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Cardiovascular and Metabolic Science

Continuation of the Revista Mexicana de Cardiología

2024

- The lack of CPR teaching
- In search of an appropriate risk scale for Mexicans
- Heart block in a patient with transposition of the great arteries and *situs inversus*
- Atypical presentation of *Vagococcus fluvialis* in a cardiac pacing device
- Calcium modification technique to overcome a balloon uncrossable occlusion
- Protocol for certification as a cardio-protected area in Mexico

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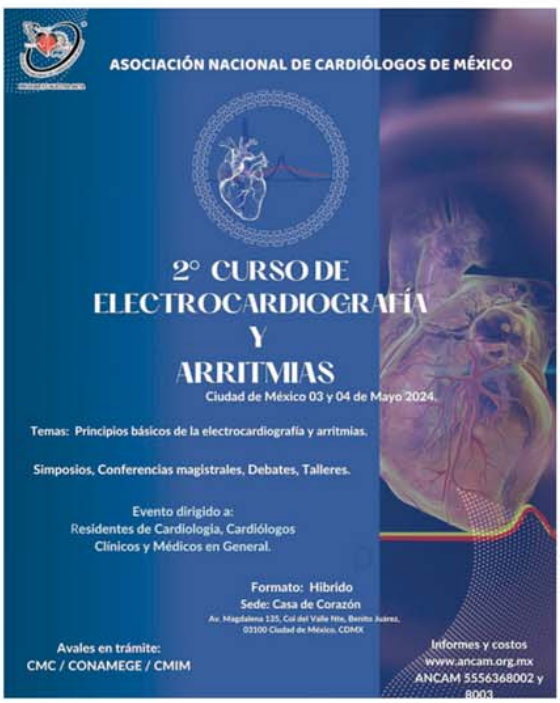

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Editorial

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The lack of CPR teaching in Mexico

La falta de enseñanza de RCP en México

Jorge Álvarez de la Cadena-Sillas*

Cardiovascular diseases are the leading cause of death in the world. Among them, the presence of sudden cardiac death (SCD) stands out.[1] The prompt activation of the emergency medical service (EMS), the early initiation of CPR by witnesses, and the use of the AED improve the prognosis of survival and complications of the victim.[2] In this context, international CPR recommendations increasingly insist on teaching these maneuvers to first responders and witnesses, especially in the context of out-of-hospital cardiac arrest (OHCA),[3] which is where witnesses are the ones who can initiate the rescue maneuver's attention to victims.[4] In Mexico, there is no free CPR training program for the open population either at the government level or by Non-governmental Organizations (NGOs). There are only separate efforts, and most of them are not free and are taught mainly to people who request them and at some cost. Furthermore, we think that the fact that SCDs are mostly produced as OHCA and the evidence that the performance of early detection by witnesses leads to greater survival. It should be the reason for providing education that reaches the majority of the population,[5] as I said before, for free. In this sense, we think that the recommendations made by ANCAM in its initial program to save a life with just your hands should be a turning point to extend CPR education to the Mexican population by an NGO, but taking advantage above all of the learning capacity of the school population[6] this should also be a government program at the national level in primary schools. Multiple studies show that teaching CPR and CPR maneuvers in schoolchildren is accompanied by a[7-9] reduction in morbidity and mortality in patients with OHCA. We think that this type of writing should raise awareness among political authorities to consider the importance of teaching this type of maneuver in training not only at the level of the school population but also at the secondary level where it is shown that the population is more receptive and potentially suitable for the application of CPR maneuvers and make it mandatory in high-risk populations such as those seeking to obtain a driving license, and places with a high concentration of people such as airports, stadiums, shopping centers, airports, gyms, sports centers, etc. Finally, the idea is to reduce a real health problem that causes great deterioration in the health of Mexicans, their families, and their workplaces, and that also translates into economic problems for the country since most of the victims are people of productive age.

Let us help raise awareness in the general population and especially in our governments and make it easier for the teaching of CPR to reach the majority of Mexicans finally.

REFERENCES

1. Atwood C, Eisenberg MS, Herlitz J, Rea TD. Incidence of EMS-treated out-of-hospital cardiac arrest in Europe. Resuscitation. 2005; 67 (1): 75-80.
2. Meaney PA, Bobrow BJ, Mancini ME, Christenson J, de Caen AR, Bhanji F et al. Cardiopulmonary resuscitation quality: improving cardiac resuscitation outcomes both inside and outside the hospital. A consensus statement from the American Heart Association. Circulation. 2013; 128 (4): 417-435.
3. Greif R, Lockey AS, Conaghan P, Lippert A, De Vries W, Monsieurs KG. European resuscitation council guidelines for resuscitation 2015. Section

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10. Education and implementation of resuscitation. Resuscitation. 2015; 95: 288-301.
4. Vaillancourt C, Verma A, Trickett J, Crete D, Beaudoin T, Nesbitt L, Wells GA, Stiell IG. Evaluating the effectiveness of dispatch-assisted cardiopulmonary resuscitation instructions. Acad Emerg Med. 2007; 14 (10): 877-883.
5. Gallagher EJ, Lombardi G, Gennis P. Effectiveness of bystander cardiopulmonary resuscitation and survival following out-of-hospital cardiac arrest. JAMA. 1995; 274 (24): 1922-1925.
6. Böttiger BW, Van Aken H. Kids save lives. Training school children in cardiopulmonary resuscitation worldwide is now endorsed by the World Health Organization (WHO). Resuscitation. 2015; 94: A5-A7.
7. Iserbyt P, Theys L, Ward P, Charlier N. The effect of a specialized content knowledge workshop on teaching and learning basic life support in elementary school: a cluster randomized controlled trial. Resuscitation. 2017; 112: 17-21.
8. Mpotos N, Isebyrt P. Children saving lives: training towards CPR excellence levels in chest compression based on age and physical characteristics. Resuscitation. 2017; 121: 135-140.
9. López UMC, Freire TM, Rasines SR, Iglesias GA. RCP na aula: programa de enseñanza de la reanimación cardiopulmonar básica para estudiantes de secundaria. Emergencias. 2012; 24: 76.

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ORIGINAL RESEARCH

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In search of an appropriate risk scale for Mexicans. The insufficiencies of the Globorisk scale

En busca de una escala de riesgo adecuada para los mexicanos. Las insuficiencias de la escala Globorisk

Alejandra Meaney,* Martha Yolanda Martínez-Marroquín,‡ Virginia Samaniego-Méndez,§ Carlos Fernández-Barros,¶ Isabel Hidalgo,‖ Nayeli Nájera,** Guillermo Ceballos,** Eduardo Meaney**

Keywords:
cardiovascular risk, Globorisk tool, TG/HDL-c quotient, Lindavista score.

Palabras clave:
riesgo cardiovascular, sistema Globorisk, cociente TG/C-HDL, puntaje Lindavista.

ABSTRACT

Introduction: risk scales are helpful in the primary prevention of cardiovascular (CV) diseases to detect high-risk subjects. In Mexico, scales developed in populations very different from ours are used. Recently, the use of the Globorisk tool in Mexico has been proposed. We have shown that the ACC/AHA scale underestimates the risk measured with the TG/HDL-c index and the so-called Lindavista score. We now compare these last to the risk calculated with the Globorisk tool, whose original estimates were adjusted to national data. **Material and methods:** the sum of the abnormalities in the data of 2,602 healthy subjects (age, gender, body mass, waist, lipid profile, and blood glucose) is the Lindavista score. This and the quartile values of the TG/HDL-c index were compared with the Globorisk risk estimate for Mexico. **Results:** Lindavista risk and TG/HDL-c ratio values have a very high linear correlation, but Globorisk underestimates the risk. **Conclusion:** any scale that does not consider traits and factors that are highly prevalent in our population (abdominal obesity and lipid triad) can correctly express the risk. While waiting to develop our scale that encloses the anthropometric and cardiometabolic traits of the Mexican population, the TG/HDL-c index is proposed as a valuable, economical, and practical tool for estimating the risk of our population.

RESUMEN

Introducción: *las escalas de riesgo son útiles en la prevención primaria de las enfermedades cardiovasculares (CV) para detectar sujetos de alto riesgo. En México se utilizan escalas desarrolladas en poblaciones muy diferentes a la nuestra. Recientemente, se ha propuesto el uso de la herramienta de Globorisk para la población mexicana. Hemos demostrado que el baremo ACC/AHA subestima el riesgo medido con el índice TG/C-HDL y el llamado puntaje Lindavista. Ahora comparamos estos últimos con el riesgo calculado con la herramienta Globorisk, cuyas estimaciones originales se ajustaron a los datos nacionales.* ***Material y métodos:*** *la sumatoria de las anormalidades de los datos de 2,602 sujetos sanos (edad, género, masa corporal, cintura, perfil de lípidos y glucemia) conformaron el puntaje Lindavista. Éste y los valores cuartilares del índice TG/C-HDL se compararon con la estimación del riesgo Globorisk para México.* ***Resultados:*** *el riesgo Lindavista y los valores del cociente TG/C-HDL tienen una muy alta correlación lineal, pero Globorisk subestima gruesamente el riesgo.* ***Conclusión:*** *ningún baremo que no tome en cuenta rasgos y factores muy prevalentes en nuestra población (obesidad abdominal y tríada lipídica) expresa correctamente el riesgo. En espera de desarrollar nuestro propio baremo que tome en cuenta los rasgos antropométricos y cardiometabólicos de la población mexicana, se propone al índice TG/C-HDL como una herramienta útil, económica y práctica para la estimación del riesgo de nuestra población.*

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INTRODUCTION

Until now, one of the most solid paradigms of contemporary cardiovascular (CV) medicine is that estimating risk to tailor specific prophylactic measures according to the magnitude of the calculated danger is essential in the primary prevention of CV diseases.[1] Under that idea, several risk scores have been introduced in the last decades based on ample adult population cohorts comprising both sexes.[2-10] Using multiple regression analysis, where the different risk factors were used as independent or explanatory and diverse fatal and non-fatal outcomes as dependent or predicted variables, multiple regression equations were generated to predict the absolute risk of those outcomes, generally over ten years. Because these seminal cohort studies are expensive, complex, and long-lasting, without exception, they were generated in developed countries. Physicians from less advanced nations are forced to use these risk scales even though their populations are strikingly different from an ethnic, nutritional, anthropometric, and cultural point of view. However, as Ueda stated, «Risk equations developed in one population cannot be applied to other populations, or even used in the same population years after they were developed because mean CVD risk and CVD risk factor levels vary across populations and over time».[6]

In our country, the risk scales that are more attractive to physicians are the United States American College of Cardiology/American Heart Association atherosclerotic cardiovascular disease (ASCVD) risk scale (ACC/AHA ASCVD risk scale),[7] the European SCORE2 and SCORE2OP,[8,9] and the international Globorisk.[10]

However, our group has insisted on the necessity of developing a risk scale appropriate to Mexicans, given the peculiar and distinctive features of our predominant mestizo population: high prevalence, mainly of the central type, of overweight and obesity (O/O), genetic predisposition to insulin resistance and the so-called «metabolic syndrome», atherogenic dyslipidemia, and type 2 diabetes (DM2).[11-14]

A clinical guide on dyslipidemia focused on the Mexican population was recently published,[15] in which, among many debatable topics and conclusions, the use of the Globorisk tool for risk estimation in primary prevention was recommended. Although the guide is intended to be a product of a broad national consensus, many concepts and findings of several national research groups, such as ours, are not reflected in many of the recommendations and conclusions of the document mentioned above.

More recently, our group published a work in which we showed that since the ACC/AHA ASCVD risk scale does not consider some highly prevalent risk factors in our country, its calculation grossly underestimates the cardiovascular risk of the Mexican population.[16] We compared the risk estimated by the US scale against the values of the ratio between triglycerides (TG) to the cholesterol of the high-density lipoproteins (HDL-c), the TG/HDL-c index, a simple, inexpensive, and easy-to-get risk marker, and also with the Lindavista scale, still under study, derived from anthropometric data, blood glucose, lipids, and blood pressure from the primary prevention study of the same name.[13] The ACC/AHA ASCVD scale coincides with the TG/HDL-c index and the Lindavista score only at the extremes. Still, in patients with high or moderate risk, according to our markers, the US scale continues to consider them at intermediate risk. The present work is an extension of the previous one but now scrutinizes the usefulness of another risk score system, the Globorisk tool, to correctly assess the CV risk of Mexicans.

MATERIAL AND METHODS

The Lindavista study's methodology and results and the «Lindavista scale» proposal have been described elsewhere.[13,16] A non-probabilistic sample was assembled with subjects of both sexes, aged 35 or older, without a history of atherosclerotic diseases, diabetes, or any systemic severe disease, who were invited to participate in a long-range primary prevention program on cardiovascular (CV) risk factors. The participants were randomly allocated into two groups: one, in which the follow-up was done by cardiologists trained in prevention, and another cared for by their private or institutional

general physicians. Institutional ethics and research committees approved the protocol, which was conducted under the standards of Good Clinical Practices,[17] and following ethical[18] and legal[19] standards, including the mandatory obtention of informed consent.

The following data were obtained from all participants' clinical examinations and laboratory tests: age, sex, and smoking status were registered. From weight (in kg) and height (in cm), body mass index was calculated (BMI, kg/m^2). Abdominal circumference was measured in cm. According to standard specifications, systemic systolic and diastolic blood pressures (SBP, DBP) were measured in mm Hg with mercurial sphygmomanometers.[20] Fasting glycemia and lipid profile: total cholesterol (TC), TG, HDL-c were obtained in mg/dL by colorimetric assay kits following manufacturers' instructions. Low-density lipoprotein cholesterol (LDL-c) was estimated through the Friedewald formula[21] (LDL-c = TC-HDL-c/(TG/5) if concentrations of TG were below 300 mg/dL. If not, instead of LDL-c, the non-HDL cholesterol estimation was used as a substitute: non-HDL-c = TC-HDL-c.

The summation of these eleven variables yields the «Lindavista score» (LS). Each variable was assigned a value between -3 to +3, according to its amount, following established criteria and, sometimes, arbitrarily. The greater the sum, the higher the CV risk, according to the concept of «risk aggregation».[22] The highest possible value of the sum would be 33. The LS was estimated in all subjects of the cohort.

The TG/HDL-c index[23] was estimated from the lipid values as a CV and cardiometabolic index.

CV risk was also assessed using the Globorisk tool based on data from eight prospective cohort studies.[10] The laboratory version of the score considers smoking, systolic blood pressure, diabetes, and TC to develop regression equations predicting the 10-year risk of sudden death and fatal and non-fatal episodes of ischemic heart disease and stroke.[6] There are risk-colored-code charts for 182 nations, recalibrating the original risk score according to country-specific mean risk factor levels and CVD rates. According to the color code of the charts, it can be assumed that the first two categories in green (< 5, 5-9%) correspond to the lowest risk; the yellow one (10-19%) to moderate risk; the one in orange color (20-29%) to high risk and those with different tones of red (30-39, 40-50, and more than 50%) to very high risk *(Table 1)*.[24]

Statistical analysis. Data was analyzed using GraphPad Prism version 7.00 for Windows (GraphPad Software Inc., San Diego, CA, USA). Correlation coefficients among the Globorisk, Lindavista risk, and TG/HDL indexes were done using Pearson's correlation coefficient formula. A p-value < 0.05 was considered statistically significant.

RESULTS

We test the LS score in all cohort subjects, comparing its values against the TG/HDL-c index, a risk score proposed since the Framingham observations.[23] To calibrate the LS, their values were divided into quartiles and compared against those of the TG/HDL-c quotient, corresponding to the quotient figures of < 3.3, 3.3-4.6, 4.7-6, and > 6 to quartile values of the LS of Q1, 0 to 4.9; Q2, from 5 to 8.9; Q3, from 9 to 13; and Q4, greater than 13 scores.[16] Arbitrarily, we named those LS intervals of low, borderline, intermediate, and high-risk categories, following the ACC/AHA ASCVD risk scale nomenclature.[7,16]

The comparison between the TG/HDL-c index and the Globorisk score is shown in *Figure 1*, while the relation between Globorisk and LS is shown in *Figure 2*.

DISCUSSION

Humanity, despite belonging to a single race, comprises numerous ethnic groups that have marked phenotypical differences. Although this statement is a truism, it has not been completely assimilated into the modern medical imagination. For example, not long ago, the results of the INTERHEART study indicated another truism: that a set of nine well-known risk factors is responsible for 90% of the attributable risk of coronary heart disease (CHD).[25] Although this study produced some nonsense results, like considering that «psychosocial stress» is the third most important

Table 1: Lindavista risk score.

Risk factor grading	Scoring	Risk factor grading	Scoring
Female, (years)		Systemic diastolic blood pressure, (mmHg)	
< 30	-3	< 90	0
30-39	-1	90-99	1
40-49	0	100-109	2
50-59	1	≥ 110	3
> 60	2	Fasting glycemia, (mg/dL)	
Male, (years)		< 100	0
< 30	-1	100-126	1
30-39	0	127-140	2
40-49	1	≥ 140	3
50-59	2	Total cholesterol, (mg/dL)	
> 60	3	< 200	0
Smoking, (daily consumption)		200-239	1
Never smokers or former smokers (at least in the last year)	0	240-279	2
		≥ 280	3
Cigarette consumption			
1-5	1	Triglycerides, (mg/dL)	
6-10	2	< 150	0
> 10	3	150-199	1
Body mass index, (kg/m^2)		200-499	2
< 25	0	≥ 500	3
25-29.9	1	HDL-c, (mg/dL)	
30-34.9	2	≥ 60	0
≥ 35	3	40-59	1
Abdominal circumference in women, (cm)		30-39	2
< 80	0	< 30	3
80-84.9	1	LDL-c, (mg/dL)	
85-89.9	2	< 100	0
≥ 90	3	100-129	1
Abdominal circumference in men, (cm)		130-159	2
< 90	0	≥ 160	3
90-94.9	1	Total score	
95-99.9	2		
≥ 100	3		
Systemic systolic blood pressure (mm Hg)			
< 140	0		
140-159	1		
160-179	2		
≥180	3		

The sum expresses the number and severity of risk factors. The grading of some factors was done, in some cases, taking the standard categories (BMI or BP, for example). In other cases, the different gradation was arbitrary, as in the case of abdominal obesity.

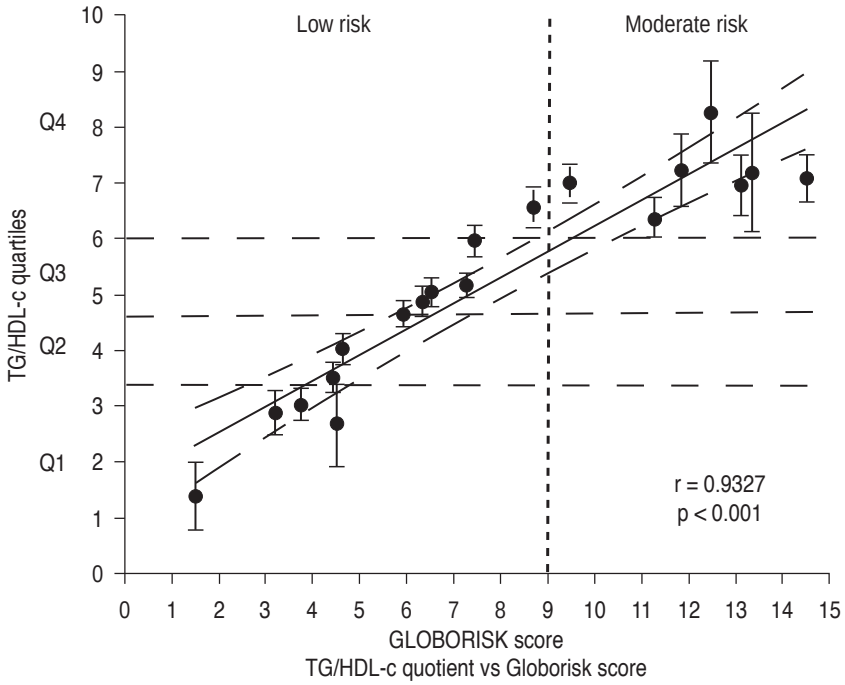

Figure 1:

TG/HDL-c index vs Lindavista score. A straight linear relation exists between TG/HDL-c quotient and Globorisk scores, with a high correlation coefficient. However, the highest values of the TG/HDL-c index correspond to the lowest Globorisk scores categories, signaling that this system significantly underestimates the cardiovascular risk of the Lindavista study population.

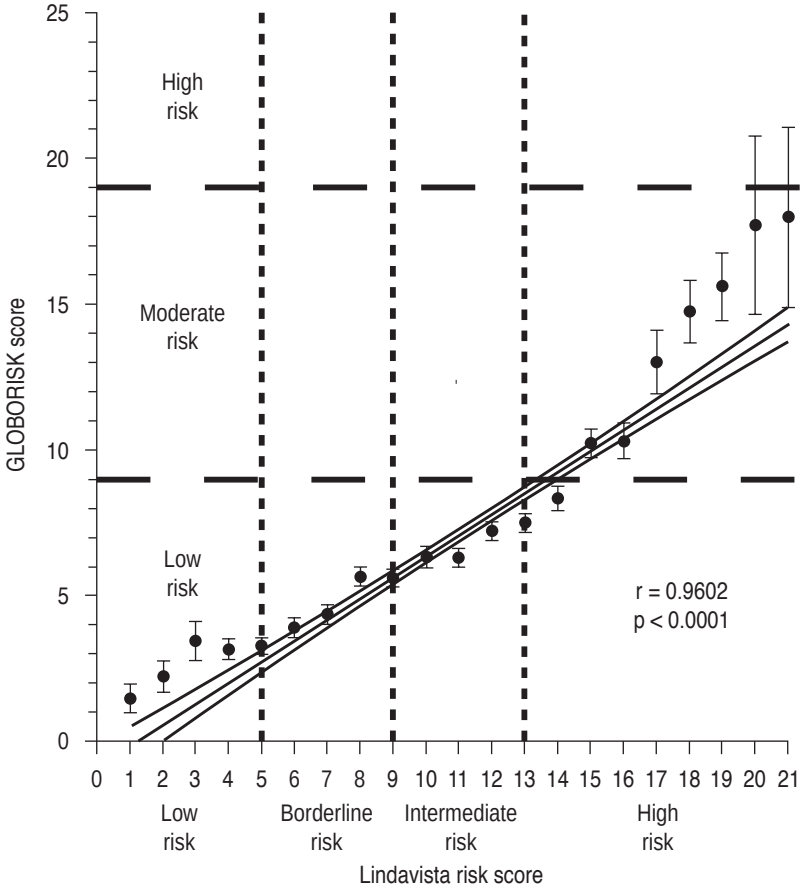

Figure 2:

GLOBORISK score vs Lindavista score. Despite a straight linear correlation between both risk scales, Globorisk does not coincide with the estimations of the Lindavista score. Even those with the highest LS summations are qualified in the low and moderate Globorisk scores.

determinant of CHD, above even obesity, hypertension, and diabetes, its worst defect is to state that these results are observed «worldwide in both sexes and at all ages in all regions»,[25] a way to reject the fact of the biodiversity that characterizes the human gender. To begin with, only six Latin American countries were considered (Argentina, Brazil, Colombia, Chile, Guatemala, and Mexico), leaving out most of the American nations.[26] Secondly, the Mexican population studied reached a meager number of 8 cases and 17 controls from a single research center.[26] What solid conclusions can be derived from this scanty number, which, in addition to making matters worse, did not constitute a paired set? Thirdly, the results of a previous, more rigorous although much less extensive, Latin America case-control study were already known (and probably inspired the INTERHEART design), assembling data from the FRICAL study (enclosing the subjects of four Latin American countries: Argentina, Cuba, Mexico, and Venezuela).[27] Our country contributed with 200 cases and 200 controls, still a small number, but without doubt considerably larger than that of the Mexican contribution to the INTERHEART study. The FRICAL study showed remarkable differences among the participating nations, entirely dissimilar from the anthropometric, nutritional, and ethnic points of view. For example, hypercholesterolemia was very important in Cuba as an infartogenic risk factor while having a bordering consequence among Mexicans. On the contrary, diabetes mellitus was prominently significant in Mexico and almost negligible in Cuba. The phenotypic differences between the distinct ethnic groups and their mixtures turn Latin America just into a geographical or geopolitical term rather than a homogeneous ethnic region. So, the problem is not determining the CV risk factors but rather their relative importance, which changes from community to community and country to country. Due to the above facts, the risk scales developed for a particular population cannot be applied to another.

Considering that CV risk is substantially different across populations due to known multiple determinants from genetic, epigenetic, nutritional, environmental, psychosocial, educational, and cultural nature, plus the differences in the quality, the access, and the coverage amplitude of the health systems, the Globorisk tool recalibrates the original data replacing age-and-sex-specific average risk factor and the levels of the risk factors observed in the health surveys of several nations, and also with the CVD death rates from the World Health Organization.[28] The Cohorts Consortium of Latin America and the Caribbean (CC-LAC), led by the researchers of the Harvard T.H. Chan School of Public Health, one of the leading institutions in the development of the Globorisk tool, estimated the discriminatory and calibration capacities of the system in the risk estimation using pooled data from nine prospective Latin American cohorts enclosing 21,378 subjects.[29] By using Harrell's C-statistic or concordance index, which signals the discriminatory power of a predictive system model, the researchers determined a reasonable index higher than 0.7. The data's calibration was obtained by estimating the slopes (close to 1) of different linear regression equations. Despite the impeccable mathematical management, and focusing only on the Mexican situation, we can say that the two cohorts used in the Consortium exercise have significant limitations. The Mexican Teachers' Cohort[30] is a cancer-oriented project, enclosing mainly premenopausal female schoolteachers (just 1.8% of participants were male, from a single Federal state), relatively young. As far as we know, no biochemical or blood pressure data were collected, and except for a single sub-study on the role of sunlight in preventing the increase in carotid intima-media thickness, the study group has had no other publication directed at the cardiovascular or cardiometabolic areas.[31] Although this study may be important for studying the epidemiological behavior of different tumors in women, as designed, it has no use in determining cardiovascular risk. For its part, the cohort of the Health Workers study[32] comprised personnel from Mexican governmental health institutions. Just 9,267 of all participants were adults from two cities in Central Mexico (Cuernavaca, Morelos, and Toluca, State of Mexico), relatively young (mean age around 43.6 ± 14 years). The sample was biased

towards women (70%). Although at baseline, BMI, waist circumference, glycemia, the whole basic lipid profile, and blood pressure were measured, and their results are concordant with other cohort and epidemiologic studies,[11,13] the following assessment, done six years later, just comprised 1,855 persons, to which 1,286 new recruited subjects were added. To our knowledge, only one cardiovascular study has been published with data from this cohort, a binational comparison with US citizens of Mexican origin, which showed that the nationals of our country have a lower proportion of traditional CV risk factors than their counterparts living in the United States.[33] The limited regional representativeness, the young mean age of the cohort, the fact that the participants were part of the medical and paramedical staff, the bias towards women, and the lack of follow-up to determine CV outcomes, make this study unsuitable for any adjustment of the original Globorisk equations.

On the other hand, GLOBORISK charts utilize only a reduced number of risk factors, which are insufficient to encompass the complex genetic, nutritional, and metabolic conditions of the Mexican population plagued by a dysmetabolic O/O epidemic.[34-36]

In the study preceding the current one, already mentioned,[16] we documented the underestimation of risk provided by the ACC/AHA ASCVD risk scale. In comparison, the Globorisk tool performs even worse. As shown in *Figures 1 and 2*, while a high cardiovascular and cardiometabolic risk, secondary to a high frequency of dysmetabolic abdominal obesity, characterizes the Lindavista study population, the Globorisk scale grossly underrates the risk. As the more atherogenic milieu in the current Mexican population is given for the ominous consequences of the binomial insulin resistance/hyperinsulinism, essentially atherogenic dyslipidemia and systemic inflammation, any score risk system that no includes abdominal obesity and concentration of TG is improper to test in a population like ours.

The LS was only used as proof of the concept called the aggregation of risk, i.e., meaning that the more risk factors a person accumulates, and the higher or more serious they are, the more pronounced the CV risk. In this context, the LS keeps a close linear correlation with the TG/HDL-c index, a reliable and worldwide accepted CV risk marker, with prognostic and therapeutic relevance.[16,23,37-41] It is surprising that despite the numerous works recently published in national and international journals from several Mexican research groups, the use of this valuable risk marker is entirely ignored by most clinicians and lipid researchers in our country.

The data shown here indicate that the Globorisk tool performs poorly in detecting CV risk in our population. The highest values of both the LS and the TG/HDL-c correspond to a low GLOBORISK score. The three tools only coincide in low-risk subjects. In a country where 40-50% of the adult population suffers from the so-called metabolic syndrome,[13,34,42] whose pathophysiological basis is binomial insulin resistance/hyperinsulinism, the concentration of TG cannot be ignored.

A common argument used to disregard the value of hypertriglyceridemia as a vascular risk factor is based on the debatable relative failure of fibrates to lower the CV risk, which underpins the refusal of many of our lipid experts, in line with the US guidelines, to consider the pathogenic power of TG. This attitude was further reinforced by the results of the recent study with pemafibrate, a new selective peroxisome proliferator-activated receptor α modulator, which did not demonstrate any reduction in cardiovascular risk in patients with diabetes despite a descent of 26.2% of TG concentration.[43] In comparison, twenty-five years ago, the VA-HIT study encompassing a male population on secondary prevention with low HDL-c levels and LDL-c levels < 140 mg/dL, with or without hypertriglyceridemia, tested the use of gemfibrozil (without statins) on coronary risk reduction. The active treatment reduced TC by 4%, TG by 31%, and increased HDL-c by 6% without any significant reduction of LDL-c. An absolute risk reduction of coronary events was observed of 4.4% (with an NNT [number necessary to treat] of just 22) and a 22% descent of relative risk compared to placebo.[44] It was evident that the risk reduction was a consequence mainly of the descent of triglyceridemia and not because of the decrease in LDL-c. The reanalysis of several studies on

different fibrates shows that these reduce CV risk in patients with hypertriglyceridemia and low HDL-c (as commonly seen in dysmetabolic O/O). This reduction is not observed in subjects without dyslipidemia, as it is entirely expected.[45] Faced with all this evidence, the failed results of the pemafibrate study only disqualify this drug itself and not the entire group of fibrates. The indisputable fact is that one of the consequences of hypertriglyceridemia is the increased production of small, dense LDL particles, highly atherogenic. On the other hand, there is increasingly robust evidence worldwide that elevated TG concentrations are an important, unavoidable vascular risk factor.[46-53] There is some evidence, which needs to be confirmed and expanded, that atherogenic dyslipidemia, a result of insulin resistance, is the most critical lipid mechanism of myocardial infarction in our country.[54]

Until a prospective study is carried out to determine the relative weight of the different determinants of CV risk in our heterogeneous population, it would be advisable to use the more straightforward and reliable TG/HDL-c index to estimate it.

REFERENCES

1. Lloyd-Jones DM. Cardiovascular risk prediction. Basic concepts, current status, and future directions. Circulation. 2010; 121: 1768-1777. doi: 10.1161/CIRCULATIONAHA.109.849166.
2. Wilson PW, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. Circulation. 1998; 97: 1837-1847. doi: 10.1161/01.cir.97.18.1837.
3. WHO CVD Risk Chart Working Group. World Health Organization cardiovascular disease risk charts: revised models to estimate risk in 21 global regions. Lancet Glob Health. 2019; 7: e1332-e1345. doi: 10.1016/S2214-109X(19)30318-3.
4. D'Agostino RB, Grundy SM, Sullivan LM, Wilson P, for the CHD Risk Prediction Group. Validation of the Framingham coronary heart disease prediction scores: results of a multiple ethnic groups investigation. JAMA. 2001; 286: 180-187. doi: 10.1001/jama.286.2.180.
5. Conroy RM, Pyorala K, Fitzgerald AP, Sans S, Menotti A, De Backer G et al. Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE project. Eur Heart J. 2003; 24: 987-1003. doi: 10.1016/s0195-668x(03)00114-3.
6. Ueda P, Woodward M, Lu Y, Hajifathalian K, Al-Wotayan R, Aguilar-Salinas CA et al. Laboratory-based and office-based risk scores and charts to predict 10-year risk of cardiovascular disease in 182 countries: a pooled analysis of prospective cohorts and health surveys. Lancet Diabetes Endocrinol. 2017; 5: 196. Available in: https://doi.org/10.1016/S2213-8587(17)30015-3
7. Goff DC Jr, Lloyd-Jones DM, Bennett G, Coady S, D'Agostino RB, Gibbons R et al. Expert Work Group Members. 2013 ACC/AHA Guideline on the assessment of cardiovascular risk. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014; 129 [Suppl 2]: S49-S73. doi: 10.1161/01.cir.0000437741.48606.98.
8. SCORE2 working group and ESC Cardiovascular risk collaboration. SCORE2 risk prediction algorithms: new models to estimate 10-year risk of cardiovascular disease in Europe. Eur Heart J. 2021; 42: 2439-2454. Available in: https://doi.org/10.1093/eurheartj/ehab309
9. SCORE2-OP working group and ESC Cardiovascular risk collaboration. SCORE2-OP risk prediction algorithms: estimating incident cardiovascular event risk in older persons in four geographical risk regions. Eur Heart J. 2021; 42: 2455-2467. Available in: https://doi.org/10.1093/eurheartj/ehab312
10. Hajifathalian K, Ueda P, Lu Y, Woodward M, Ahmadvand A, Aguilar-Salinas CA et al. A novel risk score to predict cardiovascular disease risk in national populations (Globorisk): a pooled analysis of prospective cohorts and health examination surveys. Lancet Diabetes Endocrinol. 2015; 3: 339-355. doi: 10.1016/S2213-8587(15)00081-9.
11. Meaney E, Lara-Esqueda A, Ceballos-Reyes GM, Asbun J, Vela A, Martínez-Marroquín Y et al. Cardiovascular risk factors in the urban Mexican population: the FRIMEX study. Publ Health. 2007; 121: 378-384. doi: 10.1016/j.puhe.2006.11.008.
12. Fanghanel-Salmón G, Gutiérrez-Salmeán G, Samaniego V, Meaney A, Sánchez-Reyes L, Navarrete U et al. Obesity phenotypes in urban middle-class cohorts; the PRIT-Lindavista merging evidence in Mexico: the OPUS PRIME study. Nutr Hosp. 2015; 32: 182-188. doi: 10.3305/nh.2015.32.1.8646.
13. Meaney A, Ceballos-Reyes G, Gutiérrez-Salmean G, Samaniego-Méndez V, Vela-Huerta A, Alcocer L et al. Cardiovascular risk factors in a Mexican middle-class urban population. The Lindavista Study. Baseline data. Arch Cardiol Mex. 2013; 83: 249-256. doi: 10.1016/j.acmx.2013.05.002.
14. Palloni A, Beltrán-Sánchez H, Pinto G, Wong R. Adult obesity, disease and longevity in Mexico. Salud Publica Mex. 2015; 57 Suppl 1(01): S22-S30. doi: 10.21149/spm.v57s1.7586.
15. Pavía-López AA, Alcocer-Gamba MA, Ruiz-Gastelum ED, Mayorga-Butrón JL, Mehta R, Díaz-Aragón FA et al. Guía de práctica clínica mexicana para el diagnóstico y tratamiento de las dislipidemias y enfermedad cardiovascular aterosclerótica. Arch Cardiol Mex. 2022; 92 (Supl): 1-62. doi: 10.24875/ACM.M22000081.
16. Martínez-Marroquín Y, Meaney A, Samaniego-Méndez V, Nájera N, Ceballos G, Fernández-Barros C et al. The TG/HDL-c Lipid Ratio as a cardiovascular risk marker in a Mexican urban middle-class population: Do we

need a risk score tailored for Mexicans? J Clin Med. 2023; 12 (18): 6005. doi: 10.3390/jcm12186005.
17. Dixon JR. Guidelines on good clinical practice. Int Digest Health Legis. 1999; 6: 65-74. doi: 10.1080/105294199277860.
18. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA. 2013; 310: 2191-2194. doi: 10.1001/jama.2013.281053.
19. Diario de la Federación. [(accessed on November 12 2023)]. Available in: http://www.salud.gob.mx/cnts/pdfs/LEY_GENERAL_DE_SALUD.pdf
20. Pickering TG, Hall JE, Appel LJ, Falkner BE, Graves J, Hill MN et al. Recommendations for blood pressure measurement in humans and experimental animals: Part 1: Blood pressure measurement in humans: a statement for professionals from the Sub-committee of Professional and Public Education of the American Heart Association Council on High Blood Pressure Research. Circulation. 2005; 111: 697-716. doi: 10.1161/01.CIR.0000154900.76284.F6.
21. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma without the use of12 the preparative ultracentrifuge. Clin Chem. 1972; 18: 499-502. doi: 10.1093/clinchem/18.6.499.
22. Bjornsen K, Aven T. Risk aggregation: what does it really mean? Reliab Eng Syst Saf. 2019; 191: 106524. https://doi.org/10.1016/j.ress.2019.10652.
23. Gaziano JM, Hennekens CH, O'Donnell CJ, Breslow JL, Buring JE. Fasting triglycerides, high-density lipoprotein, and risk of myocardial infarction. Circulation. 1997; 96: 2520-2525. doi: 10.1161/01.CIR.96.8.2520.
24. Barua L, Banik PC, Shariful Islam SM, Faruque M. Application of country-specific Globorisk score to estimate next 10 years risk of cardiovascular diseases and its associated predictors among postmenopausal rural women of Bangladesh: a cross-sectional study in a primary care setting. Lifestyle Med. 2021; 2: e32. Available in: https://doi.org/10.1002/lim2.32
25. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet. 2004; 364: 937-952. doi: 10.1016/S0140-6736(04)17018-9.
26. Lanas F, Avezum A, Bautista LE, Diaz R, Luna M, Islam S et al. Risk factors for acute myocardial infarction in Latin America: the INTERHEART Latin American study. Circulation. 2007; 115: 1067-1074. doi: 10.1161/CIRCULATIONAHA.106.633552.
27. Ciruzzi M, Schargrodsky H, Pramparo P, Rivas Estany E, Rodriguez Naude L, De la Noval Garcia R et al. Attributable risks for acute myocardial infarction in four countries of Latin America. Medicina. (Buenos Aires). 2003; 63: 697-703.
28. Cohorts Consortium of Latin America and the Caribbean (CC-LAC). Derivation, internal validation, and recalibration of a cardiovascular risk score for Latin America and the Caribbean (Globorisk-LAC): A pooled analysis of cohort studies. The Lancet Regional Health – Americas. 2022;9: 100258. https://doi.org/10.1016/j.lana.2022.100258.
29. Cohorts Consortium of Latin America and the Caribbean (CC-LAC). Derivation, internal validation, and recalibration of a cardiovascular risk score for Latin America and the Caribbean (Globorisk-LAC): a pooled analysis of cohort studies. Lancet Reg Health Am. 2022; 9: 100258. Available in: https://doi.org/10.1016/j.lana.2022.100258
30. Lajous M, Ortiz-Panoso E, Monge A, Santoyo-Vistrain R, García-Anaya A, Yunes-Díaz E et al. Cohort profile: the Mexican teachers' cohort (MTC). Int J Epidemiol. 2017; 46 (2): e10. doi: 10.1093/ije/dyv123.
31. Aguilar M, Muñoz-Aguirre P, Cortés-Valencia A, Flores-Torres MH, Catzin-Kuhlmann A, López-Ridaura R et al. Sun exposure and intima-media thickness in the mexican teachers' cohort study. J Womens Health (Larchmt). 2023; 32: 366-374. doi: 10.1089/jwh.2022.0135.
32. Denova-Gutiérrez E, Flores YN, Gallegos-Carrillo K, Ramírez-Palacios P, Rivera-Paredez B, Muñoz-Aguirre P et al. Health workers cohort study: methods and study design. Salud Publica Mex. 2016; 58: 708-716. Available in: http://dx.doi.org/10.21149/spm.v58i6.8299.
33. Morales LS, Flores YN, Leng M, Sportiche N, Gallegos-Carrillo K, Salmerón J. Risk factors for cardiovascular disease among Mexican-American adults in the United States and Mexico: a comparative study. Salud Publica Mex. 2014; 56: 197-205. doi: 10.21149/spm.v56i2.7335.
34. Bernal-Reyes R, Icaza-Chávez ME, Chi-Cervera LA, Remes-Trocheb JM, Amieva-Balmori M, Priego-Parra BA et al. Prevalence and clinical-epidemiologic characteristics of a Mexican population with metabolic (dysfunction) associated fatty liver disease: an open population study. Rev Gastroenterol Mex. 2023; 88: 199-207.
35. Rojas-Martínez R, Aguilar-Salinas CA, Romero-Martínez M, Castro-Porras L, Gómez-Velasco D, Mehta R. Trends in the prevalence of metabolic syndrome and its components in Mexican adults, 2006-2018. Salud Publica Mex. 2021; 63: 713-724. doi: 10.21149/12835.
36. Sohail M, Palma-Martínez MJ, Chong AY, Quinto-Cortés CD, Barberena-Jonas C, Medina-Muñoz SG et al. Mexican Biobank advances population and medical genomics of diverse ancestries. Nature. 2023; 622: 775-783. doi: 10.1038/s41586-023-06560-0.
37. García-Ortiz H, Barajas-Olmos F, Contreras-Cubas C, Córdova EJ, Centeno-Cruz F, Mendoza-Caamal EA et al. The genomic landscape of Mexican Indigenous populations brings insights into the peopling of the Americas. Nat Commun. 2021; 12: 5942. Available in: https://doi.org/10.1038/s41467-021-26188-w
38. Murguía-Romero M, Jiménez-Flores JR, Sigrist-Flores SC, Espinoza-Camacho MA, Jiménez-Morales M, Piña E et al. Plasma triglyceride/HDL-cholesterol ratio, insulin resistance, and cardiometabolic risk in young adults. J Lipid Res. 2013; 54: 2795-2279. doi: 10.1194/jlr.M040584.
39. Jeppesen J, Hein HO, Suadicani P, Gyntelberg F. Relation of high TG-low HDL cholesterol and LDL cholesterol to the incidence of ischemic heart disease. An 8-year follow-up in the Copenhagen male study.

Arterioscler Thromb Vasc Biol. 1997; 17: 1114-1120. doi: 10.1161/01.atv.17.6.1114.
40. Kosmas CE, Rodriguez Polanco S, Bousvarou MD, Papakonstantinou EJ, Peña Genao E et al. The triglyceride/high-density lipoprotein cholesterol (TG/HDL-C) ratio as a risk marker for metabolic syndrome and cardiovascular disease. Diagnostics (Basel). 2023; 13: 929. doi: 10.3390/diagnostics13050929.
41. Yokoyama K, Tani S, Matsuo R, Matsumoto N. Increased triglyceride/high-density lipoprotein cholesterol ratio may be associated with reduction in the low-density lipoprotein particle size: assessment of atherosclerotic cardiovascular disease risk. Heart Vessel. 2019; 34: 227-236. doi: 10. 1007/s00380-018-1247-9.
42. Gutiérrez-Solis AL, Datta Banik S, Méndez-González RM. Prevalence of metabolic syndrome in Mexico: A systematic review and meta-analysis. Metab Syndr Relat Disord. 2018; 16: 395-405. doi: 10.1089/met.2017.0157.
43. Das Pradhan A, Glynn RJ, Fruchart J-C, MacFadyen JG, Zaharris ES, Everett BM et al. Triglyceride lowering with Pemafibrate to reduce cardiovascular risk. N Engl J Med. 2022; 387: 1923-1934. doi: 10.1056/NEJMoa2210645.
44. Rubins HB, Rubins SJ, Collins D, Fye CL, Anderson JW, Elam MB et al. Gemfibrozil for the secondary prevention of coronary heart disease in men with low levels of high-density lipoprotein cholesterol. N Engl J Med. 1999; 341: 410-418. doi: 10.1056/NEJM199908053410604.
45. Tenenbaum A, Fisman EZ. "If it ain't broke, don't fix it": a commentary on the positive-negative results of the ACCORD Lipid study. Cardiovasc Diabetol. 2010; 9: 24. doi: 10.1186/1475-2840-9-24.
46. Essilfie G, Shavelle DM, Tun H, Platt K, Kobayashi R, Mehra A et al. Association of elevated triglycerides and acute myocardial infarction in young Hispanics. CRM. 2016; 17: 510-514. Available in: http://dx.doi.org/10.1016/j.carrev.2016.06.001
47. Arca M, Colivicci F, D'Erasmo L, Borghi C, Veronesi C et al. Association of hypertriglyceridemia with all-cause mortality and atherosclerotic cardiovascular events in a low-risk Italian population: the TG-REAL Retrospective Cohort Analysis. J Am Heart Assoc. 2020; 9: e015801. doi: 10.1161/JAHA.119.015801.
48. Saadatagah S, Pasha AK, Alhalabi L, Sandhyavenu H, Farwati M, Smith CY et al. Coronary heart disease risk associated with primary isolated hypertriglyceridemia; a population□based study. J Am Heart Assoc. 2021; 10: e019343. doi: 10.1161/JAHA.120.019343.
49. Farnier M, Zeller M, Masson D, Cottin Y. Triglycerides and risk of atherosclerotic cardiovascular disease: an update. Arch Cardiovasc Dis. 2021; 114: 132-139. Available in: https://doi.org/10.1016/j.acvd.2020.11.006.
50. Sarwar N, Danesh J, Eiriksdottir G, Sigurdsson G, Wareham N, Bingham S et al. Triglycerides and the risk of coronary heart disease. 10 158 incident cases among 262 525 participants in 29 western prospective studies. Circulation. 2007; 115: 450-458. https://doi.org/10.1161/CIRCULATIONAHA.106.637793
51. Aberra T, Peterson ED, Pagidipati NJ, Mulder H, Wojdyla DM, Philip S et al. The association between triglycerides and incident cardiovascular disease: what Is "optimal"? J Clin Lipidol. 2020; 14: 438-447.e3. doi: 10.1016/j.jacl.2020.04.009.
52. Vallejo-Vaz AJ, Corral P, Schreier L, Raya KK. Triglycerides and residual risk. Curr Opin Endocrinol Diabetes Obes. 2020; 27: 95-103. doi: 10.1097/MED.0000000000000530.
53. Ye X, Kong W, Zafar MI, Chen L-L. Serum triglycerides as a risk factor for cardiovascular diseases in type 2 diabetes mellitus: a systematic review and meta-analysis of prospective studies. Cardiovasc Diabetol. 2019; 18: 48. Available in: https://doi.org/10.1186/s12933-019-0851-z
54. Estrada-García T, Meaney A, López-Hernández D, Meaney E, Sánchez-Hernández O, Rodríguez-Arellano E et al. Hypertension and lipid triad are the most important attributable risks for myocardial infarction in a middle-class urban Mexican population. Ann Nutr Metab 2013; 63 (Suppl 1): 1343 (abstract).

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Complete heart block in an adult patient with isolated congenitally corrected transposition of the great arteries and *situs inversus*

Bloqueo auriculoventricular completo en un paciente adulto con transposición congénitamente corregida de grandes arterias aisladas y situs inversus

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Keywords:
congenitally corrected transposition of the great arteries, complete heart block, congenital heart disease, adult, *situs inversus*.

Palabras clave:
transposición congénitamente corregida de grandes arterias, bloqueo auriculoventricular completo, cardiopatía congénita, adulto, situs inversus.

ABSTRACT

Congenitally corrected transposition of the great arteries (ccTGA) is a rare congenital heart disease. Many patients remain asymptomatic when no cardiac lesions are present (isolated ccTGA). In ccTGA, the atrioventricular conduction system may be abnormal, resulting in progressive dysfunction and, eventually, a Complete Heart Block (CHB). In ccTGA with *situs inversus*, the conduction pathway resembles a normal tract, but the atrioventricular node is located posteriorly. Compared with *situs solitus*, spontaneous CHB is uncommon in ccTGA patients with *situs inversus*. We report the case of a 40-year-old female without previous medical conditions or having a family or personal history of heart disease presented with loss of consciousness. At admission, electrocardiography revealed bradycardia, CHB, and hypertrophy of the right ventricle. Cardiovascular imaging tests detected an isolated ccTGA with *situs inversus* and levocardia. The Holter monitor revealed intermittent CHB. Exercise testing demonstrated chronotropic incompetence. An epicardial pacemaker was implanted, and the patient was discharged symptom-free. At a two-years follow-up remains asymptomatic. This case illustrates the importance of cardiovascular imaging in defining cardiac anatomy, ruling out other congenital heart defects, and facilitating pacing therapy in complex congenital heart disease. Congenital heart disease patients should be treated by a multidisciplinary team with expertise in permanent pacing.

RESUMEN

La transposición congénitamente corregida de grandes arterias (TccGA) es una cardiopatía congénita poco común. Muchos pacientes permanecen asintomáticos cuando no hay lesiones cardiacas presentes (TccGA aislada). En la TccGA, el sistema de conducción auriculoventricular puede ser anormal, lo que resulta en una disfunción progresiva y, finalmente, en un bloqueo auriculoventricular (BAV) completo. En la TccGA con situs inversus, la vía de conducción se asemeja a un tracto normal, pero el nódulo auriculoventricular se ubica posteriormente. En comparación con el situs solitus, el BAV completo espontáneo es poco común en pacientes con TccGA con situs inversus. Se presenta el caso de una mujer de 40 años sin enfermedades previas ni con antecedentes familiares o personales de cardiopatías que presentó pérdida de conciencia. Al ingreso, el electrocardiograma reveló bradicardia, BAV completo e hipertrofia del ventrículo derecho. Estudios de imagen cardiaca detectaron una TccGA aislada con situs inversus y levocardia. El monitoreo Holter reveló BAV completo intermitente. Las pruebas de esfuerzo demostraron incompetencia cronotrópica. Se le implantó un marcapasos epicárdico y la paciente fue dada de alta asintomática. Tras dos años de seguimiento permaneció asintomática. Este caso ilustra la importancia de imagen cardiovascular para definir la anatomía cardiaca, descartar otras cardiopatías congénitas y facilitar la terapia de estimulación cardiaca en cardiopatías congénitas complejas. Los pacientes con cardiopatías congénitas deben ser tratados por un equipo multidisciplinario con experiencia en estimulación cardiaca permanente.

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INTRODUCTION

Acongenitally corrected transposition of the great arteries (ccTGA) is a rare congenital heart disease characterized by discordant atrioventricular and ventriculo-arterial connections.[1,2] The right atrium (RA) enters the morphological left ventricle (LV), which rises to the pulmonary artery, and the left atrium (LA) communicates with the morphological right ventricle (RV), which gives rise to the aorta.[2] Among the associated lesions are ventricular septal defects (70%), pulmonary stenosis (40%), and dysplastic systemic tricuspid valves.[1] The clinical course of adults with ccTGA is relatively unknown, with cases of isolated ccTGA rarely developing complications before adulthood.[1,3,4] In most cases, the position of the atrioventricular node and the bundle of his is abnormal, resulting in abnormal atrioventricular conduction.[1] In patients with ccTGA and *situs inversus*, complications are lower than in patients with situs solis, including Complete Heart Block (CHB).[4] Visceroatrial *situs inversus* with ccTGA is a rare congenital condition.[5,6] Given the rarity of this condition, there are limited reports of CHB in adult patients with isolated ccTGA and *situs inversus*. Therefore, we report a case of symptomatic intermittent CHB in an adult patient with ccTGA, *situs inversus*, and levocardia who required pacing therapy.

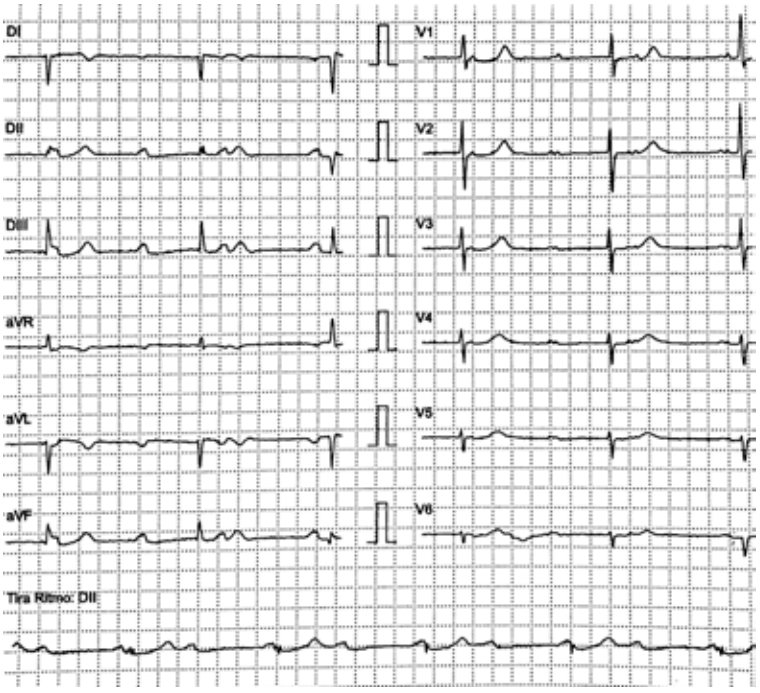

Figure 1: Initial 12-Lead electrocardiogram: atrioventricular dissociation, right ventricular hypertrophy, normal QRS voltage and duration, a prolonged QT interval, no ST-segment elevation or depression, and negative T waves in leads DI, aVR, and aVL.

CASE PRESENTATION

A 40-year-old female was admitted to the emergency department after briefly losing consciousness at work in the last 12 hours. The patient felt well before and immediately following the episode, and there was no apparent trauma or confusion. As part of her initial evaluation at another center, an electrocardiogram revealed a CHB *(Figure 1)*, which led to her referral to this facility. The patient denied having any previous medical conditions or having a family or personal history of heart disease and also denied taking any medications.

On examination at admission, she was afebrile, with a blood pressure of 125/67 mmHg and a heart rate of 40 beats/min. The cardiovascular examination revealed a high-pitched and loud grade 4/6 pansystolic murmur in the tricuspid valve area, which increased upon inspiration.

On admission, electrocardiography revealed a CHB with right ventricular hypertrophy *(Figure 2)*. In addition, the blood tests were relevant for high cholesterol and triglyceride levels, with the rest of the studies in the normal range *(Table 1)*.

Transesogapheal echocardiography revealed a mirror-image atrial arrangement, with right-sided LA connected to a morphological RV with an emerging aorta, a left-sided RA connected to a morphologic LV with an arising pulmonary artery, a right ventricular ejection fraction (RVEF) of 38%, an estimated pulmonary artery systolic pressure of 106 mmHg, mild pulmonary regurgitation, intact interatrial and interventricular septums, moderate tricuspid regurgitation, and no intracavitary thrombus. Cardiac computed tomography revealed an isolated ccTGA with visceroatrial *situs inversus* and levocardia *(Figures 3 and 4)*.

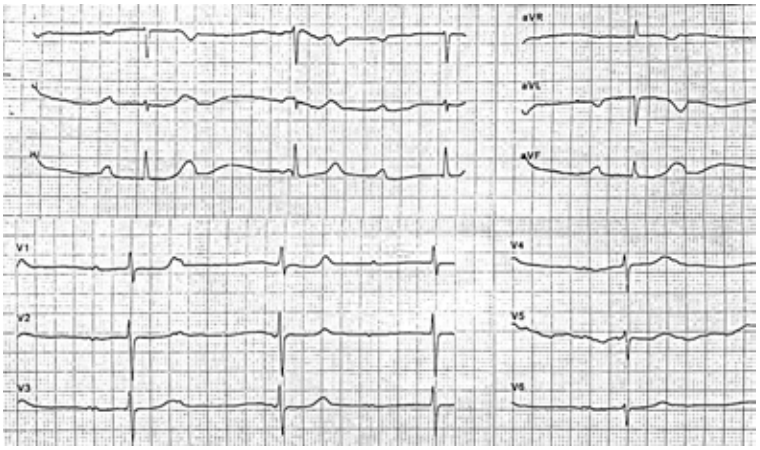

Figure 2: 12-Lead electrocardiogram on admission: atrioventricular dissociation, right ventricular hypertrophy, normal QRS voltage and duration, a prolonged QT interval, no ST-segment elevation or depression, and negative T waves in leads DI, aVR, and aVL.

The Holter monitor showed intermittent CHB alternated with sinus rhythm and premature ventricular contractions *(Figure 5)*. In the exercise testing, the patient achieved 4.6 METS, showed chronotropic incompetence, and was suspended by fatigue *(Figure 6)*.

Based on the results of these studies, a permanent epicardial pacemaker was implanted; the patient was discharged symptom-free and with a functioning pacemaker. At a two-year follow-up, the patient remained asymptomatic, and a TTE showed RVEF 38% with moderate tricuspid regurgitation with a functional pacemaker.

DISCUSSION

Described by Von Rokitansky in 1875, ccTGA accounts for approximately 0.5% of all congenital heart defects, with limited information on adult patients.[7]

Concerning the conduction system, the atrioventricular node and His bundle follow an unusual path, and many patients have dual AV nodes. Second anomalous AV nodes and bundles are usually anterior, and the long, penetrating bundle is prone to fibrosis with increasing age. As a result, the conduction system is somewhat tenuous, with the

Table 1: Blood tests on admission.

Test	Result	Reference [range]
Leukocytes (10^3/µL)	7.02	5-10
Hemoglobin (g/dL)	14.4	14-18
Hematocrit (%)	45.7	42-52
MCV (fL)	78.9	80-95
MCH (pg)	24.9	27-31
MCHC (g/dL)	31.7	32-36
Platelets (10^3/µL)	280	130-400
Glucose (mg/dL)	103	74-106
Creatinine (mg/dL)	1.02	0.6-1.2
Urea (mg/dL)	30.3	18-50
AST (U/L)	39	13-39
ALT (U/L)	52	7-52
Total bilirrubin (mg/dL)	0.56	0.3-1
Albumin (g/dL)	3.9	3.5-5.7
Globulin (g/dL)	2.9	1.9-2.7
Total protein (g/dL)	6.8	6.4-8.9
LDH (U/L)	195	140-271
GGT (U/L)	60	9-64
AP (U/L)	114	34-104
Creatin kinase (U/L)	83	21-232
Creatin kinase MB (U/L)	13.8	0-10
Troponin I (ng/L)	< 1.5	0-19
Sodium (mEq/L)	136	136-145
Potassium (mEq/L)	4.2	3.5-5.1
Chloride (mEq/L)	106	98-107
Total cholesterol (mg/dL)	223	0-200
Triglyceride (mg/dL)	232	0-150
HDL (mg/dL)	46	32-92
HbA1c (%)	5.7	4-6.5
Total T3 (ng/mL)	0.87	0.87-1.78
Total T4 (µg/dL)	8.41	6.09-12.23
Free T4 (ng/dL)	0.83	0.61-1.12
TSH (UI/mL)	1.73	0.34-5.6

MCV = mean corpuscular volume. MCH = mean corpuscular hemoglobin. MCHC = mean corpuscular hemoglobin concentration. AST = aspartate aminotransferase. ALT = alanine aminotransferase. LDH = lactate dehydrogenase. GGT = gamma glutamyltransferase. AP = alkaline phosphatase. HDL = high-density lipoprotein. HbA1c = glycosylated hemoglobin. T3 = thiiodothyronine. T4 = thyroxine. TSH = thyroid-stimulating hormone.

incidence of complete AV block rising at 2% per year.[2,8,9]

In 10% of ccTGA cases, *situs inversus* is present; in this condition, the conduction pathway resembles a normal tract with an atrioventricular node located posteriorly.[4,10] Levocardia usually exists with *situs solitus*, but dextrocardia can complicate the anatomical presentation in approximately 25% of the cases.[10]

In the literature, no significant differences in ventricular septal defect, pulmonary tract stenosis, and long-term mortality were found between ccTGA with *situs inversus* or *situs solitus*. There was, however, a lower incidence of nonsurgically related CHB (0 vs 42%, p = 0.032), development of CHB in 7.4 years (12.5 vs 57%, p = 0.045), tricuspid valve anomalies (0.0 vs 50%, p = 0.01), overall complications (25 vs 73%, p = 0.034) and heart failure (p = 0.038).[4]

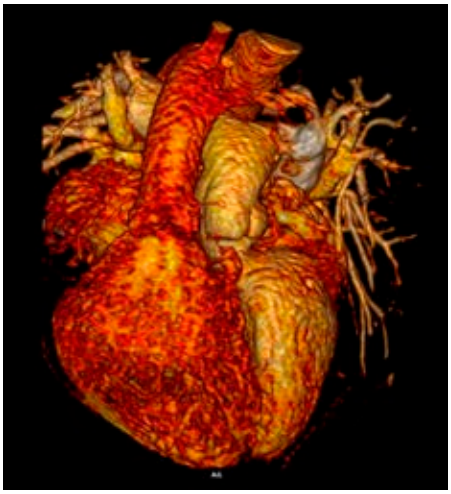

Figure 4: Cardiac computed tomography: 3D reconstruction exhibiting right-sided anterior aorta emerging from right ventricle with a left-sided posterior pulmonary trunk arising from left ventricle.
RV = right ventricle. LV = left ventricle.

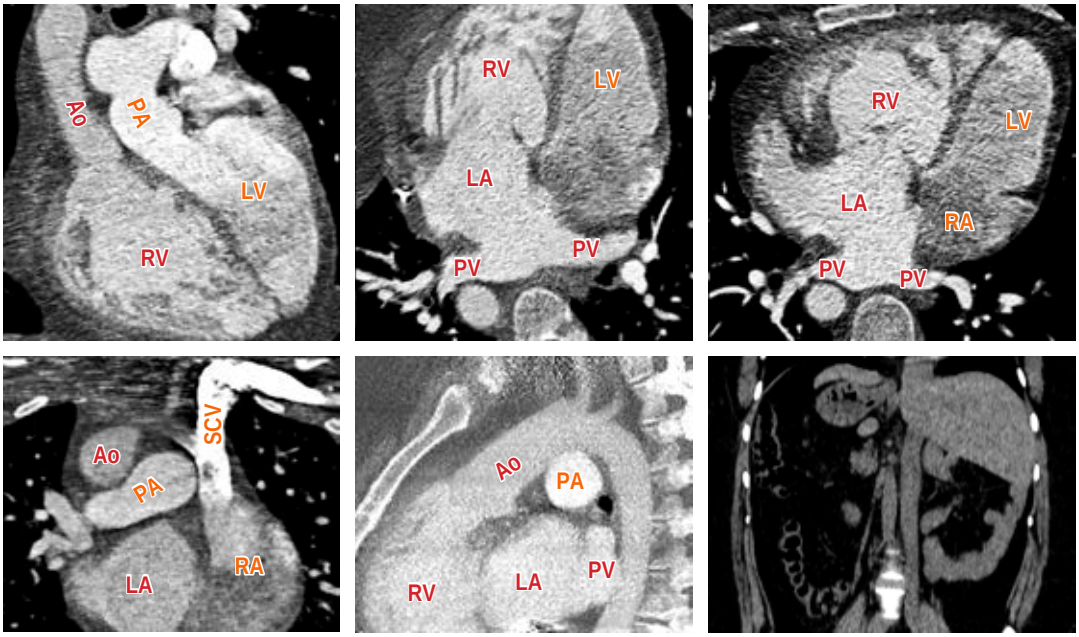

Figure 3: Cardiac computed tomography: visceroatrial *situs inversus*: left-sided inferior cava vein, right-sided abdominal aorta, right-sided liver, left-sided stomach, mirror-image atrial arrangement with L-looping of ventricles. Ventriculoarterial discordance: a right-sided morphologic right ventricle with an arising aorta and a left-sided morphologic left ventricle with an emerging pulmonary artery. Atrioventricular discordance: right-sided left atrium receiving pulmonary vein drainage communicates with the tricuspid valve to right ventricle, while left-sided right atrium receiving cava vein drainage communicates with the mitral valve to left ventricle.
RV = right ventricle. LV = left ventricle. LA = left atrium. RA = right atrium. Ao = aortic. PA = pulmonary artery. PV = pulmonary vein. SCV = superior cava vein.

The radiographic and electrocardiographic findings often lead to the diagnosis of ccTGA when symptoms are absent and physical findings are subtle.[1,8,10] Electrocardiograms frequently reveal ventricular hypertrophy and atrial enlargement, even in the absence of other cardiac lesions.[1,10] To confirm the diagnosis of ccTGA, cardiac imaging is essential, which aids in defining cardiac anatomy despite clinical suspicion.[1]

Pacemaker implantation may be justified in patients who suffer from symptomatic chronotropic incompetence. Current recommendations for cardiac pacing in patients with congenital heart disease and high-degree atrioventricular block are as follows: a)

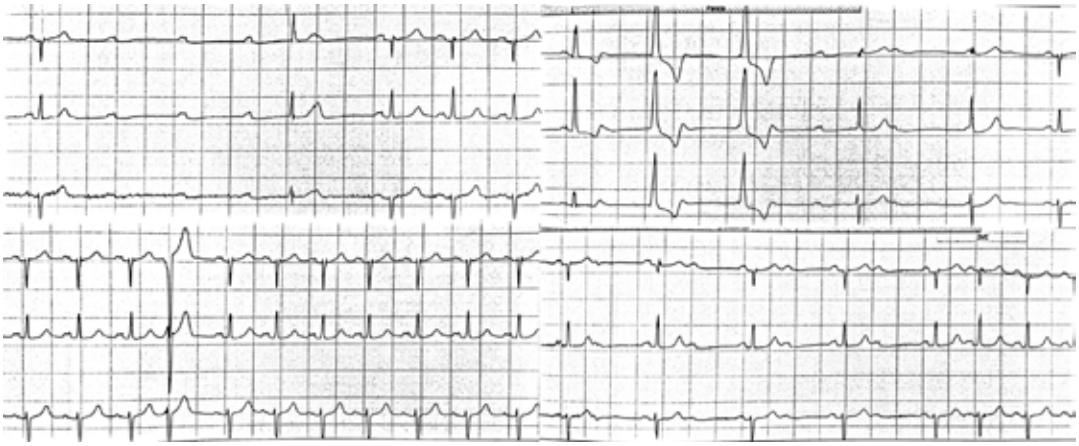

Figure 5: Holter monitor: intermittent complete heart block alternated with sinus rhythm and premature ventricular contractions.

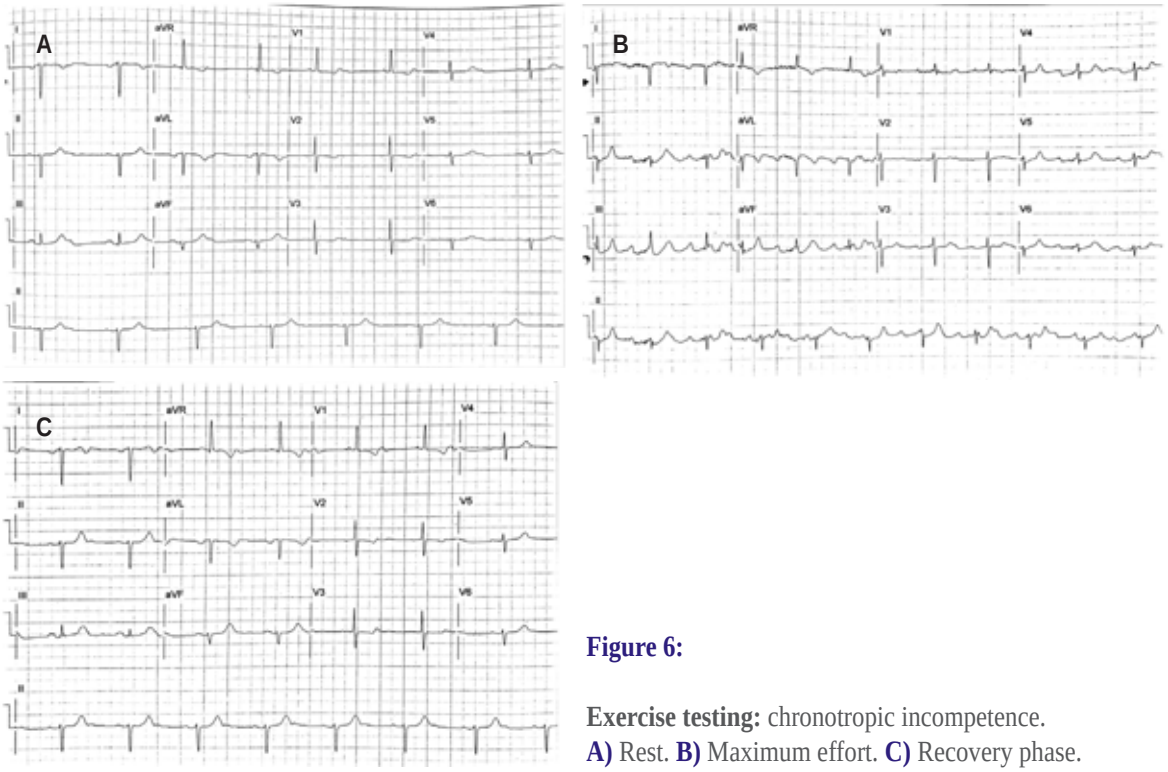

Figure 6:

Exercise testing: chronotropic incompetence. **A)** Rest. **B)** Maximum effort. **C)** Recovery phase.

symptoms, b) pauses > 3 times the cycle length of the ventricular escape rhythm, c) broad QRS escape rhythms, d) prolonged QT interval, e) complex ventricular ectopy, and f) the mean daytime heart rate < 50 beats/min.[11]

The patients have a reduced life expectancy; 50% would still be alive at 60 years of age if they did not have associated lesions. Additionally, no evidence exists that medical treatment is associated with preventing heart failure or improving outcomes.[1]

Surgery is generally reserved for symptomatic and asymptomatic patients with evidence of deteriorating RV function and worsening tricuspid regurgitation. Intervention in asymptomatic patients with preserved RV and tricuspid valve functions without any other septal defects is controversial.[10]

CONCLUSIONS

Isolated ccTGA usually does not manifest symptoms until adulthood; CHB results from abnormalities in the atrioventricular conduction system associated with discordant atrioventricular and ventriculoarterial connections. Patients with *situs inversus* and ccTGA have a lower incidence of CHB than those with *situs solitus*. In this group of patients, cardiovascular imaging studies are essential for defining cardiac anatomy and facilitating pacing therapy.

REFERENCES

1. Baumgartner H, De Backer J, Babu-Narayan SV, Budts W, Chessa M, Diller GP et al. 2020 ESC Guidelines for the management of adult congenital heart disease. Eur Heart J. 2021; 42(6): 563-645.
2. Warnes CA. Transposition of the great arteries. Circulation. 2006; 114(24): 2699-2709.
3. Auer J, Pujol C, Maurer SJ, Nagdyman N, Ewert P, Tutarel O. Congenitally corrected transposition of the great arteries in adults-a contemporary single center experience. J Cardiovasc Dev Dis. 2021; 8(9): 113.
4. Oliver JM, Gallego P, Gonzalez AE, Sanchez-Recalde A, Brett M, Polo L et al. Comparison of outcomes in adults with congenitally corrected transposition with *situs inversus* versus *situs solitus*. Am J Cardiol. 2012; 110(11): 1687-1691.
5. Sohns JM, Steinmetz M, Schneider H, Fasshauer M, Staab W, Kowallick JT et al. *Situs inversus* totalis with congenitally corrected transposition of the great arteries: insights from cardiac MRI. Springerplus. 2014; 3: 601.
6. Lachhab F, Ajaja R, Fikri I, Amellal M, Otmani Y, Amri R et al. Transposition of the great arteries in *situs inversus totalis*. World J Pediatr Congenit Heart Surg. 2011; 2(3): 520-522.
7. Amaral F, Valente AM, Manso PH, Gali LG, Braggion-Santos MF, Rocha JM et al. Congenitally Corrected Transposition of the Great Arteries in the Adult. Braz J Cardiovasc Surg. 2022; 37(4): 534-545.
8. Kutty S, Danford DA, Diller GP, Tutarel O. Contemporary management and outcomes in congenitally corrected transposition of the great arteries. Heart. 2018; 104(14): 1148-1155.
9. Spigel Z, Binsalamah ZM, Caldarone C. Congenitally corrected transposition of the great arteries: anatomic, physiologic repair, and palliation. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu. 2019; 22: 32-42.
10. Kumar TKS. Congenitally corrected transposition of the great arteries. J Thorac Dis. 2020; 12(3): 1213-1218.
11. Glikson M, Nielsen JC, Kronborg MB, Michowitz Y, Auricchio A, Barbash IM et al. 2021 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy. Eur Heart J. 2021; 42(35): 3427-3520.

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An unexpected germ: atypical presentation of *Vagococcus fluvialis* pocket infection in a cardiac pacing device

Un germen inesperado: presentación atípica de infección de bolsillo de dispositivo de estimulación cardiaca por Vagococcus fluvialis

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Keywords:
cardiac implantable electronic devices, complications, pocket infection, endocarditis, *Vagococcus fluvialis*.

Palabras clave:
dispositivos de estimulación eléctrica cardiaca implantables, complicaciones, infección de bolsillo, endocarditis, Vagococcus fluvialis.

ABSTRACT

Advances in cardiac implantable electronic devices (CIED) technology have enabled them to play a relevant role in heart disease. Although complications have decreased, CIED-related infection persists as one of the problems that has the greatest impact on the patient and the health system. Infections due to unusual germs generate additional morbidity and increased costs of care but can have a favorable course with early diagnosis and treatment. The case of a patient with clinical signs and symptoms of CIED pocket infection by *Vagococcus fluvialis*, without systemic infection or endocarditis, is presented for the first time in the literature. Timely treatment allowed a favorable evolution. New diagnostic and therapeutic challenges come from the hand of more complex patients.

RESUMEN

El avance en la tecnología de los dispositivos de estimulación eléctrica cardiaca (DEEC) ha permitido que ocupen un papel relevante en enfermedades cardiacas. Aunque las complicaciones han disminuido, la infección relacionada con DEEC persiste como uno de los problemas que mayor impacto tienen para el paciente y el sistema de salud. Las infecciones por gérmenes inusuales generan morbilidad adicional y costos aumentados en la atención, pero pueden cursar con una evolución favorable con un diagnóstico y tratamiento tempranos. Se presenta por primera vez en la literatura, el caso de un paciente con signos y síntomas clínicos de infección de bolsillo de DEEC por Vagococcus fluvialis, *sin infección sistémica ni endocarditis. El tratamiento oportuno permitió una evolución favorable. Nuevos retos diagnóstico y terapéuticos vienen de la mano de pacientes más complejos.*

INTRODUCTION

Advances in cardiac implantable electronic devices (CIED) technology have enabled them to play a relevant role in complex diseases such as heart failure or sudden arrhythmic death. Although complications have decreased, CIED-related infection persists as one of the problems that has the greatest impact on the patient and the health system.[1]

Antibiotic prophylaxis has consistently reduced infection rates[2] and is a settled recommendation.[3,4] However, various series report current infection rates close to 1-2%. The causative agents are usually *Staphylococcus aureus* and *Staphylococcus epidermidis* (or another coagulase-negative). Other infectious microorganisms such as *Enterococcus*, *Streptococcus*, *Candida*, etc.[4] have also been reported. Atypical microorganisms, such as *Vagococcus fluvialis*, have a different clinical course, from slowly developing infections to rapidly progressive courses.[5]

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CASE PRESENTATION

An 84-year-old male patient with a history of type 2 diabetes mellitus, arterial hypertension, atrial fibrillation, and heart failure with reduced left ventricular ejection fraction (LVEF) (30%). Additionally, an atrioventricular block was documented, reason for which he has a cardioresynchronizer (CRTD) as a primary prevention strategy and treatment of heart failure.

After a trauma in the vicinity of the device implantation site, a larval picture of local inflammatory signs began that was intensifying and made him consult four months after the initial event. Significant edema, warmth, and redness in the device area are documented on initial evaluation. He had no fever or compromised general condition. The initial paraclinical tests included a normal blood count and CRP. A transesophageal echocardiography was performed, which showed a normal LVEF and ruled out endocarditis. Blood cultures were negative. A PET CT was performed that showed increased uptake, thickening of the walls of the generator pocket, a moderate amount of surrounding inflammatory fluid, and mediastinal lymphadenopathies *(Figure 1)*.

Due to evidence suggestive of infection at the device implant site, he was taken to a CRTD explant with electrode extraction and temporary pacemaker implantation.

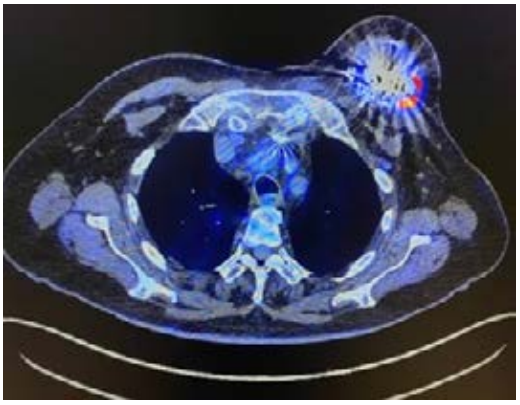

Figure 1: Positron emission tomography-computed tomography (PET-CT) scan: hyperenhancement in the pocket area, thickening of the generator pocket walls, moderate amount of inflammatory fluid around it, and mediastinal adenopathies.

During the procedure, abundant fibrotic but very friable tissue was observed that compromised the capsule and the underlying tissue, which was mostly resected and without evidence of purulent material coming out. Subsequently, manual extraction of electrodes is performed. Resected tissue and electrode tips are sent for microbiological analysis and pathology *(Figure 2)*.

Immediately after withdrawal, empirical antibiotic therapy recommended by infectology with cefazolin and daptomycin is initiated, which is received for three days. The subsequent evolution of the patient is favorable. The final report of the electrode and tissue culture shows growth of *Vagococcus fluvialis* *(Figure 3)*, for which antibiotic therapy with ampicillin-sulbactam was adjusted, which he received for an additional 11 days. At the end of the antibiotic cycle, a single-chamber pacemaker was implanted on the contralateral side, with antibiotic prophylaxis with vancomycin.

DISCUSSION

Improvements in CIED technology have allowed their use in increasingly complex diseases and patients. Likewise, the longevity of the population and the higher prevalence of heart rhythm diseases in older patients explain the notable increase in implantation rates in various countries.[6] Concomitantly, the risks related to the procedure may increase given the profile of patients operated on: CIED-related infection has significant impacts on morbidity, mortality, and costs for the health system,[7] therefore it is important to perform an active search once the suspicion is made. Antibiotic prophylaxis has proven to be an indispensable resource to reduce the risk of infection. Several studies have evaluated the use of combined therapies and compared them with cephalosporins as an initial alternative. However, they have not consistently shown additional benefits: incremental therapy with vancomycin reduced the risk of infection by 23% (although not statistically significantly).[8]

Despite prophylaxis, infection rates between 1-4% continue to be reported in various series. In a recent study reported by the authors, the device infection rate was less than 1% in

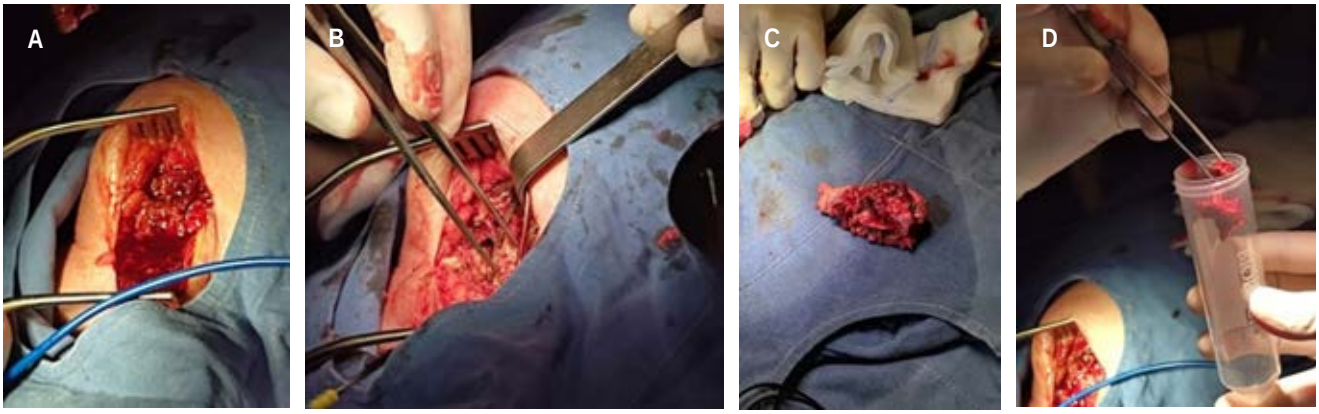

Figure 2: A-B) Fatty fibrotic tissue involving capsule and underlying tissue, absence of purulent material. **C)** Very friable tumor-like tissue, which is mostly resected. **D)** Sent for analysis, including electrode tip.

997 patients.[9] In addition, it is known that multiple factors can influence a higher risk of infection: diabetes, heart failure, previous anticoagulation, the presence of two or more electrodes, and the time of the procedure, among others.[10]

Related risk factors can be classified as patient-related, procedure-related, and device-related. Regarding the patient, chronic kidney disease, diabetes mellitus, chronic obstructive pulmonary disease, the use of corticosteroids, and a history of previous device infection are important. In those related to the procedure, postoperative hematoma and the use of anticoagulants are important. Moreover, in relation to the device, abdominal pockets, and epicardial leads, the use of a defibrillator (with or without resynchronization therapy) increases the risk.[10,11] The PADIT authors found significant risk factors for infection and created a score to predict that risk (prior procedures [P], age [A], depressed renal function [D], immunocompromised [I], and procedure type [T]). A score ≥ 7 poses a risk of hospitalization for infection $\geq 3.4\%$.[12]

The pathogens responsible for the infection are predominantly gram-positive (72.3%), with Staphylococcus aureus (31.6%) and coagulase-negative *Staphylococcus* (29.9%) being the most frequent.[8] Less frequent germs are *Corynebacterium species*, *Propionibacterium acnes*, *Gram-negative bacilli*, *Candida* spp, and non-tuberculous mycobacteria.

There are even unusual germs called atypical. A recent series found that they were responsible for 5.4% of device infections. Among the pathogens identified were *Pantoea species*, *Kocuria species*, *Cutibacterium acnes*, *Corynebacterium tuberculostearicum*, *Corynebacterium striatum*, *Stenotrophomonas maltophilia*, and *Pseudozyma ahidis*. They are recognized as pathogens when there are two positive blood cultures or tissue or electrode cultures with the growth of said microorganism.[5] Infection by such atypical germs usually evolves favorably and responds well to directed antibiotic treatment and removal of the device.

The case presented is, to our knowledge, the first reported case of CIED infection related to *Vagococcus fluvialis*. *Vagococcus* spp. is a gram-positive, catalase-negative, facultatively anaerobic coccus that comprises 14 species, of which only 2 cause infection in animals, including *Vagococcus fluvialis*. It is associated with infections in pigs, cattle, cats, and horses.[13] It was initially described by Hashimoto et al. in 1974, then in 1989, it was classified by Collins et al.,[14] but the first time it was reported in humans was in 1997 by Teixeira et al.,[15] when it was isolated from the peritoneal fluid of a dialysis patient who had been bitten by a lamb. Subsequently, it has been reported in bone infections,[16] dental infections,[17] and in some cases of endocarditis.[18] *Vagococcus fluvialis* infections usually occur in skin, soft,

and osteoarticular tissues and more frequently in diabetic patients. In humans, it is difficult to identify their role as a pathogen because they are usually part of polymicrobial cultures.[13]

The evolution of the patient was very favorable after the extraction. Latent presentation, with few systemic inflammatory symptoms and scant inflammatory response in paraclinical tests, should guide the search for unusual germs. The clinical history, always valuable, shows how a trauma near the device implant site could be related to the development of the infection. Although common pathogens should always be sought out, we can sometimes find unusual culprits.

CONCLUSIONS

Infection of the pocket of cardiac electrical stimulation devices is a known problem that increases the morbidity and mortality of patients, therefore it is essential to perform an active search once the suspicion is made. The diagnostic process not only involves sophisticated paraclinical tests, but also a clinical history that evaluates risk factors and circumstances that favor certain types of germs. Early, targeted treatment based on an interdisciplinary group favors the best outcomes.

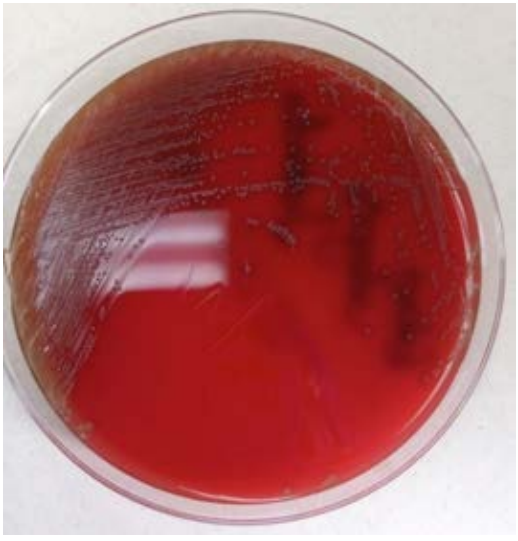

Figure 3: Colony formation of *Vagococcus fluvialis* on MacConkey agar.

REFERENCES

1. Wilkoff BL, Boriani G, Mittal S, Poole JE, Kennergren C, Corey GR et al. Impact of cardiac implantable electronic device infection: a clinical and economic analysis of the WRAP-IT trial. Circ Arrhythm Electrophysiol. 2020; 13 (5): e008280.
2. De Oliveira JC, Martinelli M, Nishioka SA, Varejao T, Uipe D, Pedrosa AA et al. Efficacy of antibiotic prophylaxis before the implantation of pacemakers and cardioverter-defibrillators: results of a large, prospective, randomized, double-blinded, placebo-controlled trial. Circ Arrhythm Electrophysiol. 2009; 2 (1): 29-34.
3. Padfield GJ, Steinberg C, Bennett MT, Chakrabarti S, Deyell MW, Bashir J et al. Preventing cardiac implantable electronic device infections. Heart Rhythm. 2015; 12 (11): 2344-2356.
4. Longtin Y, Gervais P, Birnie DH, Wang J, Alings M, Philippon F et al. Impact of choice of prophylaxis on the microbiology of cardiac implantable electronic device infections: insights from the prevention of arrhythmia device infection trial (PADIT). Open Forum Infect Dis. 2021; 8 (11): ofab513.
5. Kohli U, Hazra A, Shahab A, Beaser AD, Aziz ZA, Upadhyay GA et al. Atypical pathogens associated with cardiac implantable electronic device infections. Pacing Clin Electrophysiol. 2021; 44 (9): 1549-1561.
6. Glikson M, Nielsen JC, Kronborg MB, Michowitz Y, Auricchio A, Barbash IM et al. 2021 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy. Eur Heart J. 2021; 42 (35): 3427-3520.
7. Sohail MR, Henrikson CA, Braid-Forbes MJ, Forbes KF, Lerner DJ. Mortality and cost associated with cardiovascular implantable electronic device infections. Arch Intern Med. 2011; 171 (20): 1821-1828.
8. Krahn AD, Longtin Y, Philippon F, Birnie DH, Manlucu J, Angaran P et al. Prevention of arrhythmia device infection trial: the PADIT trial. J Am Coll Cardiol. 2018; 72 (24): 3098-3109.
9. Gómez-Valencia AR, Aristizábal-Aristizábal J, Ocampo-Moreno D, Fernández-Turizo MJ, Galindo-Quintero MC, Vásquez-Trespalacios EM et al. Characterization of patients undergoing cardiac implantable electronic device implantation in a tertiary center: emphasis on complications. Cardiovasc Metab Sci. 2021; 32 (2): 72-81.
10. Polyzos KA, Konstantelias AA, Falagas ME. Risk factors for cardiac implantable electronic device infection: a systematic review and meta-analysis. Europace. 2015; 17 (5): 767-777.
11. Rattanawong P, Kewcharoen J, Mekraksakit P, Mekritthikrai R, Prasitlumkum N, Vutthikraivit W et al. Device infections in implantable cardioverter defibrillators versus permanent pacemakers: a systematic review and meta-analysis. J Cardiovasc Electrophysiol. 2019; 30 (7): 1053-1065.
12. Birnie DH, Wang J, Alings M, Philippon F, Parkash R, Manlucu J et al. Risk factors for infections involving cardiac implanted electronic devices. J Am Coll Cardiol. 2019; 74 (23): 2845-2854.
13. Racero L, Barberis C, Traglia G, Loza MS, Vay C, Almuzara M. Infections due to *Vagococcus* spp.

microbiological and clinical aspects and literature review. Enferm Infecc Microbiol Clin (Engl Ed). 2021; 39 (7): 335-339.
14. Collins MD, Ash C, Farrow JA, Wallbanks S, Williams AM. 16S ribosomal ribonucleic acid sequence analyses of lactococci and related taxa. Description of *Vagococcus fluvialis* gen. nov., sp. nov. J Appl Bacteriol. 1989; 67 (4): 453-460.
15. Teixeira LM, Carvalho MG, Merquior VL, Steigerwalt AG, Brenner DJ, Facklam RR. Phenotypic and genotypic characterization of *Vagococcus fluvialis*, including strains isolated from human sources. J Clin Microbiol. 1997; 35 (11): 2778-2781.
16. Matsuo T, Mori N, Kawai F, Sakurai A, Toyoda M, Mikami Y et al. *Vagococcus fluvialis* as a causative pathogen of bloodstream and decubitus ulcer infection: Case report and systematic review of the literature. J Infect Chemother. 2021; 27 (2): 359-363.
17. Schirrmeister JF, Liebenow AL, Pelz K, Wittmer A, Serr A, Hellwig E et al. New bacterial compositions in root-filled teeth with periradicular lesions. J Endod. 2009; 35 (2): 169-174.
18. Jadhav KP, Pai PG. A rare infective endocarditis caused by *Vagococcus fluvialis*. J Cardiol Cases. 2019; 20 (4): 129-131.

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External calcium modification technique to overcome a balloon uncrossable chronic total occlusion: a report of two cases and review of the literature

Técnica de modificación externa del calcio para superar una oclusión total crónica no superable con balón

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Keywords:
chronic total occlusion, balloon, uncrossable lesion, external calcium modification.

Palabras clave:
oclusión total crónica, balón, lesión incruzable, modificación externa del calcio.

ABSTRACT

Introduction: chronic total occlusion is the most challenging part of percutaneous coronary intervention. In balloon uncrossable lesions, the wire can be advanced throughout the lesion to the distal part of the vessel, while the balloon can not. **Case report:** in this scenario, there are very few options to perform. Herein, we present two cases of balloon uncrossable chronic total occlusion, in which all the other methods were unsuccessful. **Conclusion:** we called this technique «external calcium modification» in which a balloon uncrossable lesion was overcome by cracking the calcified plaque via balloon inflation in the subintimal area over an intentionally directed wire around the calcium in subintimal space.

RESUMEN

Introducción: *la oclusión total crónica es la parte más desafiante de la intervención coronaria percutánea. En lesiones que no se pueden cruzar con balón, el alambre puede avanzar a lo largo de la lesión hasta la parte distal del vaso, mientras que el balón no.* ***Reporte de un caso:*** *en este escenario, hay muy pocas opciones para realizar. En este documento presentamos dos casos de oclusión total crónica no superable con balón en los que todos los demás métodos no tuvieron éxito.* ***Conclusión:*** *llamamos a esta técnica «modificación externa del calcio» en la que la lesión que no se puede cruzar con el balón se superó rompiendo la placa calcificada mediante el inflado del balón en el área subintimal sobre un alambre dirigido intencionalmente alrededor del calcio en el espacio subintimal.*

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INTRODUCTION

Developing novel equipment and techniques enables more challenging chronic total occlusion (CTO) lesions. On the other hand, despite these improvements, uncrossable lesions still remain to be a problem. Herein, report the rechanneling of a balloon uncrossable heavily calcified left anterior descending artery (LAD) artery CTO by cracking the calcified plaque with balloon inflation in the subintimal area, and we call this technique «external calcium modification».

CASE REPORT

A 66-year-old male with typical angina and a history of failed CTO percutan was referred to our CTO tertiary center for retry. Echocardiography revealed an ejection fraction of 45%. MRI study demonstrated viability in the LAD region. Coronary angiography revealed a long LAD CTO over 20 mm with heavy calcification *(Figure 1A)*. The J-CTO score was four since the first attempt in another center had failed due to the inability of the wire passage.[1] The cap of the CTO was

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semi-ambiguous. The wire was able to be advanced through the highly calcified lesion with the support of a microcatheter, but the microcatheter and even low-profile balloons could not be advanced despite good backup with 7 fr femoral access and an EBU catheter in place *(Figure 1B)*. First of all, the microcatheter was exchanged with a more supportive one, and the calcified lesion was tried to be drilled. The second step was using a guide extension catheter in order to increase support. Upon failure, an anchor balloon was inflated in the septal branch. A blimp scoring balloon was used in combination with an anchor balloon and deep-seated guide extension.[2] Leopard crawl technique and grenadoplasty were also tried, but both failed.[3] The other options were the STAR technique, which will probably lead to the loss of many side branches, and the retrograde approach, with a low chance of success due to unfavorable collaterals. If we wanted to use a rotaablator, we first had to pass a rotawire through the microcatheter, and since the microcatheter could not be advanced, there was a risk of losing the original wire, which was in the true lumen due to the long distance of the CTO. Moreover, the patient refused.

Since the balloon uncrossable lesion was covered with a high calcium burden, cracking the calcification with a balloon advanced over a subintimal hydrophilic wire was another option. A fielder XT-A guidewire was advanced around the CTO lesion in the subintimal area *(Figure 1C)*. A 2*12 mm balloon was inflated at 8 atm over the wire in the subintimal area to crack the calcification from outside. After extraluminal plaque modification, the subintimal wire and the balloon were withdrawn. A microcatheter was then advanced with the support of an anchor balloon over the original true lumen wire *(Figure 1D)*. Then the procedure was successfully completed with balloon predilatation and stent implantation *(Figure 1E-F)*.

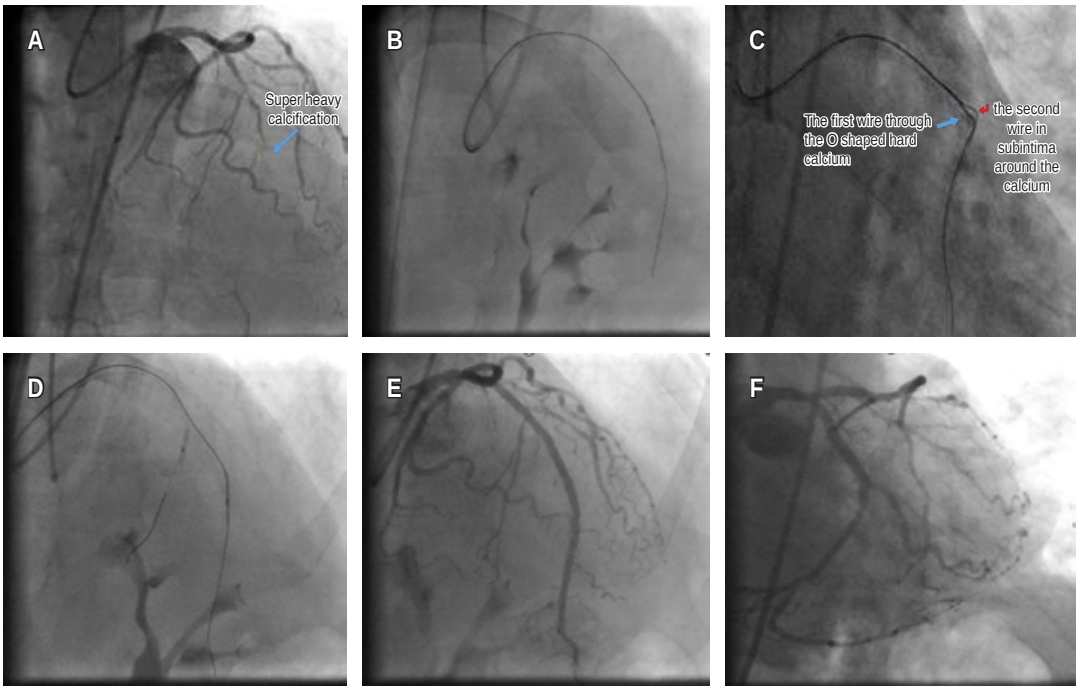

Figure 1: A) The blue arrow shows super heavy calcification. **B)** The wire could be advanced, but the microcatheter failed to pass the chronic total occlusion body. **C)** The blue arrow shows the second wire in the subintima around the calcium. **D)** Following balloon inflation in the subintimal area, the microcatheter then could be advanced with the support of an anchor balloon. **E-F)** Final appearances in cranial and caudal views.

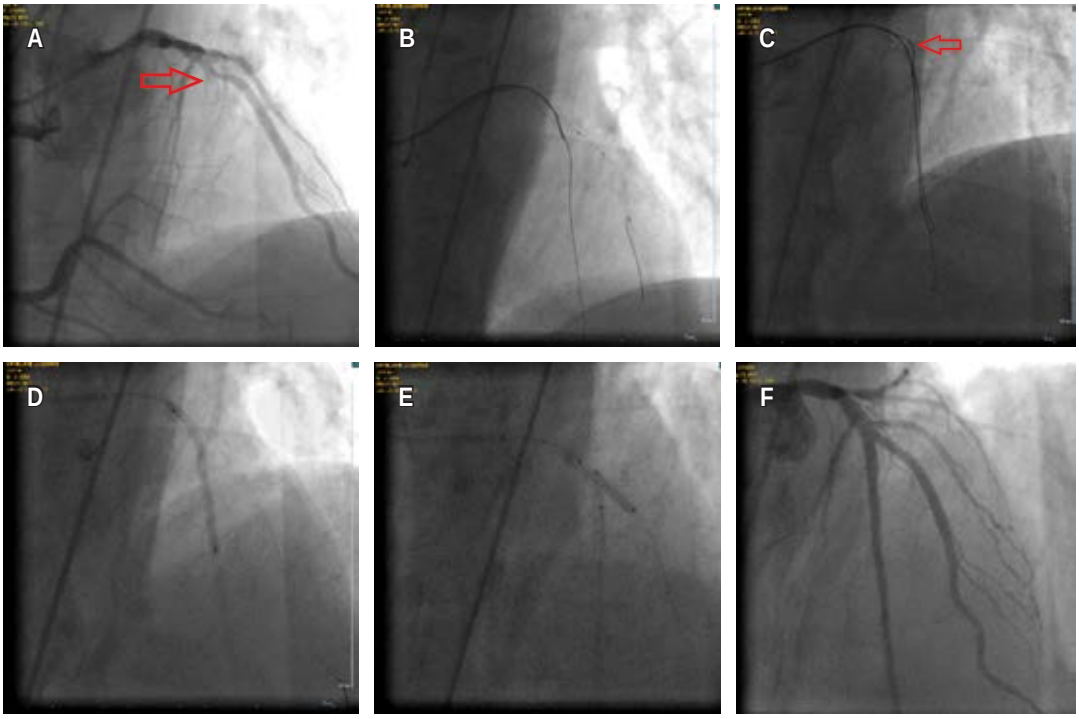

Figure 2: A) The red arrow shows the ambiguous proximal cap. **B)** The microcatheter could not be advanced despite the support of an anchor balloon. **C)** The red arrow shows the knuckled hydrophilic wire going down in the subintimal area around the calcium. **D)** Implantation of a 3 × 38 mm DES in the left anterior descending artery. **E)** Implantation of a 2.75 × 20 mm DES in the diagonal branch via TAP technique. **F)** Final appearance.

The second case was a 55-year-old male with a history of cerebrovascular disease. He was also referred to our CTO tertiary center for retry PCI of LAD CTO lesion with heavy calcification and a J-CTO score of 3 *(Figure 2A)*. MRI revealed viability in the anterior wall and a large diagonal at the proximal cap. Again, all the steps mentioned above failed to advance the microcatheter over the wire, which could be advanced to the distal part of the vessel through the true lumen *(Figure 2B)*. A hydrophilic wire was again knuckled and advanced around the CTO body in the subintimal space *(Figure 2C)*. A 2 × 12 mm balloon was advanced over this wire and inflated at 6 atm. After cracking the external calcium, the microcatheter could be advanced over the wire in the true lumen. A 3 × 38 mm Drug-Eluting Stent (DES) was implanted in the LAD *(Figure 2D)*. Then, a 2.75 × 20 mm DES was implanted in the diagonal branch using the TAP technique, and the procedure was finished successfully *(Figure 2E-F)*.

DISCUSSION

Herein, we report a bail-out intervention for overcoming an uncrossable balloon CTO by cracking the calcium with an NC balloon in the subintima. We call this technique «external calcium modification».

The usual steps to overcome this problem are increasing the support by using femoral access, longer sheaths, and stronger guide catheters such as Amplatz or EBU. Using anchor balloon or super anchor balloon technique, extra support wires, deep-seated guiding extension gears, smaller or hydrophilic coated dedicated CTO balloons, and blimp or dedicated microcatheters may also be helpful. Usually, it takes a combination of these steps to overcome the lesion, but sometimes more advanced techniques like leopard crawl and propofol-soaked or lubricated rota wire passage might be needed. Finally, intentional antegrade

dissection reentry (ADR) and external luminal plaque modification can be an option. The STAR technique was not preferred in our case, considering the absence of a stingray catheter in the cath lab and the possible loss of side branches. To the best of our knowledge, the only case in the literature was presented by Christopoulos G et al, defining the subintimal external crush technique for a balloon uncrossable chronic total occlusion. Also, in this case, high calcification that hampered the crossing of the balloon was cracked by subintimal balloon inflation that allowed subsequent balloon crossing.[4] Some review papers presented algorithms for a balloon uncrossable lesion, which consists of augmented guide catheter support (larger guide catheter with a more supportive shape, long arterial sheaths, deep engagement, guide catheter extension, anchor wire, buddy wire, and anchor balloon) and lesion modification techniques (grenadoplasty, dedicated microcatheters, excimer laser, seesaw balloon-wire cutting technique, multi-wire plaque crushing technique and crowbar effect technique). On the other hand, this external calcium modification technique is mentioned briefly in these papers with a lack of experience.[5,6] Thus, our paper presenting two cases of external calcium modification technique will add unique information to the balloon uncrossable CTO knowledge.

CONCLUSIONS

Consequently, the external calcium modification technique, which consists of plaque modification using a balloon in subintimal space (over an intentionally directed wire in subintima and around the calcium) and cracking the calcium from the outer vessel structure, is an advanced risky procedure that can be used as a last resort in experienced operators' hands with high success and low complication rates.

REFERENCES

1. Morino Y, Abe M, Morimoto T, Kimura T, Hayashi Y, Muramatsu T et al. Predicting successful guidewire crossing through chronic total occlusion of native coronary lesions within 30 minutes: the J-CTO (Multicenter CTO Registry in Japan) score as a difficulty grading and time assessment tool. JACC Cardiovasc Interv. 2011; 4 (2): 213-221. doi: 10.1016/j.jcin.2010.09.024.
2. Dens J, Holvoet W, McCutcheon K, Ungureanu C, Coussement P, Haine S et al. A prospective, multi-center, randomised controlled trial for evaluation of the effectiveness of the Blimp scoring balloon in lesions not crossable with a conventional balloon or microcatheter: the BLIMP study. Acta Cardiol. 2023; 78 (1): 86-90. doi: 10.1080/00015385.2022.2058676.
3. Kazuhiro A, Taichiro H, Takayuki S. Efficacy of lacrosse NSE using the "leopard-crawl" technique on severely calcified lesions. J Invasive Cardiol. 2013; 25 (10): 555-564.
4. Christopoulos G, Kotsia AP, Rangan BV, Vo M, Alaswad K, Karmpaliotis D et al. "Subintimal external crush" technique for a "balloon uncrossable" chronic total occlusion. Cardiovasc Revasc Med. 2017; 18 (1): 63-65.
5. Dash D. Korean circ interventional management of "balloon-uncrossable" coronary chronic total occlusion: is there any way out? J. 2018; 48 (4): 277-286. doi: 10.4070/kcj.2017.0345.
6. McQuillan C, Jackson MWP, Brilakis ES, Egred M. Uncrossable and undilatable lesions-A practical approach to optimizing outcomes in PCI. Catheter Cardiovasc Interv. 2021; 97: 121-126. Available in: https://doi.org/10.1002/ ccd.29001

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Positioning

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Suggested protocol for certification as a cardio-protected area in Mexico. Positioning of a group of experts

Protocolo sugerido para la certificación de espacios cardioprotegidos en México. Posicionamiento de un grupo de expertos

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Keywords:
protocol, cardio-protected area, sudden cardiac death, automatic external defibrillator, cardiopulmonary resuscitation.

Palabras clave:
protocolo, espacios cardioprotegidos, muerte súbita cardiaca, desfibrilador automático externo, reanimación cardiopulmonar.

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ABSTRACT

Sudden Cardiac Death (SCD) and Out-of-Hospital Cardiac Arrest (OHCA) are global public health problems suffered by ≈3.8 million people annually; they represent a challenge in public health, which leads us to work on regulations, legislation, and consensus to implement the formation of protected Cardio areas in Mexico. The increase in cardio-protected spaces and the use of Automatic External Defibrillators (AED) in the world have contributed to improving the survival of OHCA. The use of AEDs and early public access defibrillation requires training for non-medical personnel, who are generally the first to assist and start the chain of survival, with basic and efficient Cardiopulmonary Resuscitation (CPR) until emergency services arrive at the scene of the incident. In this article, we present a structured guide to the steps that must be followed to accredit a cardio-protected space in Mexico and distinguish between public access defibrillation and a cardio-protected area.

RESUMEN

La muerte súbita cardiaca (SCD, por sus siglas en inglés) y el paro cardiaco extrahospitalario (OHCA, por sus siglas en inglés) es un problema de salud pública mundial que padecen ≈3.8 millones de personas al año. Representa un reto en salud pública, por lo que nos lleva a trabajar en reglamentos, legislaciones y consensos para lograr implementar la formación de espacios cardioprotegidos en México. El aumento en los espacios cardioprotegidos y uso de desfibrilador automático externo (DAE) en el mundo, han contribuido a mejorar la supervivencia del OHCA. El uso de DAE y la desfibrilación temprana de acceso público, requiere de entrenamiento al personal no médico, quienes generalmente son los primeros en asistir e iniciar la cadena de la supervivencia, con una reanimación cardiopulmonar básica (RCP) y eficiente hasta que lleguen al lugar del incidente los servicios de emergencias. En este escrito se mencionan los problemas actuales en México y alternativas de solución para los mismos. En el presente artículo mencionamos una guía estructurada de los pasos que se deben seguir para poder acreditar un espacio cardioprotegido en México y hacer la diferencia entre desfibrilación de acceso público y espacio cardioprotegido.

INTRODUCTION

Out-of-hospital cardiac arrest (OHCA) is a world health problem.[1] It is calculated that sudden cardiac death (SCD) represents 30% of the mortality of cardiovascular origin and 20% of the total causes of death in adults.[2-4] The actual incidence is hard to determine and may vary in each country. However, in countries like the United States

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of America or European Countries, it is calculated that it is between 41-155 cases for every 100,000 habitants yearly in populations older than 45 years;[5-7] this incidence is ten times less frequent in younger patients.[8] The survival rate is meager depending on the population studied. It is of vital importance to have a survival chain. This implies a simple and valuable conceptual method that requires coordination in each of the actions to employ. The successful performance of cardiopulmonary resuscitation (CPR) during an OHCA requires the intervention of the community trained in basic CPR. They can initially detect and notify the emergency system of the CPR in process and use an automated external defibrillator (AED)[9,10] if necessary. Basic CPR (BLS) knowledge is relevant to the general population since, usually, the first responder of an OHCA is not a health-related professional.[11,12]

Recommendations for public access defibrillation (PAD) were first published by the American Heart Association in 1992 and later by the European Resuscitation Council in 1998.[13,14]

Since then, several efforts have been made worldwide to increase the use of AEDs in areas with high incidence of OHCA, prepare community members to use them, and create protected areas. These measures, immediate CPR bystander and early AED use could increase the chance of survival by up to 50-74%.[15-17]

THE PROTOCOL

This article presents a structured guide to accredited areas as cardio-protected in México, defining them as any space or building that can ensure an adequate response to an event of sudden cardiac death within its facilities.[18] Therefore, it must be differentiated from public access defibrillation, where an AED may be available for the general population's use without necessarily being considered a cardio-protected space.

The protocol is designed so that in the vast majority of SCD cases, victims can be defibrillated in no more than 5 minutes, with initiation of high-quality CPR within the first minutes, activation of Emergency Medical Services (EMS) in the first 2 minutes of the SCD event, and transferred, in the shortest possible time, to a health institution with installed capacity for subsequent care, with the ultimate goal of rescuing the highest percentage of SCD victims from death, but also ensuring that they have a good neurological recovery and are functional in society.[19]

This protocol is not intended to be an error-free and infallible tool for recovering SCD victims in the country. It is based on the certification protocol for cardio-protected spaces of the Spanish Society of Medicine and Safety at Work. Since it is a protocol with precise and easy-to-apply recommendations, it is expected to provide the best results for possible victims of SCD within the facilities of a cardio-protected space in most cases.

The first step is to have enough AED to cover a temporal radius of 2.5 minutes between the victim and the AED. Therefore, the location and number of AED needed must be strategically planned so that any SCD victim within the cardio-protected space facilities can be detected and have fast access to high-quality CPR and an AED.[20]

Therefore, the following recommendations regarding AED equipment must be considered:

DEFIBRILLATOR AND DISTRIBUTOR

1. Defibrillator
   a. COFEPRIS must authorize the defibrillator equipment used in the facilities (Federal Commission for the Protection against Health Risks) to be used as AED in our country.
   b. The AED must have the following characteristics: a biphasic wave, patches for adults and pediatrics, and batteries in good condition.
2. Distributor
   a. The distributor must be registered as a company authorized (COFEPRIS) to sell medical-sanitary material.
   b. The company must have specific civil liability insurance for defibrillators, sales management information, expiration dates, and an equipment maintenance program.

WHERE TO PLACE THE AED

1. The installation of defibrillators will depend on the physical space available, so an AED must be within a temporal radius of 2.5 minutes for timely defibrillation of an SCD victim in less than 5 minutes.
   a. This may include ample physical space, as remote delivery systems, such as drones, can ensure the timely delivery of the AED anywhere on the property.
2. They must be installed in visible and easily accessible places, within reach of everyone, and used approved displays for easy identification.
3. They must be identified in the property's evacuation plans.
4. There must be a sign identifying the existence of the AED and its signage.

Once the first steps of the protocol have been covered, it is necessary to have an action plan to have sufficient personnel trained in basic CPR and the use of AEDs in the cardio-protected space facilities. It must ensure adequate personnel for all the pre-established locations of the AEDs and for the time that people remain within the cardio-protected space. If the building is open 24 hours a day, it must have trained personnel on all shifts.

It is essential to emphasize the timed drills of the action protocol for an SCD victim within the cardio-protected area facilities, with a desirable timing of at least four training exercises per year, to maintain adequate knowledge of the protocol by the staff and ensure attention to a victim in less than 5 minutes.

Also, the EMS must be immediately activated, with a previously established agreement between the cardio-protected areas, the EMS provider, and the reference hospital where the victims will be transferred for subsequent specialized treatment. All of this must be supported in writing in a physical and virtual manual, accessible and known by all staff.

TRAINING FOR THE USE OF THE AED

1. Companies that opt for the cardio-protected area certification must have sufficient workers trained in basic CPR and using AEDs to cover all areas where the AEDs were installed, for as long as the people remain inside the property.
2. They must have a certificate of completing a course on the importance of public access to defibrillation and a current course (no older than two years) in basic CPR and use of AEDs, given by an officially established training center and endorsed.[21]
3. In addition, there must be a program of quarterly timed drills to ensure personnel's correct action in the event of an SCD event, with an adequate response and timely defibrillation.
   a. Recognition of the SCD victim and activation of the EMS in less than 2 min.
   b. Start high-quality CPR immediately after EMS activation, ideally within the first 2 minutes of SCD.
   c. Timely defibrillation before the first 5 minutes of SCD.
   d. The EMS (high-tech ambulance) should arrive within the first 15 minutes and, if necessary, within 30 minutes of the property's EMS activation.
4. Write a response in case of SCD on the property and provide evidence on how it is disseminated to its workers, especially to the personnel directly responsible for an AED on the property.
5. The protocol must include the full names of the people responsible for each DEA and the substitute in case of absence from work due to any situation.
6. There must be a control center or response center within the property in charge of:
   a. Activate the EMS with the health institution with which you have the agreement.
   b. Ensure timely delivery of the AED if remote delivery systems (drones) are used.
   c. Maintain direct communication with the EMS and those responsible for access to the property to avoid delays in your arrival and departure.
7. The property considered for the certification of a cardio-protected area must have a log of the care of all SCD that is treated in its

facilities, with the specific attention times: With the general data of the SCD victim, activation time of the EMS, initiation of high-quality CPR, timely defibrillation, arrival time of the EMS, and time of transfer and arrival of the victim to the receiving health institution.
8. Each SCD event must be registered in the RENAPACE (National Registry of Out-of-Hospital Cardiac Arrests)[22] to have an adequate incidence of cases at the national level and subsequent protocol standardization.
9. A company or institution legally certified and endorsed in advice and evaluation of the cardio-protected area program may be contracted to implement the response protocol for an SCD on the property.

It is worth commenting on the importance of maintaining the AEDs that are established within the cardio-protected area, which is why the following is recommended:

MAINTENANCE

1. The correct condition of the equipment and its accessories must be guaranteed. In addition, the necessary accessories for the proper operation of the equipment and spare parts must be available, making rapid replacement possible or, where appropriate, ensuring that the supplier can provide the spare part within the next 24 hours.
2. The necessary spare parts are adult and pediatric patches and batteries. Likewise, these are within their validity dates with their corresponding logs by the property or the authorized provider of said services.
3. The biomedical department of the same institution or the authorized supplier must have a maintenance program or contract.

As mentioned in step number 3, it is crucial to have a service provision agreement with a certified hospital with specialized care capacity for SCD victims and with the EMS provider for safe and quick transfer of the victim.

AGREEMENT WITH THE INSTITUTION PROVIDING ADVANCED HOSPITAL SERVICES

To be sure the chain of survival will be complete in an SCD victim, the building's facilities,[23,24] must have:

1. An agreement or contract with a health services institution that has the possibility of continuing to provide adequate medical care to a victim of SCD, so it must have at least one Intensive Care Unit or Cardiovascular Intensive Care Unit, as well as access available to a hemodynamics room 24/7, 365 days a year.
2. Preferably, the agreement should be made with a health institution certified under the standards of the General Health Council, which has high-tech ambulance and medical personnel specialized in high-risk transfers.
3. In the written protocol for response to an MSC in the property, as well as in the physical locations of the AEDs, the emergency telephone number must be specified to which they should call when there is a suspicion of an MSC or in default is the number 911 for the EMS in the region.
4. The person responsible for the property must disseminate this emergency number, as well as infographics of the response protocol for an MSC, not only to its workers but to all the public who have access to its facilities daily. With the aim that everyone knows the protocol and, if necessary, can use it promptly.
5. Virtual tools available for mobile devices or equipment with Bluetooth technology or WiFi access may be used to keep people aware of the protocol's existence and activate it in case of an MSC within its facilities.

Finally, this process must not be considered finite, so it must be carried out bi-annually to ensure that the cardio-protected areas protocols are current and renewed.

RENEWAL

1. The renewal of the certificate must be biennial. To obtain this, the requirements mentioned above must be met.

2. The corresponding renewal process must be requested in advance, and all the necessary documentation for verification will be required.

This protocol covers the most important aspects to take into account to carry it out in a cardio-protected area to save the lives of SCD victims. We are sure they will give us pleasant surprises in applying it directly in their spaces, such as using new technologies for timely access to the AED, such as through drones, remotely controlled or autonomous vehicles, virtual CPR training, and AED use, etcetera.

These practices must be carried out in México to achieve cardio-protection areas and, finally, SCD, an important health problem in our country.

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REFERENCES

1. Gallagher EJ, Lombardi G, Gennis P. Effectiveness of bystander cardiopulmonary resuscitation and survival following out-of-hospital cardiac arrest. JAMA. 1995; 274 (24): 1922-1925.
2. Nichol G, Laupacis A, Stiell IG, O'Rourke K, Anis A, Bolley H et al. Cost-effectiveness analysis of potential improvements to emergency medical services for victims of out-of-hospital cardiac arrest. Ann Emerg Med. 1996; 27 (6): 711-720.
3. Dami F, Carron PN, Praz L, Fuchs V, Yersin B. Why bystanders decline telephone cardiac resuscitation advice. Acad Emerg Med. 2010; 17 (9): 1012-1015.
4. Rea TD, Eisenberg MS, Culley LL, Becker L. Dispatcher-assisted cardiopulmonary resuscitation and survival in cardiac arrest. Circulation. 2001; 104 (21): 2513-2516.
5. Kim F, Nichol G, Maynard C, Hallstrom A, Kudenchuk PJ, Rea T et al. Effect of prehospital induction of mild hypothermia on survival and neurological status among adults with cardiac arrest: a randomized clinical trial. JAMA. 2014; 311 (1): 45-52.
6. Vaillancourt C, Verma A, Trickett J, Crete D, Beaudoin T, Nesbitt L et al. Evaluating the effectiveness of dispatch-assisted cardiopulmonary resuscitation instructions. Acad Emerg Med. 2007; 14 (10): 877-883.
7. Berg RA, Hemphill R, Abella BS, Aufderheide TP, Cave DM, Hazinski MF et al. Part 5: adult basic life support: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2010; 122 (18 Suppl 3): S685-705.
8. Hallstrom A, Cobb L, Johnson E, Copass M. Cardiopulmonary resuscitation by chest compression alone or with mouth-to-mouth ventilation. N Eng J Med. 2000; 342 (21): 1546-1553.
9. Nichol G, Thomas E, Callaway CW, Hedges J, Powell JL, Aufderheide TP et al. Regional variation in out-of-hospital cardiac arrest incidence and outcome. JAMA. 2008; 300 (12): 1423-1431.
10. Ong ME, Shin SD, De Souza NN, Tanaka H, Nishiuchi T, Song KJ et al. Outcomes for out-of-hospital cardiac arrests across 7 countries in Asia: the pan asian resuscitation outcomes study (PAROS). Resuscitation. 2015; 96: 100-108.
11. Cummins RO, Ornato JP, Thies WH, Pepe PE. Improving survival from sudden cardiac arrest: the "chain of survival" concept. A statement for health professionals from the Advanced Cardiac Life Support Subcommittee and the Emergency Cardiac Care Committee, American Heart Association. Circulation. 1991; 83 (5): 1832-1847.
12. INEGI Comunicado de prensa NÚM. 24/22 24 Enero 2022, páginas 1-40. Disponible en: https://www.inegi.org.mx/contenidos/saladeprensa/boletines/2022/dr/dr2021.pdf
13. Guidelines for cardiopulmonary resuscitation and emergency cardiac care. Emergency Cardiac Care Committee and Subcommittees, American Heart Association. Part II. Adult basic life support. JAMA. 1992; 268: 2184-2198.
14. Bossaert L, Handley A, Marsden A, Arntz R, Chamberlain D, Ekstrom L et al. European Resuscitation Council guidelines for the use of automated external defibrillators by EMS providers and first responders: a statement from the Early Defibrillation Task Force, with contributions from the Working Groups on Basic and Advanced Life Support, and approved by the Executive Committee. Resuscitation 1998; 37: 91-94.
15. Álvarez de la Cadena-Sillas J, Asensio LE, Martinez DD, Urzúa GA et al. Out of hospital Cardiac Arrest (OHCA), first steps to know and follow in Mexico to have cardioprotected territories. A point of view of a group of experts. Arch Cardiol Mex. In press.
16. Valenzuela TD, Roe DJ, Nichol G, Clark LL, Spaite DW, Hardman RG. Valenzuela TD, Roe DJ, Nichol G et al. Outcomes of rapid defibrillation by security officers after cardiac arrest in casinos. N Engl J Med. 2000; 343: 1206-1209.
17. Baekgaard JS, Viereck S, Moller TP, Ersboll AK, Lippert F, Folke F. The effects of public access defibrillation on survival after out-of-hospital cardiac arrest: a systematic review of observational studies. Circulation 2017; 136: 954-965.
18. Gantzel NC, Andelius LC, Hansen CM, Blomberg SNF, Christensen HC, Kjolbye JS et al. Bystander interventions and survival following out-of-hospital cardiac arrest at Copenhagen International Airport. Resuscitation 2021; 162: 381-387.
19. Urzúa-González AR, Rivera-Chávez MJ, Zapién-Villegas R, Huaracha-López PA. Cardio protected areas in Mexico. Arch Cardiol Mex. 2020; 90 (2): 207-215.
20. Marijon E, Narayanan K, Smith K, Barra S, Basso C et al. The lancet commission to reduce the global burden of sudden cardiac death: a call for multidisciplinary

action. Lancet. 2023; 402 (10405): 883-936. doi: 10.1016/S0140-6736(23)00875-9.
21. Al Haliq SA, Khraisat OM, Kandil MA, Al Jumaan MA, Alotaibi FM et al. Assessment on CPR knowledge and AED availability in Saudi malls by security personnel: public safety perspective. J Environ Public Health. 2020; 2020: 7453027.
22. Wyckoff MH, Greif R, Morley PT, Ng KC, Olasveengen TM et al. Collaborators. 2022 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations: Summary From the Basic Life Support; Advanced Life Support; Pediatric Life Support; Neonatal Life Support; Education, Implementation, and Teams; and First Aid Task Forces. Circulation. 2022; 146 (25): e483-e557.
23. Martínez-Duncker RD, Urzúa-González AR, Aguilera-Mora LF, Laínez-Zelaya JS, Álvarez de la Cadena-Sillas J et al. Espacios cardioprotegidos en México: acciones para prevenir la muerte súbita cardiaca. Una postura de profesionales de la salud. Salud Pública Mex [Internet]. 2023; 65 (4): 407-415.
24. Cánovas MC, Salas RJM, Sánchez-Arévalo MS, Pardo Ríos M. Should the CRA chain of survival be the survival cycle? Rev Esp Cardiol (Engl Ed). 2018; 71 (5): 412-413.

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