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Editorial

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Exercise: the undervalued and less-used medicine

Ejercicio: la medicina menos valorada y utilizada

Cristy Mariely Ortiz-Calderón*

We have witnessed in the current era of significant advances in both clinical research, therapeutics, and biotechnology, a considerable increase in global life expectancy, which according to the WHO/PAHO, went from 66.8 years in 2000 to 75.5 in 2022.[1] Mexico is no exception, with an increase in life expectancy from 71 in 1990 to 74.4 years in 2022.[2] However, the leading causes of death remain unchanged. In this regard, cardiovascular diseases have occupied the top lethal positions for decades, constituting significant public health problems and originating enormous socioeconomic costs in Mexico, as it happens worldwide.[3-5] In our country, heart disease is and has been the first general cause of mortality, except in the worst years of the COVID-19 pandemic, when this disease competed with heart disease for the first place as a cause of death. However, with the significant decrease in cases and diseases of this viral infection last year, heart disease has the undisputed first place in the general mortality table in all ages and genders.[6]

Among the main factors causing an increase in mortality from all causes and a range of cardiovascular diseases, stand out both the sedentary lifestyle and physical inactivity,[7] which despite their relevance in public health and their wide daily use, they are still used interchangeably in the wrong way, as are other terms, such as exercise. This fact reveals the remarkable lack of knowledge in general and the little diffusion on the subject, even among cardiologists.

A sedentary lifestyle or sedentary behavior is defined as the predominance in the daily life of actions in wakefulness with an energy expenditure of ≤ 1.5 METs when sitting, reclining, or lying down. Physical activity is any body movement produced by skeletal muscle that causes energy expenditure. A physically inactive person performs less than 150 minutes of moderate-intensity activity per week or equivalent.[7] A MET (metabolic equivalent of task) is the amount of oxygen consumed while the individual is sitting at rest (about 3.5 milliliters of oxygen per kilogram of body weight per minute). A MET represents the intensity of the activity carried out and allows the estimation of the physical functional capacity of a person since it expresses energy expenditure during the physical effort.[8]

On the other hand, it should be noted that exercise is a particular form of physical activity that is planned, structured, and repetitive, with an intermediate or final end, and that requires the obtaining or maintaining of physical aptitude («fitness») and cardiopulmonary, musculoskeletal, and general health.[9] Functional capacity, also called exercise tolerance (or colloquially named «physical condition»), is defined by the WHO as a measure of the ability of the body to function efficiently and effectively in occupational and recreational activities, being physiologically defined by the maximal oxygen consumption (VO_2 max), that is, the product of cardiac output and the arteriovenous oxygen difference (Q * cA-cVO_2).[10] The VO_2 max is the limiting capacity of the body to absorb, distribute and use oxygen. This gas is indispensable in the aerobic mitochondrial generation of ATP in the performance of physical activity for more than 4-5 minutes.[11-13]

* Cardiology, cardiac rehabilitation. Centro Médico Nacional Siglo XXI, IMSS.

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START OF THE IDEA OF EXERCISE AS TREATMENT

Physical exercise has been utilized since ancient times for maintaining or attaining health. Historical references can be found in the old Chinese civilization (2500 BC), as well as in ancient Greek and Roman cultures, where the concept of exercise was part of the ideas of Plato (427-327 BC), Hippocrates (460-370 BC), and Galen (129-210 AC). In prominent city-states such as Sparta, exercise was considered a valuable cultural, social, religious, and political asset. Therefore, physical exercise was part of general education in that society from early ages and throughout life.[14] In modern times, this idea has evolved to the point that, nowadays, exercise is considered a therapeutic intervention. Like any other therapy, its prescription must be tailored for each person, according to everyone's characteristics and clinical condition, to obtain optimal response and benefits. Depending on the therapeutic goal, each component of the exercise session (described with the acronym «FITT»: frequency, intensity, time, and type) must be considered. Of course, as in any other therapeutic or preventive intervention, adherence and permanence are of greater relevance. Moreover, a well-structured exercise plan's preventive and curative effects can be attained with minimal or no additional cost and potential savings on future healthcare.

HOW SHOULD EXERCISE BE PRESCRIBED?

The basic principles of exercise prescription have been described using the «FITT» concept (frequency, intensity, time, and type).

I. Frequency. It is recommended that exercise be carried out on most days (minimum three per week), with a goal of at least 150 min/week to preserve health, although it is variable if there is already some pathology.
II. Intensity. It is critical to achieving better aerobic fitness and has the most significant impact on risk factors. It is usually expressed in kcal/min or METs.
III. Time. The intensity of the exercise is inversely related to the time. The training frequency and duration provide the total expenditure energy (minimum recommendation equals 1,000 kcal/week or 10 MET/h/week).
IV. Type. There are broadly three types of exercise: dynamic, wrongly known as «aerobics» (because there are examples of a pure dynamic exercise, like the 100 hundred meters run in which the runner spends principally the scarce ATP molecules created by the phosphagen system and the anaerobic glycolytic path), the static type (or «strength»), and the combination of both («resistance»).
V. Mode. Continuous moderate exercise (MCE) is the most evaluated, although high-intensity (HIIT) interval training programs have been proposed in recent years.[9]

Generally, when a therapeutic product promises many benefits for a wide range of pathologies with minimal risk, it is not a panacea but quackery. Exercise is the only therapeutic and preventive intervention that has proven this claim with scientific facts.

EXERCISE IN HEALTHY SUBJECTS

There is strong evidence of the contribution of regular physical activity to the prevention of various pathologies, even at an early age, and the inverse relationship between a good functional capacity and population mortality and morbidity. Some proven preventive benefits are:

a) Children and adolescents: improvement of bone health and weight (children from 3 to 5 years old). A better cognitive function, less risk of depression (6 to 13 years), and better cardiopulmonary and muscular fitness (6-17 years). It also prevents dangerous behavioral decisions related to tobacco smoking, alcohol abuse, the consumption of an unhealthy diet, or violence, promoting in this way healthier social environments.[10,15,16]
b) In adults: exercise decreases mortality from all causes and cardiovascular disease, reduces the probability of suffering cardiovascular events, including stroke and myocardial infarction, and lowers the

risk of hypertension, diabetes, dyslipidemia, and a variety of cancers in several organs (bladder, breast, colon, endometrium, esophagus, kidney, lung, and stomach). Furthermore, it improves mental health (cognitive functions and sleep, reducing the risk of anxiety, depression, and dementia). In addition, exercise contributes to weight loss and prevents weight recovery, resulting in a better overall quality of life.

c) Special groups: in pregnant women, exercise lowers the risk of gaining excess weight and developing gestational diabetes and postpartum depression. In the elderly, exercise lowers the risk of injuries from falls, reduces osteoporosis, and promotes healthy aging.[10,13,15]

EXERCISE IN ILLNESS

In various chronic medical conditions, exercise has also shown its usefulness. Regular physical activity controls cardiovascular risk factors, such as diabetes mellitus, dyslipidemia, obesity, and high blood pressure.[17] In heart failure, especially the variety with «reduced ejection fraction (HFrEF)», exercise diminishes the number of hospitalizations and mortality and enhances the quality of life.[18] Additionally, exercise abates numerous clinical outcomes in an extended range of disparate diseases, such as rheumatic conditions (systemic lupus erythematosus,[19-21] spondyloarthritis,[22] osteoarthritis, rheumatoid arthritis, psoriatic arthritis, systemic sclerosis disease, and gout[19]). Furthermore, it benefits mental conditions such as depression,[23] stress, anxiety,[24] schizophrenia, other forms of dementia, and neurodegenerative diseases such as Parkinson's disease and multiple sclerosis.[20] The benefits of exercise extend to different malignant entities, both solid tumors and those of blood origin, during or after therapy and even in advanced stages, to the point that exercise has also been proposed as adjuvant therapy to chemotherapy and radiotherapy.[25-27] Likewise, the advantages of exercise extend to musculoskeletal and pulmonary disorders, such as lower back pain and osteoporosis[20,27-29] chronic obstructive pulmonary disease, asthma, and cystic fibrosis, among others.

EXERCISE RISKS

The frequency of serious complications reported during a stress test is minor and less reported in modern times since they can be prevented and because the test's contraindications and the patient's previous stratification have played an essential role in reducing the inherent risk. One of the most extended studies in this regard, carried out by Gibbons et al. for ten years, included more than 70,000 treadmills up to maximal effort tests, which reported only six severe complications, including one death, with a rate of 0.8 complications per 10,000 tests.[30] On the other hand, in a recent prospective study conducted from 2002 to 2013 with patients between 35 and 65 years old who presented sudden death, only 5% (63 cases) occurred during sports activities (incidence of 21.7 per 1 million per year).[31] In recent years there has been developed a new training modality called «HIIT» (an acronym for high-intensity interval training) that has shown some benefits over the traditional mode MICT (moderate-intensity continuous training). However, it has been observed that the frequency of acute cardiac events is six times higher than with a moderate workload. Nevertheless, as the intensity of the prescription is essential in the training of high-performance athletes,[32] a previous complete clinical assessment is indispensable.

IMPORTANCE OF EXERCISE ON PUBLIC HEALTH

Current evidence indicates that physical inactivity represents a severe threat to general and cardiovascular health. In contrast, even moderate-to-vigorous physical activity considerably impacts the prevention of several potentially lethal or disabling pathologies. Although evidence signals that better preventive benefits are attained with full compliance with international expert recommendations, even a modest exercise can abate cardiovascular morbidity and mortality to some degree.[5]

WHAT CAN BE DONE?

It is essential to broaden the investigations, mainly those focused on the adequate

prescription in each pathology, since better tailoring the prescription according to the different kinds of patients. Furthermore, as health personnel, we also should recognize all the benefits of exercise, so it should be considered an established form of therapy. At the same time, health personnel must promote, educate, and make timely referrals to specialists in the field, and have to preach by example, as it is known that words can move, but the example can convince. Unfortunately, according to ENSANUT, more than half of the Mexican population of both genders are sedentary.[33] There is no doubt that this trait contributes not only to the dissemination of the epidemic of obesity that ravages our nation but, more seriously, to the continuous increment of atherosclerotic diseases, the first cause of general mortality among us in current days.

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Correspondence:
Cristy Mariely Ortiz-Calderón
E-mail: dra.cristyortiz.cardiologia@gmail.com

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Original research

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Initial results of the National Survey of Cardiovascular Risk Factors in Mexican women: «ENAFARC Mexico»

Resultados iniciales de la Encuesta Nacional de Factores de Riesgo Cardiovascular en la mujer mexicana: «ENAFARC México»

Adriana Puente-Barragán,* Alejandra Madrid-Miller,‡ Patricia Nuriulú-Escobar,§ Yoloxochitl García-Jiménez,¶ Germán Anguiano-Torres,‖ ENAFARC Mexico Research Group

Keywords: traditional risk factors, sex-specific risk factors, female cardiovascular disease, female risk factors.

Palabras clave: *factores de riesgo tradicionales, factores de riesgo sexo-específicos, enfermedad cardiovascular en la mujer, factores de riesgo de la mujer.*

ABSTRACT

Introduction: cardiovascular disease (CVD) continues to be the leading cause of death worldwide in women, associated with different cardiovascular risk factors (CVRF), both traditional, sex-specific and emerging. **Objective:** to know the frequency of traditional and sex-specific CVRF in the Mexican female population based on the National Survey of Cardiovascular Risk Factors (ENAFARC Mexico) results. **Material and methods:** surveys collected by doctors, nutritionists or nursing staff were conducted in 23 cities in Mexico. An individual standardized questionnaire with closed answers, anthropometry and laboratory tests was applied, aimed at women who attended primary care, specialty care and detection campaigns in the open population. **Results:** analysis included 2,304 surveys. The average age was 53.4 to 15.8 years old. Rich carbohydrate and saturated fat diets were reported in 51 to 62%, sedentary lifestyle in 60.5%, obesity in 32.7%, hypertension in 41.2%, dyslipidemia in 34.5%, diabetes in 21.3%, and 51.2% had metabolic syndrome criteria. 54.4% were in the postmenopausal stage; of these, 22.1% with premature menopause and 47% had at least two added risk factors (OR 2.91, 95% CI 2.56-3.31). Hypertensive disorders of pregnancy were significantly associated with the development of chronic hypertension ten years after delivery (OR 2.53 with 95% CI 1.93-3.31). **Conclusions:** there is a high frequency of traditional, sex-specific and emerging CVRF in Mexican women, mainly in postmenopausal. The etiology seems to be multifactorial and importantly related to various sociocultural determinants.

RESUMEN

Introducción: *la enfermedad cardiovascular (ECV) sigue siendo la principal causa de muerte a nivel mundial en las mujeres, asociada a diferentes factores de riesgo cardiovascular (FRCV) tanto los tradicionales como los ligados al sexo y los emergentes.* ***Objetivo:*** *conocer la frecuencia de los FRCV tradicionales y sexo-específicos de la población femenina en México, con base en los resultados de la Encuesta Nacional de Factores de Riesgo Cardiovascular (ENAFARC México).* ***Material y métodos:*** *se realizaron encuestas recolectadas por médicos, nutriólogos o personal de enfermería, en 23 ciudades de México. Se aplicó un cuestionario individual estandarizado con respuestas cerradas, antropometría y exámenes de laboratorio, dirigidas a mujeres que acudían a consulta de atención primaria, de especialidad y campañas de detección en población abierta.* ***Resultados:*** *se incluyeron en el análisis 2,304 encuestas. La edad promedio fue de 53.4 ± 15.8 años. Con alimentación rica en carbohidratos en 62% y grasas saturadas en 51.2%, así como sedentarismo en 60.5%. Cursaban con obesidad 32.7%, 41.2% con hipertensión arterial, 34.5% con dislipidemia, 21.3% con diabetes y 51.2% con síndrome metabólico. Por otro lado, 54.4% estaban en etapa menopáusica, de éstas 22.1% con menopausia prematura y 47% contaban con al menos dos factores de riesgo agregado (OR 2.91, IC 95% 2.56-3.31). Los trastornos hipertensivos del embarazo se asociaron significativamente al desarrollo de hipertensión crónica 10 años después del parto (OR 2.53 con IC 95% 1.93-3.31).* ***Conclusiones:*** *existe una elevada frecuencia de FRCV tradicionales, sexo-específicos y emergentes en la mujer mexicana, principalmente durante la menopausia. La etiología parece ser multifactorial e importantemente relacionada a diversos determinantes socioculturales.*

* Cardiologist, Head of the Cardiology Medical Section CMN 20 de Noviembre, ISSSTE. Head of the Chapter on Cardiovascular Diseases in Women, ANCAM. Mexico.
‡ Cardiologist, Master of Science, Member of the Chapter of Cardiovascular Diseases in Women, ANCAM. Mexico.
§ Echocardiographer Cardiologist, Cardiovascular Prevention Clinic. Pachuca, Hidalgo.
¶ Interventional Cardiologist, UMAE Hospital de Especialidades No. 14. Veracruz, Mexico.

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‖ Cardiologist, Sagittarius Medical Center, Cardiometabolic Prevention Center. Zapopan, Jalisco, México.

ENAFARC Mexico Research Group.

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INTRODUCTION

Cardiovascular disease (CVD) remains the leading cause of death worldwide. In women, CVD is the leading cause of morbidity and mortality in Mexico and throughout the world.[1,2] Overall, 1 in 3 women die of CVD, and 45% of women over the age of twenty have some CVD. Women in Mexico are twelve times more likely to die from acute myocardial infarction than from breast or cervical cancer. However, the information diffusion, awareness and education, both by health personnel and the population, is low, leading to its downplaying importance. Cardiovascular risk factors (CVRF) are essentially the same in men and women, known as traditional, such as hypertension, diabetes mellitus, dyslipidemia, obesity, sedentary lifestyle, and smoking. Additionally and related to the multiple activities that women carry out in daily life, in the family, at work and in the social environment, there are other risk factors called emerging or less recognized, such as depression, anxiety and other psychosocial disorders, which have an important role in the development of CVD.[3,4] Likewise, women have unique CVRF or sex-specific related to biological determinants (sex, age, genetics, race, ethnicity and family history), such as polycystic ovary syndrome, hormone replacement therapy, premature menopause (surgical or natural), conditions associated with pregnancy (gestational diabetes, hypertensive disorders, preterm delivery or low birth weight products) and systemic inflammatory and autoimmune diseases, which are not precisely specific to the female sex.[5-7] However, women are affected in greater proportion by these conditions than men. These CVRFs increase the future risk of CVD and are associated with an increase in the probability that women will develop CVD over the years, up to two or three-fold than in men, the disease will progress differently, and therapeutic response may not be the same.[3,8,9]

Women's life expectancy has increased, so by the year 2030; there will be 1,200 million women older than 50.[10] That is, they will be going through a critical period in terms of the presence of CVRF and the development of CVD, which manifests itself more frequently in women between 50 and 65 years of age. Often the importance and detection of traditional and sex-specific CVRF in women go unidentified by both women and the medical community (general practitioners, family doctors, gynecologists, cardiologists, and other specialists), which increases morbidity-mortality in women.

There are reports in the literature regarding the frequency of traditional CVRF in Mexican women. However, to date, no reports have also included in their analysis the frequency of sex-specific and emerging CVRF. Consequently, it is unknown which is the impact these may have on their cardiovascular health. Therefore, knowledge of them is essential to develop strategies to reduce cardiovascular risk in women, provide timely treatment and subsequently reduce CVD mortality. The objective of this article is to identify the frequency of traditional and sex-specific CVRF in Mexican females, based on the results of the National Survey of Cardiovascular Risk Factors (ENAFARC Mexico).

MATERIAL AND METHODS

The survey data was collected by medical doctors, nutritionists, or nursing staff in twenty-three cities in Mexico through direct interviews and filling out a survey consisting of a standardized questionnaire, controlled information with closed answers, physical measurements, and laboratory examinations *(Figure 1)*. The health personnel who supported the registration process received training and a manual standardized for measurements. The surveys included women who attended primary or specialty care consultation, as well as during community screening campaigns, who met the following selection criteria: older than 18 years, with or without a history of CVD, who had a complete register of the survey of CVRF in women (ENAFARC Mexico) and informed consent signature. Those cases that did not have complete lipid and glycemic profile laboratory tests were excluded. Standardized survey information included demographic data, pathological and non-pathological medical history, identification of traditional risk factors (diabetes, hypertension, dyslipidemia, obesity,

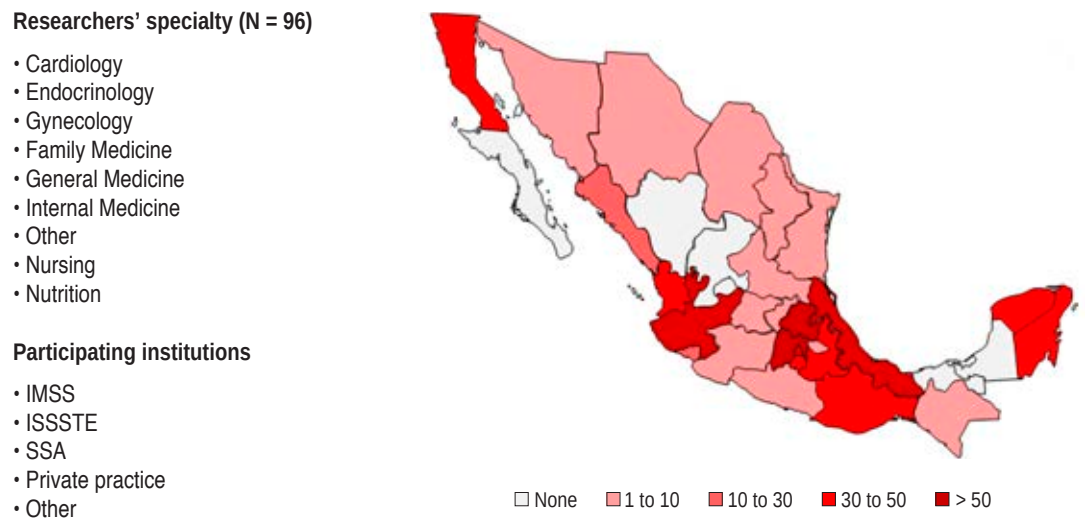

Figure 1: Participants in the survey registry.
IMSS = Mexican Social Security Institute. ISSSTE = Institute of Social Security and Services for State Workers. SSA = Secretary of Health.

metabolic syndrome), sex-specific and emerging risk factors, inflammatory diseases, including the clinical background of having suffered from COVID-19, thyroid disease and psychosocial factors (depression, anxiety disorders, family or workplace violence, sleep disorders), medical history of CVD and its treatment.

Physical measurements included: weight, height, abdominal circumference, blood pressure, heart rate, respiratory, temperature, laboratory examination: lipid profile and glycemia. Weight was measured on a weighing machine with the woman wearing light clothing without shoes, and the body mass index (BMI) was calculated as weight in kilograms divided by the square of the height in meters. Overweight or obesity was defined as BMI ≥ 24.0 kg/m^2. Cardiovascular risk stratification included the calculation of the atherogenic index, risk calculation using the ASCVD (atherosclerotic cardiovascular disease) algorithm,[11] and the Globorisk prediction model.[12] We consider exercise when carrying out the planned physical activity of moderate intensity for at least 150 min per week. Diagnosis of diabetes mellitus was considered based on the diagnostic criteria of the American Diabetes Association: for new cases (fasting glucose ≥ 126 mg/dL, casual glucose ≥ 200 mg/dL plus symptoms or tolerance curve with glucose ≥ 200 mg/dL at 2 hours) or the history of the diagnosis reported by the patient or glycated hemoglobin ≥ 6.5%. For blood pressure assessment, we used an aneroid sphygmomanometer or electronic (oscillometric) devices; three measurements were made with an interval of one min between each measurement, with the patient at resting, in a sitting position for three minutes, and the highest pressure was recorded. Hypertension was considered when the systolic blood pressure was equal to or greater than 140 mmHg or diastolic equal to or greater than 90 mmHg, according to the European Society of Cardiology classification, the European Society of Hypertension and the Consensus on systemic arterial hypertension in Mexico;[13,14] when the woman surveyed referred to having antihypertensive treatment or having no history of previous diagnosis, in the presence of high blood pressure and once external factors that could cause transient elevation of blood pressure had been ruled out, such as recent physical or mental exertion, intake of coffee, tea, or any other stimulating substance in at least one hour prior to taking blood pressure. Dyslipidemia was considered if there was a previous diagnosis or treatment or if laboratory tests reported elevated levels of cholesterol (≥ 240 mg/dL), triglycerides (> 150 mg/dL), low-density lipoproteins (LDL-c) > 130 mg/dL or decreased high-density lipoproteins cholesterol (HDL-c) < 50 mg/dL. Active

smoking was defined if, at the time of inclusion or in the previous six months, they had smoked or had a history of smoking in the five years before presenting any cardiovascular pathology. A former smoker was considered when they had quit smoking more than six months before their inclusion or more than five years before any CVD diagnostic, and non-smoker when she had never smoked or had smoked less than 100 cigarettes in her entire life.

We defined metabolic syndrome using the National Cholesterol Education Program Adult Treatment Panel III (ATP III) criteria. The habit of a healthy diet was considered if they consumed more than five servings of fruits and vegetables per day, consumption of fish or foods rich in omega-three fatty acids at least two times per week, and predominance in the frequency of unsaturated or polyunsaturated fats, low in the fat of animal origin and carbohydrates, at least six days per week. Pregnancy complications included were: gestational hypertension, preeclampsia, eclampsia, HELLP syndrome, carbohydrate intolerance, gestational diabetes, gestational dyslipidemia, preterm delivery, and macrosomic product. Moreover, the psychosocial factors were: previous diagnosis of depression, anxiety syndrome, sexual or work-related violence, sleep disorders (defined as difficulty falling asleep or staying asleep, trouble getting adequate rest or waking up tired, sleepiness or excessive fatigue during the day, history of obstructive sleep apnea, and sleeping time of fewer than eight hours).

Statistical analysis: only the surveys with 100% of the registered information were considered for analysis. The dichotomous variables are presented by means of frequencies and percentages. The results obtained from the continuous variables are expressed by measures of central tendency and dispersion according to their distribution, such as median and interquartile ranges (25 and 75%) or mean with standard deviation (SD). The bivariate evaluation of dichotomous variables was performed with the χ^2 test and the odds ratio with a 95% confidence interval.

Table 1: Demographic characteristics and lifestyle habits (N = 2,304).

Characteristic	n (%)
Age in years [mean ± SD]	53.41 ± 15.77
Occupation	
Freelance worker or professional	270 (11.72)
Employee	841 (36.50)
Retired	195 (8.46)
Homemaker	926 (40.19)
Unemployed	42 (1.82)
Student	30 (1.30)
Economic income level	
Higher	136 (5.90)
Middle	1,099 (47.70)
Lower	901 (39.11)
Poor or near-poor	168 (7.29)
Exercise	837 (36.33)
Intense	38 (4.54)
Moderate	302 (36.08)
Mild	497 (59.38)
Sedentary	1,394 (60.50)
Exercise duration	
> 150 min	409 (48.86)
< 150 min	428 (51.14)
Dietary habits	
1. Intake of vegetables and fruit:	
≥ 5 servings/day	639 (27.73)
< 5 servings/day	1,665 (72.27)
2. Consumption of fish and omega 3 products at least 2 times a week	859 (37.28)
3. Predominant consumption of mono and polyunsaturated fats	1,041 (45.18)
4. Saturated fat or trans-fat intake excess	1,175 (51.00)
5. Carbohydrates intake excess	1,429 (62.02)
6. Daily salt intake	
< 1.5 g/day (low)	486 (21.09)
1.5 to 2.3 g/day (limited)	1,517 (65.84)
> 2.3 g/day (rich)	280 (12.15)
Consumption of alcoholic beverages	
Never	1,431 (62.11)
One or fewer drinks per day, or < 7 drinks per week	847 (36.76)
Two or more drinks per day, or 8 or more drinks per week	27 (1.17)

RESULTS

Of the total of 2,499 participants, 159 were excluded because the information was incomplete, and 36 were duplicated; 2,304 were included in the analysis. The average age was 53.4 ± 15.8 years; 48.1% were married, 25% single, 12.3% widows, 7.7% lived in free union, and 6.8% divorced. Regarding the level of education, 33.1% completed college, 8% had postgraduate studies, 23.5% reached senior

Table 2: Frequency of the most common traditional and emerging risk factors (N = 2,304).

Risk factors	n (%)
Traditional risk factors	
Sedentary lifestyle	1,394 (60.5)
Current smoking	200 (8.7)
Diabetes	492 (21.3)
Hypertension	1,124 (48.8)
Dyslipidemia	1,417 (61.5)
Metabolic syndrome	1,181 (51.2)
Obesity/overweight	1,576 (70.0)
Overweight	849 (36.8)
Obesity	754 (32.7)
Emerging risk factors	
Thyroid disease	216 (9.4)
COVID-19	588 (25.5)
Depression	568 (24.6)
Anxiety disorders	666 (28.9)
Domestic violence	252 (10.9)
Workplace violence	109 (4.7)
Sleep disorders	1,188 (51.6)
Physical examination [median and interquartile ranges 25 and 75%]	
BMI (kg/m^2)	27.57 [64.3-13.7]
Abdominal perimeter (cm)	90 [156-44]
SBP (mmHg)	120 [220-60]
DBP (mmHg)	75 [120-50]
Laboratory examination [median and interquartile range 25 and 75%]	
Glucose (mg/dL)	98 [89-109]
Total cholesterol (mg/dL)	174 [148-203]
Triglycerides (mg/dL)	155 [108-187]
LDL-c (mg/dL)	100 [76-127]
HDL-c (mg/dL)	46 [38-57]
No c-HDL (mg/dL)	125 [100-155]

Frequency of the most common traditional and emerging risk factors. Traditional and emerging risk factors are frequent in the women surveyed.
SD = standard deviation. DM = diabetes mellitus. BMI = body mass index. SBP = systolic blood pressure. DBP = diastolic blood pressure. LDL-c = low-density lipoprotein cholesterol. HDL-c = high-density lipoprotein cholesterol. No c-HDL = no c-HDL cholesterol. Values are expressed as median and interquartile ranges due to the non-normal distribution of the data.

high school or technical career, 14.8% junior high school, 17.1% only had some elementary school level, and 2.7% without scholar education. Two-fifths of the women (40.2%) were housework, and 48.2% additionally worked (the majority as some company employees and only 24% were self-employed or independent professionals); 86.8% had a medium or low-income level. The proportion of women who exercised at moderate to high intensity and ate a healthy diet was only 17% and 8.8%, respectively; however, a diet rich in carbohydrates (62%) and saturated fats (51%), low in consumption of vegetables or fruits (72.3%) predominated; most of the women reported having a low alcohol consumption, 62.1% denied consumption of alcoholic beverages *(Table 1)*.

Traditional CVRF

A history or confirmed diagnosis of diabetes mellitus was reported in 21.3% (n = 492). Additionally, 76 women without a confirmed diagnosis had fasting blood glucose > 126 mg/dL; hypertension in 41.2% (n = 949), but it was found that 175 women without a previous diagnosis of hypertension had pressures equal to or greater than 140/90 mmHg, giving a total of 48.8% (n = 1,124); and dyslipidemia in 34.5% (n = 795). However, in women without having been previously diagnosed, total cholesterol levels > 240 mg/dL were found in 81, triglycerides > 150 mg/dL in 599, HDL-c < 50 mg/dL in 584 and LDL-c > 130 mg/dL in 260, that is, in 622 additional women were detected with some dyslipidemia, which added to those previously diagnosed gives a total of 61.5% (n = 1,417). The median evolution time of diabetes, hypertension and dyslipidemia was nine, ten and three years, respectively. Overweight or obesity was found in 70% (n = 1,634) of all women (32.7% with BMI > 30 kg/m^2), 70.3% (n = 1,620) with abdominal obesity, 99% of these were associated with a diet rich in carbohydrates and saturated or trans fats. 24.6% (n = 566) of the participants had an earlier diagnosis of metabolic syndrome. Additionally, it was found that 615 women met three or more criteria according to the ATP III definition, giving a total of 51.2% (n = 1,181) women with metabolic syndrome. *Table 2* shows the frequencies and values reported from the physical measurements and laboratory examinations.

Regarding diabetic women, 48% had different obesity degrees, and 36.6% were overweight. Similarly, in hypertensive women, the frequency of obesity was high 41.8% and overweight 38.8%. Current smoking was reported by only 8.7% (n = 200) and 5.1% (n = 118) had quit smoking within the last five years.

Sex-specific and emerging CVRF

We found that premature menopause was the most frequent sex-specific factor (n = 277), followed by postmenopausal hormone replacement therapy (n = 171), use of hormonal contraceptives (n = 521), early menarche (before 11 years of age) and polycystic ovary syndrome (n = 203 and n = 165, respectively). More than half of the women (54.4%) included were in the menopausal and postmenopausal stage (n = 1,253); of these, 76.1% were overweight or obese, 58.5% (n = 733) with hypertension, 48.3% (n = 607) dyslipidemia and 28.7% (n = 360) diabetes; 47% had at least two risk factors (OR 2.91, 95% CI 2.56-3.31) and 34.2% (n = 428) with metabolic syndrome (OR 2.70, 95% CI 2.30-3.18).

In the women who reported having had at least one pregnancy (n = 1,914), the most common history was preterm delivery in 22.8% (n = 316), followed by hypertensive disorders of pregnancy 22.1% (n = 277), of which preeclampsia was the most frequent 44.4% (n = 122); low birth weight product 10.1% (n = 194) and macrosomic product in 8.6% *(Figure 2)*. Half of the women with a history of hypertensive disorders during pregnancy developed hypertension ten years after delivery (OR 2.53 with 95% CI 1.93-3.31). A low percentage of women reported having had diabetes or gestational dyslipidemia (2.4% and 0.73%, respectively).

Regarding inflammatory and immunological diseases, a history of systemic lupus erythematosus was found in 0.8% (n = 12), rheumatoid arthritis in 2.8% (n = 65), and thyroid disease in 9.4% (n = 216). A history of breast cancer was recorded in 1.48% (n = 34), and 28 of them received chemotherapy, radiotherapy or combined therapy. Confirmed diagnosis of COVID-19 was reported in 25.5% (n = 588), 70 received oxygen therapy, only 36 with intrahospital treatment, and four required mechanical ventilatory support.

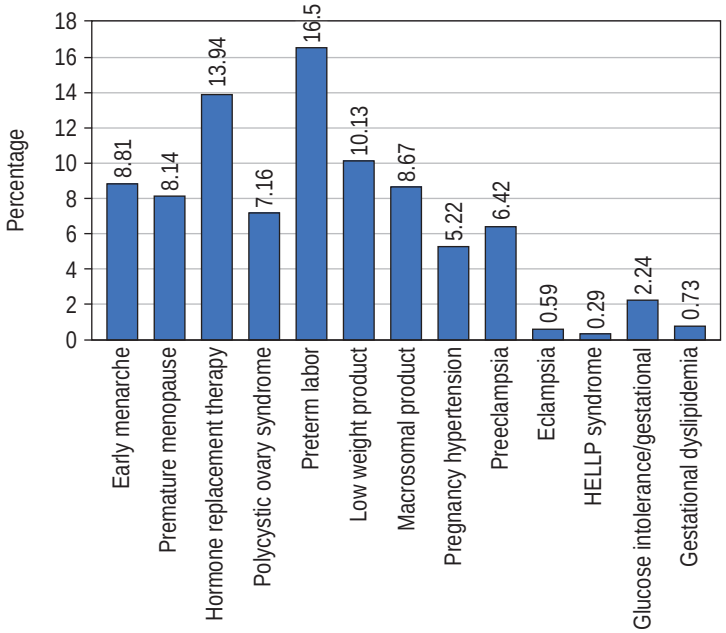

Figure 2: Sex-specific risk factors frequency. Frequency of sex-specific factors in percentage frequency.
HELLP syndrome = hemolysis syndrome, elevated liver enzymes, thrombocytopenia.

DISCUSSION

To our knowledge, this is the first report evaluating the frequency of traditional and sex-specific risk factors in the same population of Mexican women. We found that overweight or obesity, hypertension, and dyslipidemia were positioned as the three main traditional risk factors for CVD. The predominant risk factor, and apparently with the greatest impact on health in the women participating in our study, was overweight or obesity, with its highest frequency in the menopausal and postmenopausal stages. The frequency of hypertension that we found was similar to that reported in the INTERHEART study,[15] which included women who had undergone myocardial infarction cared for in medical units in 52 different countries and which reported 53% with hypertension. Nevertheless, in this study, abdominal obesity and psychosocial problems report with a lower frequency (45.6% and 45.2%, respectively) than we found.

On the other hand, the prevalence of abdominal obesity reported in large studies carried out in the community in our country, such as ENSANUT[16] and the National Study of Health and Aging in Mexico (ENASEM)[17] was higher (89.6%), but less frequency of dyslipidemia and hypertension. Similarly, we found a higher frequency of hypertension and dyslipidemia than that reported in the FRIMEX IIa study,[18] which reported 71.5% of obesity in women, but 21.5% hypertension and 40% dyslipidemia. It is important to note that 52% of the women in our study had not been previously diagnosed with dyslipidemia.

Being overweight and obese was associated with a poor-quality diet, rich in carbohydrates and fats of animal products, and a lack of exercise, according to our study. It is important to highlight that in women in the menopausal and postmenopausal stages, hypertension and dyslipidemia were found more frequently, as well as the clustering of two or more risk factors than in women in the premenopausal stage, mainly in overweight and obese women. A high percentage of women with diabetes and hypertension have different degrees of obesity, which suggests that their treatment does not include a comprehensive approach with lifestyle changes, healthy eating, and exercise. Furthermore, the high frequency of psychosocial factors such as depression, anxiety, and sleep disorders reported in our study population could also contribute. It is known that sleep disorders, both in quantity hours of sleep and in quality, have an impact on CVRF, mainly in the development of obesity and metabolic syndrome; this alteration occurred in a high percentage of the population studied, and it was mainly significantly associated in the menopausal and postmenopausal stage.

In contrast to what was reported by Benschop L et al. in 2019,[19] that up to 32% of women with hypertensive disorders during pregnancy developed chronic hypertension in the first ten years after delivery, compared to 11% of women with normotensive pregnancies, we found that 50% of the women who reported having the history developed hypertension in the same period, indicating the need to carry out long-term follow-up and establish preventive measures in women with this disorder in our population.

Despite our population's economic and cultural development, urban changes, lifestyle behaviors, and poor nutrition favor the presence of different CVRFs and, therefore, the rapid increase in cardiovascular morbidity and mortality related to them. Timely scrutiny and management of both traditional, sex-specific, and emerging risk factors are important to consider as part of the clinical evaluation of women at all life cycle stages, which should include laboratory examinations with complete lipid profiles as well as and blood glucose analysis.

Limitations

Although the study covered different cities in our country and an open population, almost half of the cases included in this study were obtained from surveys conducted in consultation with medical specialists, and most of the women lived in urban areas, which could be overestimating the frequency of factors such as hypertension and dyslipidemia, as well as psychosocial factors. The results presented are preliminary in the first analysis of ENAFARC Mexico.

CONCLUSIONS

In this first analysis of ENAFAC Mexico, we found a high frequency of traditional, sex-specific, and emerging CVRF in Mexican women, mainly after menopause. The etiology appears multifactorial and is importantly related to various sociocultural determinants in women. Unhealthy lifestyles in women have undoubtedly favored the high frequency of obesity and overweight in our population. The metabolic problems in women in the menopausal stage are associated with an increase in the presence of different risk factors and an increase in their cardiovascular risk. It is necessary to establish strategies in a timely manner for the early detection of all CVRF in women, and they must be informed of their higher risk and implement measures for a healthy lifestyle.

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ENAFARC Mexico Research Group:

Dr. Francisco Gerardo Padilla Padilla (Jalisco)
Dra. Silvia Elena Zavaleta Castillo (CDMX)
Dra. Nilda Gladys Espínola Zavaleta (CDMX)
Dra. Laura Marina Castillón Rodríguez (Nayarit)
Lic. Noemí del Socorro Salazar Díaz (Quintana Roo)
Dra. Ana Elena Ancona Vadillo (CDMX)
Dra. Delia de los Ángeles López Palomo (Yucatán)
Dra. María Guadalupe Parra Machuca (Jalisco)
Lic. Andrea Paola Serrano Martínez (Morelos)
Dra. Gladis Faustino Maravilla (Edo. Mex.)
Dra. Andrea Auryn Núñez Ruiz (CDMX)
Dra. Marianela Rodney Ortega (Puebla)
Dr. Carlos Obeth Ferreyra Solorio (Edo. Mex.)
Dr. Filiberto Alejo Díaz Aragón (Oaxaca)
Dra. Leidy Laura Pérez Martínez (Hidalgo)
Lic. Francisco Fuentes Ramírez (CDMX)
Dra. María Fabiola Barbosa García (Hidalgo)
Dr. Arturo Guerra López (Baja California)
Dr. Luis Eng Ceceña (Sinaloa)
Dra. Flor Agruel Trujillo Narváez (Baja California)
Dr. José de Jesús Tapia Conde (Tlaxcala)
Dra. María de Lourdes Basurto Acevedo (CDMX)
Dra. Aline Meza Díaz (Quintana Roo)
Dra. Elsa Margarita Arrieta Maturino (CDMX)
Dra. Lucelli Yáñez Gutiérrez (Querétaro)
Dra. Lilia Amezcua Gómez (CDMX)
Dr. Enrique Ramos Cházaro (Puebla)
Dr. Reynaldo Nicolás Vázquez (Oaxaca)
Dr. Manlio Segismundo Quiroz Salas (CDMX)
Dr. Miguel Ángel Macías Franco (Puebla)
Dr. Norberto Matadamas Hernández (Guerrero)
Dr. Héctor Vicente Bayardo Solórzano (Quintana Roo)
Dra. Leticia Nevárez Rivera (Chihuahua)
Dra. Itzel Atziry Martínez Pineda (Puebla)
Dra. Norma Cerón Enríquez (Puebla)
Dr. Francisco José Castrejón Aivar (Guanajuato)
Dra. Leidy Laura Pérez Martínez (Hidalgo)
Dr. Rafael Bustos Romero (Veracruz)
Dr. Juan Carlos Becerra Martínez (Jalisco)
Dra. Claudia Raquel Flores Rodríguez (Quintana Roo)
Dra. Sandra Graciela Rosales Uvera (CDMX)
Dr. Manuel Cabada Gamboa (Jalisco)
Dr. Luis Antonio Moreno Ruiz (CDMX)
Dra. Josefina Flores Miranda (Hidalgo)
Dr. César Téllez Calderón (Puebla)
Dr. Sergio Miguel Porras Catarino (Puebla)
Dr. José Rafael Cuauhtémoc Acoltzi Vidal (Colima)
Dra. Silvia Susana Gómez Delgadillo (Jalisco)
Dra. Anabell Pérez Ortiz (Tamaulipas)
Dra. Abishnaed Eileen Hernández Torres (Veracruz)
Dra. María de Lourdes Serna Herrera (Edo. Mex.)
Dr. César Augusto López Peláez (Oaxaca)
Dr. Carlos Alberto Romo Vicente (Jalisco)
Dr. Juan Antonio Huembes Camacho (Puebla)
Dra. Zabdy Elienai Frayre García (Chihuahua)
Dr. Gustavo Solache Ortiz (Querétaro)
Dra. Elizabeth González Alvarado (CDMX)
Dr. Carlos Alfredo Narváez Oriani (CDMX)
Dr. Luis Ángel Ruiz Chamorro (Quintana Roo)
Dra. Sandra Angélica Chi Pool (CDMX)
Dra. Tania Ramírez García (Querétaro)
Dra. Sandra Gabriela Tapia Luque (CDMX)
Dra. Lizbeth Delgadillo Medrano (Hidalgo)
Lic. Elisa Zárate Chavarría (CDMX)
Dra. Sonia Guillermina Jiménez González (Oaxaca)
Dra. Verónica Amalia Náñez Olivas (Sinaloa)
Dr. José Luis Leiva Pons (San Luis Potosí)
Dra. Eva María Picos Bovio (Nuevo León)
Dr. Ángel Cuauhtémoc Rivas Armenta (Sonora)
Dra. Talía Maritza Leal Alvarado (Puebla)
Dr. Juan Carlos Pino Padrón (Puebla)
Dra. Margarita López Hernández (Hidalgo)
Dra. Grecia Rosángela Pérez Siller (Jalisco)
Dr. Rodolfo Arturo Ruiz Nieves (Jalisco)
Dr. Jorge Flores Estrella (Colima)
Dra. Ana Cecilia Curiel Arias (Jalisco)
Lic. Alejandra Hernández Muñoz (CDMX)
Dra. Linda Gabriela Gutiérrez Delgado (Coahuila)
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Dra. Arlem Liliana Vázquez Cerda (Chiapas)
Dr. José Luis Lázaro Castillo (Edo. Mex.)
Dr. Luis Alberto Cervantes Chávez (Michoacán)

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Correspondence:
Alejandra Madrid-Miller
E-mail: ammiller@live.com.mx

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Clinical case

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Single ventricle in a 28-year-old adult, history and present of a non-surgical heart

Ventrículo único en adulto de 28 años de edad, historia y actualidad de un corazón no quirúrgico

Juan Antonio Herrera-Morales,* César Alejandro Becerra-Gutiérrez,‡ Kevin Eduardo Cazares-Hernández,§ Víctor Isidro Palomares-Alonso¶

Keywords: univentricular heart, pulmonary arterial hypertension, congenital heart disease, complex single ventricle.

Palabras clave: *ventrículo único, hipertensión arterial pulmonar, defectos cardiacos congénitos, ventrículo único complejo.*

ABSTRACT

Introduction: the single ventricle is a rare pathology within adult congenital heart disease. This is a group of severe abnormalities of the heart structure that follow developmental errors, resulting in a single ventricular chamber. In this population, pharmacological measures are ineffective in preventing progression to end-stage heart failure. However, surgical procedures help to extend survival and quality of life. **Objective:** to report the case of congenital heart disease with low prevalence. **Clinical case:** the case of a 28-year-old man with a history of cyanogenic congenital heart disease, univentricular heart type with undetermined morphology and double outflow tract is presented; the patient was diagnosed since his first year of life, which has only received medical management. **Conclusions:** unfortunately, being a rare congenital heart disease in adults, there are few references to medical management. If they are not submitted to surgical intervention at an early age, which offers a greater quality of life and survival, some patients die during infancy due to heart failure.

RESUMEN

Introducción: *el ventrículo único es una patología poco frecuente dentro de las cardiopatías congénitas en el adulto. Este es un grupo de anomalías graves de la estructura del corazón tras un mal desarrollo, que da como resultado una sola cámara ventricular. En esta población las medidas farmacológicas son poco eficaces para evitar la progresión de una falla cardiaca terminal; sin embargo, existen procedimientos quirúrgicos que ayudan a alargar la supervivencia y la calidad de vida.* ***Objetivo:*** *reportar el caso de una cardiopatía congénita en el adulto de baja prevalencia.* ***Caso clínico:*** *se presenta el caso de un hombre de 28 años con antecedente de cardiopatía congénita cianógena de tipo corazón univentricular de morfología indeterminada con doble vía de salida diagnosticada desde su primer año de vida, que ha llevado solamente manejo médico.* ***Conclusiones:*** *desafortunadamente, al ser una cardiopatía congénita poco frecuente en los adultos, existen pocas referencias sobre su manejo médico. Si no son sometidos a intervención quirúrgica en edades tempranas, lo que ofrece mayor calidad de vida y supervivencia, algunos pacientes fallecen durante la lactancia debido a insuficiencia cardiaca.*

* Medical Student. Nuevo Hospital Civil de Guadalajara «Juan I Menchaca».
‡ Medical Student, Centro Médico Nacional de Occidente, IMSS.
§ Medical Student, Hospital Regional de Autlán de Navarro.
¶ Clinical Cardiologist, Clínica Hospital No. 24 Ciudad Guzmán, ISSSTE.

Centro Universitario del Sur, Universidad de Guadalajara.

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INTRODUCTION

Univentricular physiology includes a series of cardiac malformations that result in systemic and pulmonary circulation depending on a single ventricular cavity (right, left or indeterminate ventricle), and there is usually a small accessory chamber that functions exclusively as a reservoir. According to the morphology of the systemic ventricle, ventricular failure will be earlier, as well as the presence of arrhythmias that can lead to deterioration of the functional class and death.[1]

Congenital heart defects are the most common congenital disorders, with an incidence of 1:100 in live newborns.[2] The univentricular heart is a pathology with very low prevalence within congenital heart defects, a group of anomalies in the heart's structure after a poor development that results in a

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single ventricular chamber. There are different types of morphologies depending on the dominant ventricle: right ventricle (50-57%), left ventricle (42-43%) or indeterminate type (0-2%).[1,3] This anatomical change also has functional changes, including volume overload in the ventricle, a decrease in systemic oxygen saturation, and even non-restrictive systemic pressure flow increases the pressures of the pulmonary vasculature.[4] The management of these patients is surgical at an early age, generally with the Fontan procedure, improving the survival of these patients. However, there is very little information about its medical management in adults.[2]

CASE PRESENTATION

Important background

28-year-old man, known since his first year of life with cyanogenic congenital heart disease of the univentricular heart type with undetermined morphology with a double outflow tract, not having pulmonary restriction and developed pulmonary arterial hypertension, with a PAP of 41 mmHg and a PAWP of 35 mmHg, without previous measurements at the time of diagnosis. Therefore, it was not considered a candidate for corrective or palliative surgery and was maintained with medical treatment. Since he was 12 years old, he developed polyglobulia and has been monitored with a frequent saline exchange. So far, the patient has not presented complications that threaten the patient's life.

Clinical presentation

The patient went to the cardiology department for a follow-up of single ventricular congenital heart disease. He referred to dyspnea (NYHA grade II/CG-WHO II) and intermittent headache. On admission, vital signs with a heart rate of 82 beats per minute, respiratory rate of 18 breaths per minute, blood pressure of 90/60 mmHg, temperature of 36.5 ºC and oxygen saturation of 90% on room air.

Physical examination reveals a conscious and oriented patient with conjunctival hyperemia, jugular plethora (grade I), sustained apical impulse, displaced to the sixth intercostal space in the left anterior axillary line, pansystolic and diastolic murmur predominantly in the pulmonary area (Harvey-Levine classification IV/VI), S2 unfolded and reinforced in P2, in plateau configuration, irradiated to the left mid-axillary line, with tactile fremitus, in the thoracic and pelvic limbs with the presence of clubbing *(Figure 1)*.

Clinical studies and imaging test

The electrocardiogram showed sinus rhythm, with a heart rate of 82 beats per minute and a deviated QRS axis to the right, with a wide and notched P wave in DI and the second negative P wave component in V1 suggesting left atrial growth. In DII, the P wave is acuminate, which suggests right atrial growth. Large voltages are also observed in the QRS complex, which can be measured in V2 with an R wave of 9 mV and an S wave of 43 mV, suggesting both ventricular hypertrophy, and systolic and diastolic overload. Analyzing the same QRS complex, the Katz-Wachtel sign is

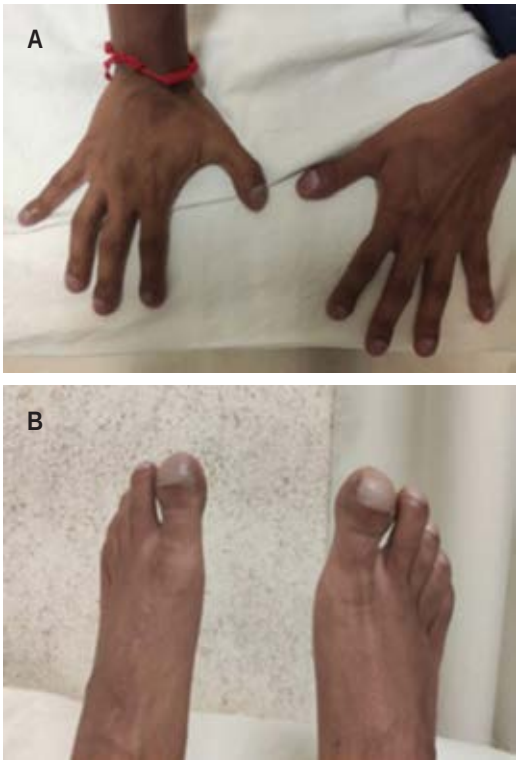

Figure 1: A) Thoracic. **B)** Pelvic limbs with acropachy.

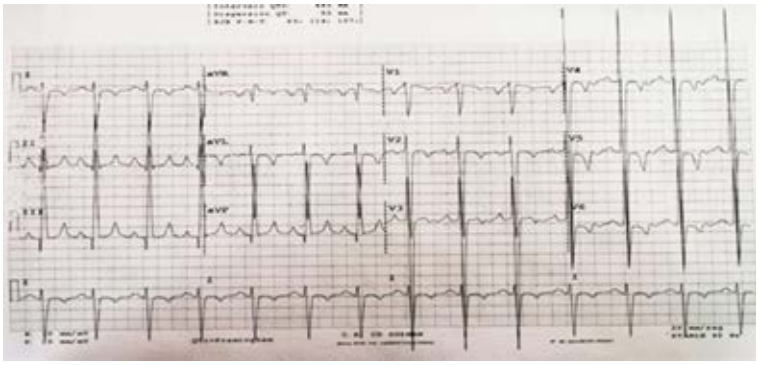

Figure 2: 12-lead electrocardiogram suggesting atrial chamber enlargement, ventricular enlargement and overload.

observed, characterized by voltages ≥ 50 mm in the intermediate precordial leads, generally observed when there is a ventricular septal defect *(Figure 2)*.

The transthoracic echocardiogram shows a single ventricle *(Figure 3)* that reveals a maximum ventricle dimension of 11 cm in diastole, a ventricular wall thickness of 2.02 cm, without abnormalities in its segmental mobility, with an absence of interventricular septum. Both atria were 5.7 cm, with moderate mitral and tricuspid valve regurgitation corroborated with the doppler effect. Dilatation of the root of the pulmonary artery of 4.49 cm, with pulmonary valve regurgitation, also corroborated with the Doppler effect. The chest X-ray shows grade III cardiomegaly, with a cardiothoracic index of 0.63 at the expense of the left profile, and with data that suggests PAH, such as a notably dilated arch of the pulmonary artery *(Figure 4)*. Prior to this, right heart catheterization was performed at 17-years-old, where a PAP of 41 mmHg and a PAWP of 35 mmHg were found.

Treatment

The patient is currently receiving pharmacological therapy with captopril 12.5 mg every 12 hours, digoxin 0.25 mg every 24 hours, sildenafil 20 mg every 8 hours and spironolactone 25 mg every 24 hours as a diuretic. He is also given supplemental oxygen with nasal prongs at 3 L/min as ambulatory management. In addition to this, he is given saline pheresis every 3 or 4 months. This procedure was done by placing the patient in a semi-fowler position, canalizing with a 0.9% saline solution with 500 cm^3 for 4 hours and nasal prongs placed with oxygen at 3 L/min. Subsequently, approximately 700 mL

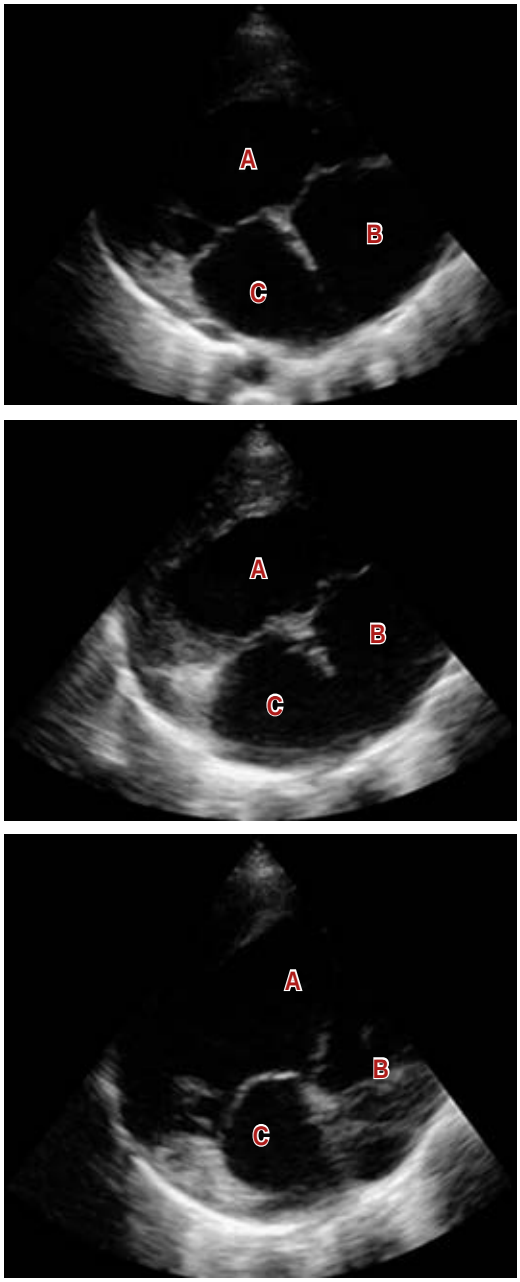

Figure 3: Transthoracic echocardiography with large single ventricle and myocardial hypertrophy evidence. **A)** Shows the single ventricle and its large dimensions; **B)** and **C)** show the right and left atrial, respectively, also with large dimensions.

Figure 4: Posteroanterior chest X-ray with grade III cardiomegaly.

of blood was drawn, the patient was observed, and vital signs were monitored every hour until discharge.

DISCUSSION

The single ventricle is a complex congenital cardiac pathology of low incidence, found in approximately 1.5% of individuals with congenital heart disease.[5] In a cohort study conducted in Wales and England between 2000 and 2018, among 53,615 patients born who went under intervention for complex congenital heart disease, only 3% had univentricular heart disease.[6] This can have univentricular variations and typical characteristics, among which are: hypoplastic left heart syndrome, tricuspid atresia, Ebtein's anomaly, double outlet right or left ventricle, or an atrioventricular canal defect.[7] Right ventricular hypoplasia is the most common form of the single ventricle, seen in 2:10,000 births, with a higher incidence in men.[8] When there is no early surgical intervention in the first three years of age, survival at 14 years is 50% in carriers of single ventricle left ventricle carriers and at four years in 50% of patients with ventricular indeterminate.[2,9]

Depending on the physiology of the single ventricle, a series of palliative surgical procedures is required. The first stage is the Norwood procedure performed in the first week of life, which consists of reconstructing the aortic arch at the right ventricle outlet, creating a stable and restrictive pathway for blood flow either from the systemic artery or from the functional ventricle. The second stage is the Glenn procedure between three and five months of age, which consists of removing the aortic shunt and performing an anastomosis of the superior vena cava to the pulmonary artery. The third and final stage is the Fontan procedure, which consists of anastomosis of the inferior vena cava to the pulmonary artery and a fenestration between the right atrium and the inferior vena cava, to reduce the load on the single ventricle.[1] This procedure has an operative mortality of less than 5%, and the 30-year survival rate is 85%.[2,9] Over time, the Fontan circulation impacts other systems by increasing systemic venous pressure, mainly resulting in hepatic congestion. However, the main causes of mortality change by not having a surgical process in patients with a single ventricle, the main ones being heart failure at an early age or arrhythmias.

The clinical presentation of a single ventricle will depend on its morphology since there may be a decrease in pulmonary outflow (Qp), differences in pulmonary vascular resistance (Rp), aortic obstruction, different functionality in the valves atrioventricular and right, left or indeterminate ventricular morphology. Pulmonary obstruction and Rp will determine Qp, which will impact the presentation of heart failure, complications and the patient's prognosis.[10] For example, patients with severe pulmonary obstruction will reduce Qp, leading to severe heart failure; in patients with moderate pulmonary obstruction, the Qp is near normal, and therefore heart failure may be mild. On the other hand, in patients without pulmonary obstruction, the Qp will depend on the Rp; if the Rp is low, the heart failure will be severe, but if the Rp is high (for example, in the Eisenmenger effect), as is the case with our patient, the heart failure will not be as severe, and survival will be greater.[11,12]

The aforementioned drugs have a specific reason for which they are administered, as the increase in diuresis, the improvement of

cardiac output and the decrease in pulmonary pressures have contributed to lengthening the time of cardiac remodelling.

Currently, the patient is a professional. He goes every two months for a physical examination and laboratory tests, including hematology, renal and liver function. However, the patient has decided not to go to cardiac rehabilitation.

CONCLUSIONS

Unfortunately, being a rare congenital heart disease in adults, there are few references about medical management in this age group. It is necessary to develop and broadcast strategies for an early diagnosis, as a principal objective to identify pediatric patients with cardiovascular diseases, who's, upon suspicion of a cardiovascular problem are references in time for a follow and treatment which improves the expectation and quality of life. If they are not managed during childhood, it is necessary to refer these types of patients for specialized follow-up of their underlying pathology, and the work of a multidisciplinary team to prevent aggravation or damage to other systems.

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Correspondence:
Víctor Isidro Palomares-Alonso
E-mail: victorisidropalomaresalonso@outlook.com

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Trap-door thoracotomy as an ideal access route for internal cardiac massage and repair of subclavian vessels

Toracotomía Trap-door *como vía de acceso ideal para masaje cardiaco interno y reparación de vasos subclavios*

Osvaldo Valdés-Dupeyrón,*,‡ Gino K Alvia-del Castillo,‡ Lidia Espinales-Casanova,‡ Javier Gonzáles-Robles,§ Lisette Rodríguez-Marcos,¶ Natacha Lois-Mendoza§

Keywords:
subclavian artery lesions, Trap-door thoracotomy, subclavian artery revascularization, internal cardiac massage.

Palabras clave:
lesiones de arteria subclavia, toracotomía Trap-door, *revascularización de arteria subclavia, masaje cardiaco interno.*

ABSTRACT

Introduction: subclavian vessel injuries remain rare and highly lethal. Patients with these types of injuries can present with neck and upper chest hematoma, hemorrhage, and signs of upper limb ischemia. Trap-door thoracotomy allows wide exposure of the thoracic cavity and base of the neck, providing rapid access to the heart, subclavian vessels, pulmonary ileus, and other anterior mediastinal structures. **Objective:** to describe the trap-door thoracotomy as the ideal approach for internal cardiac massage and subclavian vascular repair in hemodynamically unstable patients. **Cases presentation:** two patients with severe subclavian artery injuries are presented. They underwent emergency surgery using a trap-door thoracotomy, where bypass was performed from the ascending aorta to the left axillary artery with a polytetrafluoroethylene prosthesis in the first case and bypass from the left carotid artery to the left subclavian artery with an inverted saphenous vein in the second patient. **Conclusion:** the trap-door thoracotomy allows optimal access to the subclavian vessels and the heart if cardiopulmonary resuscitation is needed in critically ill patients.

RESUMEN

Introducción: *el traumatismo de vasos subclavios no es frecuente. Pueden presentarse en forma de hemorragia, hematoma en cuello y tórax superior, signos de hipoperfusión distal y choque. La toracotomía* Trap-door *permite una exposición amplia de la cavidad torácica y base del cuello que proporciona un acceso rápido a corazón, vasos subclavios, íleo pulmonar y demás estructura del mediastino anterior.* ***Objetivo:*** *describir la toracotomía de* Trap-door *como vía de acceso ideal para masaje cardiaco interno y reparación de vasos subclavios en pacientes graves.* ***Presentación de casos:*** *se presentan dos pacientes con lesiones severas de arterias subclavias que fueron intervenidos de forma emergente mediante toracotomía* Trap-door, *donde se realizó derivación de aorta ascendente a arteria axilar izquierdas con prótesis de politetrafluoroetileno en el primer caso y derivación de arteria carótida izquierda a arteria subclavia izquierdas con vena safena invertida en el segundo paciente.* ***Conclusión:*** *la toracotomía* Trap-door *permite el acceso óptimo de vasos subclavios y corazón en caso de necesitar realizar reanimación cardiopulmonar en pacientes graves.*

* ORCID: 0000-0003-3419-2381
‡ Hospital Regional «Dr. Verdi Cevallos Balda» Manabí, Ecuador.
§ Department of Health Specialties of the Technical University of Manabí, Ecuador.
¶ Department of Internal Medicine, Hospital de Especialidades de Portoviejo, Manabí, Ecuador.

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INTRODUCTION

Subclavian vein (SV) and subclavian artery (SA) injuries are relatively uncommon because they are vessels of short extension protected by osteoarticular structures of the thoracic cavity. These injuries represent 1 to 9% of all vascular trauma cases, with 90% being caused by a penetrating mechanism secondary to stab and firearm injuries, and only 5% originate from the blunt trauma mechanism.[1-3]

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A subclavian vascular injury is suspected when trauma to the upper third of the chest wall located in the clavicle or supraclavicular fossa is associated with a decreased or absent pulse in the upper limb of the same name, hemorrhage, local hematoma, shock, and first rib fracture.[1] Concomitant involvement of the subclavian vein and subclavian artery occurs in 20% of cases, with brachial plexus injury occurring in a third of these traumas, increasing mortality from 10 to 35%.[4]

The unilateral anterior cervico-sterno-thoracotomy or «Trap-door» incision was first described in 1979 by Masaoka et al. It is performed in a supine position with the neck extended; it includes a high median sternotomy (MS) that communicates with an anterior incision at the level of the fourth intercostal space and another transverse incision at the base of the neck, dividing the infrahyoid muscles. The anterior flap is retracted as an open book to expose structures such as the pulmonary apex and hilum, subclavian vessels and brachial plexus.[5] It also offers access to other structures, such as the supra-aortic arteries, for proximal vascular control and heart if a more effective cardiopulmonary resuscitation is required to perform direct cardiac massage in patients with hemodynamic instability.

CASES PRESENTATION

Case 1

A 19-year-old male was brought by relatives with a penetrating injury caused by a gunshot to the left shoulder. On physical examination, the patient was hypotensive (85/55 mmHg), with a giant hematoma in the shoulder and left hemithorax. The neurological examination revealed spastic paraplegia of the lower limbs, absence of left axillary, brachial, and radial pulses, homonymous hand coldness and cyanosis.

Chest X-ray revealed a bullet in the upper left hemithorax at the level of the fourth cervical vertebrae. Four units of red blood cells and two plasma were requested, and two grams of intravenous (IV) cefazolin were given. Emergency surgery is then indicated.

The patient suffered cardiac arrest during anesthetic induction. The left anterior thoracotomy was done through the fourth intercostal space. The ventricles appeared to be fluctuating on palpation when the pericardium was opened *(Figure 1A)*, and the cardiac monitor demonstrated fine ventricular fibrillation. Manual cardiac massage and external electrical defibrillation with 250 Joules were performed until hemodynamic stabilization was achieved.

A large hematoma displacing the left lung is found, and the trap-door incision is completed with dislocation of the left sternoclavicular joint *(Figure 1B)*, exposing the subclavian vessels and anterior mediastinum. After hematoma evacuation, a neurovascular injury with loss of the subclavian segments of the SV, SA, and brachial plexus was found. In addition, an aortic hematoma was found at the origin of the subclavian artery, making it impossible to perform the anastomosis to the descending aorta or left carotid (LC) artery.

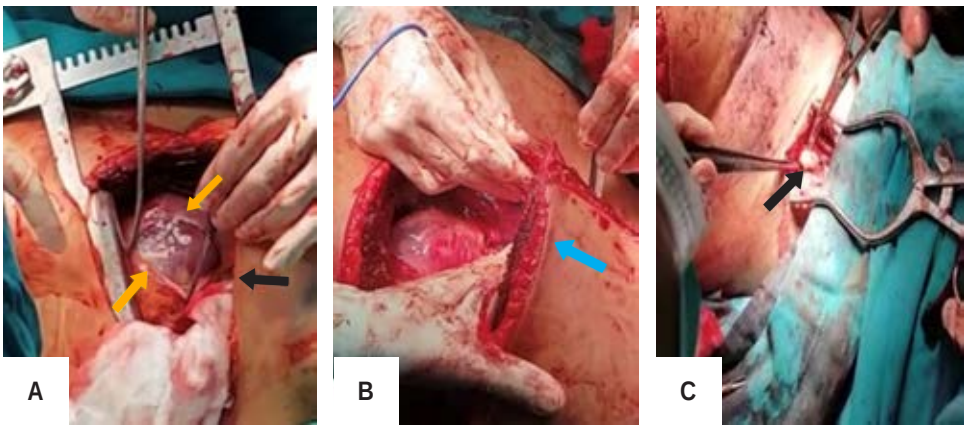

Figure 1:

Surgical procedure of case 1. **A)** Opening of pericardium and exposure of the heart (yellow arrows), heart in ventricular fibrilation (black arrow). **B)** Trap-door thoracotomy showing wide exposure of the mediastinum (blue arrow). **C)** Left axillary artery dissection (black arrow).

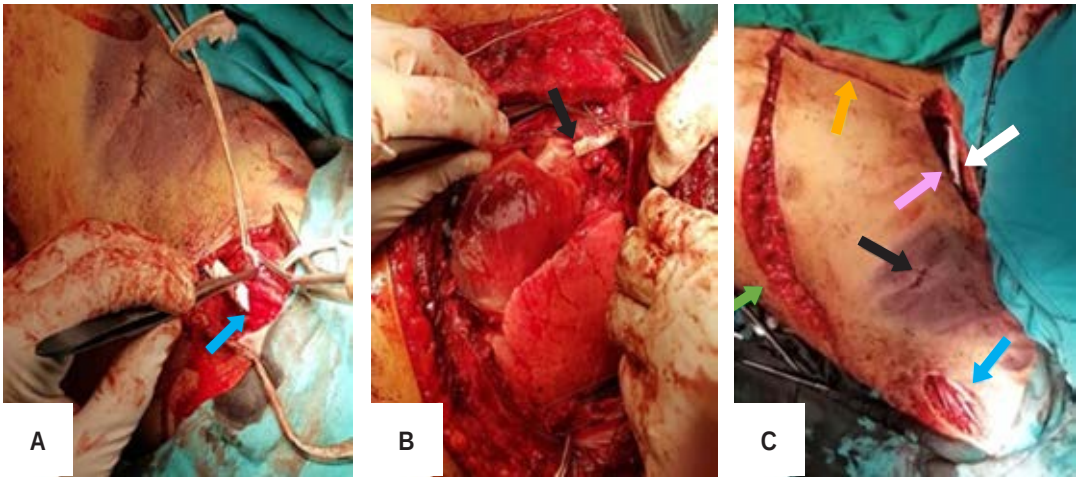

Figure 2: Surgical procedure of case 1. **A)** Preparation for suturing the polytetrafluoroethylene prosthesis with the left axillary artery (blue arrow). **B)** Suture of polytetrafluoroethylene prosthesis and ascending aorta (black arrow). **C)** Trap-door thoracotomy with sternotomy closure (yellow arrow), anterolateral thoracotomy closure (green arrow), cervicotomy closure (pink arrow), extrathoracic course of the polytetrafluoroethylene prosthesis (white arrow) suture between the prosthesis and axillary artery (blue arrow), bullet entry hole (black arrow).

The bleeding source was controlled with ligation of subclavian vessels and dissection of the left axillary artery *(Figure 1C)*. Partial clamping and bypass of the ascending aorta to the left axillary artery with a polytetrafluoroethylene (PTFE) prosthesis were performed *(Figure 2A)*, *(Figure 2B)* and arterial flow restoration of the left upper limb was achieved. Hemostasis was checked, and the chest wall was closed, showing how the trap-door thoracotomy was left. The thorax outlet of the PTFE prosthesis is also observed *(Figure 2C)*. Five minutes after the closure of the thoracic cavity, the patient presented ventricular fibrillation that resolved with defibrillation with 300 Joules.

The patient was transferred to the recovery room with inotropic support with a mean arterial pressure above 60 mmHg. Twelve hours after the surgical procedure, about 500 mL of blood was drained from the chest tube. Prolonged prothrombin time (PT) and activated partial thromboplastin time (aPTT) were found in coagulation tests. There was no evidence of residual hemothorax on chest X-ray images. Transfusion of two red blood cells and two plasma units were requested, and 500 mg of IV tranexamic acid every eight hours was indicated. There was a hemodynamic improvement within 48 hours postoperatively, but extreme bradycardia persisted, and the possibility of referring the patient to a tertiary center for pacemaker placement was assessed. Epinephrine and atropine were added, but the heart rate did not improve. The patient died 72 hours after the surgical procedure.

Case 2

An 18-year-old male was brought to the emergency department with blunt chest trauma and a left humerus fracture due to a motorcycle accident. On physical examination, the patient was hypotensive (90/57 mmHg), with a giant hematoma in the shoulder and left hemithorax. Left upper limb deformity due to humerus fracture was observed. There were signs of limb ischemia with absence of axillary and radial pulses.

Chest X-ray revealed a left humerus fracture, and a chest tomography showed a giant hematoma in the upper left hemithorax. Three red blood cells and two plasma units were requested, and two grams of IV cefazolin were given.

Emergency surgery was decided due to the patient's hemodynamic instability. General endotracheal anesthesia was indicated, and inotropic support with norepinephrine was started due to severe hypotension. Left anterior

thoracotomy was done through the fourth intercostal space, where the patient presented bradycardia and asystole, for which it was necessary to perform cardiac massage. After hemodynamic stabilization, a giant hematoma displacing the left lung is found. Vascular control of the mammary artery was performed, and the trap-door thoracotomy was completed with the dislocation of the left external clavicular joint to expose the subclavian vessels and the anterior mediastinum *(Figure 3A)*.

A five centimeter SA laceration with lesions of the SV and brachial plexus were found.

Ligation of various bleeding sources and hematoma drainage was done. The intrathoracic LC artery was dissected, and a vascular bypass was performed from this artery to the distal end of the SA with the left greater saphenous vein *(Figure 3B)*. A spontaneous arterial pulse and an arterial saturation greater than 95% of the upper left limb were observed. The SV was repaired with a 6/0 polypropylene suture.

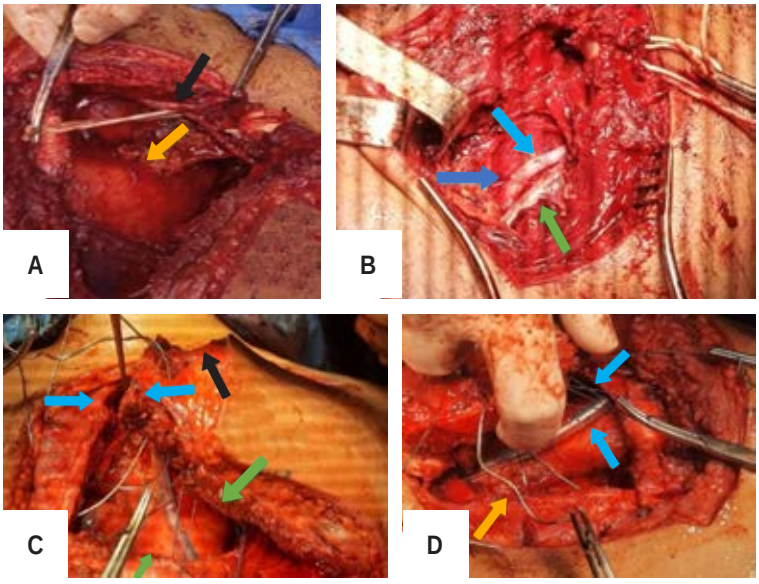

Figure 3: Surgical procedure of case 2. **A)** Trap-door thoracotomy with control of the mammary artery (black arrow) and exposure of the heart and pericardium (yellow arrow). **B)** Anastomosis of the saphenous vein with the left subclavian artery, saphenous vein (light blue arrow), subclavian artery (blue arrow), subclavian vein (green arrow). **C)** Closing trap-door thoracotomy: sternotomy closure (blue arrows), anterolateral thoracotomy closure (green arrows), cervicotomy closure (black arrow). **D)** Thoracic cavity closure: sternum wires (yellow arrow), anterolateral thoracotomy closure with pericostal stitches (blue arrow), chest tube (light blue arrow).

Hemostasis was checked, and a chest tube was placed in the extrapleural space. The thoracotomy was closed with wires in the sternum and pericostal sutures on the thoracotomy *(Figure 3C and D)*. A fasciotomy was performed due to humerus fracture in the proximal third of the arm.

The patient was transferred to the recovery room with inotropic support of norepinephrine 8 mL/h, 1 gram of ceftriaxone IV every 8 hours and 500 mg of amikacin IV every 12 hours. The chest tube output was low. However, the X-ray showed moderate effusion, so repositioning a new chest tube in the intrapleural space was required *(Figure 4A)*, which drained 700 mL of hematic fluid. The extrapleural chest tube was removed 28 hours later *(Figure 4B)*.

Endotracheal extubation and intrapleural chest tube removal were performed within 72 hours postoperatively. The patient remained in the intensive care unit for 5 days and was then transferred to the ward, where was assessed by the neurosurgery and traumatology team for brachial plexus injury and humerus fracture, respectively. The patient was discharged from the hospital 15 days later. Since then, the patient has been in constant evaluation for 2 years, with a chest CT angiography that demonstrated graft patency *(Figure 4C and D)*, although the brachial plexus injury has caused immobility and atrophy of the left shoulder and upper limb.

DISCUSSION

The prognosis of trauma to the subclavian vessels depends on variables such as type of injury, affected vessel, degree of hemorrhage, and the time between injury and specific treatment. Demetriades et al. reported that 44% of his patients had isolated SV lesions, 39% had SA lesions, and 17% had combined artery and vein injuries.[6] Similar results were obtained by Lin et al, where the concomitant arterial and venous injuries were identified in 24 of the 54 patients of their study.[4] In the present study, the severity of the clinical picture indicated emergency surgical treatment in both patients.

Mortality from isolated SV lesions can be up to 80%, significantly higher than in the presence of arterial or combined subclavian injury.[6] Another study reported death in half of the

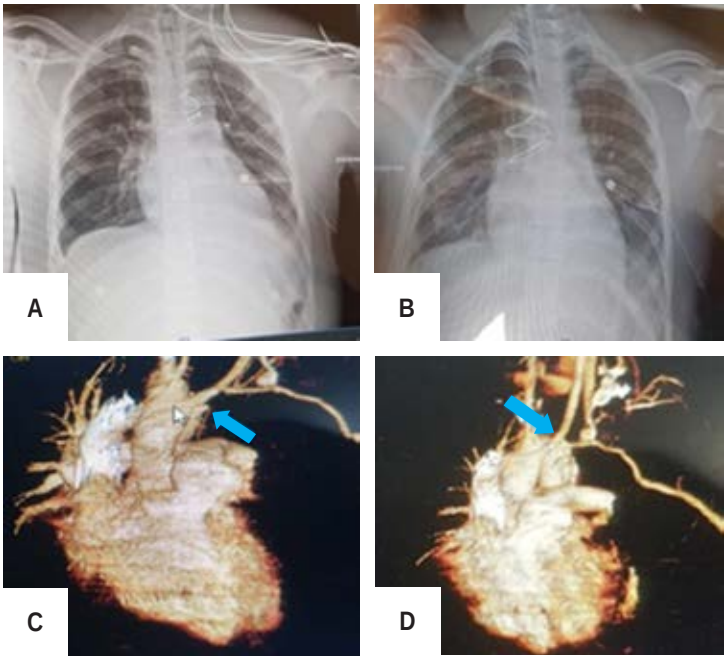

Figure 4:

Post-surgical follow-up of case 2. **A)** Chest X-ray with left intrapleural and extrapleural tubes. **B)** Left intrapleural tube. **C)** CT angiography of the chest, proximal end of the subclavian artery (blue arrow). **D)** Anastomosis between the carotid artery and saphenous vein (blue arrow).

patients with isolated SV lesions.[3] This could be associated with embolus or continuous venous bleeding. Some authors state that subclavian vessel injuries can sometimes be suspected clinically. Physical examination findings in SA lesions include the absence of pulses in upper extremities, brachial plexus palsy, audible murmur, supraclavicular hematoma, first rib fracture, and active bleeding.[7,8]

Primary identification of subclavian vascular injuries is often made intraoperatively due to the patient's hemodynamic instability, which precludes the possibility of obtaining imaging studies to corroborate the diagnosis. The patients in our report presented with giant hematomas of the upper left hemithorax, with a humerus fracture and a gunshot wound to the cervical spine, respectively. Computed tomography angiography provides the best diagnostic information to identify subclavian vascular injuries.[9]

The choice of surgical approach and incision type is one of the essential points to maintaining the patient's hemostasis; this depends on the injured side and the location of arterial and venous interruption. For some authors, the standard approach for left-sided trauma is anterolateral thoracotomy with a posterior supraclavicular or infraclavicular incision, while right-sided injuries are generally treated with an MS with supraclavicular extension.[10] MS has also been successfully used to expose the left subclavian artery, which provides a wide operative field, and allows rapid vascular control.[9] In our cases, the classic «Trap-door» thoracotomy surgical technique was used, which has been associated with a higher incidence of severe postoperative bleeding and respiratory complications.[3,11]

The unilateral anterior cervical-sterno-thoracotomy incision or «Trap-door» incision was first described as a route of exposure for Pancoast tumors of the superior sulcus.[5] Since then, it has been used by thoracic surgeons as an approach to lung and upper mediastinum tumors. It also allows a better view of large vessels of the mediastinum and neck.[12] In our patients, this approach was considered an ideal technique, with the minor modification of performing sternoclavicular dislocation due to its rapid access to the subclavian vessels. It was also possible to expose the heart to perform internal cardiac massage and, at the same time, perform proximal vascular control to avoid profuse bleeding.

The lack of exposure of the medial and distal subclavian vessels is a disadvantage of

this approach. Supraclavicular or infraclavicular incisions expose the subclavian vessels but require the surgeon to perform external cardiac massage with the impossibility of proximal vascular control if profuse bleeding is presented. The trap-door technique should be considered an ideal approach to perform an effective cardiac massage to achieve cardiopulmonary resuscitation and control of SA lesions.

The endovascular approach as a treatment option for penetrating and blunt injuries of the subclavian vessels is relatively new. It includes polytetrafluoroethylene (PTFE)-coated endoprostheses with an expandable or self-expandable balloon.[13,14] This approach has been commonly used for pseudoaneurysms and left SA lesions due to its thoracic location compared to the right SA, which is extrathoracic.[2]

Most subclavian vascular injuries require significant open intervention for proper management.[15] Posner concluded that open anatomic repair is the most desirable option to prevent subclavian steal syndrome, claudication, or ischemia leading to limb amputation.[16]

Long-term morbidity is closely related to the presence of associated brachial plexus injuries.[17] In the study conducted by Graham, brachial plexus injuries were observed in 34% of the patients.[18] Unfortunately, cases of complete brachial plexus transection and secondary nerve repair may only return minimal functional improvement and leave the patient with permanent functional disability. In our study, brachial plexus injury was present in both patients.

CONCLUSION

The trap-door thoracotomy allows optimal access to structures like the mediastinum, hilum and lung parenchyma. Its wide exposure provides proximal and distal vascular control of the great vessels, an essential requirement to achieve adequate repair of such structures. Its cervical extension offers exposure of the proximal and medial course of the subclavian vessels below the clavicle. It also helps to expose the heart and pericardium to perform an effective internal cardiac massage in critically ill patients.

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Correspondence:
Osvaldo Valdés-Dupeyrón
E-mail: osvaldovaldesdupeyron@gmail.com

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Left atrial myxoma: the importance of cardiovascular imaging in the long-term follow-up of breast cancer survivors

Mixoma auricular izquierdo: importancia de la imagen cardiovascular en el seguimiento a largo plazo de las sobrevivientes de cáncer de mama

José Martín Alanís-Naranjo,* Cielmar Galeana-Abarca,‡ Marco Antonio Rentería-Galicia,§ Esbeidira Aranet Arroyo-Martínez,¶ María Azalea Loredo-Alanís,‖ Thelma Rodríguez-López**

Keywords:
atrial myxoma, breast cancer, cardiovascular imaging, second primary tumor, oncologic follow-up, cardio-oncology.

Palabras clave:
mixoma auricular, cáncer de mama, imagen cardiovascular, segundo tumor primario, seguimiento oncológico, cardio-oncología.

ABSTRACT

The incidence of cancer patients with cardiac diseases requiring surgery is rising as the population ages, and early detection of cancer and the use of new therapies are increasing survival rates. Cardiac tumors, despite their rarity, are an integral part of the cardio-oncology practice and require diagnosis and treatment. In recent years, the incidence of cardiac tumors has risen due to advancements in multimodality imaging, which have become more accessible and widespread. The association between treated breast cancer and myxoma could be considered a mere coincidence, but a few documented cases exist. We report the case of a patient with a history of breast cancer who presented, upon follow-up, a left atrial cardiac mass on cardiovascular imaging and underwent immediate surgery. This case illustrates the importance of Cardio-Oncology Clinics during the follow-up of breast cancer survivors.

RESUMEN

La incidencia de pacientes con cáncer y enfermedades cardiacas que requieren cirugía aumenta a medida que la población envejece. La detección temprana del cáncer y el uso de nuevas terapias aumentan las tasas de supervivencia. Los tumores cardiacos, a pesar de su rareza, son una parte integral de la cardio-oncología, requiriendo diagnóstico y tratamiento. En los últimos años, la incidencia de tumores cardiacos ha aumentado debido a los avances en los estudios de imagen, que se han vuelto más accesibles. La asociación entre el cáncer de mama y el mixoma podría considerarse una mera coincidencia, pero hay pocos casos documentados. Presentamos el caso de una paciente con antecedente de cáncer de mama que, durante el seguimiento, presentó una masa cardiaca en la aurícula izquierda en estudios de imagen cardiovascular y, de inmediato, fue intervenida quirúrgicamente. Este caso ilustra la importancia de las Clínicas de Cardio-Oncología durante el seguimiento de las sobrevivientes de cáncer de mama.

* Internist, Cardiology Resident.
‡ Cardiologist, Cardiovascular Imaging Specialist.
§ Cardiovascular Surgeon.
¶ Cardiologist, Echocardiographist.
‖ Pathologist.
** Cardiologist.

Hospital Regional 1° de Octubre ISSSTE. Mexico City, Mexico.

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INTRODUCTION

Cancer patients with a cardiac disease requiring surgery are becoming more common as the population ages, and early cancer diagnosis and new therapies are increasing survival rates.[1] Despite the rarity of cardiac tumors, they are an integral part of the cardio-oncology practice and require diagnosis and treatment. According to their site of origin, neoplastic tumors can be primary or secondary (metastatic).[2,3] Most primary cardiac tumors are benign (up to 90%).[4] These tumors have increased in incidence in the last ten years due to advances in multimodality imaging, which has become more accessible and widespread.[3,4] The most common benign heart tumor is cardiac myxoma, a mobile, intracavitary, round, or oval-shaped tumor. When it is present in the left atrium, it is frequently attached to the fossa

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ovalis by a stalk. The patient may be symptomatic (with obstructive, embolic, or constitutional symptoms) or asymptomatic, and the tumor may be found incidentally during routine cardiac imaging.[2,5] The association between treated breast cancer and cardiac myxoma could be considered a mere coincidence, but a few documented cases exist.[1]

We report the case of a patient with a history of breast cancer who presented, upon follow-up, a left atrial cardiac mass on cardiovascular imaging and underwent immediate surgery.

CASE PRESENTATION

A 59-year-old Mexican woman presented at the Cardio-Oncology (C-O) clinic was referred by her oncologist due to the finding of an intracardiac mass in her routine transthoracic echocardiogram (TTE). In 2013 she was diagnosed with invasive ductal breast carcinoma (Node + ER-/PR-/ERBB+). She received four cycles of neoadjuvant chemotherapy (TAC: docetaxel, doxorubicin, and cyclophosphamide). Then she continued with trastuzumab. The patient also underwent right breast mastectomy, axillary lymph node resection and radiation therapy (total dose of 50 Gy). Because of the potentially cardiotoxic therapy received, periodic echocardiograms were performed. Since then, the patient has been asymptomatic and cancer-free, according to a recent oncological examination.

Eight years after the breast cancer diagnosis, a transthoracic echocardiogram revealed a heterogeneous, pedicled, mobile mass attached to the interatrial septum without obstruction to the flow across the mitral orifice, suggesting a left atrial myxoma. Because of these findings, the oncologist referred her to the C-O clinic.

In addition, her past medical history revealed metabolic syndrome and non-alcoholic fatty liver disease. Her family history was negative for cardiovascular disease and cancer. Physical examination revealed stable vital signs, no murmurs, clear lungs, and a previous mastectomy scar. Routine laboratory parameters were within normal limits. The electrocardiogram *(Figure 1)* and chest radiograph were unremarkable.

Transesophageal echocardiography revealed a 26 × 16 × 14 mm heterogeneous, lobulated, mobile mass in the left atrium, attached to the interatrial septum, and without obstruction to the flow across the mitral orifice *(Figure 2)*.

Furthermore, a cardiac tomography showed a mass suggesting myxoma adjacent to the interatrial septum *(Figure 3)*. There were no significant lesions in the coronary arteries, and the calcium score was 0 Agatston units.

Two months later, the patient underwent cardiac surgery, which revealed an atrial multilobular mass with hemorrhagic areas *(Figure 4)*. A histopathological examination confirmed the diagnosis of cardiac myxoma *(Figure 5)*. The patient remained symptom-free after the surgery and during follow-up.

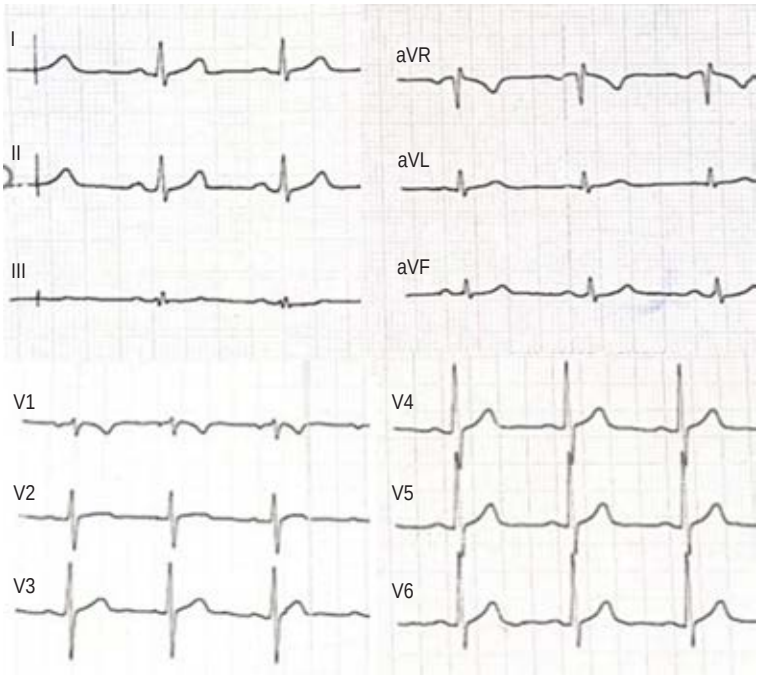

Figure 1: 12-lead electrocardiogram.

DISCUSSION

Oncologists and hematologists refer cancer patients to the C-O clinic to assess chemotherapy or radiotherapy's potential deleterious cardiovascular effects. Echocardiography is the most commonly used imaging technique for assessing these effects and detecting lesions within the heart.[6]

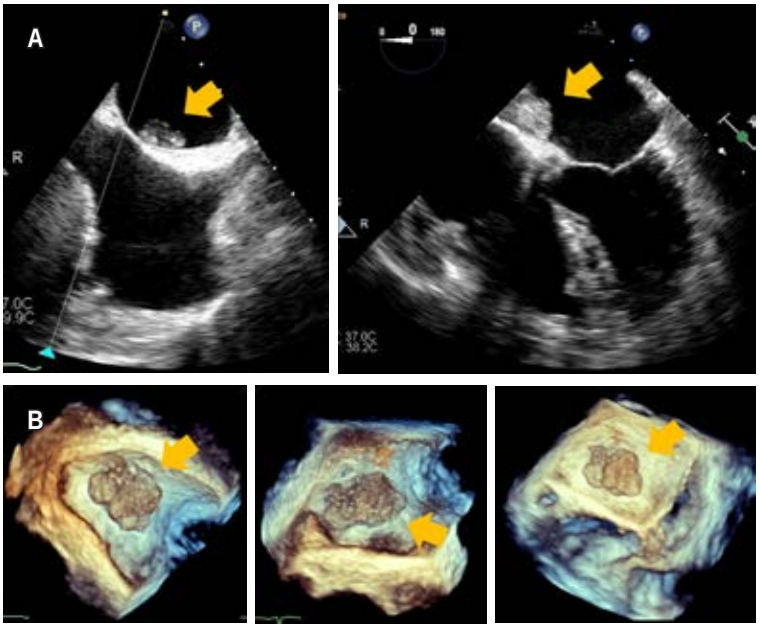

Figure 2: Transesophageal echocardiography. **A)** Heterogeneous, lobulated mass in the left atrium attached to the interatrial septum. **B)** Real-time 3-dimensional echocardiography (RT3DE) image.

A high risk of long-term cardiovascular toxicity is associated with specific cancer treatments, including anthracycline chemotherapy and radiotherapy. These effects may occur 5-10 years after the initial treatment, resulting in up to six times more common coronary artery disease and heart failure than in the general population. The long-term effect of trastuzumab is unknown beyond ten years. A cancer survivor with a very high risk of future cardiovascular disease fulfills the following characteristics: 1) Very high baseline cardiovascular toxicity risk pre-treatment, 2) Doxorubicin ≥ 400 mg/m^2, 3) Radiotherapy > 25 Gy, 4) RT > 15-25 Gy + Doxorubicin ≥ 100 mg/m^2. Therefore, TTE should be considered at years 1, 3, and 5 after completion of cardiotoxic cancer therapy and every five years after that in asymptomatic, very high-risk adult cancer survivors.[7]

The literature on cardiac surgery in patients previously treated for breast cancer remains limited.[1] A cardiac tumor diagnosed after breast

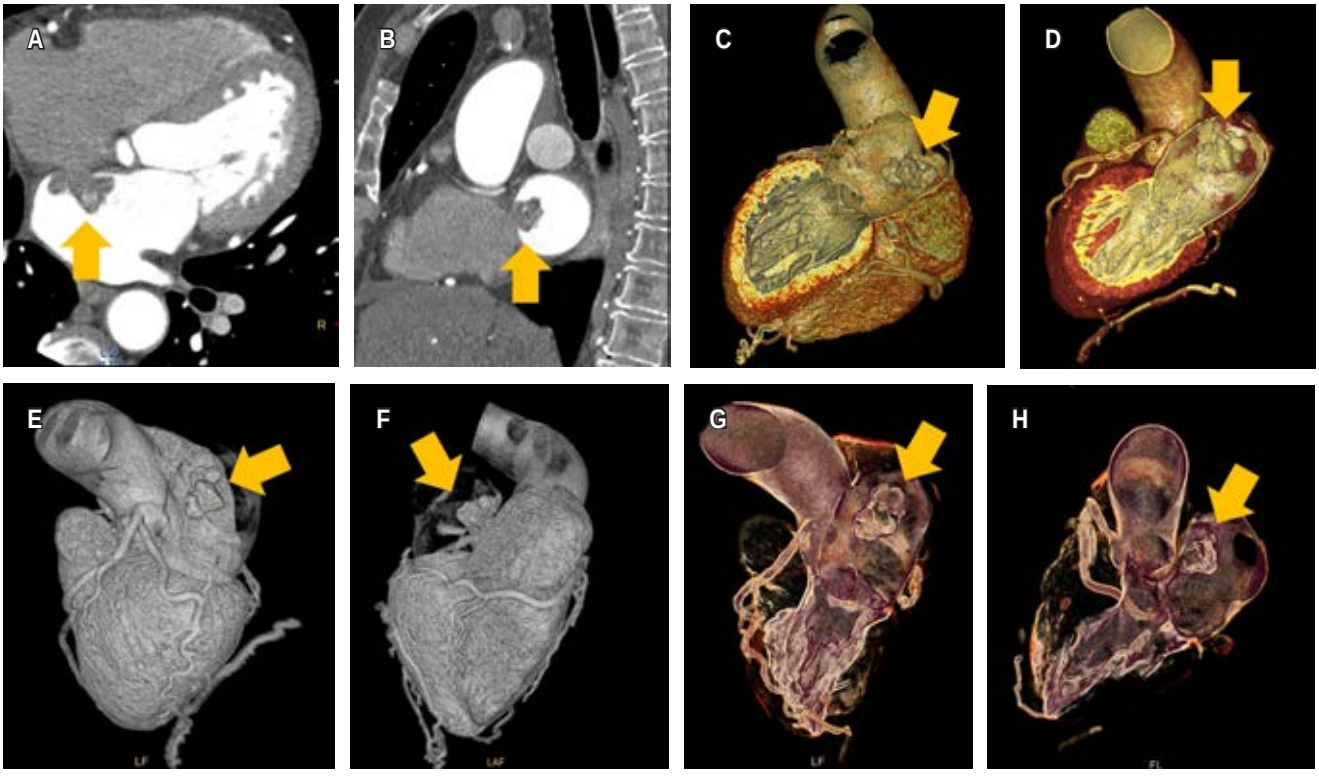

Figure 3: Cardiac computed tomography. **A)** and **B)** A mass in the left atrium on contrast-enhanced cardiac computed tomography (arrow). **C-H)** 3D reconstruction of the left atrial chamber with a mass (arrow).

cancer is a rare finding.[8] The patient may be asymptomatic, and the lesion can be found incidentally, as in the present case. In imaging diagnoses of a cardiac mass, 47% corresponded to benign masses, including myxomas (20%); 64% of patients had a history of malignancy, which included breast cancer (5%).[9]

The authors of a case-control study of autopsy cases concluded that it is challenging to assess the correlation between cardiac myxoma and other neoplasms because it is a condition that is uncommon in life and sometimes goes undetected. As a result of diagnosis suspicion bias, the knowledge that the patient has been diagnosed with one disease (neoplasm) influences the intensity of their search for another condition.[10] Some case reports, however, describe cardiac myxomas as a late complication in cancer survivors, hypothesizing that chemotherapy, radiotherapy, or immunosuppression[11-13] may have contributed to the tumor's growth.[14,15]

Cardiac tumors are rare, and any space-occupying mass noted on cardiovascular imaging modalities should be considered as part of the differential diagnosis. Many types of tumors exist, including neoplastic and nonneoplastic lesions and masses. Neoplastic lesions are further classified into primary and secondary tumors (metastatic), all of which can be classified as benign or malignant. Primary cardiac tumors may originate from the pericardium or the myocardium but are generally benign.[2,4] Myxomas represent about 50% of all benign intracardiac tumors. They are predominant in the left atrium in 75% of cases, and in the right atrium, in 20% of cases. Bronchial, breast, melanoma, lymphoma, and leukemia are the most common cancers metastasizing to the heart.[6]

A cardiac tumor may be symptomatic or discovered incidentally during an evaluation for an unrelated physical condition or problem.[2] The tumor's size, location, and mobility determine symptoms and signs of myxoma. The tumor can produce symptoms by interfering with valvular function, resulting in left ventricle obstruction or congestive heart failure. Myxomas of the left atrium have a high incidence of brain embolisms; therefore, surgical treatment should be performed as soon as possible.[4,5]

A Carney complex (CNC) is a rare hereditary genetic condition that can be inherited autosomally dominant or sporadic.[6] This syndrome is caused in most patients by a defect of the PRKAR1A gene. It consists of multiple endocrine neoplasms and lentiginosis characterized by abnormal pigmentation of the skin and mucosa, myxomas primarily of the heart, skin, and breast, endocrine neoplasms, psammomatous melanotic schwannomas, breast ductal adenomas, osteochondromyxomas, and

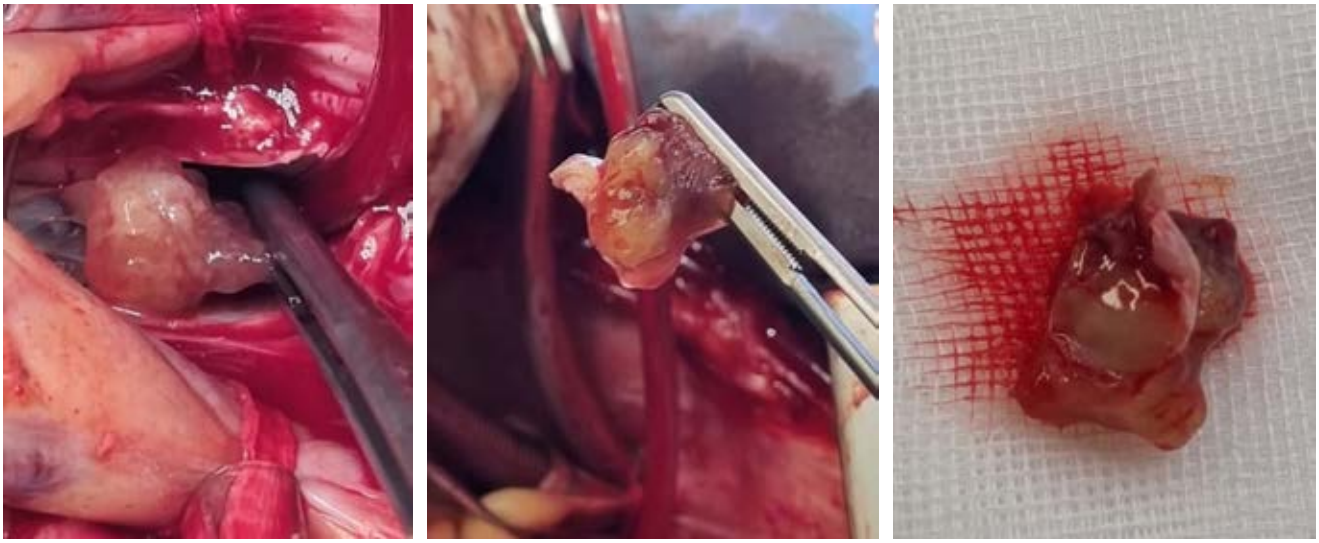

Figure 4: Intraoperative view of a left atrial multilobulated mass with hemorrhagic areas.

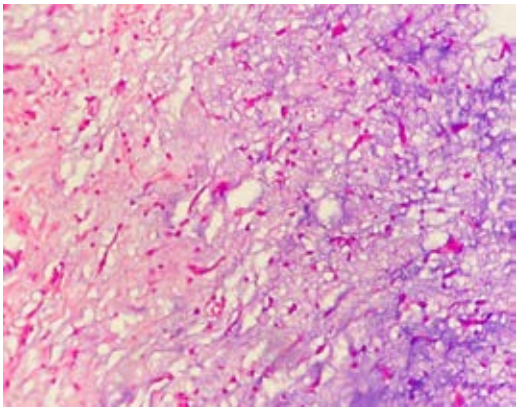

Figure 5: Photomicrograph showing spindle-shaped cells in a myxoid and hemosiderin background.

other non endocrine tumors.[16] To exclude this possibility, measurement of endocrine hormone levels in patients with recurrent myxomas is necessary.[4,6] In C-O clinics, cardiac myxomas are sometimes seen in breast cancer patients; however, the relationship between breast cancer and cardiac myxoma is seldom reported in patients without the Carney complex.[6]

Although obtaining a histopathologic specimen is the gold standard for diagnosis, multimodality imaging can often pinpoint the cause of a cardiac mass.[2,17] Since two-dimensional transthoracic echocardiography is available and portable, it is often used first for diagnosis. It provides radiation-free and inexpensive images of tumors and minor, highly mobile masses, such as masses originating from valves, as well as assessing the size and location of tumors.[2] Paolisso et al. have recently identified some echocardiographic parameters that help predict malignancies and minimize diagnostic delay. It is important to recognize that contrast echocardiography is a valuable tool, but not all echocardiography laboratories have access to ultrasound-enhancing agents.[18] However, in addition to inadequate acoustic windows, which are particularly problematic in obese and chronic pulmonary disease patients, these studies lack tissue characterization.[2]

The use of computed tomography (CT) for assessing cardiac masses has become increasingly popular, mainly when other imaging modalities are not diagnostic or contraindicated. As a result of electrocardiographic gating, motion-related artifacts are minimized, and lesion margins and their relationship to tissue planes are more precisely delineated, which is especially beneficial when planning surgical procedures. However, radiation exposure, risk of contrast-induced nephropathy, and limited soft tissue and temporal resolution of CT scans are disadvantages compared to magnetic resonance imaging.[2]

A cardiac CT usually reveals a smooth or slightly villous intracavitary mass with low attenuation. Therefore, arterial phase contrast enhancement may not appear, and cine image reconstruction may be used to determine the lesion's mobility and attachment. Malignancy may be suspected, however, if local invasion, feeding vessels, hemorrhage, involvement of more than one cardiac chamber, and pericardial effusion are detected.[2]

Surgical resection is essential for a histological diagnosis and prevents significant complications such as embolization. It has a low mortality rate and a favorable long-term outcome. As approximately 10 to 15% of these tumors recur, generally near the original site, an echocardiogram should be performed annually for at least four years.[2,5]

CONCLUSIONS

Asymptomatic patients with previously treated breast cancer may present a second primary tumor, as in this case: a cardiac myxoma. Furthermore, chemotherapy, radiotherapy, or immunosuppression may contribute to the development of a second primary tumor. Therefore, as part of the long-term survivorship care after breast cancer treatment, it is imperative to perform regular clinical examinations and cardiovascular imaging to establish an early diagnosis and treatment. This case illustrates the importance of Cardio-Oncology Clinics during the follow-up of breast cancer survivors. In addition, echocardiography provides a method of detecting small tumors in breast cancer survivors who are still asymptomatic.

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Correspondence:
Thelma Rodríguez-López, M.D.
E-mail: thelma8rl@gmail.com

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Atrial fibrillation and obesity: two epidemic diseases with complex interactions

Fibrilación auricular y obesidad: dos enfermedades epidémicas con interacciones complejas

Jorge Álvarez de la Cadena-Sillas,* Enrique Asensio-Lafuente,*
Elsa De la Chesnaye,‡ Gerardo Rodríguez-Diez§

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ABSTRACT

Atrial fibrillation (AF) is a chronic degenerative and multifactorial disease with increasing prevalence and incidence that might even reach epidemic proportion, as with obesity. A highly prevalent problem worldwide. The combination of both conditions represents higher morbidity and mortality risks, and obesity is a risk factor for AF and worse outcomes of this complex arrhythmia. In the present work, we review the pathophysiological interactions between obesity and AF, the beneficial effects of obesity control on AF outcomes and the potentiation of better results with the current treatments for AF.

RESUMEN

La fibrilación auricular (FA) es una enfermedad crónica compleja, degenerativa y multifactorial cuya prevalencia e incidencia aumentan, de modo que puede considerarse una verdadera epidemia, como ocurre con la obesidad. La combinación de ambas enfermedades supone un mayor riesgo de morbilidad y mortalidad. La obesidad por sí misma es un factor de riesgo para la FA y se asocia con una peor evolución de esta compleja arritmia. En el presente trabajo, se revisan las interacciones fisiopatológicas entre obesidad y FA, así como los efectos positivos del control de la obesidad en la FA y la obtención de mejores resultados con las terapias disponibles en la actualidad para la arritmia.

* Instituto de Corazón de Querétaro. Querétaro, México.
‡ Unidad de Investigación Médica en Enfermedades Metabólicas, Centro Médico Nacional Siglo XXI, Instituto Mexicano del Seguro Social. Ciudad de México, México.
§ Servicio de Electrofisiología, Centro Médico Nacional 20 de Noviembre, Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado. Ciudad de México, México.

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INTRODUCTION

Atrial fibrillation (AF), a degenerative, progressive, and multifactorial disease, is the most common persistent arrhythmia in adults and is considered an epidemic in this century. It is degenerative because prevalence and incidence increase with age, translating into an increase in mortality and a poor quality of life. The estimated prevalence of AF in adults is between 2 and 4%, and it will grow twofold due to population aging and a better capacity for arrhythmia diagnosis.[1] AF is a progressive disease and a risk factor for cerebrovascular accidents (CVA) in up to 25% of ischemic etiology.[2]

OBESITY AS A DISEASE AND RISK FACTOR FOR ATRIAL FIBRILLATION

Obesity prevalence has increased worldwide, and Mexico is not an exception: 46% of women between 30 and 59 years and 35% of men have obesity; this pathology is considered a modifiable risk factor for many cardiovascular diseases, including AF.[1,2] The Framingham heart study shows that for every unit of body mass index (BMI) increase, there is a 4% growth in the risk of AF regardless of the patient's sex.[3] Body mass index is still an independent risk factor with a linear relationship when adjusted to other risk factors or heart conditions.[4] The Women's Health Study, designed exclusively to associate

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gender with the risk of developing AF in 34,309 patients, followed by a mean time of 12.9 years, showed that such risk was directly proportional to BMI augmentation. At the same time, an increase in BMI of more than 25%, even in the short term, also increased the incidence of AF.[2,4]

Moreover, obesity is associated with cardiovascular risk factors that elevate the risk of AF, such as diabetes, hypertension, metabolic syndrome, cardiac failure, coronary artery disease, chronic disease, and obstructive sleep apnea (OSA).[1,5,6] The seep heart study showed that patients with respiratory problems related to OSA have a fourfold incidence of AF and non-sustained ventricular tachycardias.[5,6]

Obesity modifies hemodynamic regulation, neurohumoral, metabolic inflammatory, and autonomic system functions.[2,4,6,7] Changes in the hemodynamic regulation derived from obesity also include increased cardiac output due to increased systolic volume and left ventricular hypertrophy with diastolic dysfunction of several degrees. If this condition is sustained, increases in the end-diastolic pressure will lead to diastolic dysfunction and left atrium enlargement, causing high venous pressure, and retrograde pulmonary capillary pressure, exacerbating the clinical symptoms.[2,4,6,8]

The physiopathologic relationship between obesity and AF is complex and unclear since obesity is considered a proinflammatory systemic state related to adipokine dysregulation. In patients with a respiratory pathology such as OSA, the inflammation is aggravated by hypoventilation and secondary hypoxia, which will stimulate the liberation of more inflammatory cytokines such as the tumor necrosis factor-alpha, interleukin 1-beta and interleukin-6 among others.[2,4,8] Obesity and OSA could also increase the possibility of AF recurrence in patients submitted to an AF ablation procedure.[1]

Emphasis has been placed on the relevance of both pericardial fat and epicardial adipose tissue in the induction of the inflammatory immune response mediated by the paracrine action of the adipokines. Under this hormonal influence, the fat infiltration in the atrial myocardium and the myocardial remodeling can lead to significant fibrosis, more evident in the left atrium.[6,7] The inflammatory cytokines and chemokines could be responsible for the dysfunction of ion channels and atrial fibrosis, which will induce reentry circuits in AF.[2,6,7] Adipokines are bioactive proteins located and secreted predominantly in the adipose tissue. They participate in systemic mechanisms like energy and lipid metabolism, insulin sensitivity, and angiogenesis.[9] However, plenty of evidence suggests these molecules exist in various tissues, including the myocardium.[10] They act through different signaling pathways in many physiological processes, including cardiovascular function.[11]

Even though the mechanisms by which adipokines are involved in the development of atrial fibrillation have not been elucidated yet, several studies have addressed this issue by describing an association between anti-inflammatory and pro-inflammatory adipokines with the onset of AF.[12] Nevertheless, the results reported are scarce and contradictory. For instance, some authors stated no association between the anti-inflammatory adipokine adiponectin and the risk of stroke, whereas others reported the opposite. The same occurred with other adipokines like apelin, chemerin, and resistin; therefore, it is likely that the results reported in epidemiological studies would not suffice to implement adipokine-dysregulated levels as biomarkers for AF prevention.[13] Thus, combined clinical, epidemiological, and molecular approaches should be considered to improve AF outcomes.

On the other hand, it is common for obese people to present enlargement of the left atrium, specifically if the indexed volume of the body surface area evaluates the latter. Also, it is common to find adipose tissue infiltration of the atrial myocardium and anomalies in the systemic inflammatory response due to adipose tissue enlargement in abdominal and epicardial fat.[14]

At the cellular level, electromechanical atrial remodeling leads to a fragmentation of the endoplasmic reticulum, causing changes in protein folding and localization, especially those related to autonomic connections. Also, mitochondrial adaptations to impaired cellular homeostasis have been observed. In this context, it is known that mitochondria of metabolically stressed atrial tissue from both human and animal models present an increased production of reactive oxygen species. The latter and advanced glycation end products

lead to inflammation and the promotion of cardiovascular diseases, including diabetic cardiomyopathy and AF.[14] Therefore, cardiac chambers do not need to dilate or tension to increase in the parietal myocardium for AF to appear and perpetuate.

The use of direct anticoagulants in overweight or obese patients reduces the risk of suffering any systemic embolism myocardial infarction (MI), and pulmonary thromboembolism (PTE) (OR: 0.75; CI 95%: 0.66 a 0.84 and OR: 0.62; CI 95%: 0.54 to 0.70, respectively) as opposed to what happens in patients with a BMI less than 25 kg/m^2 body surface.[15] This phenomenon is known as the «obesity paradox». Obese patients could have a better prognosis than those with a normal BMI; however, no randomized controlled studies confirm this observation.[6,8,15] This phenomenon could result from better metabolic reserves, less cachexia, and increased mass and muscular tone. These changes could be due to the renin-angiotensin-aldosterone system's activation and an increased cytokine level with a protective effect against the cardiovascular drugs used in hypertension treatment, most prevalent in these subjects. Despite all these associations, the observation has yet to be reported within an observational cohort study or in studies with long-term follow-ups.[8,16]

Direct oral anticoagulants or the antagonists of vitamin K are indicated in patients with obesity and AF, just like they are recommended to all patients with arrhythmia, even if their BMI is more than 40-50 kg/m^2 BS. No antiplatelets are recommended in any patient with atrial fibrillation.[17-25]

EFFECTS OF WEIGHT LOSS

It has also been observed that weight loss is directly related to a diminished arrhythmic burden and improved symptoms.[26,27] The LEGACY study[28] showed that patients with AF that were able to reduce their corporal weight by more than 10% of their initial weight at the beginning of the study had six times more probability of being free of AF or other atrial arrhythmias in a five-year follow-up compared to patients that did not lose weight, or that had a weight reduction inferior than 3%.[2,8,28] In the REVERSE-AF study,[29] 88% of the patients with a sustained weight reduction of 10% of the basal body weight went from persistent AF to paroxistic or no AF at al. The same study found that 86% of the patients that could reduce their body weight were free of arrhythmias during the follow-up. Although this measure delays an ablation procedure, this should not be a factor in not performing or delaying pulmonary vein isolation in patients with an indication for the procedure. Despite these observational data, it has not been demonstrated that weight reduction in patients with AF diminishes the long-term risk of embolic events or other clinical adverse outcomes such as mortality, ictus, or hospitalization due to cardiac failure.[2,8]

As mentioned earlier, there seems to be a complex relationship between obesity and AF. The physiopathological mechanisms include many factors; however, the direct intervention of weight reduction positively affects the progression of the arrhythmia. This kind of intervention is low-cost, and the significant results reinforce the importance of preventing and controlling cardiovascular risk factors. Implementing public health policies in this regard should be more efficient in reaching more population sectors, thus reducing the health, social, and economic burdens of arrhythmias expected to be more prevalent soon.

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Correspondence:
Enrique Asensio-Lafuente, MD
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