult-to-control hypertension?

2. The first study on RSD was Simplicity HTN-1 with 50 pts with HR, with a reduction in office systolic BP (SBP) of 27 mmHg and diastolic BP (DBP) of 17 mmHg at one year, and with reductions in 88 patients at three years of 32 mmHg in SBP and 14 mmHg in DBP, with no significant adverse events.¹¹ The Symplicity HTN-2 study included 106 patients with HR who were randomized to RSD (n = 52) or medical treatment (n = 54) with a reduction in office SBP of 32 and DBP of 11 mmHg in the RSD group compared with a reduction of 1/0 mmHg in SBP/DBP in the control group, with no evidence of significant adverse events related to RSD. The Symplicity HTN-3 study included 535 HR pts randomized 2:1 to RSD vs a Sham procedure where the RSD group reduced 14 mmHg and the Sham group 11 mmHg, therefore the difference between groups at six months did not reach the statistical difference of more than 5 mmHg for the efficacy outcome, the primary safety endpoint was met with no significant adverse events in the RSD group. The final 36-month follow-up of this study was published in Lancet in 2022 demonstrating a reduction in office SBP of 26 mmHg in the RSD group vs 5 mmHg in the Sham group (p < 0.0001) and a reduction in ABPM of 15.6 mmHg in the RSD group vs 0.3 mmHg in the Sham group (p < 0.0001). Since the publication of HTN-3 in 2014, changes have been made to the radiofrequency denervation catheter, transitioning from monopolar to tetrapolar, self-expanding, and coiled devices, such as the Spyral. Additionally, an ultrasound-based catheter, known as the Paradise System, has also been developed. The results of subsequent studies were performed with these technologies. The HTN Spyral Off Med study again demonstrated proof of concept for denervation in 331 patients,

166 in the DSR group and 165 in the control group (Sham). These patients did not receive pharmacological treatment to evaluate the pure response to DSR. The safety and efficacy endpoints were met, with statistical differences in favor of the DSR group. Subsequently, the Spyril HTN ON Med study included patients with difficult-to-control hypertension and BP between 140 and 170 mmHg and randomized them to DSR vs. Sham. At 36 months of follow-up, the differences in ABPM for blood pressure were: the RSD group had a reduction in SBP/DBP of $-18.7/-11.9$ mm Hg, while the Sham group had a reduction of $-8.6/-6$ mmHg. These differences were statistically significant ($p = 0.0039$ for SBP and $p = 0.0055$ for DBP), with the additional benefit of a 24-hour effect observed through ABPM for RSD compared to the Sham group. Additionally, the Sham group had a greater need for increased antihypertensive medication load than the RSD group. The DENERHTN study analyzed 101 patients with HBP, of which 48 were assigned to the RSD + randomized sequence antihypertensive escalation (RSAHT) group versus the RSAHT group alone. The conclusion was that the RSD group at six months reduced daytime SBP on ABPM by -15.8 mmHg vs. -9.9 mmHg in the SSAHT group alone, a baseline-adjusted difference of -5.9 mm Hg (-11.3 to -0.5 ; $p = 0.0329$). The RADIANCE-HTN TRIO study, which utilized ultrasound technology, enrolled 136 patients with hypertension, randomizing 69 to receive RSD and 67 to receive Sham treatment. In this study, RSD reduced SBP by 4.5 mmHg more on ABPM than the control group within six months, representing a statistically significant difference. It is worth noting that the primary safety endpoints have been fully met in all previous studies.²⁷

3. RSD is approved as an adjunct to pharmacological therapy to help manage patients with heart rhythm disorders (HR). There is no position from any Latin American society regarding the treatment or the algorithm to follow for determining candidates for it. The proposal is to develop

an algorithm for selecting candidate patients by guidelines and algorithms for patients with RH. It is suggested that, if the position is favorable regarding RSD, the steps to follow are to determine:

- a. Which patient should be considered HR?
 - b. Objectively and practically rule out pseudo-resistance.
 - c. Establish ABPM as a fundamental part of the HR study algorithm.
 - d. Prioritize those patients at higher cardiovascular risk, who are most susceptible to adverse events and in whom BP control has an even greater benefit (the fundamental objective of MACARENHA).
 - e. Establish a practical algorithm to rule out secondary hypertension.
 - f. Emphasize avoiding therapeutic inertia.
 - g. Recommend the establishment of an expert group to determine therapeutic options and consider the patient's decision.
 - h. Suggest appropriate pathways for a patient to undergo a safe and effective procedure performed by experienced operators.
4. RSD is a minimally invasive treatment that is safe and effective in significantly reducing SBP and DBP in patients with RH, in conjunction with drug treatment. Its durability, as evidenced by at least 3 years of follow-up, has been proven, and it offers a 24-hour effect. This therapy should be regulated to establish its proper use based on scientific evidence and prevent its abuse.

How would digital health be useful in MACARENHA?

Cardiovascular diseases are the leading cause of death in Mexico and worldwide. Despite significant advances in pharmacological treatments and invasive procedures for the management of acute myocardial infarction, it remains the leading cause of mortality globally. Furthermore, an increase in the prevalence of other chronic diseases such as heart failure, atrial fibrillation, aortic valve stenosis,

chronic kidney disease, fatty liver disease, and cognitive impairment, among others, has been observed.²⁸

1. High blood pressure is frequently associated with multiple cardiometabolic risk factors, such as obesity, diabetes, and dyslipidemia. Together, these factors contribute to multi-organ damage, affecting vital organs such as the heart, brain, liver, and kidneys. The high prevalence of these risk factors, combined with the low control rates observed in most countries, underscores the urgent need to adopt innovative strategies to address this issue. In this context, digital health, new technologies, and artificial intelligence are emerging as key tools to optimize both the diagnosis and comprehensive management of these conditions.
2. To address the problem of controlling high blood pressure and cardiometabolic risk factors in Mexico and Latin America, it is crucial to consider the unique characteristics of the region, including unequal access to health services, the high prevalence of obesity and diabetes, and economic constraints. Specific and tailored solutions are proposed below.
3. Strengthening primary care through the use of digital technologies for mass training, employing a multidisciplinary approach that involves health personnel (physicians, nurses, nutritionists, social workers, psychologists, etc.) to enhance primary prevention, detection, and comprehensive management of hypertension and associated cardiometabolic risk factors via standardized protocols.
4. Promoting digital health through the use of electronic medical records, mobile applications, voice assistants, and portable electronic devices, such as digital sphygmomanometers, glucometers, digital scales, and rhythm strip electrocardiographs, considering indigenous languages and different literacy levels. Train healthcare personnel and patients in the use of digital tools and artificial intelligence to enhance their care and treatment.²⁸
5. Education and prevention campaigns: highlight and promote a healthy lifestyle

from childhood, focusing on proper nutrition and physical activity. Implement educational programs in schools and textbooks, and increase the use of mass media, including social media and digital platforms, to enhance knowledge and understanding.²⁸

6. Promote public policies: health regulations on sugary drinks, ultra-processed foods, and easy labeling. Promote recreational spaces that promote physical activity, such as parks and bike paths.
7. Encourage the use of artificial intelligence and big data: Enhance traditional risk prediction and stratification systems, and implement regional databases, such as the RIHTA (Registro de Hipertensión Arterial), to inform clinical and public health decisions. Develop pharmacogenomics, personalized medicine, and AI-based therapies.
8. Increase international collaboration: A collaborative approach is required among governments, health institutions, academia, industry, and civil society. Furthermore, it is essential to adapt these approaches to local specificities within Mexico and Latin America, prioritizing equity and sustainability.
9. The use of digital health, new information technologies, wearable devices, and artificial intelligence has not only proven to be key tools for improving patient education but also has the potential to significantly increase the diagnosis, monitoring, and follow-up rates of patients with multiple cardiometabolic risk factors and multisystem organ damage. Within the framework of the MACARENHA Connection, these emerging technologies promise to optimize care and clinical outcomes comprehensively (*Figure 3*).

What would be the preventive approach? MACARENHA's vision

Primordial Prevention

1. Focused on avoiding the onset of CVRFs before they develop.²⁹ Involves changes in public policies, improvements in the context at the macro

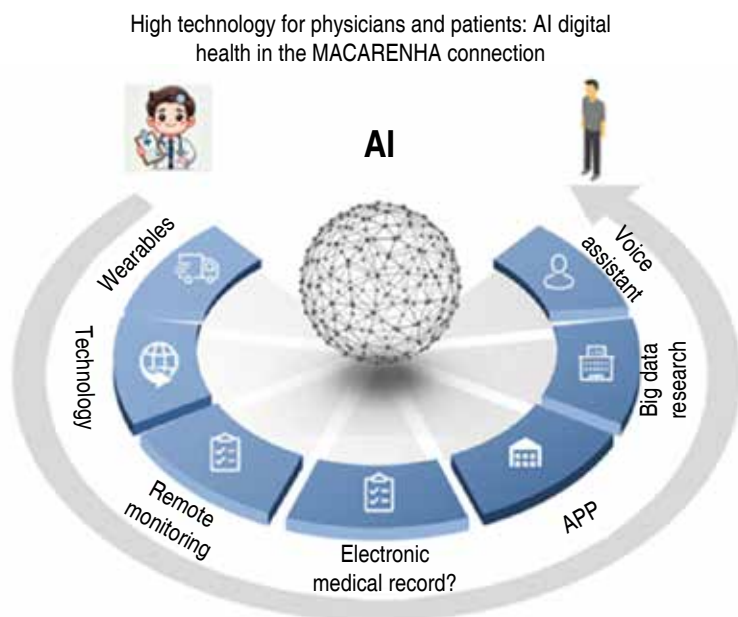


Figure 3: Artificial intelligence in the context of MACARENHA.

AI = artificial intelligence.

MACARENHA = Metabolic-Adipose-Cardio-Arterial-Renal-Entero-Hepatic-Neurological-behavior in Hypertension.

level, encompassing the physical, urban, economic, environmental, and social environments, as well as changes in individual behavior.

- a. For example, programs that promote physical activity and healthy eating from childhood.
- b. Promotion of Healthy Lifestyles: Promoting regular physical activity and a balanced diet are cornerstones of this initiative.
- c. Educational campaigns that increase awareness about CVRFs.
- d. Access to Preventive Health Care: Facilitate universal access to health services that promote prevention, periodic health checkups, and campaigns for correct blood pressure measurement.

Primary prevention: intervention in individuals already with CVRF³⁰

1. For GREHTA, it is essential to focus on people who already have high blood pressure (disease/risk factor).

2. The goal is to prevent progression to established cardiovascular disease.
3. Key strategies include early detection and diagnosis, appropriate pharmacological management of hypertension and risk factors such as obesity, DM, dyslipidemia, etc.
4. The recently published study «Overweight, Obesity and Age: The Main Determinants of Cardiovascular Risk Aggregation in the Current Mexican Population: The FRIMEX III Study», by Eduardo Meaney et al., establishes that in developed countries, hypertension behaves according to the so-called «law of thirds», in developing countries it behaves like the well-known «law of halves», and that in Mexico, control is only 8%, which is alarming.

Secondary prevention, according to the WHO, is intended for the early detection of incipient disease (before clinical manifestations appear). It means searching for diseases as early as possible in «apparently healthy» subjects.

5. And the WHO continues: «It includes actions resulting from early diagnosis and timely treatment, particularly for arterial hypertension in its early stages, by conducting periodic check-ups and monitoring the patient, monitoring its progress, and detecting any possible sequelae (target organ damage) promptly. Secondary prevention refers to the strategies and measures implemented to control and manage hypertension in individuals who have already been diagnosed with this condition, to prevent complications and improve quality of life».
6. An unquestionable aspect, starting with primary prevention and predominantly in secondary prevention, is the importance of follow-up in secondary prevention and the suspected diagnosis of hypertension-mediated organ damage (HMOD). Accordingly, in this MACARENHA connection, we highlight the metabolic involvement (fasting blood glucose, HbA1c, weight control, CRP, thyroid hormone), as well as the effects on the heart, blood vessels, brain, kidney, and liver, among others, proposing basic studies to investigate these effects. Several international societies have already emphasized this comprehensive

approach to hypertension management in different ways.³¹

Tertiary Prevention

1. According to the WHO, it refers to actions related to the complete recovery of the clinically manifest disease, through correct diagnosis and treatment, and physical, psychological, and social rehabilitation in cases of disability or sequelae, thus seeking to reduce them (Figure 4).^{32,33}

What other ways are there to prevent cardiovascular risk?

Role of influenza vaccination³⁴⁻³⁷

In Mexico, for the last six years (2016-2023), cardiovascular disease has been the leading cause of death, surpassed only by COVID-19 infection in 2022. Other respiratory illnesses, such as seasonal influenza and pneumonia, have also been among the top 10 causes of death in Mexico in recent years, according to the National Institute of Geographical and Statistical Information (INEGI).

Key Messages

1. All patients with high blood pressure must receive an annual influenza vaccination.
2. Include all adults aged 50 years and above in the universal vaccination program with standard doses, regardless of comorbidities.

As earlier prevention, maximal benefit

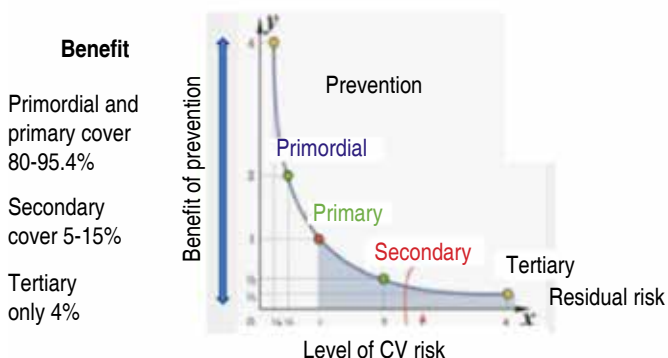


Figure 4: Comprehensive cardiovascular prevention. CV = cardiovascular.

3. The use of a high-dose differentiated influenza vaccine is recommended for adults over 60 years of age (it will be available in Mexico shortly).
4. According to the latest report from the World Health Organization (WHO) (Global Respiratory Virus Activity Weekly Update No. 503), the activity of seasonal influenza viruses and SARS-CoV-2 remains at inter-epidemic levels in Mexico, even elevated in other countries around the world.
5. According to the WHO, there are estimated to be over 3.5 million cases of seasonal influenza each year, resulting in up to 650,000 deaths annually.
6. We know that diseases such as influenza, pneumonia, and COVID-19 are more than just respiratory illnesses, as they also cause uncontrolled cardiovascular risk factors, including diabetes and high blood pressure, in adults. These infections are directly related to an increase in neurological, renal, and cardiovascular complications such as cerebrovascular events (CVA), encephalopathy, acute kidney failure, acute myocardial infarction (AMI), heart failure, myocarditis, and venous thromboembolism.
7. The mechanisms by which these infections increase the risk in these patients derive from effects generated by the acute respiratory disease, such as hypoxemia (with increased myocardial oxygen demand), increased inflammatory cytokines that cause hypercoagulability, and increased adrenergic activity, which can lead to the rupture of an atheromatous plaque, causing atherothrombosis at the coronary, cerebral, or peripheral levels. In addition, the viruses can lodge directly at the vascular, myocardial, or cerebral levels, causing myocarditis or encephalitis. Undoubtedly, the impacts of vaccination against influenza viruses.
8. COVID-19 and pneumococcus have been beneficial in the global and Mexican population with cardiovascular risk factors. For example, it is estimated that influenza vaccination in older adults reduces cardiovascular death and death from all causes by up to 41%.
9. According to the vaccination guidelines for the 2024-25 winter season in Mexico, the

target population for the pneumococcal vaccine is all adults over 60 years of age, while for influenza, the target population is children from six months to five years of age, adults over 60 years of age, as well as at-risk populations such as pregnant women, healthcare personnel, children, and adults in general with comorbidities such as diabetes, morbid obesity, chronic lung diseases, kidney failure, immunocompromised individuals, and cardiovascular disease. These guidelines also recommend vaccination for COVID-19 in this same group of patients, except for children under five years of age and adults with acquired or congenital chronic cardiovascular diseases that require prolonged use of salicylates. It is not clear whether all patients with essential hypertension are considered comorbid or high-risk patients. Another aspect to consider is that ages with high influenza mortality rates, such as those between 50 and 60 years of age, are not eligible for influenza vaccination in Mexico.

10. All adults over 60 years of age must achieve and maintain 95% pneumococcal vaccination coverage.
11. Vaccination against influenza and other infections, such as COVID-19 and pneumococcus, in patients with hypertension and the MACARENHA connection is essential for preventing complications and reducing morbidity and mortality in these patients in Mexico.

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Gym benefits?

¿Beneficios del gimnasio?

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We had a recent admission in our clinic of a 33-year-old man with a frontal fracture after a syncope-related hit. The patient happened to have an acute massive pulmonary embolism with severe right ventricular failure, with final survival after seven days in hospital, including three days of intensive care.

This young man is a bodybuilder with gym-strain training tailored by an instructor and a nutritionist who prescribed polypharmacy including clenbuterol, oxymetholone, carnitine betaine anhydrous, L-carnitine tartrate, glycine propionyl L-carnitine, creatine, and glutamine, plus several plant-based powders.

On the same discharge day, we received another one, a 29-year-old male with palpitations; another gym-staff and esthetics-oriented nutritionist victim, receiving indications of strain escalation, high carbohydrate diet, and polypharmacy with beta-alanine, creatine monohydrate, caffeine anhydrous, *Juniperus communis*, hordenine HCL, dimethylethanolamine, *Rauwolfia vomitoria* extract (alpha yohimbine), and *Huperzine serrata*, on a bottle called Psychotic Blend. This patient had sinus tachycardia, ventricular extrasystoles, hyperglycemia, and up to three times the upper normal level of creatine phosphokinase (CPK). The patient came accompanied by his girlfriend, who also had a mesomorphic habitus and the same treatment. He was not surprised when we informed him about the significant CPK elevation. He explained to us that the purpose of muscle damage is to accelerate muscle buildup.

Who doubts the benefits of physical training, including gym strain, with obvious wellness and life expectancy gain, especially through

cardiovascular risk reduction?¹ Nonetheless, these athletes receive dangerous instructions from trainers and nutritionists, oriented towards beauty over health, recommending wrong diets, and polypharmacy that exposes them to potentially harmful drug interactions.²

The problem exposed here discloses several issues, starting with the personal need for beauty over the need for early death prevention, the trainers with strategies of fast muscle growth based on muscle damage, multiple drug compounds masked as nutritional supplements, and nutritionists prescribing them.

The cardiological community must be prepared to attend to severe complications from the training of healthy and sick persons under the advice of these professionals. I also mention sick patients as I remember a case of a man with coronary bypass on oral anticoagulation who had a catastrophic complication after a prescribed intense 3-hour daily strain training.

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Atherogenic risk profiles and cardiovascular risk assessment in hospitalized patients with type 2 diabetes

Perfiles de riesgo aterogénico y evaluación del riesgo cardiovascular en pacientes hospitalizados con diabetes tipo 2

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Palabras clave:

cardiología, aterogénica, diabetes mellitus, riesgo cardiovascular.

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ABSTRACT

Introduction: cardiovascular diseases are the leading cause of morbidity and mortality among individuals with type two diabetes mellitus, affecting adults aged 20 to 79 years. **Objective:** the study aims to correlate atherogenic risk factors with the duration of diabetes diagnosis to determine the cardiovascular risk of patients in a hospital ward. **Material and methods:** this observational, correlational, and cross-sectional study was conducted at the Center of Medical Specialties of the *Instituto de Seguridad Social del Estado de Tabasco* from January to June 2024. A representative sample of three hundred forty-three patients was selected from a population of 3,193, using a 95% confidence level and a five percent margin of error. The Framingham cardiovascular risk prediction table was adapted, achieving validation with a Cronbach's alpha coefficient of 0.770. **Results:** among the three hundred forty-three patients evaluated, 39 (11.4%) were found to have a high risk of experiencing a cardiovascular event within the next 10 years. A significant positive correlation was found between cardiovascular risk and the duration since the diagnosis of type 2 diabetes, with a p-value of 0.003. **Conclusion:** the findings confirm that the duration of diabetes is a significant determinant of cardiovascular risk in hospitalized patients.

Abbreviations:

ARFs = Atherosclerotic Risk Factors
BMI = Body Mass Index
CKD = Chronic Kidney Disease
CVD = Cardiovascular Diseases
CVR = Cardiovascular Risk

RESUMEN

Introducción: las enfermedades cardiovasculares son la causa principal de morbilidad y mortalidad en personas con diabetes mellitus tipo 2, afectando a adultos entre 20 y 79 años. **Objetivo:** el estudio busca una correlación entre los factores de riesgo aterogénicos con el tiempo de diagnóstico de diabetes para determinar el riesgo cardiovascular que tienen los pacientes en una sala de hospitalización. **Material y métodos:** este estudio observacional, correlacional y transversal se llevó a cabo en el Centro de Especialidades Médicas del Instituto de Seguridad Social del Estado de Tabasco, desde enero hasta junio de 2024. Se seleccionó una muestra representativa de 343 pacientes de una población total de 3,193, utilizando un nivel de confianza del 95% y un margen de error del 5%. Se adaptó la tabla de predicción de riesgo cardiovascular de Framingham, logrando una validación con un coeficiente de Alpha de Cronbach de 0.770. **Resultados:** entre los 343 pacientes evaluados, la distribución del riesgo cardiovascular fue de 39 (11.4%) pacientes que presentan un riesgo alto de experimentar un evento cardiovascular en los próximos 10 años. Se encontró una correlación positiva significativa entre el riesgo cardiovascular y el tiempo desde el diagnóstico de DM2 con un valor de $p = 0.003$. **Conclusión:** los hallazgos confirman que la duración de la diabetes es un determinante significativo para el riesgo cardiovascular en los pacientes hospitalizados.

DM2 = Type 2 Diabetes Mellitus
IDF = International Diabetes Federation
INEGI = Instituto Nacional de Estadística y Geografía (National Institute of Statistics and Geography)
SD = Standard Deviation

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INTRODUCTION

Cardiovascular disease is the leading cause of morbidity and mortality in individuals with type 2 diabetes mellitus (DM2), especially in adults aged 20 to 79 years.¹ This disease has gained increasing relevance as a health concern due to its high prevalence and the severe complications it causes.

In Mexico, the prevalence of type 2 diabetes is also alarming. According to the 2021 World Diabetes Day Statistics report from the Instituto Nacional de Estadística y Geografía (INEGI), 10.3% of the population aged 20 years or older (equivalent to 8,542,718 individuals) has been diagnosed with diabetes mellitus. By 2001, 16.1% of the population aged 53 years or older had been diagnosed with diabetes (14.1% in men and 17.8% in women). By 2021, this percentage had risen to 25.6% (22.5% in men and 28.1% in women).² However, it is estimated that around 60% of individuals with type 2 diabetes are unaware they have the disease, which significantly increases the risk of severe complications, including cardiovascular diseases, renal failure, and other related issues.³

The complications associated with type 2 diabetes have a devastating impact on global health. According to the Diabetes Atlas of the International Diabetes Federation (IDF), complications of DM2 caused approximately 4.2 million deaths worldwide in 2019.¹ These complications include cardiovascular diseases, renal failure, blindness, and amputations, which severely affect patients' quality of life and represent a significant portion of hospital admissions. Diabetes complications often require urgent intervention and early diagnosis, which includes proper treatment.⁴

Globally, it is estimated that a heart attack occurs every four seconds. In the United States, this event happens every 26 seconds, while in Mexico, it is estimated to occur every three minutes.^{5,6} INEGI reports that although mortality rates from type 2 diabetes have decreased in recent years, from 119.5 per 100,000 inhabitants in 2020 to 89.4 in 2022, diabetes remains one of the leading causes of death, especially among adults aged 65 years and older. By 2023, mortality rates continued to decrease compared to those reported in 2022.⁷

Atherogenic risk factors in type 2 diabetes

DM2 often develops years before clinical diagnosis and is strongly associated with various atherosclerotic risk factors (ARFs). These ARFs directly contribute to the progression and severity of DM2, including dyslipidemia, hypertension (HTN), and obesity, all of which significantly elevate cardiovascular risk in these patients.^{8,9} Therefore, identifying and managing these risk factors is essential to reducing the incidence and severity of cardiovascular diseases (CVD) in individuals with DM2.¹⁰

Cardiovascular risk in type 2 diabetes mellitus

Cardiovascular risk (CVR) refers to the probability of developing CVD, such as coronary artery disease, stroke, or peripheral arterial disease. Alarming, around 80% of deaths in individuals with DM2 result from vascular complications, with ischemic heart disease accounting for 40% and cerebral ischemia for 10%.

Patients with DM2 often face a combination of risk factors that exacerbate their CVR, including tobacco use, physical inactivity, nonadherence to treatment regimens, prolonged disease duration, and the presence of complications.^{11,12} Notably, the duration of diabetes is a key determinant, as extended progression increases the risk of conditions affecting multiple organ systems.¹³

Cardiovascular risk and hospitalization of patients

Hospitalized patients with DM2 are at heightened risk of developing severe vascular complications due to multiple predisposing factors. Scientific evidence highlights that cardio-atherogenic factors often influenced by lifestyle can disrupt blood flow and lead to critical cardiac events.¹⁴⁻¹⁶

In Mexico, during the first quarter of 2024, the Epidemiological Surveillance System for DM2 recorded 11,083 hospitalizations of patients diagnosed with DM2, with Tabasco reporting the highest number of cases. Among these, the most common comorbidities included hypertension (affecting 6,705 individuals, 60.50%), obesity (1,488 cases, 13.43%), and chronic kidney disease (CKD) (1,433 cases,

12.93%). Hypertension is a major trigger for life-threatening events like acute myocardial infarction and cerebrovascular accidents, as evidenced by SINAVE data.¹⁷

Early intervention in glucose control

Timely intervention in glucose control to achieve the recommended HbA1c targets ($\leq 7\%$) significantly reduces the onset and progression of DM2-related complications. However, the benefits of intensive glycemic control take time to manifest, making early intervention particularly advantageous for younger patients. Weight loss of 10 to 15% also contributes to substantial metabolic improvements.¹⁸

For example, studies demonstrate that early glycemic control is associated with a lower incidence of microvascular complications, such as retinopathy and nephropathy, as well as a delay in the progression of macrovascular complications like myocardial infarction. These findings highlight the importance of early and sustained glycemic management to improve long-term outcomes in DM2 patients.

Adapted Framingham risk score for hospitalized DM2 patients

The Framingham Risk Score has been adapted to address limitations in assessing CVR among hospitalized DM2 patients. The original version does not adequately account for factors such as treatment regimens, body mass index (BMI), duration of disease, or gender differences, which are elements critical for accurate risk estimation in this population.¹⁹⁻²²

This modified score incorporates these variables, providing a more tailored and reliable assessment of CVR in hospitalized DM2 patients. By offering a contextualized risk evaluation, the adapted score enhances clinical decision-making and supports the prioritization of interventions aimed at reducing cardiovascular morbidity and mortality.

The objective of this study is to establish a correlation between the time of being diabetic and the presence of atherogenic risk factors to understand better and define the cardiovascular risk profile of patients hospitalized with type 2 diabetes mellitus (DM2).

MATERIAL AND METHODS

An observational, correlational, and cross-sectional study was conducted. The study population consisted of patients diagnosed with DM2 who were hospitalized at the Medical Specialty Center of the *Instituto de Seguridad Social del Estado de Tabasco (ISSET)*, Mexico, between January and June 2024.

The sample size was calculated by a random test from a population of 3,193 patients, with a confidence level of 95% and a margin of error of five percent, resulting in a sample of 343 patients.

Following the corresponding authorization from the Teaching Committee of the ISSET and obtaining the JI-LCT-179 registry from the Research Center of the *Universidad Juárez Autónoma de Tabasco*, patients aged 40 to 79 years with clinical records and social security numbers were identified.

Rationale for adjusting the risk score

Diabetes mellitus is a well-established risk factor for microvascular (e.g., retinopathy, nephropathy) and macrovascular (e.g., coronary artery disease, stroke) complications. However, appropriate treatment can significantly delay or even prevent these serious outcomes, emphasizing the importance of personalized cardiovascular risk assessments.

Patients hospitalized with DM2 are often exposed to additional risk factors, such as acute metabolic dysregulation, immobility, and stress, which can accelerate the progression of vascular complications and increase the likelihood of fatal outcomes.

To conduct a comprehensive cardiovascular risk assessment, the Framingham Risk Score was adjusted to include additional variables that are particularly relevant for hospitalized patients with type 2 diabetes mellitus (DM2). While the Framingham Risk Score is widely validated for predicting cardiovascular risk in the general population, it may not fully account for the unique risk factors seen in hospitalized DM2 patients.

To address these limitations, the score was adapted to include the following: Time since diabetes diagnosis, Documented complications in the past five years, and Adherence to

diabetes treatment. These adjustments are intended to provide a more nuanced and accurate risk stratification for this specific group (Figures 1 and 2).

The data were collected from clinical records in accordance with the ethical guidelines established in NOM-004-SSA3-2012, the General Health Law, and the Federal Law on the Protection of Personal Data Held by Private Parties. The information collected included age, sex, body mass index, blood pressure, lipid profile, HbA1c levels, and any documented complications related to diabetes.

The study adhered to the principles of the Declaration of Helsinki, ensuring the protection of the health, rights, and dignity of the participants. This included obtaining informed consent, safeguarding personal information, and assessing the risks and benefits associated with the research.

RESULTS

Upon examination of the sociodemographic data, the mean age with a standard deviation (SD) was 59.66 ± 9.57 years, with a predominance of females, representing 180 (52.5%) of the

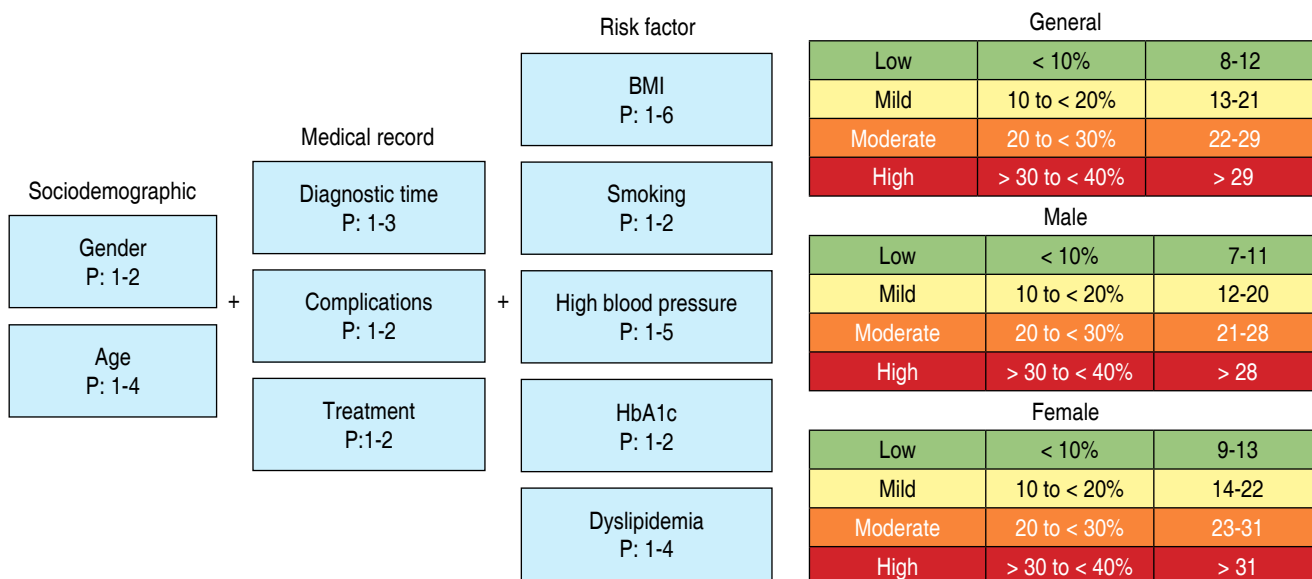


Figure 1: Adaptation of the cardiovascular risk table in hospitalized patients.

Source: prepared by the authors based on the Framingham Risk Score.

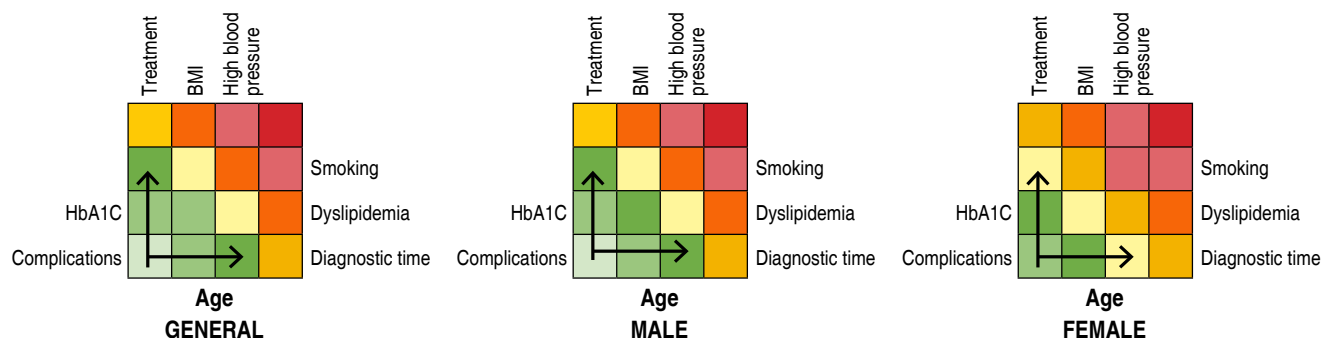


Figure 2: Colorimetry between variables and cardiovascular risk factors in patients with type 2 diabetes mellitus. Differences are observed based on gender, with emphasis on the influence of treatment, body mass index (BMI), and time of diagnosis.

records. Marital status was also examined, with 249 (72.6%) patients being married (Table 1), which could potentially influence adherence to treatment and emotional support.

A review of the clinical records revealed that 337 patients (98.3%) had complete records. Of this subset, 243 patients (78%) had more than 10 years with the diagnosis of diabetes. Furthermore, 320 (93.5%) patients had been hospitalized in the last five years due to mild complications, and 305 (89.5%) patients had an active treatment plan (Table 2).

The mean and standard deviation of body mass index (BMI) was 27.50 ± 6.13 , with 132 (38.5%) patients classified as overweight at the time of the study. Additionally, 87.7% of patients were non-smokers.

Regarding arterial hypertension, 65.3% of patients were hypertensive. Among them, 36.7% had controlled hypertension, while 28.6% had uncontrolled hypertension, further categorized as grade I (18.7%), grade II (7.9%), and grade III (2%). This highlights that while a significant proportion of patients achieved blood pressure control, a considerable subgroup remains with moderate to severe hypertension, elevating their risk for cardiovascular events.

In the glycemic control section, 52.4% of patients demonstrated effective glycemic control. Regarding dyslipidemia, 63.6% of patients had normal cholesterol and triglyceride

Table 1: Sociodemographic variables (N = 343).

	n (%)
General age*	59.66 ± 9.57
Male*	60.06 ± 9.36
Female*	59.30 ± 9.70
Gender	
Male	163 (47.5)
Female	180 (52.5)
Marital status	
Single	80 (23.3)
Married	249 (72.6)
Divorced	8 (2.3)
Common-law	6 (1.7)

* Data presented as mean ± standard deviation.

Table 2: Clinical data of the patients (N = 343).

	n (%)
Duration of illness (years)	
Less than 5	48 (14.0)
Between 5 to 10	52 (15.2)
More than 10	243 (70.8)
Complications < 5 years	
Presented complications	320 (93.5)
No complications	23 (6.7)
Treatment	
With treatment	307 (89.5)
Without treatment	36 (10.5)
Clinical record	
Complete record	337 (98.3)
Incomplete record	6 (1.7)

levels (Table 3). A modified table was used to calculate cardiovascular risk, revealing that 44 patients (12.8%) had low risk, 132 patients (38.5%) had mild risk, 128 patients (37.3%) had moderate risk, and 39 patients (11.4%) had high risk of experiencing a cardiovascular event within the next 10 years (Table 4; Figure 3).

Spearman's correlation analysis revealed positive correlations between BMI and dyslipidemia ($p = 0.158$, $p = 0.003$), hypertension ($p = 0.200$, $p < 0.001$), and smoking ($p = 0.118$, $p = 0.029$), indicating that BMI is a primary cardiovascular risk factor. Dyslipidemia was also significantly associated with hypertension ($p = 0.299$, $p < 0.001$) and poor diabetes control as indicated by HbA1c ($p = 0.119$, $p = 0.028$), which in turn predisposes individuals to cardiovascular disease (Table 5).

DISCUSSION

This study identified a significant prevalence of moderate and high cardiovascular risk in patients with type 2 diabetes, particularly in those with hypertension, poor glycemic control, and obesity. Our results contrast with those reported by Bacuilima-Zhañay et al.,⁴ in whom low cardiovascular risk predominated over five years. This difference could be explained by the population characteristics and the better glycemic control observed in their sample,

Table 3: Cardiovascular risk factors (N = 343).

	n (%)
General BMI*	27.50 ± 6.13
Male*	23.03 ± 3.88
Female*	23.37 ± 3.91
Body mass index	
Underweight	24 (7.0)
Normal weight	88 (25.7)
Overweight	132 (38.5)
Obesity grade I	63 (18.4)
Obesity grade II	23 (6.7)
Obesity grade III	13 (3.8)
Smoking	
No	301 (87.7)
Yes	42 (12.3)
Hypertension	
Non hypertensive	119 (34.7)
Controlled	126 (36.7)
Grade I	64 (18.7)
Grade II	27 (7.9)
Grade III	7 (2.0)
Type 2 diabetes mellitus	
Controlled (glucose < 130 mg/dL o HbA1c < 7%)	180 (52.5)
Uncontrolled (glucose > 130 mg/dL o HbA1c > 7%)	163 (47.5)
Dyslipidemia	
Normal cholesterol and triglycerides	218 (63.6)
Mixed dyslipidemia	72 (21.0)
Hypertriglyceridemia > 150 mg/dL	39 (11.4)
Hypercholesterolemia > 200 mg/dL	14 (4.1)

* Data presented as mean ± standard deviation.

The variability of factors associated with cardiovascular risk is evident. Body mass index (BMI) and smoking status show the greatest variability, indicating significant differences among individuals. Additionally, outliers in weight categories and dyslipidemia suggest relevant extreme cases that warrant further detailed analysis. The highest medians in BMI and smoking underscore their potential impact on cardiovascular risk.

which reduced the proportion of long-term cardiovascular complications.

Compared to Vega-Jiménez et al.,¹⁹ our population has a higher rate of glycemic control

(52.4% versus 41%), which correlates with a higher proportion of moderate and high risk in our study. These results highlight the influence of glycemic control on cardiovascular risk classification, a finding consistent with previous literature. Similarly, Zamora-Fung et al.²³ reported 80.2% of their population as low risk, which could also be attributed to better glycemic control (58.7%) compared to our sample.

The study by Zalapa-Farias et al.,²⁴ which reported a similar prevalence of dyslipidemia (41%), underscores the importance of glycemic control as a key determinant. Although both populations have a high prevalence of dyslipidemia, the lower proportion of patients with glycemic control in their population (41% versus 52.4% in our study) may explain the observed differences in risk classification.

On the other hand, Poll-Cabrera et al.²⁵ included additional factors, such as hypertriglyceridemia and chronic kidney disease, in their cardiovascular risk assessment, which were not included in our sample. This may explain the higher prevalence of severe cardiovascular risk in their population compared with the 11.4% high risk observed in our study. The inclusion of these factors could enrich future predictive models and provide a more comprehensive view of cardiovascular risk in patients with type 2 diabetes.

Finally, a comparison with Garza-López et al.,²⁶ who used the Framingham model, highlighted the limitations of this model, particularly its inability to take into account factors such as obesity or duration of diabetes. In contrast, our approach using a modified model allowed for a more balanced distribution of cardiovascular risk, highlighting the importance of adapting models to the specific characteristics of the population studied.

In conclusion, our findings underscore the importance of a personalized approach to cardiovascular risk assessment and management in patients with type 2 diabetes. Factors such as glycemic control, hypertension, and obesity should be prioritized in prevention and treatment strategies. In addition, the inclusion of additional comorbidities and the validation of predictive models tailored to different population contexts are key areas for future research.

CONCLUSION

Comprehensive management of type 2 diabetes should be carefully tailored to the individual needs of each patient. This includes not only glycemic control but also management of major comorbidities, including hypertension, obesity, and other cardiovascular risk factors. The introduction of advanced pharmacological therapies, including Glucagon-Like Peptide-1 (GLP-1) receptor agonists (GLP-1 RAs) and SGLT2 inhibitors (SGLT2is), has demonstrated additional benefits beyond glucose lowering. These therapies have been shown to contribute significantly to cardiovascular and renal protection. These developments should be accompanied by the provision of ongoing diabetes self-management education and support (DSMES) programs, which are essential to improve adherence, optimize clinical outcomes, and reduce the risk of long-term complications.

The study results show that the cardiovascular risk profile of hospitalized patients with type 2 diabetes varies widely. The majority of patients are at moderate cardiovascular risk, while a small proportion are at high risk, particularly those with poor adherence. This finding underscores the importance of early intervention and close monitoring of glycemic control and comorbidities to reduce the risk of cardiovascular complications.

Factors such as the duration of diabetes and the presence of comorbidities, including high

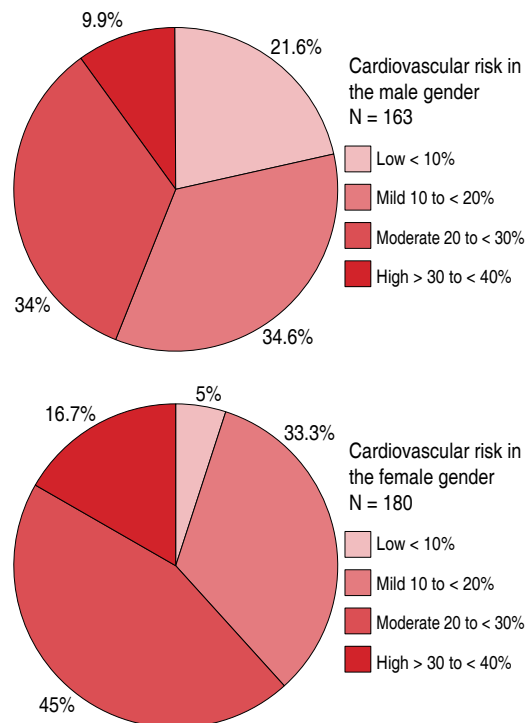


Figure 3: Percentage of cardiovascular risk by gender. Cardiovascular risk by gender: the distribution of cardiovascular risk stratified by gender is observed. Men exhibit a higher percentage of low risk (21.6 vs. 9.9% in women), while women show a higher prevalence of moderate risk (45 vs. 34% in men) and high risk (12.2 vs. 16.7% in men), highlighting significant differences in the epidemiology of cardiovascular risk between both genders.

Table 4: Cardiovascular risk (N = 343).	
Grouped	n (%)
Low risk (< 10%)	44 (12.8)
Mild risk (10 to < 20%)	132 (38.5)
Moderate risk (20 to < 30%)	128 (37.3)
High risk (> 30 to < 40%)	39 (11.4)

10-year cardiovascular risk according to the Framingham risk score in patients diagnosed with type 2 diabetes mellitus attended at the Medical Specialties Center of the *Instituto de Seguridad Social del Estado de Tabasco* between January-June 2024.

body mass index and poor glycemic control, have been identified as key determinants of cardiovascular risk profile. Modification of the Framingham Risk Score to incorporate these specific factors related to type 2 diabetes has improved the predictive ability of the model, allowing for more accurate cardiovascular risk stratification. This adjustment facilitates the early identification of high-risk patients and enables the implementation of preventive strategies.

From a clinical perspective, the results suggest that an integrated and personalized approach that addresses both appropriate glycemic control and management of associated comorbidities is critical to reducing cardiovascular risk in hospitalized patients with type 2 diabetes. It is imperative that treatment be individualized, that adherence

Table 5: Correlations between atherogenic cardiovascular risk factor variables.

Variables	BMI	DP	Smoking	HTN	DM2
Time since DM2 diagnosis	0.158* p = 0.003	–	0.147* p = 0.006	–	–
Body mass index	–	0.158* p = 0.003	0.118‡ p = 0.029	0.200* p < 0.001	–
Dyslipidemia	0.158* p = 0.003	–	–	0.109‡ p = 0.044	0.299* p < 0.001
Smoking	0.118‡ p = 0.029	–	–	0.225* p < 0.001	–
Hypertension	0.200* p < 0.001	0.109‡ p = 0.044	0.225* p < 0.001	–	0.119‡ p = 0.028
Control of diabetes by HbA1c	–	0.299* p < 0.001	–	0.119‡ p = 0.028	–

* Correlation is significant at the 0.001 level (two-tailed). ‡ Correlation is significant at the 0.005 level (two-tailed). BMI = Body Mass Index. DP = primary dyslipidemia. HbA1c = hemoglobin A1c. HTN = Arterial Hypertension. DM2 = Type 2 diabetes mellitus (control of type 2 diabetes mellitus by HbA1c).

to the therapeutic regimen be promoted, and that the influence of social and emotional factors in disease management be considered. The integration of these elements may have a significant impact on improving long-term outcomes and quality of life for patients.

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Declaration of confidentiality and patients consent

Research protocol: «*Atherogenic risk profiles and cardiovascular risk assessment in hospitalized patients with type 2 diabetes*» with protocol folio JI-LCT-179. This protocol has been previously analyzed and accepted by the Research Committee of the Academic Division of Health Sciences of the *Universidad Juárez Autónoma de Tabasco*.

The authors confirm that they have complied with the pertinent work protocols for the use of patient data. In addition, the authors confirm that the patient has been duly informed and has given written informed consent for the publication of his or her images and other clinical information in the journal without any identifying details in order to safeguard his or her right to privacy. Furthermore, the authors attest that no form of generative artificial intelligence has been employed in the preparation of this manuscript or in the creation of figures, graphs, tables, or their corresponding captions or legends.

Clinical trial registration and approval number protocol folio JI-LCT-179, previously analyzed and accepted by the Research Committee of the Academic Division of Health Sciences of the *Universidad Juárez Autónoma de Tabasco*.

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Perception among family members and physicians about the recommendation for family members to learn cardiovascular resuscitation in patients at high risk for sudden cardiac arrest

Percepción de familiares y médicos sobre la recomendación de aprender reanimación cardiopulmonar para familiares de pacientes con alto riesgo de parada cardíaca súbita

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Keywords:

cardiopulmonary resuscitation learning, heart disease, out-of-hospital cardiac arrest, layperson cardiopulmonary resuscitation, survey.

Palabras clave:

aprendizaje de reanimación cardiopulmonar; cardiopatía, paro cardíaco extra-hospitalario, reanimación cardiopulmonar por personas sin entrenamiento médico profesional, encuesta.

ABSTRACT

Introduction: most out-of-hospital cardiac arrests (OHCA) in patients with cardiovascular disease occur at home or in the vicinity of relatives. Someone in the patient's entourage should be able to administer cardiopulmonary resuscitation (CPR). We conducted two surveys to evaluate if CPR learning is suggested to patients and relatives by their physician and to the patients to know their perception in that regard. **Material and methods:** two surveys were conducted among physicians (cardiologists) and patients (heart disease). All were voluntary and anonymous. Physicians were contacted through an internet survey tool that included both private and public practices, and patients responded in the waiting room of private practices located in private hospitals. Responses were analyzed as categorical variables with the χ^2 test and, when necessary, Student's t-test. **Results:** one hundred and eighty-four cardiologists and 432 patients responded. Among physicians, 95.7% see high-risk OHCA patients, and 97.8% consider «important» or «very important» that someone close to them is able to perform CPR. Physicians think that less than 5% of family members are able to do so, and 59% suggest always, or almost always, the need for someone to learn CPR. Among patients, 95.1% consider «important» that «somebody» knows how to perform CPR in their vicinity, 32.8% think someone close knows how to do so, and in 65.5% of them, someone (friends and family 73.6%, their physician 14.1%) has suggested CPR learning. **Conclusions:** there is

RESUMEN

Introducción: la mayoría de los paros cardíacos extrahospitalarios (PCEH) en enfermos cardiovasculares ocurren en casa o cerca de familiares. Alguien en el entorno del paciente debería poder administrar maniobras de reanimación cardiopulmonar (RCP) básicas y activar a los servicios médicos de emergencia (SME). Se hicieron encuestas para evaluar si se sugiere a los pacientes y familiares aprender RCP y a los pacientes para conocer su percepción. **Material y métodos:** se aplicaron dos encuestas sencillas de comprensión y aplicación rápidas, una a médicos (cardiólogos) y otra a pacientes con enfermedad cardiovascular. Todas fueron anónimas y voluntarias. A los médicos con práctica privada y pública se les aplicó con una herramienta de internet y a los pacientes en la sala de espera de prácticas privadas en hospitales privados. Las respuestas se analizaron como variables categóricas con χ^2 y t de Student en caso necesario. **Resultados:** se obtuvieron 184 respuestas de cardiólogos y 432 de pacientes con enfermedad cardiovascular. El 95.7% de los médicos dijo ver pacientes con alto riesgo de PCEH y el 97.8% consideran importante o muy importante que alguien cercano sepa dar RCP; creen que en menos del 5% de los casos ocurre esto y el 59% de ellos sugieren siempre o casi siempre que alguien aprenda. El 95.1% de los pacientes cree importante que «la gente» sepa dar RCP. El 32.8% de ellos cree que alguien cercano sabe hacerlo. Al 65.5% alguien (familiares y amigos 73.6%, su médico 14.1%) le ha sugerido que aprendan RCP. **Conclusiones:** aparentemente existe una percepción generalizada sobre la importancia de la RCP

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a generalized perception of the importance of CPR learning in the proximity of heart patients, but apparently, few people actually know how to do it. Patients consider that their main sources of information are family and friends.

en el entorno del enfermo cardiovascular, sin embargo, en apariencia, poca gente está capacitada para realizarla. La mayoría de los pacientes considera que su principal fuente de información y sugerencias son amigos y familiares.

Abbreviations:

CPR = Cardiopulmonary Resuscitation

EMS = Emergency Medical Services

OHCA = Out-of-Hospital Cardiac Arrests

INTRODUCTION

Out-of-Hospital Cardiac Arrests (OHCA) is a health problem: more than 350,000 occur each year in the US, most of them at home (73.4%), 16.3% in a public space, and 10.3% in nursing homes.¹ Although some older people or heart disease patients might live alone, many others in different age or disease groups have relatives or care-takers with them, and it would be desirable that someone in that environment could administer cardiopulmonary resuscitation (CPR) and alert the emergency medical services (EMS) to treat an OHCA when the patient is not terminal.² Several efforts have been made to improve CPR learning and performance by family members or relatives. Nevertheless, several barriers persist: some of them might be cultural, and others come from concerns about the patient's welfare. Paradoxically, there seems to be a high awareness about the usefulness of CPR in the general population.

In Mexico, this has not been explored, and there is no knowledge about the public's perception concerning CPR performance as a layperson, nor about the importance of CPR as a life-saving intervention or the obstacles a layperson might encounter to perform it. In the same way, there are very few studies about prehospital cardiac arrest in Mexico, so epidemiological information is scarce as well.^{3,4} It has been estimated that there are 33,000 to 55,000 sudden cardiac death events in Mexico each year,^{5,6} and most of them happen out of a medical facility. It is well proven that the earlier CPR and defibrillation are applied in an OHCA, the better the survival odds for the patient.^{7,8} It also has to be pointed out that about 10% will survive hospital discharge, but once this point is

attained, approximately 90% of patients survive the first year.⁹ Hence, a relative or care-taker close to the cardiovascular patient with a high-risk disease should be able to timely detect cardiac arrest, start CPR, activate the EMS, and ask for a defibrillator in an attempt to increase survival rates.

We decided to make an initial approach to these issues in a group of persons at high risk of OHCA, such as cardiac disease patients and the physicians who treat them on an outpatient basis. We sought if physicians (Cardiologists) who treat these individuals suggest that patients' relatives learn CPR maneuvers on a regular basis and what perception patients have on the subject. To this purpose, we designed a simple questionnaire for physicians and another survey for patients.

MATERIAL AND METHODS

Two different surveys were developed to investigate if CPR learning is considered relevant for cardiovascular patients' relatives and if it is suggested in an outpatient setting. Both surveys and the protocol were approved by the Hospital H+'s Querétaro Bioethics committee (Approval letter sent to the publisher).

The survey intended for physicians was designed to be completed online. It was tested for clear language, easy response, and short duration on ten cardiologists within a private practice setting. It included seven questions. Some of them were multiple choice (3), and others were a scale (4) of percentages («How many of your patient's relatives do you consider know how to perform CPR?» for example) or attitudes («How important do you believe it is for family members and relatives of people with heart disease to learn CPR?» with a five-points grading from «not important at all» to «very important»). After testing, the survey was presented to the president of one of the

Table 1: Main characteristics of the physicians that participated in the survey.

Participants' main activity	N = 184 n (%)	Main age group	Gender male n (%)	Do you see people with SCD high-risk? (YES) n (%)	I always (5) / Almost always recommend CPR learning (4) n (%)
Clinical cardiology	124 (67.4)	55 to 65 years-old (58 subjects)	104 (83.8)	116 (93.5)	69 (55.6)
Echocardiography	20 (10.9)	45 to 55 years-old (9 subjects)	10 (50)	20 (100)	11 (55)
Cardiac imaging	1 (0.5)	35 to 45 years-old	0 (0)	1 (100)	1 (100)
Interventional cardiology (hemodynamics)	18 (9.8)	55 to 65 years-old (8 subjects)	18 (100)	18 (100)	11 (61.1)
Interventional cardiology (electrophysiology)	12 (6.5)	55 to 65 years-old (5 subjects)	10 (83.3)	12 (100)	10 (83.3)
Heart failure	1 (0.5)	45 to 55 years-old	0 (0)	1 (100)	1 (100)
Cardiac rehabilitation	8 (4.3)	35 to 45 years-old (4 subjects)	4 (50)	5 (100)	4 (50)

CPR = CardioPulmonary Resuscitation. SCD = sudden cardiac death.

largest cardiological societies in our country, which has 2,200 members (according to 2022 membership records). He kindly helped us to submit the voluntary questionnaire through their mailing list as a web link to the Google Formularies app (Google, California, USA). All the surveys were anonymous: the investigators had no means to reach the answering physician or to find their contact or personal information since the mailing list was not managed by the research team, and there was no record of personal data on the survey webpage. The anonymous answers were concentrated in the «Formulary» app of Google Surveys and collected in an Excel Microsoft database as categorical variables for further statistical analysis.

We also designed a short questionnaire to evaluate the perception of cardiovascular patients attending private practice cardiology groups in Queretaro, San Miguel de Allende, and Aguascalientes. The survey was tested on twenty-five patients attending outpatient offices in Queretaro, San Miguel de Allende, and San Juan del Rio to explore and adjust language, clarity, and extension of the interview. Once validated, the survey was handed to patients

before their consultation turn, on a single piece of paper without any identification markings. If they agreed to participate, their anonymous answers were collected by the administrative assistant as they entered the office, prior to any contact with their physician. Questions included their gender and age group (less than 18 years old to more than 65 in 10-year age groups). The main questions («Do you think it is important for people to know how to perform CPR?», «Has somebody told you about the importance of CPR learning in your entourage?», and «Does someone close to you know how to perform CPR?») included three options (yes, no, I don't know). The fourth question was, «Who has told you about the need to have someone near you who can perform CPR?». The answers included friends, relatives, your physician, others, and I don't know. The data were also captured in a Microsoft Excel database and analyzed as categorical variables.

In this prospective, transversal, and descriptive study, the main results are expressed as totals and percentages and were analyzed with a χ^2 test to evaluate differences between age and gender groups among the patients or a Student's t-test when necessary.

Results

We received 184 physicians' answers (8.36% of the disclosed society's membership). The responder's main characteristics are depicted in [Table 1](#). Most colleagues (n = 76, 41.3%) were in the 55 to 65 age range, 39 (21.2%) in the 35 to 45 age range, and 37 (20.1%) in the 45 to 55 age range. Three physicians were in the

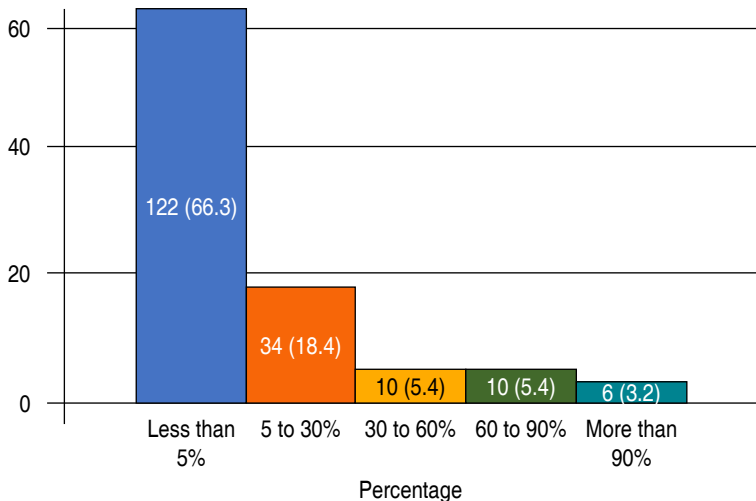


Figure 1: Response to the question: What proportion of your high-sudden-cardiac-death-risk patients' relatives do you consider are able to perform cardiopulmonary resuscitation?

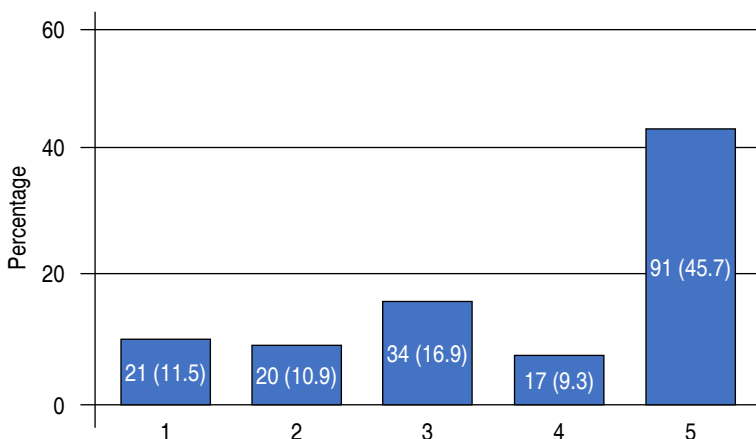


Figure 2: Responses to the question: Do you suggest that the family or close relatives of a sudden-cardiac-death-risk patient learn Cardiopulmonary resuscitation (CPR)? Number 1 indicates «Never», and number 5 indicates «Always». Digital material (file number)

25 to 35 age range (1.6%). Responders were predominantly male subjects.

Among the specialists surveyed, 176 (95.7%) stated that they care for high-sudden cardiac death risk patients. In the same group of physicians, 179 (97.8%) considered that it is important or very important for a patient's family member to learn CPR maneuvers.

In this regard, 108 (59%) cardiologists mentioned that they «always» or «almost always» suggest to a family member or a care-taker to learn CPR ([Figure 1](#)). There were some differences according to the physician's specialty. For example, 10 out of 12 electrophysiologists (83.3%) stated that they recommend their high-risk patient's families to learn CPR, while among the general cardiology practitioners, 69 of 124 (55.6%) stated the same ([Table 1](#)). When asked what proportion of the family or caregivers of their high-risk patients they thought could perform CPR, 122 (66.3%) responded that less than 5%, and 34 (18.47%) said that probably 5 to 30% of family members would be able to do so ([Figure 2](#)).

The survey was presented to 540 patients, and only 432 (80%) agreed to answer it. There were 234 (54.16%) male and 198 (45.8%) female subjects. Most of them were in the 65 or more years old group ([Table 2](#)), and 411 (95.13%) considered it important for «people» to know how to perform CPR. In 284 cases (65.5%), someone has told them about the relevance of a close relative or care-taker to be able to perform CPR. In this group, the recommendation came from a family member (145, 51.06%), a friend (64, 22.5%), or their physician (40, 14.08%). [Table 3](#) summarizes the main findings by gender and [Table 4](#) by age group. There were no significant differences between sex or age groups regarding the general patient population. Elderly patients (more than 65 years old) received significantly fewer recommendations for people around them to learn CPR, as well as the younger age group (less than 18 years old).

DISCUSSION

Layperson-provided CPR has been studied from several angles to promote its learning and wide community application with variable

Table 2: General findings in 432 patients' surveys.

Table 2: General findings in 432 patients' surveys.			
	n (%)		
Gender			
Male	234 (54.16)		
Female	198 (45.8)		
Age group (years)			
18 or less	14 (3.24)		
18-35	47 (10.88)		
35-45	79 (18.29)		
45-55	90 (20.83)		
55-65	69 (15.97)		
More than 65	132 (30.56)		
	Yes n (%)	No n (%)	I don't know n (%)
Do you believe it is important that people know how to perform CPR?	411 (95.13)	7 (1.6)	14 (3.2)
Has someone told you about the need for someone close to you to know how to perform CPR?	284 (65.51)	127 (29.17)	16 (3.7)
Does someone close to you know how to perform CPR?	142 (32.87)	208 (47.69)	82 (18.98)
Who has told you that it would be useful to have someone near you that knows how to perform CPR?	n (%)		
Friend	64 (22.54)		
Family	146 (51.06)		
Physician	40 (14.08)		
Other	38 (13.38)		
I don't know	16 (5.03)		
CPR = CardioPulmonary Resuscitation.			

degrees of success. Although CPR guidelines emphasize the need for layperson-provided CPR (Class I recommendation), they do not mention high-risk patients' close relatives or family as a specific training target.¹⁰⁻¹³ Since the 1980s, different groups identified the need to

promote CPR by relatives of patients with heart disease.^{7,8} Training this subset of individuals should probably be a class IIA recommendation since most OHCA happen at home, but it has not been emphasized. Specific limitations and directed assistance must be regarded, but a general recommendation should be envisaged and explored.

The present survey shows a positive attitude of physicians towards CPR learning, and apparently, a significant number of them suggest it to families and patients. Fifty-nine percent of the surveyed cardiologists mention that they always or almost always do it, a higher percentage than the one found 40 years ago in King County (one of the places in the world with higher bystander CPR rates and OHCA survival) by St Louis P. et al.¹⁰

On the other hand, physicians consider that few family members or at-home caretakers are able to do so. This goes in line with the findings by Cariou et al.,¹⁴ who interviewed 153 cohabitants of 127 patients and found that 3.5% of the patients' relatives learned CPR because of the new household circumstance. A study by Sato N et al.,¹⁵ found that in the case of an OHCA, it is less likely for the patient to receive CPR from a relative as opposed to a non-family bystander. The authors advance several reasons: families can suffer from emotional stress and psychological barriers to performing CPR on a known victim, the rescuer might be alone at home with the victim (because of aging couples without support), and have her/his own aging and disease issues. In Mexico, there might be some other reasons, such as legal and safety concerns, but the present survey was not designed to explore this.

A major issue seems to be the lack of availability of low-cost or no-cost training courses or facilities; thus, several options have been devised: A recent study evaluated CPR learning among patient's families through a self-learning CPR kit that included usual tools - a 20-minute video and a practice manikin - compared to a mobile device application. They found non-significant differences between both methods when measuring learning interest, although there was a trend towards better skill retention and performance among people with the «traditional» learning kit over the app.^{16,17}

Another group explored what happened when MDs were prescribed to learn CPR maneuvers by either purchasing an inflatable manikin and video at the physician’s office for self-training at home or by attending a presential CPR course. They found that patients and relatives can be motivated to purchase a training kit (9 to 24% of patients) but not to take a CPR lesson from a written prescription.¹⁷

Patients seem aware of the importance of CPR training, and most of them consider it important for «people» to learn CPR. This issue should be addressed with other tools since it raises the question: Who is to learn CPR if not people who are aware of its relevance? Many barriers seem to entangle the relative’s decision to learn and apply CPR while respecting the patient’s desires and condition,¹⁵ but it was

not the purpose of this survey to evaluate that question, which deserves local evaluation to consider idiosyncratic aspects.

An important proportion of subjects in this series have received suggestions about having someone close to them learn CPR, and the suggestion came mainly from family and friends. The lower proportion of physician-recommended CPR training referred by patients is more in line with the findings by St Louis, Mandel, and Goldberg.¹⁰⁻¹² Cardiologists surveyed in the present study are aware of the potential benefits of patients’ relatives knowing CPR and make the recommendation to a proportion of their high-risk patients.

These results suggest that there is a mismatch between physicians’ and patients’ perceptions regarding «CPR learning

Table 3: Main findings according to patients’ gender.

	Age range						Is it important people know CPR?		
	18 or less	18 to 35	35 to 45	45 to 55	55 to 65	More than 65	Yes	No	I don’t know
Male, n (%)	4 (1.71)	21 (8.97)	46 (19.66)	49 (20.94)	37 (15.81)	77 (32.91)	226 (96.58)	4 (1.71)	5 (2.14)
Female, n (%)	10 (5.05)	26 (13.13)	32 (16.16)	41 (20.71)	32 (16.16)	57 (28.79)	187 (94.44)	3 (1.52)	9 (4.55)
p M vs. F	0.030	0.087	0.172	0.476	0.461	0.178	0.145	0.437	0.086

	Has somebody told you?			Who?				Someone close know to perform CPR?			
	Yes	No	I don’t know	Friend	Family	Physician	Other	I don’t know	Yes	No	I don’t know
Male, n (%)	158 (67.52)	68 (29.06)	5 (2.14)	42 (17.95)	72 (30.77)	22 (9.40)	21 (8.97)	9 (3.85)	80 (34.19)	105 (44.87)	49 (20.94)
Female, n (%)	126 (63.64)	59 (29.80)	11 (5.56)	22 (11.11)	74 (37.37)	18 (9.09)	17 (8.59)	7 (3.54)	62 (31.31)	103 (52.02)	33 (16.67)
P M vs. F	0.199	0.434	0.035	0.021	0.075	0.456	0.444	0.432	0.263	0.070	0.128

Gender distribution: Male (M) and Female (F). Comparisons are made between genders. CPR = CardioPulmonary Resuscitation.

Table 4: Main findings according to patients' age group.

	Age group (years)							
	≤ 18 n = 14	18-35 n = 47	35-45 n = 78	45-55 n = 90	55-65 n = 69	≥ 65 n = 134	p*	p**
Male gender	4 (28.6)	21 (44.7)	46 (58.97)	49 (54.4)	37 (53.6)	77 (57.5)	NS	0.02
Is it important for people to know how to perform CPR?								
Yes	13 (92.8)	47 (100.0)	76 (97.44)	85 (94.4)	62 (89.8)	130 (97.0)	NS	NS
No	1 (7.2)	0 (0.0)	2 (2.56)	2 (2.22)	1 (1.45)	1 (0.75)	NS	NS
I don't know	0 (0.0)	0 (0.0)	0 (0.0)	3 (3.33)	7 (10.14)	3 (2.2)	NS	0.04
Has somebody told you about the need to have someone near you able to administer CPR?								
Yes	5 (35.7)	32 (68.09)	62 (79.49)	64 (71.1)	48 (69.6)	73 (54.5)	NS	NS
No	8 (57.14)	14 (29.79)	13 (16.67)	20 (22.2)	17 (24.6)	55 (41.0)	0.045	NS
I don't know	1 (7.14)	1 (2.13)	1 (1.28)	3 (3.33)	4 (5.8)	6 (4.5)	NS	NS
Who has told you?								
Friend	0 (0.0)	9 (19.1)	16 (20.51)	14 (15.56)	7 (10.1)	18 (13.4)	NS	0.0001
Family	4 (28.6)	16 (34.04)	33 (42.31)	27 (30.0)	27 (39.1)	39 (29.1)	NS	NS
Physician	1 (7.14)	5 (10.6)	8 (10.26)	7 (7.78)	8 (11.6)	11 (8.2)	NS	NS
Other	3 (21.43)	2 (4.26)	3 (3.85)	15 (16.67)	5 (7.25)	10 (7.5)	NS	NS
I don't know	0 (0.0)	2 (4.26)	0 (0.0)	9 (10.0)	1 (1.45)	4 (3.0)	NS	0.02
Does someone near you know how to perform CPR?								
Yes	2 (14.3)	19 (40.4)	27 (34.62)	37 (41.1)	25 (36.23)	32 (23.9)	NS	NS
No	8 (57.1)	18 (38.3)	48 (61.54)	34 (37.78)	31 (44.9)	69 (51.5)	NS	NS
I don't know	4 (28.6)	10 (21.3)	3 (3.85)	19 (21.1)	13 (18.8)	33 (24.6)	NS	NS

p* = between adjacent columns. p** = between less than 18 years-old and more than 65 years-old. NS = Non-Significant.

prescription». Apparently, patients feel that their physician is not the primary source for such a recommendation.

It seems that there is a lack of clarity in the communication between physicians and families: 59% of physicians say that they recommend CPR learning, but patients who receive that recommendation mention that only in 14% of cases, it came from their doctor in a general cardiology practice. This phenomenon seems in line with an «optimism bias»,¹⁸ from either the physician or the patient himself, that is, a false perception of the real risk level. If the whole interviewed population is considered, only 9% of the patients received the suggestion from their physician.

Another difference is that most cardiologists consider that less than 5% of their patients have someone near them able to perform CPR, while 32.8% of patients feel that a relative might perform CPR on them. That somehow confident perception might be a deterrent for laypersons, in this case, close relatives of a diseased person, to learn CPR, EMS activation, and automated external defibrillator use. In any case, 32% seems a low proportion of subjects able to perform CPR in high-risk populations. A recent report by CARES in the US shows that 41.2% of people with OHCA received bystander CPR, and 11.7% were treated with an AED by laypersons.¹⁹

Present results suggest that several educational components, such as poor availability and promotion of CPR courses directed to the public, cost limitations for some families, installation limitations, and poor diffusion of a «CPR culture», among others, may jeopardize CPR learning in developing countries.²⁰ Physicians have an important role in promoting CPR training, but in some instances, they do not have the necessary information to direct the family members to a specific course or training activity, sometimes even to a proper facility able to provide information and courses. Another issue could be the lenient attitude of physicians towards CPR learning in the same manner that many times we do not insist on smoking cessation, physical activity, or weight control, for example.^{6,11}

An alternative explanation could be that physicians answered the question with fear

of criticism and thus biased the result. A clear instruction to learn CPR from a trusted physician might have a significant impact on high-risk patients' survival, but that recommendation must be assertively done and followed, no matter if the physician practices in a private or public institution. Steps need to be taken to provide better information to both physicians and family members in order to increase the safety of high-risk patients in a setting that should be safer: the home.

Study limitations

The surveys were conducted in a medical setting, either through a medical office. All participants freely decided to respond to or not to the questionnaire, but the context in which it was applied might have biased some of the data obtained. Regarding the cardiological society, the participation seems low, and it can be interpreted as a lack of interest in the matter, making the people who did participate the concerned ones about it, an element that can also bias some of the results. The number of surveyed people might be another limitation, along with the fact that some of the surveyed physicians either have a mixed practice (public and private) or exclusively private or exclusively public practice.

CONCLUSIONS

There seems to be a high level of awareness among physicians and patients about the need for layperson CPR training – AED use, and there also seems to be several opportunity areas to improve how and how often physicians transmit the need for CPR learning among patients and their families. An improvement in the number of persons able to perform CPR, especially around high-risk patients, might improve survival. Establishing protocols that facilitate physicians and other health personnel to transmit information and eliminate perceived barriers to performing layperson CPR in high-risk populations is a starting point in developing countries. Those protocols should be the result of collaborative actions between society, medical associations, and policy-makers.

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Diagnostic challenge: cardiac myeloid sarcoma in a patient with acute myeloid leukemia

Reto diagnóstico: sarcoma mieloide cardiaco en un paciente con leucemia mieloide aguda

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Keywords:

cardiac myeloid sarcoma, imaging studies, cardiovascular imaging, cardiac granulocytic sarcoma, cardiac chloroma.

Palabras clave:

sarcoma mieloide cardiaco, estudios de imagen, imagen cardiovascular, sarcoma granulocítico cardiaco, cloroma cardiaco.

ABSTRACT

Introduction: myeloid sarcoma, also known as granulocytic sarcoma or chloroma, is a malignant neoplasm resulting from the infiltration of immature myeloid cells into extramedullary tissues, with an estimated incidence of 2.5-9.1% in patients with acute myeloid leukemia (AML). The heart is an uncommon site of occurrence (< 1%). Currently, there are no firmly established diagnostic or treatment guidelines for this condition. **Case report:** a 21-year-old female patient with a history of acute myeloid leukemia (translocation 9:11), diagnosed at age 16. After receiving chemotherapy, she achieved remission in October 2019. She was referred for follow-up in December 2021, presenting with wasting syndrome, palpitations, and dyspnea (NYHA II). **Conclusions:** this case highlights the rarity of cardiac myeloid sarcoma and underscores the need for the use of multimodal imaging in diagnosis and follow-up. Additionally, it emphasizes the importance of establishing specialized care pathways with a cardio-onco-hematological perspective in Mexico.

RESUMEN

Introducción: el sarcoma mieloide, también conocido como sarcoma granulocítico o cloroma, es una neoplasia maligna resultante de la infiltración de células mieloides inmaduras en tejidos extramedulares, con una incidencia estimada de 2.5-9.1% en pacientes con leucemia mieloide aguda (LMA). El corazón es un sitio poco común de aparición (< 1%). Actualmente, no existen pautas diagnósticas ni de tratamiento firmemente establecidas para esta condición. **Caso clínico:** paciente femenino de 21 años con antecedente de leucemia mieloide aguda (translocación 9:11), diagnosticada a los 16 años. Tras recibir quimioterapia logró la remisión en octubre de 2019. Fue referida para seguimiento en diciembre de 2021, presentando síndrome consuntivo, palpitaciones y disnea (NYHA II). **Conclusiones:** este caso resalta la rareza del sarcoma mieloide cardiaco y subraya la necesidad de utilizar imagenología multimodal en el diagnóstico y seguimiento. Además, destaca la relevancia de establecer rutas asistenciales especializadas con una perspectiva cardio-onco-hematológica en México.

Abbreviations:

AML = Acute Myeloid Leukemia
CMS = Cardiac Myeloid Sarcoma
MRI = Magnetic Resonance Imaging
MS = Myeloid Sarcoma

NYHA = New York Heart Association
PET = Positron Emission Tomography
PET-CT = Positron Emission Tomography-Computed Tomography scan

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INTRODUCTION

Myeloid Sarcoma (MS) is associated with childhood Acute Myeloid Leukemia (AML) and may appear before AML is diagnosed, during its course, or even in isolation without bone marrow involvement (Primary or Isolated Myeloid Sarcoma).¹ Additionally, the expression of this pathology has been linked to Myeloproliferative Disorders or Myelodysplastic Syndromes during adulthood. The presentation of MS in cardiac localization, as in this case, is uncommon and accounts for < 1% of cases, so a high index of suspicion in the clinical context is warranted.²

There are multiple risk factors for developing this condition, including chromosomal aberrations (monosomy 7, trisomy 8, and rearrangement of the MLL gene) or manifestation of subtypes of promyelocytic and myelomonocytic leukemia (according to the French-American-British [FAB] classification for AML),³ and the expression of Auer rods in leukemia cells has been described as a risk factor associated with the presentation of myeloid sarcoma.⁴

Due to the extremely rare presentation of Cardiac Myeloid Sarcoma (CMS), there are no well-established guidelines or consensus on the diagnosis, management, and treatment of this disease.

CASE PRESENTATION

This is a 21-year-old female patient, native and resident of Mexico City, with a history of acute myeloid leukemia with translocation

(9:11), diagnosed at the age of 16 (February 2019). Initially managed and treated at the *Hospital Infantil de México*, where she received chemotherapy (Table 1), and complete remission by bone marrow aspiration (BMA) was documented in October 2019. Consequently, she was referred to our center, *Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán* in December 2021, upon reaching adulthood for follow-up. This month, the patient presented with wasting syndrome, palpitations, and dyspnea (NYHA II).

Consequently, an electrocardiogram was conducted, and an echocardiogram was scheduled. A 12-lead electrocardiogram performed in December 2021 showed a First-degree AV Block, with a PR interval of 240 milliseconds (Figure 1). An echocardiogram performed in January 2022 reported an infiltrating mass of 49 × 26 mm in the lower two-thirds of the interatrial septum, with retro-aortic infiltration and at the base of the anterior leaflet of the aortic valve. A decreased global longitudinal strain of -17% and an ejection fraction of 45% were reported (Video 1 https://www.medigraphic.com/videos/cardiovascular/cms252v_1).

Differential diagnosis. Clinically, there are multiple conditions that need to be differentiated from cardiac myeloid sarcoma, because they present with a very similar clinical picture. For example, benign cardiac tumors, any type of cardiac metastasis, or even some cardiomyopathies. Additionally, we should also consider cardiac lymphomas. Due to this clinical mimicry, it is crucial to

Table 1: First chemotherapy regimen targeted for myeloid leukemia.

Phase	Chemotherapy regimen	Drugs used
Induction	ATEDox regimen	Cytarabine + mercaptopurine + etoposide + doxorubicin
Reinduction	AM regimen	Cytarabine + mitoxantrone
Consolidation	First cycle	Cytarabine + mitoxantrone
	Second cycle	Cytarabine + etoposide
	Third cycle	Cytarabine
	Fourth cycle	Cytarabine + etoposide

Note: Abstract of the chemotherapy regimen targeted for myeloid leukemia in February 2019.

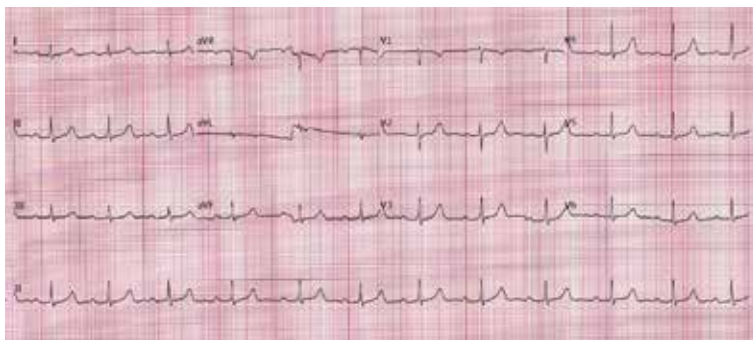


Figure 1: A 12-lead EKG is performed with the unique finding of a First-degree AV Block, with a PR interval of 240 milliseconds.

Table 2: Treatment for heart failure prescribed (January 2022).
Carvedilol 6.25 mg orally every 24 hours Dapagliflozin 5 mg orally every 24 hours Sacubitril/valsartan 50 mg orally every 12 hours
This table summarizes the medical treatment provided after the patient’s symptoms and echocardiogram indicated heart failure with reduced ejection fraction and altered global longitudinal strain.

perform immunohistochemical characterization of the lesions.

Investigations. Based on the previous findings, she was referred to the cardiology service to start treatment for heart failure (Table 2) and also a cardiac magnetic resonance imaging (MRI), Positron Emission Tomography (PET), and bone marrow aspiration (BMA) with immunofixation, cytogenetics were requested.

Magnetic Resonance Imaging was performed in January 2022, and an infiltrating mass of the interatrial septum was identified, with invasion of the anterior atrial wall and the upper third of the interventricular septum (Video 2 https://www.medigraphic.com/videos/cardiovascular/cms252v_2).

PET-CT (Positron Emission Tomography-Computed Tomography scan) performed in February 2022 reported irregular solid tissue in the interatrial septum with an SUV of 7.0 and extension surrounding the ascending aorta, as

well as focal metabolism in fatty tissue of the aortopulmonary window with an SUV of 4.8; these findings are compatible with neoplastic activity (Figure 2).

Bone Marrow Aspiration, performed in February 2022, demonstrated decreased cellularity. No blasts, 6% eosinophils. Macrophages without hemophagocytosis. Additionally, immunofixation showed weak CD45, CD117+, CD34+, CD13+ and



Figure 2:

PET-CT performed in February 2022.

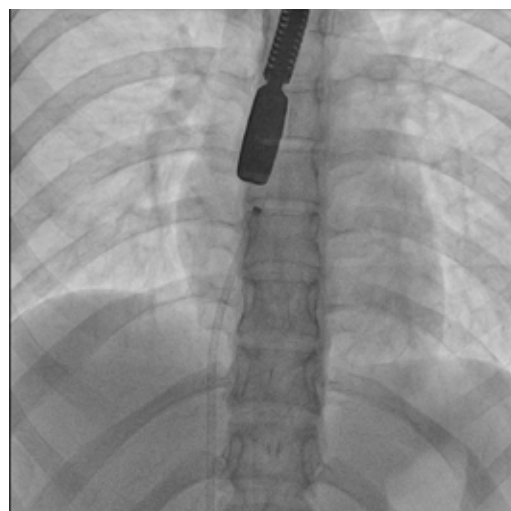


Figure 3: Biopsy performed by catheterization and guided by transesophageal echocardiography (TEE).

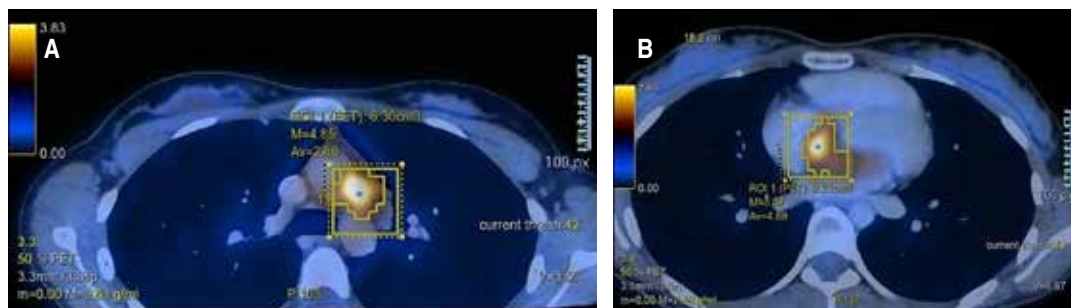


Figure 4: A) PET-CT performed in April 2022. B) PET-CT performed in April 2022.

Table 3: Second chemotherapy regimen.

Cycle	Drugs used	Dosage regimen (mg/m ²)
First	Azacitidine	75
	Venetoclax	100
Second	Azacitidine	75
	Venetoclax	100
Third	Azacitidine	75
	Venetoclax	100

CD33+. Bone biopsy showed hypocellular (50%) bone with adequate maturation without infiltration or presence of blasts.

Consequently, to characterize this lesion histopathologically, a first biopsy of the mass was performed, in March 2022 via right femoral venous catheterization guided by transesophageal echocardiography (TEE) (Figure 3) in which it was reported myocardium with CD45+ lymphocyte foci, MPO-, calretinin-, and S100-. These results were not conclusive for determining a tumor of myeloid origin.

A follow-up PET-CT was performed in April 2022, showing increased lesion activity (SUV 8.8) (Figure 4). Thus, probable disease recurrence with CMS was suspected despite the initial biopsy result. Consequently, it was decided to initiate second-line chemotherapy (Table 3).

During treatment, PET-CT follow-up in June 2022 showed reduced metabolic activity (SUV 5.6) with no changes in dimensions. Consequently, in August 2022, increased uptake despite treatment was reported (SUV 8.8), leading to a determination of refractory disease.

Afterwards, a second biopsy was performed in September 2022 to determine the histopathological origin of the mass. The reported results were as follows; MPO+, CD68+, CD4+, TdT-, HLA-DR+, lysozyme+. Therefore, these findings were consistent with the diagnosis of cardiac myeloid sarcoma. The histological sections obtained are included in the image (Figure 5).

Management and follow-up. Due to refractory disease, a rescue regimen of FLAG-IDA-VEN. Idarubicin was excluded due to the high risk of cardiotoxicity in October 2022. Afterward, three consolidation cycles of this same regimen were administered in December 2022, January 2023, and May 2023 (Table 4).

Subsequently, in February 2023, imaging studies were conducted, including a transthoracic echocardiogram, PET-CT (Figure 6), and cardiac magnetic resonance imaging, revealing persistence of the mass. However, a decrease in uptake in the PET-CT was observed, with an SUVmax of 2.5.

Due to the patient's refusal to enroll in a hematopoietic stem cell transplantation protocol and also decline in continuing chemotherapy treatment, it was decided to initiate a plan of radiation therapy sessions. It is important to note that better therapeutic outcomes have been documented with radiotherapy; therefore, this type of therapy was chosen.

A PET-CT imaging study was conducted in February 2024 (Figure 7), which showed a much more pronounced decrease in metabolic activity (1.8 SUV), compared with previous studies that showed higher metabolic activity (Figure 8). Additionally, a new echocardiogram reported an ejection fraction of 60% and a

global longitudinal strain of -19% , attributed to treatment for heart failure.

We have attached an abstract image that provides a clearer view of the case and its evolution over time (Figure 9).

DISCUSSION

In the case presented above, both the patient's initial manifestations and her hematologic/oncologic history guided the search for underlying cardiovascular pathology, employing an initial approach with echocardiography that identified the interatrial mass. Available literature highlights the importance of conventional imaging techniques (Computed Tomography and Magnetic Resonance Imaging) as pillars in the non-invasive diagnosis of CMS,⁵ which help conduct a deeper investigation into the layers, chambers, and valves involved. Similarly, other imaging methods such as echocardiography or Positron Emission Tomography (PET) play crucial roles.⁶ In the presented case, an approach through MRI was decided upon, corroborating the infiltrating mass of the interatrial septum with malignant characteristics and delineating its extension. Additionally, an initial PET-CT was performed, which showed increased metabolic activity, guiding diagnostic suspicion toward malignant neoplastic etiology; PET-CT also played a key role in patient follow-up, guiding the

diagnostic approach to the mass and assessing response to chemotherapy (refractory to second-line regimen but with partial response to the rescue regimen).⁷

Other studies such as histopathological, immunohistochemical, and molecular analyses help stratify risk and make therapeutic decisions.⁸ Typically, histopathological examination reveals an infiltrate of myeloid cells at various stages of maturation, which may exhibit granulocytic or monocytic maturation, sharing similarity with the histological appearance of Acute Myeloid Leukemia.⁹

In the presented case, although the first biopsy obtained by intervention was inconclusive, the findings of PET-CT and the t(9;11) translocation in peripheral blood guided the initiation of treatment. Subsequently, due to a lack of response to the second-line treatment regimen, a second biopsy was performed,

Table 4: FLAG-IDA-VEN regimen for refractory disease.

Fludarabine: 30 mg/m² IV daily for five days
 Cytarabine (Ara-C): 2 g/m² IV daily for five days
 Idarubicin: 12 mg/m² IV daily for three days (excluded due to high risk of cardiotoxicity)
 Venetoclax: 100 mg orally daily for the first seven days, escalating to 200 mg daily for the next seven days, up to a maximum of 400 mg daily.

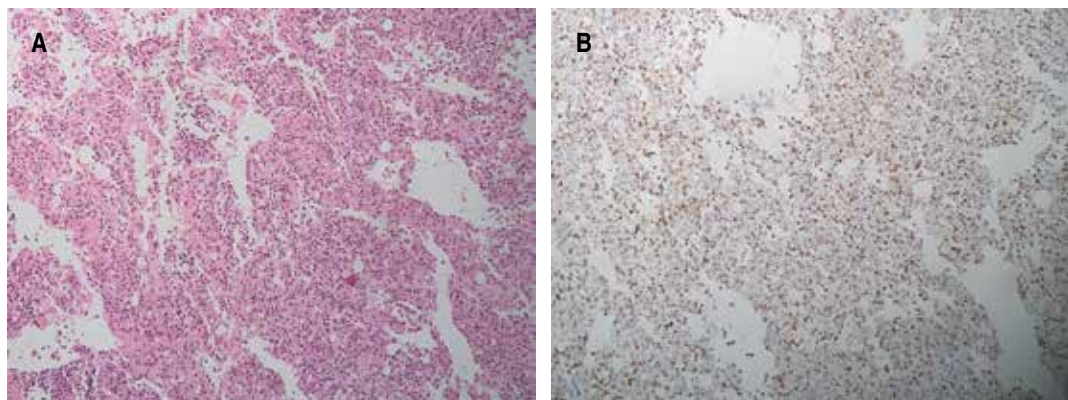


Figure 5: A) Histological section stained with hematoxylin-eosin (H&E) showing abundant infiltrate composed of small-sized cells with clefted nuclei and scant cytoplasm. **B)** Diffuse staining is observed with the myeloperoxidase (MPO) reaction.



Figure 6:
PET-CT performed
in February 2023.

which was positive for MPO, CD68, CD4 and HLA-DR, confirming the myeloid origin of the tumor. In conjunction with the patient's clinical context, set the basis for initiating rescue therapy.

Anthracyclines were not used in Acute Myeloid Sarcoma, despite being of myeloid origin, due to their association with chemotherapy-associated cardiac dysfunction. However, better therapeutic outcomes have been documented with radiotherapy, so this type of therapy was opted for, achieving follow-up for resolution of Cardiac Myeloid Sarcoma with preservation of cardiac function.¹⁰

CONCLUSIONS

1. **Rarity of the condition:** this case report underscores the rarity of cardiac myeloid sarcoma and encourages physicians to consider similar diagnoses in patients presenting with cardiac masses.
2. **Role of multimodal imaging:** this case highlights the crucial role of multimodal imaging in both diagnosing and monitoring cardiac masses, providing valuable insights for effective treatment.
3. **Collaborative approach:** the collaborative approach between hematology and cardiology services was essential in guiding the diagnosis and initiating the appropriate treatment.
4. **Need for specialized pathways:** this case emphasizes the importance of establishing and promoting healthcare pathways with a cardio-onco-hematologic perspective in Mexico to improve patient care for complex conditions.

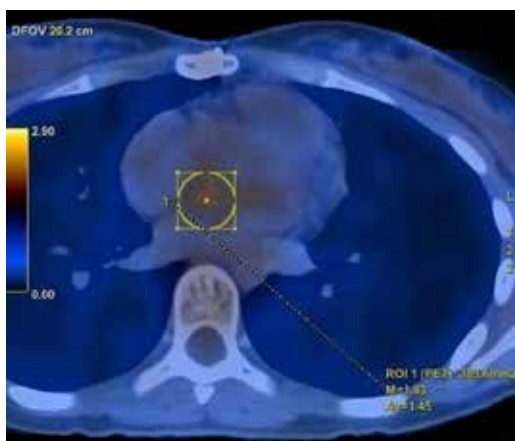


Figure 7: PET-CT performed in February 2024.

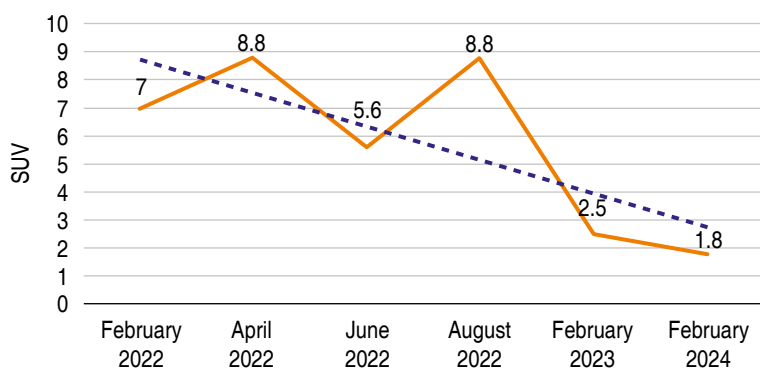


Figure 8: Changes in PET-CT standardized uptake value (SUV).

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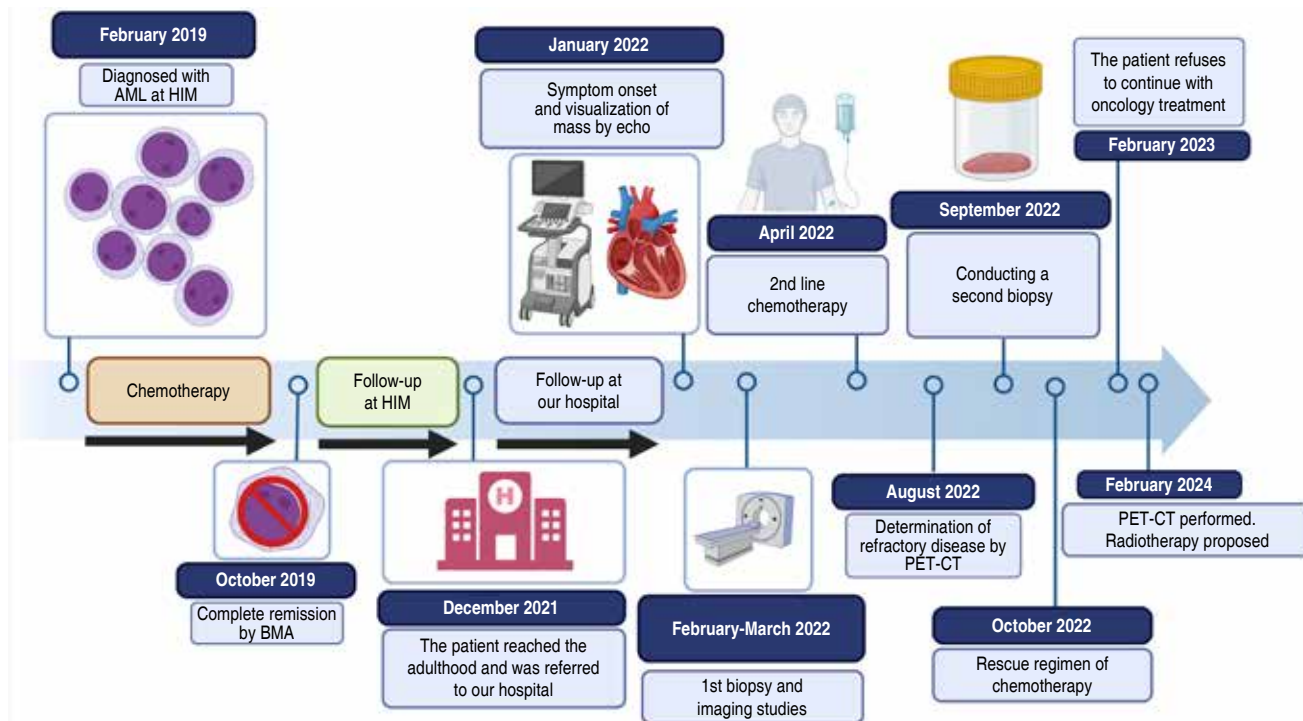


Figure 9: Abstract image that provides a clearer view of the case and its evolution over time.

AML = Acute Myeloid Leukemia. BMA = Bone Marrow Aspiration. HIM = *Hospital Infantil de México*. PET-CT = Positron Emission Tomography-Computed Tomography scan

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Case of coil dislodgement in saphenous vein graft coil occlusion in retrograde chronic total occlusion percutaneous coronary intervention

Migración de coil de un puente de vena safena durante la intervención percutánea de una oclusión crónica vía retrógrada

Arash Hashemi,* Ahmet Karagöz,‡ Melisa Uçar,§ Mehdi Zoghi,¶ Lida Ghaffari||

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Keywords:
coil, saphenous vein graft, chronic total occlusion.

Palabras clave:
coil, injerto de vena safena, oclusión total crónica.

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ABSTRACT

We report the case of a 78-year-old male with a history of coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) to the saphenous vein graft (SVG) to the obtuse marginal artery (OM). The patient presented with acute coronary syndrome and was referred for tertiary care after coronary angiography revealed in-stent restenosis in a thrombotic SVG, along with chronic total occlusion (CTO) of the left circumflex (LCx) artery. Our initial plan was intervention of SVG to OM due to stent restenosis and thrombosis. During the procedure, a balloon rupture resulted in dissection and hematoma. As a bailout intervention, native LCx with CTO ostial stenting was performed, followed by coil occlusion of the SVG. Complications arose when the coil dislodged and fragmented, leading to embolization of one particle in the descending aorta and the other in the femoral artery. Both fragments were successfully retrieved via snare. This case highlights the complexity of managing SVG-related PCI complications and the importance of careful device handling during coiling procedures.

RESUMEN

Reportamos el caso de un hombre de 78 años con antecedentes de cirugía de revascularización coronaria (CRC) e intervención coronaria percutánea (ICP) del injerto de vena safena (IVS) a la arteria marginal obtusa (MO). El paciente presentó síndrome coronario agudo y fue derivado a atención terciaria después de que la angiografía coronaria revelara reestenosis intrastent en una IVS trombótica, junto con oclusión total crónica (OTC) de la arteria circunfleja izquierda (CI). Nuestro plan inicial fue la intervención de IVS a MO debido a reestenosis del stent y trombosis. Durante el procedimiento, una rotura de balón resultó en disección y hematoma. Como intervención de rescate, se realizó stent nativo en la CI con OTC, seguido de oclusión con coil de la IVS. Surgieron complicaciones cuando el coil se desprendió y fragmentó, lo que llevó a la embolización de una partícula en la aorta descendente y la otra en la arteria femoral. Ambos fragmentos se recuperaron con éxito mediante un lazo. Este caso destaca la complejidad del manejo de las complicaciones de la ICP relacionadas con la IVS y la importancia de manipular cuidadosamente el dispositivo durante los procedimientos de colocación de la bobina.

Abbreviations:

CABG = Coronary Artery Bypass Graft
CTO = chronic total occlusion
ISR = In-Stent Restenosis
LCx = Left Circumflex Artery

OM = Obtuse Marginal
PCI = Percutaneous Coronary Intervention
SVGs = Saphenous Vein Grafts
TIMI = Thrombolysis in Myocardial Infarction

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INTRODUCTION

Saphenous vein grafts (SVGs) are frequently used in coronary artery bypass graft (CABG) surgeries to bypass occluded coronary arteries. In CABG surgery SVGs are frequently used but these grafts are prone to degeneration, atherosclerotic process, and thrombus formation often treated with coronary percutaneous intervention with balloon angioplasty and stenting leading to complications such as in-stent restenosis (ISR) and SVG failure. Management of ISR in SVGs, especially when complicated by chronic total occlusion (CTO) of native coronary arteries, presents unique challenges. This case illustrates a rare complication during the attempt to

occlude an SVG with coil embolization during retrograde CTO percutaneous coronary intervention (PCI).

CASE PRESENTATION

The patient was a 78 years old male with a history of CABG and PCI. His medical history included hypertension, hyperlipidemia and a previous PCI on the SVG to the obtuse marginal (OM) artery (*Figure 1*).

The patient presented with symptoms of acute coronary syndrome, including chest pain and shortness of breath. The ECG was in sinus rhythm and q wave was seen in D2, D3 and AVF leads. (*Figure 2*) His blood tests showed no significant values. He was referred to our center for tertiary care after coronary angiography performed at another hospital revealed a thrombotic SVG with in stent restenosis and CTO of the left circumflex artery (LCx) (*Figure 3*).

Our aim was to use the SVG as retrograde conduit for CTO PCI. During the procedure stenting was done but the stents balloon ruptured and made a huge dissection which caused a hematoma (*Figure 4*). As a bailout solution we decided to stent from the ostial LCx (*Figure 5*). To maintain a sufficient coronary perfusion, we decided to coil occlude due to Thrombolysis in Myocardial Infarction Score (TIMI) flow over 2 in this stenotic and thrombotic SVG so the competitive flow won't affect the newly opened CTO's long-term results. While coiling the donor SVG the coil dislodged. During the attempt to snare the dislodged coil with single loop snare, force by this device resulted in fracture in the dislodge coil and made two separated particles. One particle stayed in the descending aorta and the other went to the femoral artery. Both then were snared eventually (*Figure 6*).

DISCUSSION

This case highlights several key challenges in the management of post-CABG patients with PCI to SVGs. First, the management of in-stent restenosis in thrombotic SVGs poses significant risks, particularly when CTO is involved in the native coronary arteries. The decision to use the

Figure 1:

Thrombotic SVG with in-stent restenosis LCx CTO from ostial with no antegrade guide support. (J CTO Score; 4 Long, Calcified, Ambiguous proximal CAP and retry).

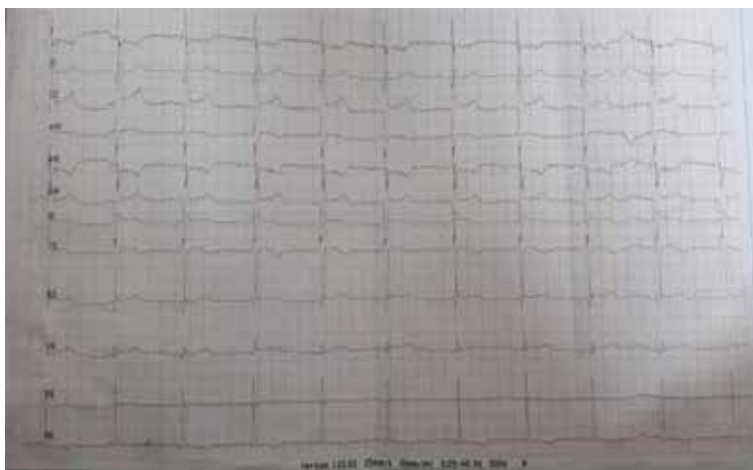
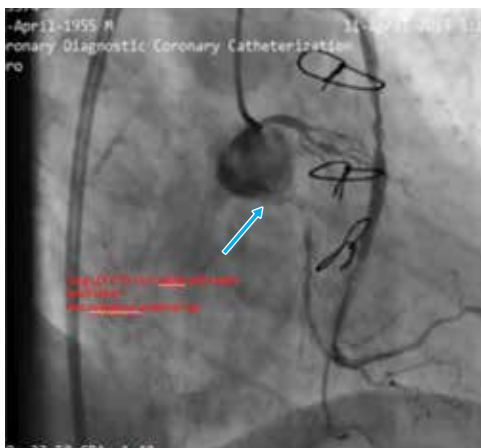


Figure 2: Sinus rhythm and q wave in D2, D3 and AVF leads.

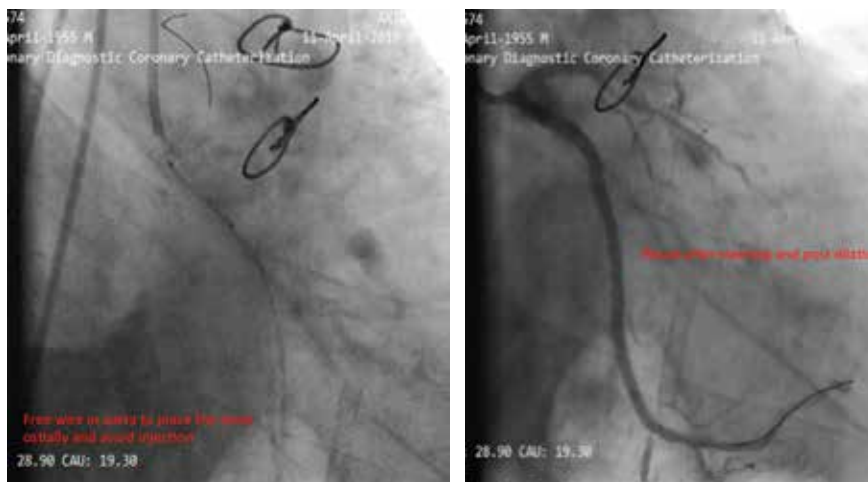


Figure 3: Attempt for CTO PCI using SVG as retrograde conduit.

Figure 4:
Stenting was done, stent's balloon ruptured the LCx and created a huge dissection and hematoma.



Figure 5:
Free wire in aorta to place the stent ostially and avoid injection. Result after stenting and post dilation.



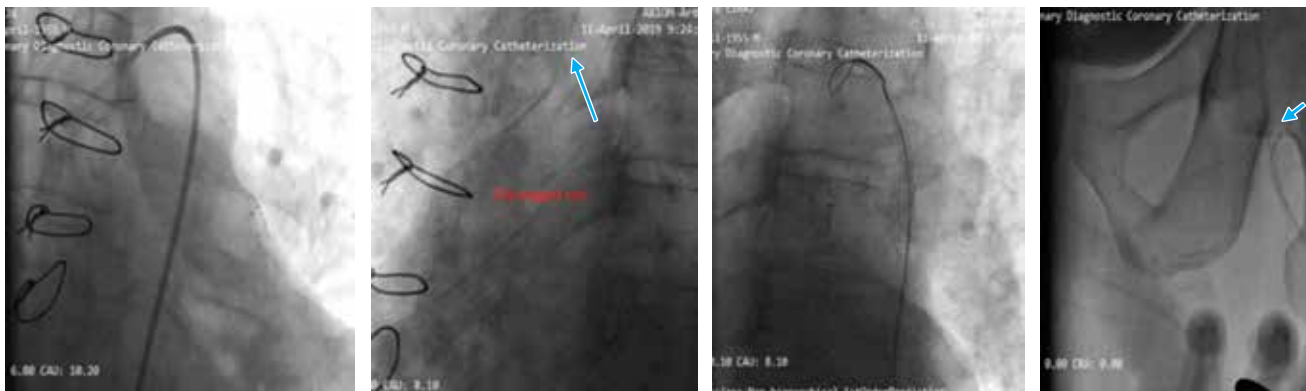


Figure 6: Dislodged coil, during the attempt to snare the dislodged coil with single loop snare; force by this device resulted in fracture in the dislodged coil and made two separated particles. Dislodged coil particle in descending aorta. Another part of the dislodged coil in the femoral artery.

SVG as a retrograde conduit was justified based on the anatomy;¹ but complications such as balloon rupture and SVG dissection underscore the importance of selecting appropriate devices and anticipating potential hazards.^{2,3}

Coil occlusion of SVGs is commonly employed to reduce competitive flow; however, in this case, coil dislodgement led to additional complications. The retrieval of coil fragments from both the descending aorta and femoral artery demonstrates the importance of having a bailout plan in such high-risk interventions.⁴

Moreover, the fracture of the coil during snaring highlights the need for careful handling of retrieval devices to avoid exacerbating complications.

Prompt and efficient operation is necessary after loop formation; as hemodynamic instability can occur quickly due to the compressive forces of looped wires on the heart.

Balloon rupture leading to dissection and hematoma is a severe complication that necessitates immediate bailout strategies, such as ostial stenting, where techniques like the Szabo technique can be helpful.⁵

When competitive flow from an SVG is present (TIMI flow ≥ 2), coil occlusion should be considered to ensure long-term patency of the newly opened CTO.⁶

CONCLUSIONS

This case underscores several important technical and procedural considerations for

managing complex PCI in post-CABG patients with SVG involvement.

Stenotic or occluded SVGs should be considered the primary retrograde route for CTO PCI when available, as they often lead to fewer complications and greater procedural success compared to other collateral routes. Coil retrieval, when necessary, is best managed with three-looped snares, which are superior to single-loop snares for preventing coil fracture and subsequent embolization. This case highlights the importance of careful procedural planning and the ability to handle unexpected complications during complex coronary interventions.

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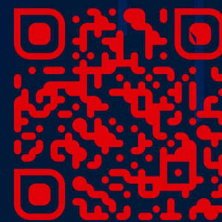
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