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PREVENIR ES NUESTRA META

- Cardioprotected spaces in Mexico
- TG/HDL-c index in the Mexican population
- Near-infrared spectroscopy (NIRS) in Mexico
- ANCAM protocol for Cardio-protected stadiums in Mexico during World Cup
- Uncertainty and probability are the basis of clinical epidemiology

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Editorial

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Cardioprotected spaces in Mexico: in theory a priority public health issue, but forgotten in reality

Los espacios cardioprotegidos en México: en teoría un problema prioritario de Salud Pública, pero olvidado en la realidad

Jorge Álvarez de la Cadena-Sillas*

«Most people spend more time and energy talking about problems than actually facing them»
Henry Ford

Cardiovascular diseases are a public health problem in Mexico and around the world, being the leading cause of death, with sudden cardiac death (SCD) accounting for at least 50% of these deaths.[1,2] Fast activation of the emergency medical services (EMS), early initiation of cardiopulmonary resuscitation (CPR), by bystanders if possible, and immediate use of an Automatic External Defibrillator (AED) can improve the victim's prognosis and reduce complications.[3,4] In this context, international CPR recommendations increasingly emphasize educating the general public on these maneuvers, as bystanders are typically the first to perform them in out-of-hospital cardiac arrest (OHCA).[5] In Mexico, public policies have not been concerned about initiating a cardioprotection program at the national level[6-8] (despite cardiovascular disease being the leading cause of death in the country). Instead, they have focused on prioritizing other programs with lower incidence and mortality rates, though these are also important. At the national level, the cardiovascular mortality rate reported by the National Institute of Statistics and Geography (INEGI), in the first semester of 2024, was an incidence of 77.6 per 100,000 inhabitants, of which between 35 and 50% of these deaths were due to SCD, representing at least double the mortality from breast cancer in women, which is 17.9 per 100,000.[9] Compare these figures with the rate of 0.7 in men and 0.3 in women per 100,000 inhabitants of fire-related deaths in Mexico.[10] However, there are strict, well-established programs in Mexico, set out in the Mexican Official Standard (NOM-002-STPS-2010),[11] that require and regulate the placement of fire extinguishers in our country, including in new or renovated buildings: public buildings, commercial and industrial establishments, medical offices and pharmacies, heavy vehicles, etc.

Likewise, the national program against breast cancer began in 2008 and continues to be supported at all levels, thanks to which mortality from this problem has been considerably reduced.[12] This program has been successful at the national level and is coupled with excellent advertising marked by the characteristic pink bow.

However, the leading cause of death in Mexico for decades has NOT had an established program, and we do not have legislation or regulations for the creation of cardioprotected spaces at ANY level. There are no health programs or legislation that demand the creation of cardioprotected spaces, defined as a place that has the equipment (AED) and personnel trained in CPR and use of AED to attend SCD events, allowing a rapid response by starting bystander cardiopulmonary resuscitation (B-CPR), which could increase the chances of survival of the victim before the

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arrival of EMS. The survival rate can reach 50-70% with the use of B-CPR early defibrillation within three to five minutes after collapse.[5]

The need exists; public and political awareness does NOT exist. Many actions are required at multiple levels, not only governmental actions through legislation on the matter, but also the efforts of the general public, private initiative, medical societies, and educational institutions, from basic schools to universities.[13] Free CPR programs for the general population (such as the one initiated by ANCAM 2024) allow the problem of SCD to be given the priority it requires, without postponing its solution.

Would it not be an excellent idea, in addition to having a national program and legislation on cardioprotection, to have an advertising program that included a green ribbon?

«No critic is more capable than I of clearly perceiving the disproportion between the problems and the solutions I offer»
Sigmund Freud

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ORIGINAL RESEARCH

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The TG/HDL-c index, a marker of atherogenic dyslipidemia, is a significant factor in the contemporary epidemiological profile of Mexico

El índice TG/c-HDL, marcador de dislipidemia aterogénica, es un factor significativo en el perfil epidemiológico contemporáneo de México

Nayelli Nájera,*,** Yara López-Dionicio,*,** Alejandra Meaney,‡ Pilar Ortiz-Vilchis,§ Guillermo Pérez-Ishiwara,¶ Gerardo Juárez,‖ Eduardo Meaney,*,‡‡ Guillermo Ceballos*,‡‡

Keywords: hypertriglyceridemia, TG/HDL index, Mexican society, lipid profile.

Palabras clave: *hipertrigliceridemia, índice TG/HDL, sociedad mexicana, perfil lipídico.*

ABSTRACT

Introduction: obesity/overweight (O/O) is the basis of the leading causes of general mortality in Mexico: ischemic heart disease and type 2 Diabetes Mellitus (2DM). The lipid triad, associated with O/O, is the most common type of dyslipidemia in our country. We analyzed the lipid profiles of a large sample of the contemporary urban population of Mexico City. **Material and methods:** sixty-eight thousand participants comprised this cohort. The clinical status, reason for the study, and whether the patient was being treated were not recorded. Total Cholesterol (TC), TriGlycerides (TG), and High-Density Lipoprotein cholesterol (HDL-c) levels were measured spectrophotometrically. Low-Density Lipoprotein (LDL-c) and non-HDL levels, and the risk ratios TC/HDL-c, LDL-c/HDL-c, and TG/HDL-c were calculated. The classification criteria were based on ATP III and European guidelines. The mean values and quartile distributions of all lipids and lipoproteins were estimated and stratified by sex. **Results:** the TC values were above the cut-off. The TG values were significantly higher than this. The HDL-c levels in both sexes remained close to the lower limit. The LDL-c levels were between 100 and 130 mg/dL in both men and women. Non-HDL-c levels never reached a cut-off of 160 mg/dL. The LDL-c/HDL-c index was below it. Interestingly, the TG/HDL-c values were above the cut-off limit. **Conclusions:** hypertriglyceridemia, caused by abdominal obesity, is the most critical lipid abnormality in the Mexican population. TG/HDL-c is a readily available, inexpensive risk marker that should be used routinely.

RESUMEN

Introducción: *la obesidad/sobrepeso (O/O) es la base de las principales causas de mortalidad general en México: cardiopatía isquémica y diabetes mellitus tipo 2 (DM2). La tríada lipídica, asociada con O/O, es el tipo más común de dislipidemia en nuestro país. Analizamos los perfiles lipídicos de una muestra amplia de la población urbana contemporánea de la Ciudad de México.* ***Material y métodos:*** *sesenta y ocho mil participantes conformaron esta cohorte. No se registró el estado clínico, el motivo del estudio ni si el paciente estaba recibiendo tratamiento. Se midieron espectrofotométricamente los niveles de colesterol total (CT), triglicéridos (TG) y colesterol unido a lipoproteínas de alta densidad (c-HDL). Se calcularon los niveles de lipoproteínas de baja densidad (c-LDL) y no HDL, y las razones de riesgo CT/c-HDL, c-LDL/c-HDL y TG/c-HDL. Los criterios de clasificación se basaron en el ATP III y las guías europeas. Se estimaron los valores medios y las distribuciones de cuartiles de todos los lípidos y lipoproteínas y se estratificaron por sexo.* ***Resultados:*** *los valores de CT estuvieron por encima del punto de corte. Los valores de TG fueron significativamente mayores que este. Los niveles de c-HDL en ambos sexos se mantuvieron cerca del límite inferior. Los niveles de c-LDL estuvieron entre 100 y 130 mg/dL tanto en hombres como en mujeres. Los niveles de c-no-HDL nunca alcanzaron un punto de corte de 160 mg/dL. El índice c-LDL/c-HDL estuvo por debajo de este. Curiosamente, los valores de TG/c-HDL estuvieron por encima del límite de corte.* ***Conclusiones:*** *la hipertrigliceridemia, causada por la obesidad abdominal, es la anormalidad lipídica más crítica en la población mexicana. TG/c-HDL es un marcador de riesgo fácilmente disponible y de bajo costo que debe usarse de forma rutinaria.*

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INTRODUCTION

Due to profound socioeconomic and cultural changes, Mexico has undergone a rapid epidemiological transition, with its impact being uneven across different regions.[1-3] One of the most significant consequences of this transition is the alarming rise in the prevalence of overweight and obesity (O/O), now the country's foremost public health issue.[3] These conditions affect nearly four-fifths of the adult population and contribute to the onset, progression, and complications of other cardiometabolic disorders, particularly the two leading causes of mortality in Mexico, ischemic heart disease and diabetes mellitus (DM).[4] This growing health crisis has placed a considerable burden on the national healthcare system, undermining workforce productivity and economic competitiveness.[5-7]

Regretfully, neither the Mexican State nor society has responded adequately to the threat posed by these lethal epidemics The combination of limited and poorly managed governmental health spending, the absence of adequate preventive public policies, insufficient training of a significant proportion of healthcare personnel in managing cardiovascular risk factors, and the widespread adoption of lifestyle and dietary habits foreign to traditional Mexican culture, particularly the high consumption of junk and processed foods,[8-11] among many other contributing factors, has led to the explosive rise in the prevalence and lethality of O/O, DM, and Atherosclerotic Cardiovascular Diseases (ASCVD).[12]

Among the main risk factors for ASCVD, dyslipidemia is overlooked by Mexican health decision-makers, who do not consider it a national public health priority.[13] As a result, many patients, including those at the highest risk, fail to achieve their therapeutic goals due to inadequate diagnosis and treatment.

In a population with such a high prevalence of O/O, it is unsurprising that one of the most common lipid disorder phenotypes is atherogenic dyslipidemia, also known as the lipid triad,[14] which is pathophysiologically and epidemiologically linked to obesity and type 2 diabetes mellitus (DM2).[15,16] This condition appears to be the most prevalent lipid disorder associated with myocardial infarction in Mexico.[16] Unfortunately, Mexican physicians often ignore or underestimate this reality, including lipid experts, who uncritically adhere to guidelines based on populations that are significantly different from ours.[17] In this context, the triglyceride/high-density lipoprotein cholesterol (TG/HDL-c) ratio,[18,19] a simple, reliable, and excellent marker of cardiovascular risk and insulin resistance,[20] which aligns well with the metabolic profile of Mexicans, is widely overlooked by most treating physicians despite substantial evidence supporting its clinical usefulness.[21]

Therefore, our study presents the results of a lipid profile analysis, including the TG/HDL-c index, in a sample of the general urban population from the middle and lower-middle economic classes.

MATERIAL AND METHODS

The study followed Good Clinical Practice guidelines, the principles outlined in the Declaration of Helsinki, and the Mexican federal regulations established in the General Law of Health.[22-24] Participants were recruited through invitations, with no specific inclusion criteria. Any individual who accepted the invitation and provided informed consent (or whose parents or guardians did so on their behalf in the case of minors) was included in the study. As a result, the cohort consisted of a non-probabilistic sample of 68,000 participants of both sexes.

Blood samples were collected from individuals referred by private physicians for clinical laboratory testing between 2012 and 2022. However, the specific reasons for these medical evaluations, whether routine check-ups, diagnostic workups, or follow-ups, remain unknown. Additionally, no data were available on participants' clinical conditions or pharmacological treatments.

Lipid and lipoprotein levels were measured using standard spectrometric laboratory methods. The analyses included total cholesterol (TC), triglycerides (TG), HDL-c, and low-density lipoprotein cholesterol (LDL-c). LDL-c was estimated using the Friedewald formula [LDL-c = TC - HDL-c - (TG/5)].[25] Non-HDL

cholesterol (non-HDL-c),[26] which represents all atherogenic lipid fractions containing apolipoprotein B100, was calculated by subtracting HDL-c from TC.

We used the lipid and lipoprotein classification criteria from the ATP III guidelines and selected risk thresholds from the European Society of Cardiology/European Atherosclerosis Society to define the risk cut-offs.[27,28] In both genders, TC and TG levels of 200 and 150 mg/dL, respectively, were considered reference points. For LDL-c, the ATP III guidelines consider an optimal value to be less than 100 mg/dL and «near optimal/above optimal», a value between 100 and 129 mg/dL.

For non-HDL-c, given that its concentration should be 30 mg/dL above LDL-c, the recommended threshold for pharmacological intervention is 130 mg/dL. In comparison, levels below 160 mg/dL were classified as «near optimal».[28] The ATP III HDL-c cut-offs for metabolic syndrome were applied to both genders. According to the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) criteria, hypoalphalipoproteinemia is diagnosed when HDL-c is < 40 mg/dL in men and < 50 mg/dL in women.[29]

Atherogenic ratios, including TC/HDL-c,[30] LDL-C/HDL-c,[31] and TG/HDL-c,[18] were calculated based on lipid and lipoprotein measurements. The cut-off value for the TC/HDL-c ratio was derived from the 1999-2014 National Health and Nutrition Examination Surveys (NHANES), where a ratio of ≥ 4.22 was positively correlated with cardiovascular mortality.[31] The LDL-C/HDL-c ratio cut-off of 2.7 was determined by averaging results from multiple studies.[32-34]

We considered findings from various studies on the TG/HDL-c ratio, which indicated average cut-off values of 2.7 for women and 3.4 for men.[35] However, given that this index varies significantly across ethnicities and clinical conditions, we also incorporated quartile values from a previous study[36] conducted on a sample of the urban middle class in Mexico City. These interquartile ranges were < 3.3, [3.3-4.6], [4.7-6], and > 6, corresponding to the four classical risk categories defined by the American Heart Association/American College of Cardiology (AHA/ACC): low, borderline, intermediate, and high risk.[37]

Finally, all lipid, lipoprotein, and ratio values were stratified by sex and plotted across decades of age, ranging from 10 to 90 years or older.

RESULTS

Table 1 summarizes the data on lipids and lipoproteins, expressed as mean and standard deviation, and categorized into quartiles. As

Table 1: Mean and standard deviation of the main lipids and lipoproteins.

Gender	TC mg/dL	TG mg/dL	HDL-c mg/dL	LDL-c mg/dL	Non-HDL-c mg/dL
Women, mean ± SD	205.5 ± 47.3	188.5 ± 149.7	50.4 ± 13.9	120 ± 56.5	147.9 ± 47.8
Percentile					
Quartile 25	171	111	41	86.53	115
Quartile 50	200	157	49	116.8	143
Quartile 75	233	219	59	152.6	176
Men, mean ± SD	199.5 ± 47.8	211.9 ± 187	46.5 ± 12.5	111.7 ± 62.1	135.2 ± 45.3
Percentile					
Quartile 25	168	115	38	84.75	104
Quartile 50	194	166	45	110.8	132
Quartile 75	226	244	52.7	139.2	162

HDL-c = high-density lipoprotein cholesterol. LDL-c = low-density lipoprotein cholesterol. Non-HDL-c = non-HDL cholesterol. SD = Standard Deviation. TC = Total cholesterol. TG = Triglycerides.

Table 2: Mean and standard deviation of atherogenic indexes, along with quartile values (N = 68,000).

Gender	TC/HDL-c mg/dL	LDL/HDL-c mg/dL	TG/HDL-c mg/dL
Women, mean ± SD	4.45 ± 1.70	2.45 ± 1.18	3.63 ± 4.93
Percentile			
Quartile 25	3.29	1.68	1.792
Quartile 50	4.17	2.31	2.838
Quartile 75	5.26	3.03	4.429
Men, mean ± SD	4.53 ± 1.62	2.64 ± 1.08	4.62 ± 9.98
Percentile			
Quartile 25	3.42	1.89	1.936
Quartile 50	4.22	2.58	3.243
Quartile 75	5.26	3.27	5.257

HDL-c = high-density lipoprotein cholesterol. LDL = low-density lipoprotein. SD = Standard Deviation. TC = Total cholesterol. TG = Triglycerides.

expected, given the nature of the survey, the data showed a considerable dispersion. When analyzing the mean and median values of lipids, lipoproteins, and their ratios, TC was found to be close to or precisely at the cut-off limit in both sexes. In contrast, both the mean and median TG values were significantly elevated, with higher levels observed in men compared to women.

Regarding HDL-c, both men and women exhibited borderline values, with women showing approximately 5 mg/dL higher levels, as expected. LDL-c concentrations in women were at the pharmacological treatment threshold, whereas in men, they were slightly lower, but still near the cut-off. The mean and median non-HDL-c values exceeded the minimum desirable limit for both sexes.

Table 2 presents the results for the atherogenic ratios. The mean and median TC/HDL-c values exceeded the cut-off of 4.2 in both sexes. For the LDL-c/HDL-c ratio, both the mean and median values were slightly below the risk threshold but remained close in both sexes. In contrast, the mean TG/HDL-c index was above the cut-off in both men and women. However, although the median value was elevated in women, it was slightly below the threshold in men. When applying the quartile values from our previous study, the overall mean TG/HDL-c ratio corresponded to the 50th percentile, with higher values observed in men compared to women.

Figures 1 to 5 present the lipid, lipoprotein, and index values analyzed in the study population stratified by age.

The data showed that TC levels *(Figure 1)* were slightly higher in women than in men. In both sexes, the highest values were observed between the ages of 40 and 70 years, when the mean values were barely above the 200 mg/dL limit, followed by a modest decline in the oldest age group.

Throughout life, from youth to old age, TG values remained similar in both sexes and consistently above the cut-off limit of 150 mg/dL, with no significant changes in the oldest groups. Notably, TG levels were higher in men than in women of all ages *(Figure 2)*.

As expected, the plasma HDL-c concentration *(Figure 3)* was slightly higher in women than in men, with no significant variations across age groups. In women, HDL-c levels remained consistently around the 50 mg/dL cut-off, while in men, differences across decades were minimal, with slightly higher values in the older groups.

LDL-c levels *(Figure 4)* remained between 100 and 130 mg/dL in both sexes across most age groups, except in the youngest and oldest

groups, where values dropped below 100 mg/dL. A decline was observed in the oldest age group, which was more pronounced in men.

Non-HDL-c levels *(Figure 5)* followed a similar pattern in both sexes. While values never reached the 160 mg/dL cut-off, women aged 40-79 years and men aged 30-69 years had levels above 130 mg/dL. Sustained decline was observed in the oldest age group.

The TC/HDL-c atherogenic ratio *(Figure 6)* was slightly above the 4.22 cut-off in women aged 30-90 years and men aged 20-80 years.

The LDL-C/HDL-c ratio *(Figure 7)* remained below the 2.7 cut-off in women; in men, it exceeded this threshold between the ages of 30 and 50. As observed with the other parameters, a decline occurred in the oldest age groups, starting at 69 years in women and 59 years in men.

Finally, the TG/HDL-c ratio *(Figure 8)* exceeded the 2.7 cut-off in women across all age decades, except for those older than 80 years. In men, the values remained above the 3.4 threshold between 20 and 80 years old. Using the quartile distribution from a Mexican population as a reference, most women in this study fell within the first and second quartiles (low and borderline risk). In contrast, most men, except for the youngest and oldest age extremes, had values corresponding to the second and third quartiles (intermediate and high risk).

DISCUSSION

This study analyzed the lipid profile of a non-probabilistic segment of the urban middle class in Mexico City, providing insight into the alarming metabolic reality of a society that has undergone a drastic shift in dietary habits over the past few decades. The widespread adoption of a Westernized diet, characterized by excessive consumption of

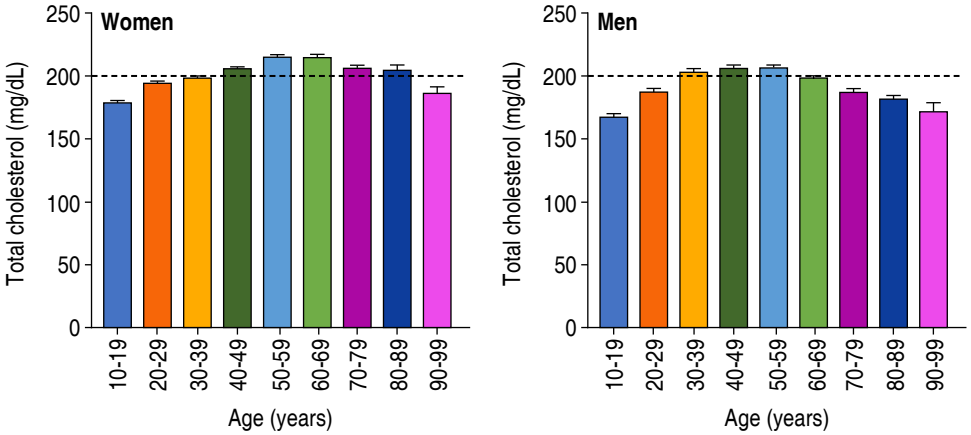

Figure 1:

Total cholesterol concentrations by age and gender. The dotted line expresses the cut-off value of this variable.

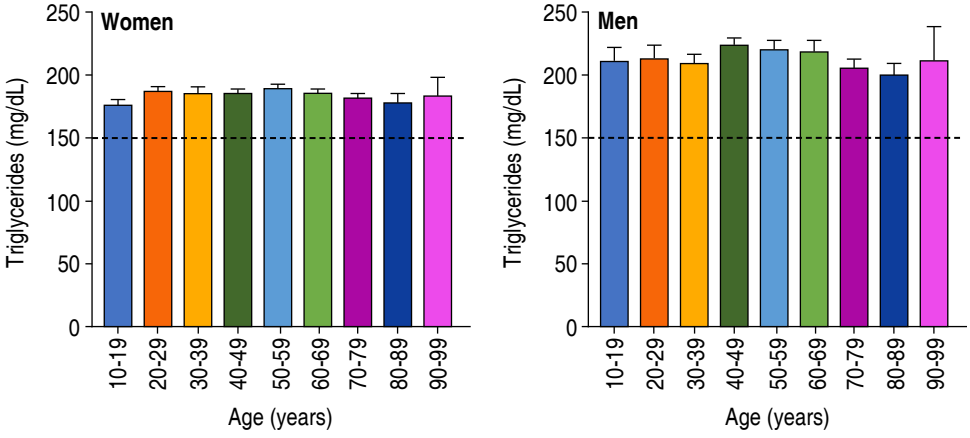

Figure 2:

Triglyceride concentrations according to age and gender. The dotted line expresses the cut-off value of this variable.

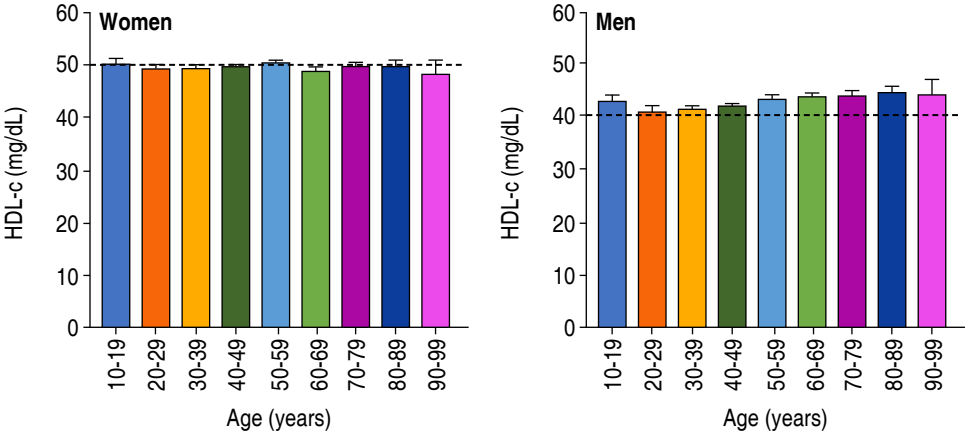

Figure 3:

HDL-c concentrations by age and gender. The dotted lines indicate the cut-off points, by gender, for this variable.

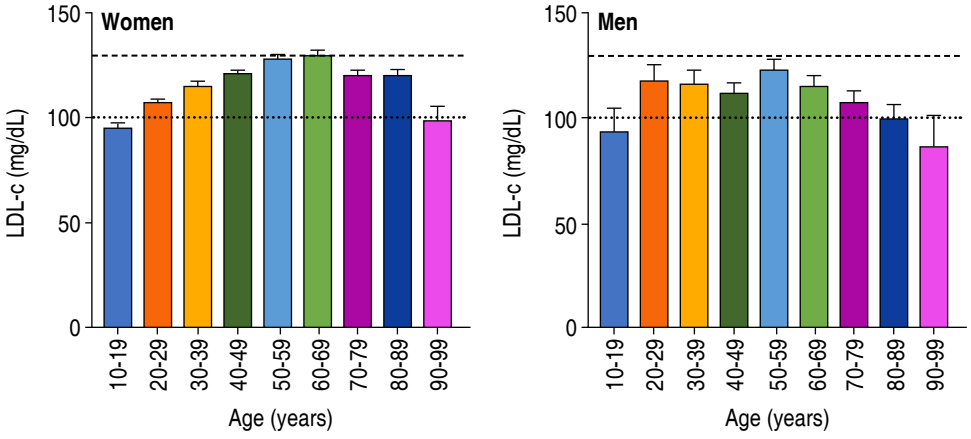

Figure 4:

LDL-c concentrations according to age and gender. Dotted lines indicate the cut-off values described in the ATP III document for the optimal level (< 100 mg/dL) and for values close to or above the optimal level (between 100 and 130 mg/dL).

junk and processed products, as well as foods rich in calories, cholesterol, and saturated fat, has been compounded by a sedentary lifestyle, contributing to the exponential rise in obesity (O/O) and its associated cardiometabolic consequences.[3,38]

Although the study design did not allow us to determine the clinical conditions of the participants, the reasons for their biochemical evaluations, or whether they were undergoing lipid-lowering treatment, the data revealed a clear pattern of dyslipidemia. Elevated TG levels were observed across all age groups, along with consistently high TG/HDL-c ratios, which were more pronounced in men than in women. Even if a proportion of participants were receiving lipid-lowering therapy, the persistence of these abnormalities suggests that current interventions do not effectively modify the underlying dyslipidemia profile of this population.

These findings highlight a concerning scenario: a population at significant cardiometabolic risk, where dyslipidemia remains prevalent despite potential medical interventions. The combination of high TG concentrations, atherogenic lipid ratios, and the increasing burden of O/O underscores the urgent need for more effective public health strategies. Addressing this issue requires comprehensive policies that promote healthier dietary habits, encourage physical activity, and improve the early detection and treatment of dyslipidemia to mitigate the long-term impact on cardiovascular health.

Certainly, LDL-c is not a primary concern in contemporary Mexican lipid epidemiology. Instead, hypertriglyceridemia and the TG/

HDL-c index, markers of insulin resistance generally associated with O/O, are of greater significance. The link between insulin resistance syndrome and lipid abnormalities is well documented.[39-42] This syndrome is strongly associated with hyperinsulinemia, which persists as long as pancreatic function is maintained. The binomial of insulin resistance and hyperinsulinemia is a significant factor in the development and progression of traits that define Metabolic Syndrome (MS).[43]

The clinical and epidemiological significance of MS lies in its predictive value for (DM2), its frequent association with this disease, and, even before diabetes manifests, its role as a cluster of cardiometabolic risk factors that contribute to severe, disabling, and potentially fatal cardiovascular and metabolic complications.[44,45]

Atherogenic dyslipidemia, also known as the lipid triad, is one of the most critical consequences of insulin resistance. Elevated TG concentrations, concomitant reduction in HDL-C mass, and increased LDL-C levels characterize this dyslipidemic profile.[46-48] However, the most concerning aspect is the significant rise in small, dense LDL particles, the most atherogenic lipid fraction.[49,50] This dyslipidemia poses a substantial threat to the health of the Mexican population, which underscores the importance of our research in understanding and addressing this issue.

The role of TG as a significant atherogenic risk factor has been debated for decades.[51-59] Although epidemiological evidence supporting this association is robust, hypertriglyceridemia is often omitted or minimized in the USA and European Dyslipidemia Risk Scores designed to estimate cardiovascular morbidity and mortality. Unfortunately, most Mexican lipid

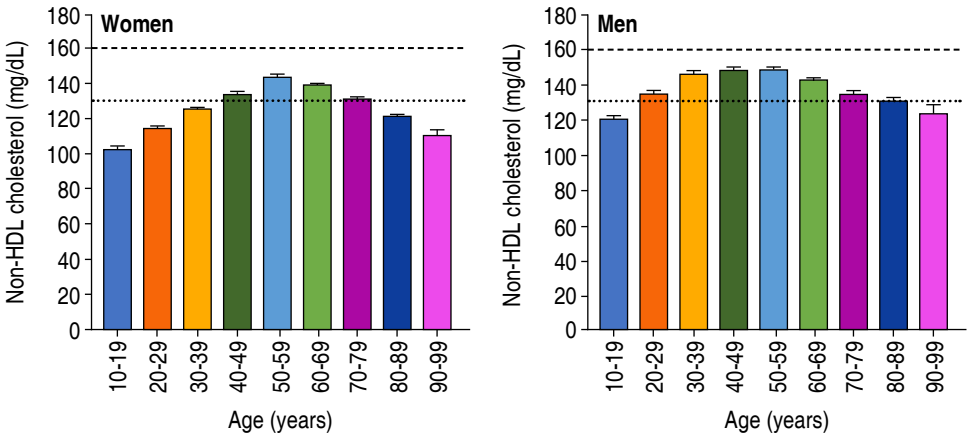

Figure 5:

Non-HDL cholesterol concentrations according to age and gender. Dotted lines indicate the cut-off values for this variable, which is 30 mg higher than the LDL-c values.

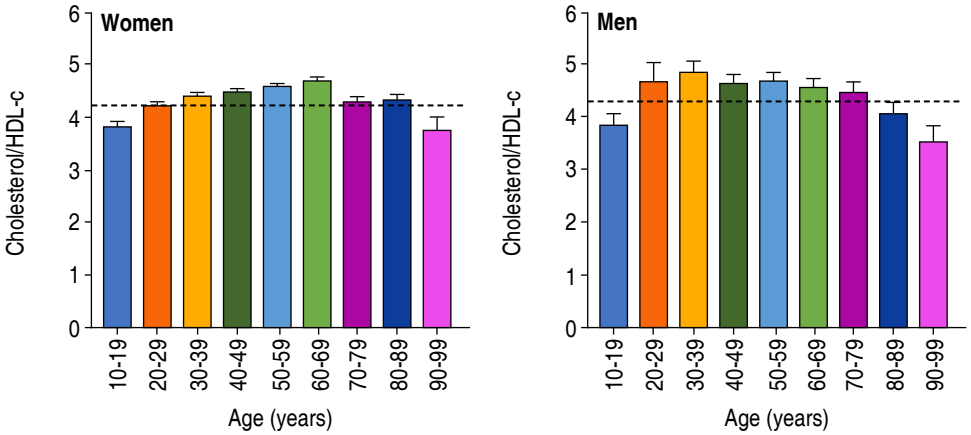

Figure 6:

TC/HDL-c ratio according to age and gender. The dotted line expresses the cut-off from the 1999-2014 National Health and Nutrition Examination Surveys (NHANES), with a positive correlation with mortality, where a ratio of ≥ 4.22 was positively correlated with mortality.

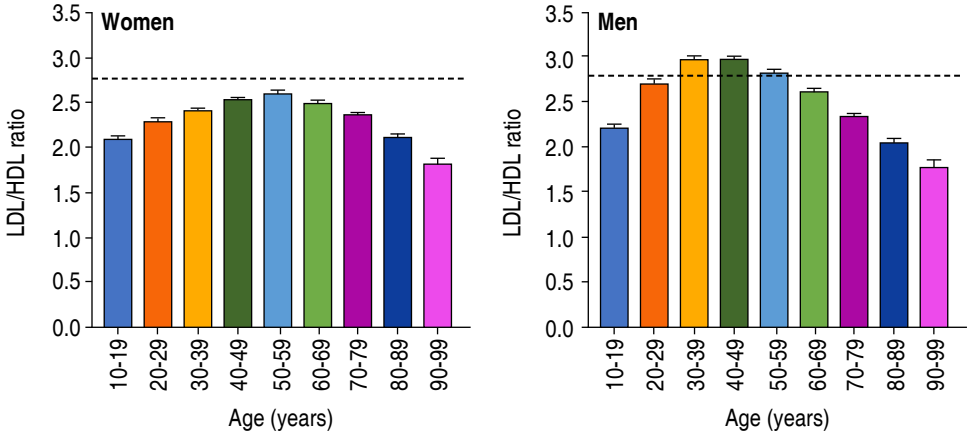

Figure 7:

LDL-c/HDL-c index according to age and gender. The dotted line indicates de LDL-C/HDL-c ratio of 2.7, determined by averaging results from multiple studies (see text).

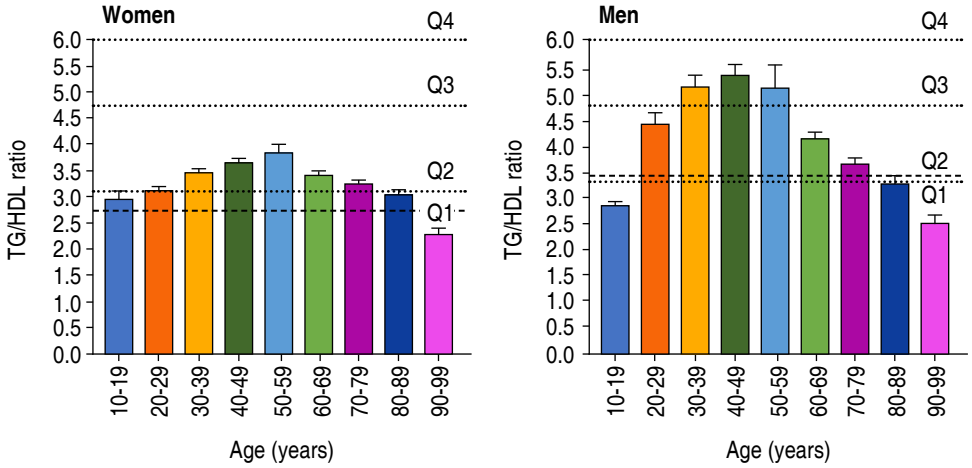

Figure 8: TG/HDL index according to age and gender. The gross dotted line indicates the cut-off values of 2.7 for women and 3.4 for men reported in various studies. The thinnest dotted lines signal the quartile values observed in a sample of the urban middle class in Mexico City (< 3.3, 3.4-4.6, 4.7-6, and > 6), which correspond to the classical risk categories (low, borderline, intermediate, and high risk) of the American Heart Association/American College of Cardiology (AHA/ACC): see text.

experts have adopted this approach. This uncritical stance is primarily due to the absence of a national risk scale that considers the anthropometric and metabolic characteristics of the Mexican population.

In previous studies,[36,60] we documented that the American College of Cardiology/American Heart Association Pooled Cohort Equations (ACC/AHA PCEs)[37] and the international GLOBORISK[61] tool fail to assess cardiovascular risk in the Mexican population accurately. These models overlooked two key pathogenic traits in our population: increased abdominal circumference and elevated TG concentrations. A more recent risk scale for primary prevention, developed by the American Heart Association, incorporates the body mass index (BMI), hemoglobin A1c, urine albumin-to-creatinine ratio, and a social deprivation index. However, surprisingly, it neglects the TG concentration and abdominal circumference, limiting its applicability.[62]

It is increasingly evident that TG are not directly atherogenic but contribute to cardiovascular risk primarily through the formation of small, dense LDL particles. These have a greater ability to infiltrate the arterial wall owing to their reduced size, increased

retention in the subendothelial proteoglycan network, and higher susceptibility to oxidation. Moreover, they are not efficiently cleared by hepatic LDL receptors and are more readily bound by arterial wall LDL receptors, exacerbating their atherogenic potential.[63,64]

Risk quotients (RQs) have long been used as valuable predictive tools.[65] The Castelli indexes or ratios[30,66] (TC/HDL-c and LDL-c/HDL-c) are based on the simple assumption that a higher numerator (LDL-c or TC, whose main component is LDL-c) combined with a lower denominator (HDL-c, the protective lipid fraction) indicates an increased coronary risk. Conversely, lower atherogenic fractions and higher HDL-c values suggest a lower risk.

Unlike these traditional ratios, the TG/HDL-c index is more complex, reflecting lipid imbalances secondary to the insulin resistance/hyperinsulinemia binomial, which is a characteristic feature of atherogenic dyslipidemia. This condition is highly prevalent in individuals with DM2, obesity, or both.[20,66] Although several recent studies have highlighted the clinical relevance of the TG/HDL-c index,[67-71] this tool has rarely been discussed in Mexican publications on lipid disorders. General practitioners and specialists use it less frequently in routine clinical practice.

The data presented here clearly demonstrate that hypertriglyceridemia is a prominent feature of the lipid profile of the contemporary Mexican population. However, unlike previous studies,[14,72-74] including some conducted by our group, the present findings did not show low HDL-c concentrations (hypoalphalipoproteinemia), the other key component of the lipid triad. There was no obvious explanation for the increased HDL-c level. Nonetheless, a recent national survey reported a similar pattern: while 48.9% of participants in a probabilistic sample had hypertriglyceridemia, only 28.3% had HDL-c levels < 40 mg/dL (21.6% of women and 35.5% of men).[75] These discrepancies warrant further investigation in future studies.

CONCLUSIONS

Even though the cohort reported in this study is not probabilistic, independent of the clinical status of the patients, and whether or not they were treated with agents that influence the concentration of serum lipids, the striking results showed an adverse lipid profile, clearly indicating an ominous picture of a population ravaged by a very severe epidemic of O/O. Hypertriglyceridemia is the most prevalent lipid disorder identified in this sample of contemporary inhabitants of Mexico City. In recent times, hypoalphalipoproteinemia (another component of atherogenic dyslipidemia) has been the most prominent lipid abnormality identified in several Mexican surveys and clinical trials; however, it was less prevalent in the present study. Nonetheless, the quotient of TG/HDL-c (a marker of insulin resistance/hyperinsulinism) was the most relevant CV risk marker. These results underline the urgent need to launch a campaign against O/O, the foundation of diabetes and ASCVD epidemics.

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Initial experience with near-infrared spectroscopy in the treatment of coronary atherosclerotic disease in Mexico

Experiencia inicial con espectroscopia de infrarrojo cercano en el tratamiento de la enfermedad aterosclerótica coronaria en México

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Keywords: near-infrared spectroscopy, intravascular ultrasound, vulnerable plaque, lipid core burden index, coronary atherosclerosis imaging.

Palabras clave: *espectroscopia de infrarrojo cercano, ultrasonido intravascular, placa vulnerable, índice de carga del núcleo lipídico, imagenología de aterosclerosis coronaria.*

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ABSTRACT

Atherosclerotic coronary artery disease (CAD) remains one of the leading causes of morbidity and mortality worldwide. In recent years, the emergence of intravascular imaging technologies has enabled more precise characterization of vulnerable plaques-those with a high lipid core burden and increased risk of rupture. Near-infrared spectroscopy (NIRS), when integrated with intravascular ultrasound (IVUS), constitutes an advanced diagnostic modality capable of identifying high-risk lesions even in the absence of non-ischemia inducing stenosis. This combined IVUS-NIRS platform enables real-time chemical characterization of atherosclerotic plaques through the lipid core burden index (LCBI), while simultaneously providing detailed structural assessment via IVUS. Recently adopted in interventional cardiology practices across Mexico and Latin America, this technology enhances risk stratification and supports more informed decision-making during percutaneous coronary intervention (PCI). In this article, we present an updated review of the technical fundamentals, clinical utility, and key evidence supporting the use of IVUS-NIRS in coronary artery disease, including pivotal findings from the LRP, PROSPECT II, and PREVENT trials. These studies highlight the predictive value and therapeutic potential of IVUS-NIRS in guiding PCI beyond conventional angiographic or physiological parameters. Additionally, we share the initial clinical experience in Mexico, including representative case images that illustrate the practical application of IVUS-NIRS in daily practice. This imaging modality provides

RESUMEN

La enfermedad coronaria ateroesclerótica (EAC) continúa siendo una de las principales causas de morbilidad y mortalidad a nivel mundial. En los últimos años, la aparición de tecnologías de imagen intravascular ha permitido una caracterización más precisa de las placas vulnerables, aquellas con una alta carga de núcleo lipídico y mayor riesgo de ruptura. La espectroscopia cercana al infrarrojo (NIRS), cuando se integra con el ultrasonido intravascular (IVUS), constituye una modalidad diagnóstica avanzada capaz de identificar lesiones de alto riesgo incluso en ausencia de estenosis inductoras de isquemia. Esta plataforma combinada IVUS-NIRS proporciona una evaluación química en tiempo real de la placa ateroesclerótica a través del índice de carga lipídica (LCBI), al tiempo que ofrece una valoración estructural detallada mediante IVUS. Recientemente incorporada a la práctica de la cardiología intervencionista en México y América Latina, esta tecnología mejora la estratificación del riesgo y facilita la toma de decisiones más informadas durante la intervención coronaria percutánea (ICP). En este artículo, presentamos una revisión actualizada sobre los fundamentos técnicos, la utilidad clínica y la evidencia clave que respalda el uso de IVUS-NIRS en la enfermedad arterial coronaria, incluyendo hallazgos fundamentales de los ensayos clínicos LRP, PROSPECT II y PREVENT. Estos estudios destacan el valor predictivo y el potencial terapéutico de IVUS-NIRS para guiar la ICP más allá de los parámetros angiográficos o fisiológicos convencionales. Asimismo, compartimos la experiencia clínica inicial en México, incluyendo imágenes representativas de casos que ilustran la aplicación práctica de

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an additional diagnostic layer that supports optimized lesion selection, guides intensification of lipid-lowering and antithrombotic therapy, and contributes to a more personalized, evidence-based approach in contemporary interventional cardiology.

IVUS-NIRS en la práctica diaria. Esta modalidad de imagen proporciona una capa diagnóstica adicional que permite optimizar la selección de lesiones, orientar la intensificación de la terapia hipolipemiante y antitrombótica, y contribuir a un enfoque más personalizado y basado en evidencia en la cardiología intervencionista contemporánea.

Abbreviations:

ACS = acute coronary syndromes
CAD = coronary artery disease
iFR = Instantaneous Wave-Free Ratio
IVUS = intravascular ultrasound
LCBI = lipid core burden index
LCP = lipid core plaque
LRP = lipid-rich plaque
NIRS = near-infrared spectroscopy
OMT = optimal medical therapy.
PCI = percutaneous coronary intervention

INTRODUCTION

The rupture of lipid-rich plaques is the principal mechanism responsible for the onset of acute coronary syndromes (ACS), including myocardial infarction and sudden cardiac death. Nevertheless, the management of coronary artery disease (CAD) has focused primarily on hemodynamically significant lesions, as assessed by either hyperemic or non-hyperemic physiological indices. In spite of that, recent evidence has demonstrated that a considerable proportion of vulnerable plaques are non-obstructive and do not induce myocardial ischemia.[1-3] The combined use of intravascular ultrasound (IVUS) and near-infrared spectroscopy (NIRS) enables accurate in vivo characterization of the chemical composition of atherosclerotic plaques and facilitates the identification of lesions that meet criteria for high rupture risk.[4-8]

For the first time, this dual-modality technology is available in Mexico. In this context, we present a review of the IVUS-NIRS platform, an overview of its clinical utility, and representative imaging cases derived from our initial experience in the country.

NIRS employs near-infrared light to interrogate the chemical properties of arterial tissue. It capitalizes on the fact that various substances absorb and scatter NIR light (wavelengths from 800 to 2,500 nm) differently across the spectrum. A NIRS spectrometer emits light into the tissue and measures the fraction of reflected light over a broad range of optical wavelengths. The output is plotted as an absorbance spectrum, with wavelength on the x-axis, allowing characterization of lipid-specific signatures.[9,10]

Lipids exhibit a characteristic absorption pattern due to the presence of carbon-hydrogen bonds in their molecular structure. This enables the generation of chemical maps, or chemograms, that highlight regions with high lipid content, quantified by the lipid core burden index (LCBI).[11] When combined with IVUS, this technology provides structural insights into plaque architecture and thickness, offering high specificity for lipid detection while producing interpretable, color-coded chemograms.[12] As with other IVUS platforms, the IVUS-NIRS system can be used *in vivo* with whole blood, without requiring contrast or saline flushes for image acquisition.[13]

Clinical evidence

There is a growing body of evidence supporting the utility of structural characterization of coronary atherosclerotic plaques.[14] Among the most pivotal studies is the prospective Lipid-Rich Plaque (LRP) trial,[15] which demonstrated that NIRS can safely and effectively identify vulnerable plaques and patients at increased risk of future coronary events. Specifically, plaques with a maxLCBI4mm ≥ 400 (cut-off value obtained from previous observational studies that found that atherosclerotic plaques causing acute coronary syndromes exhibited significantly elevated values of maxLCBI4mm ≥ 400) were associated with nearly double the risk of major adverse

cardiovascular events (MACE) compared to plaques with values < 400 (adjusted HR: 1.89; p = 0.0021) over a two-year follow-up period[16] *(Figure 1)*.

Subsequently, the PROSPECT II study evaluated the combined use of intravascular ultrasound (IVUS) and near-infrared spectroscopy (NIRS) in non-culprit arteries following a recent myocardial infarction, enrolling 898 patients with a median follow-up of four years.[8] The investigators identified three major plaque-level characteristics as predictors of adverse cardiovascular events during follow-up: high lipid burden defined by a maxLCBI4mm ≥ 324.7 (OR:7.8), plaque burden ≥ 70% (OR:12.9), and minimum lumen area (MLA) ≤ 4 mm^2 (OR:4.97). Lesions exhibiting both high lipid content and large plaque burden were associated with a 7% rate of adverse events at four years, while lesions without these features had an event rate of only 0.2%[17] *(Figure 2)*, suggesting that the combination of these two factors are the major contributors to the likelihood of atherosclerotic plaque rupture, even without taking into account the minimum luminal area.

Most recently, the PREVENT randomized controlled trial assessed the safety and efficacy of preventive PCI in non-ischemia-inducing vulnerable plaques (defined as fractional flow reserve > 0.80), compared with optimal medical therapy (OMT) alone.[18] The trial included 1,606 patients with stable CAD or acute coronary syndromes. The target lesions were not responsible for the index event, and patients were randomized to preventive PCI plus OMT (n = 803) or OMT alone (n = 803), with a two-year follow-up. Vulnerable plaques were identified based on at least two of the following criteria: MLA < 4.0 mm^2, plaque burden > 70%, maxLCBI4mm > 315, or thin-cap fibroatheroma (identified via optical coherence tomography). The incidence of the primary endpoint was significantly lower in the PCI group (0.4%) compared to the OMT group (3.4%), yielding an absolute risk reduction of 3.0% (p = 0.0003). At seven-year follow-up, the cumulative MACE rate remained lower in the PCI group (6.5%) versus the OMT group (9.4%)[19] *(Figure 3)*.

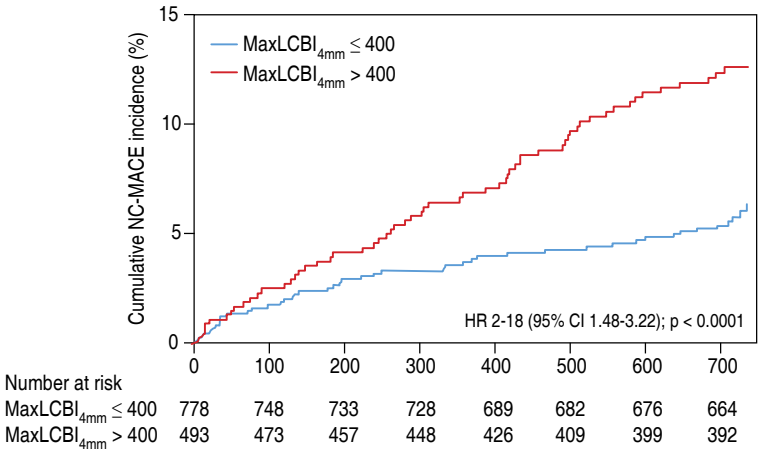

Figure 1: LRP study 24-month patient-level cumulative incidence of non-culprit MACE. Patients with maxLCBI$_{4mm}$ > 400 had an unadjusted HR of 2.18 (95% CI 1.48-3.22; p < 0.0001) and an adjusted HR of 1. 89 (1.26-2.83; p = 0. 0021) to have non-culprit MACE relative to patients with maxLCBI$_{4mm}$ of 400 or less.[15]

Technical aspects

The IVUS-NIRS catheter currently available in Mexico (DUALPRO-MAKOTO, Nippro, Japan) is compatible with 6 French or larger guide catheters and integrates both IVUS and NIRS sensors *(Figure 4)*, allowing simultaneous acquisition of structural and chemical imaging. The IVUS component operates within a frequency range of 35 to 65 MHz, which can be adjusted based on the required depth of penetration to generate high-resolution intravascular images. Automated pullback (up to 150 mm) is required for IVUS-NIRS image acquisition, with user-selectable speeds of 0.5, 1.0, or 2 mm/s. Manual IVUS image acquisition is also possible.

Once the pullback is completed, the main screen displays three key panels *(Figure 5)*. On the left, cross-sectional IVUS images are shown, with a surrounding halo indicating axial lipid distribution-red representing lipid-negative areas and yellow denoting lipid-rich zones. The upper-right panel shows the chemogram, a two-dimensional visual map that represents the probability of the presence of a lipid core plaque (LCP) within specific scan regions. High probabilities are represented in yellow, while lower probabilities gradually transition to red.

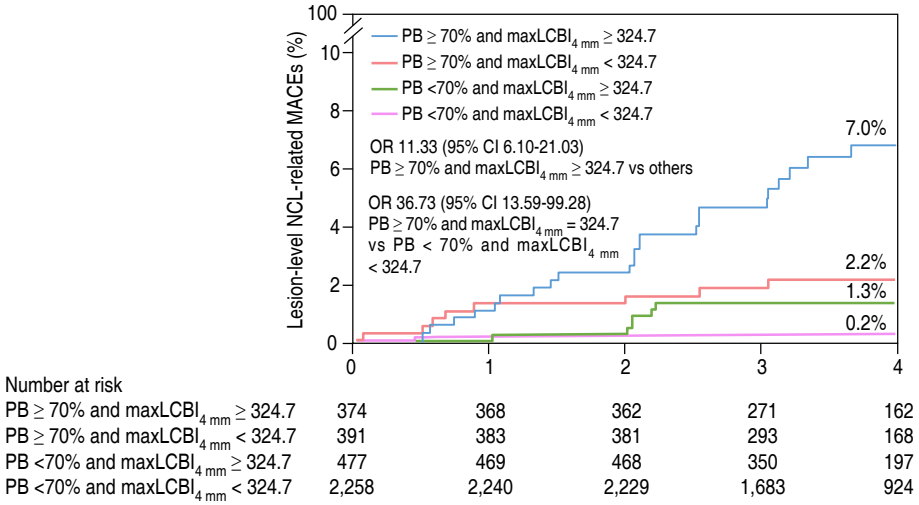

Figure 2:

Non-culprit lesion level MACEs at four years in the PROSPECT II study. The combination of high lipid content (maxLCBI4mm ≥ 324.7) and large plaque burden (≥ 70%) conferred the highest risk of MACEs (OR of 11.33) versus not having one of these plaque characteristics. Furthermore, not having both of them adjudged a very low probability of MACEs (0.2% of MACEs at four years).[8]

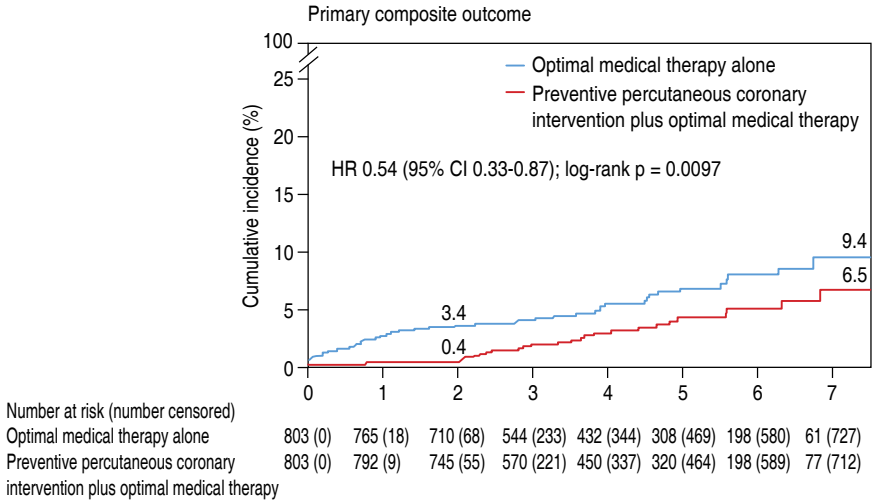

Figure 3:

Cumulative incidence of the primary composite outcome at seven years in the PREVENT trial. Although the frequency of events was low, PCI of non-ischemia-inducing lesions (plus optimal medical therapy) with high-risk characteristics resulted in fewer adverse events than optimal medical therapy alone.[18]

Yellow highlights are displayed when the lipid probability exceeds 0.6 at any point. To the left of the chemogram, the lipid core burden index (LCBI) is automatically calculated and presented. This index is derived from the ratio of positive lipid probability scores (> 0.6) to all valid lipid data points within the selected segment and is expressed on a 0-1,000 scale, reflecting low to high lipid burden. The system also displays the maximum LCBI in any predefined 4 mm segment (maxLCBI4mm), along with its exact location. The use of the 4 mm segment stems primarily from its practical implementation in early NIRS systems. Its length represents a compromise between spatial resolution and clinical relevance, allowing detection of focally dangerous areas without diluting them into longer segments. This 4 mm section of the assessed artery is quite narrow but sufficient to consider a surrogate for the circumferential extension of a lipid core, becoming the standard in clinical and validation studies, as it provides a focal and reproducible metric. The bottom-right panel provides a longitudinal IVUS image, overlaid with a block-level chemogram. This view is divided into 2 mm segments and uses a four-color scale (yellow, brown, orange, red) to summarize lipid probability from highest to lowest within each block.

Initial experience and utility in daily practice

Although the IVUS-NIRS platform has been available in Mexico for less than one year, it has rapidly proven valuable in both the diagnostic and interventional phases of coronary evaluation. During diagnostic procedures, IVUS offers high-resolution assessment of plaque morphology and vessel architecture, while NIRS provides chemical insight into intraplaque composition. During PCI, this technology allows intraprocedural assessment of stent results and identification of high-risk residual plaques.[20]

In our initial experience, in over 50 cases in an «all comers» fashion for either stable disease or acute coronary syndromes, the Makoto IVUS-NIRS system has been complication-free (0% of catheter-induced complications) and has identified multiple examples of lipid-rich atherosclerotic plaques. These findings have been used in clinical decision-making, allowing individualized treatment strategies.[21-23] Of these 54 initial cases in our experience, the information provided by IVUS-NIRS, in addition to the conventional use of IVUS for technical guidance of our PCIs, resulted in stenting of two non-culprit (two different patients) non-ischemia-inducing atherosclerotic plaques *(Figures 6 and 7)* that had been previously assessed by Instantaneous Wave-Free Ratio (iFR) but with very high risk characteristics by IVUS-NIRS, high-risk location (proximal coronary segments), and concomitant high clinical risk factors (both acute coronary syndrome context). In addition, lesions with a fibrotic appearance on IVUS were frequently observed, but with

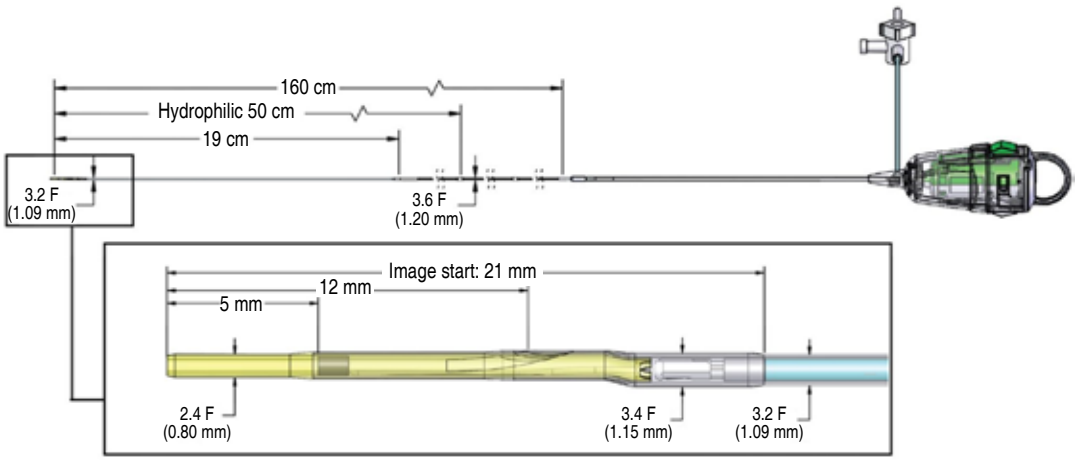

Figure 4:

Dual-Pro Makoto Catheter.[25]

Figure 5:

Main working display of the Makoto IVUS-NIRS console.
IVUS = integrated with intravascular ultrasound. NIRS = near-infrared spectroscopy.

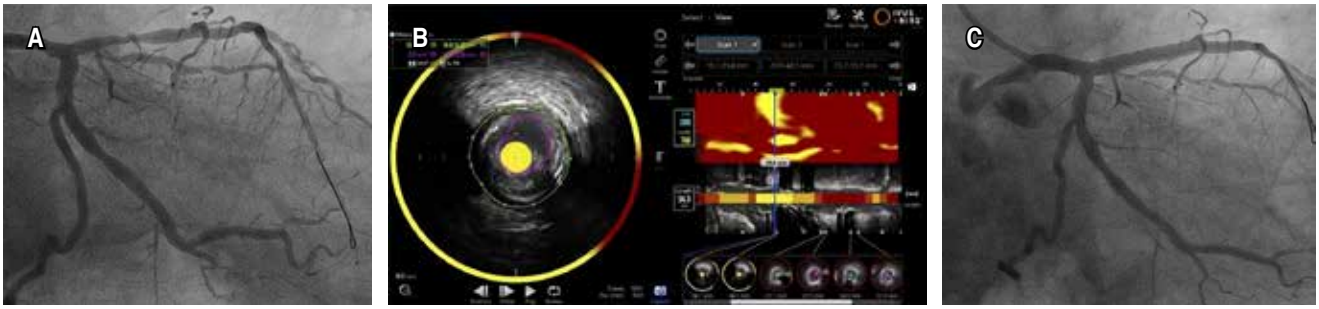

Figure 6: A) Non-ischemia inducing stenosis in the proximal Left anterior descending by Instantaneous Wave-Free Ratio (iFR 0.92). **B)** High-risk features identified by IVUS-NIRS: on the left, the axial IVUS image reveals a mixed-content atherosclerotic lesion with heterogeneous appearance and multiple intraplaque hypoechoic zones. In the upper left, measurements show a minimum lumen area (MLA) of 3.7 mm^2 and a plaque burden (PB) of 72%. The circumferential halo highlights the axial distribution of lipid content. On the right, the longitudinal chemogram demonstrates a high lipid burden with a $maxLCBI_{4mm}$ of 766. In the bottom-right, the longitudinal IVUS image combined with a block-level chemogram shows intense yellow areas representing regions of maximal lipid concentration. **C)** Angiographic result after IVUS-guided stent implantation.
IVUS = integrated with intravascular ultrasound. NIRS = near-infrared spectroscopy.

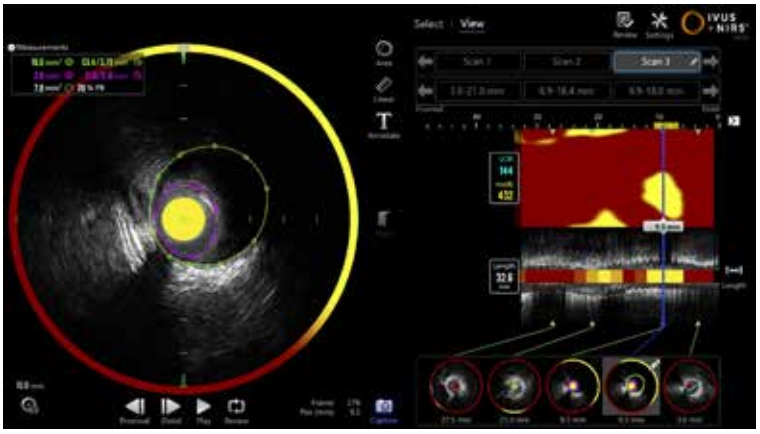

Figure 7: Atherosclerotic plaque at the right coronary artery, predominantly composed of lipid-rich content, evidenced by a $maxLCBI_{4mm}$ of 432. This finding is consistent with predominantly hypoechoic regions in the axial IVUS image. The circumferential yellow halo confirms the axial localization of intraplaque lipid. Considered a high-risk plaque by high lipid core burden, high plaque burden (70%), and a minimum lumen area of less than 4 mm^2.
IVUS = integrated with intravascular ultrasound.

considerable amount of intraplaque lipids by NIRS *(Figure 8)*. Also, the other nine non-ischemia-inducing atherosclerotic plaques with high lipid burden by IVUS-NIRS were found (maxLCBI4mm > 315) at distal coronary segments but without other characteristics associated with plaque vulnerability (MLA > 4 mm or plaque burden < 70%). Nevertheless, that discovery led to an intensification of their lipid-lowering treatment beyond that originally intended, specifically the addition of PCSK9 inhibitors to the usual statin plus ezetimibe regimen.

While a uniform consensus has yet to be established, current data suggest that a vulnerable atherosclerotic plaque-prone to rupture or erosion-is currently defined by a combination of a maxLCBI4mm > 315 on NIRS (324 in the PROSPECT trial), a minimum lumen area < 4.0 mm^2, and a plaque burden > 70% on IVUS (or a fibrous cap thickness < 65 µm on optical coherence tomography).[17] This additional diagnostic layer provided by IVUS-NIRS may, in highly selected cases, support a decision to intervene on a non-ischemia-inducing lesion with high rupture potential. Conversely, it may justify a conservative approach in borderline functional lesions that lack vulnerability features. Furthermore, identifying plaques with high lipid content should prompt intensification of lipid-lowering therapy, aggressive modification of cardiovascular risk factors (e.g., smoking cessation, treatment of hypertension or diabetes), and closer clinical follow-up.[24]

The implementation of this technology in Mexico is still associated with several challenges. There is limited availability of IVUS-NIRS consoles nationwide, and the system carries

a higher cost compared to basic intravascular ultrasound platforms. Although the acquisition of NIRS-derived images requires only a short learning curve, proper interpretation across various clinical scenarios necessitates specific training and experience.

CONCLUSION

The incorporation of IVUS-NIRS technology into interventional cardiology practice in Mexico represents a significant advancement in the structural and functional characterization of coronary atherosclerotic plaques. Historically, therapeutic decision-making has been guided primarily by angiographic and physiological criteria, which, although effective for evaluating hemodynamically significant stenoses, are limited in their ability to detect biologically vulnerable lesions at high risk of rupture. IVUS-NIRS bridges this gap by integrating two complementary modalities: near-infrared spectroscopy for direct detection of intraplaque lipid content, and intravascular ultrasound for high-resolution assessment of plaque morphology, burden, luminal dimensions, and post-PCI outcomes.

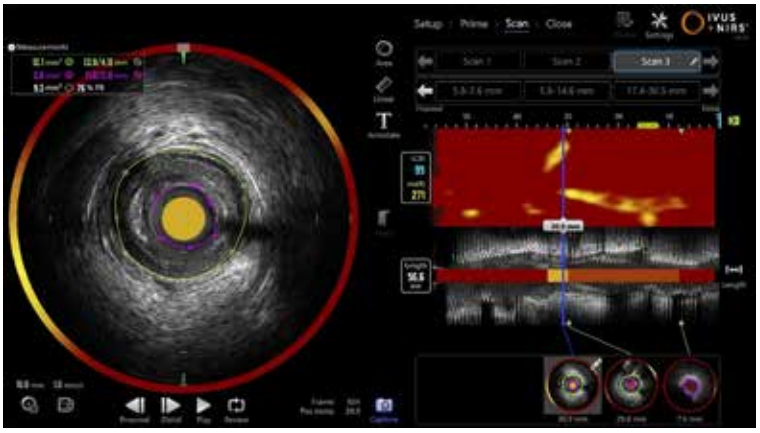

Figure 8: Image of a mixed atherosclerotic plaque at the right coronary artery. The axial IVUS image displays hypoechoic regions interspersed with isoechoic and hyperechoic areas. Evaluation of the corresponding chemogram revealed a moderate lipid burden with a maxLCBI$_{4mm}$ of 271, consistent with the mixed nature of the plaque. Notice the high plaque burden (76%) and the minim lumen area of 2.8 mm^2. The iFr of this lesion resulted in 0.82, so it was treated with stenting.
IVUS = integrated with intravascular ultrasound.

This combined imaging strategy enables more refined risk stratification, supporting percutaneous interventions tailored to the biological vulnerability of each lesion. The availability of IVUS-NIRS in Mexico and across Latin America opens the door to a new paradigm in precision cardiovascular medicine. Its integration into routine cath lab workflows has the potential not only to optimize immediate clinical outcomes but also to establish preventive strategies for high-risk patients, enabling more precise decisions regarding when to intervene and whom to target for intensified medical therapy.

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Protocol for certifying stadiums in Mexico as cardio-protected spaces in the 2026 Soccer World Cup

Protocolo para la certificación de estadios en México como espacios cardioprotegidos en el Mundial de Fútbol de 2026

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Keywords: cardioprotection protocol, stadiums in Mexico, World Cup.

Palabras clave: *protocolo de cardioprotección, estadios de México, Copa Mundial de Fútbol.*

ABSTRACT

Sudden cardiac death (SCD) events at sporting events have raised awareness due to their media impact, and soccer is no exception. The next International Federation of Association Football (FIFA, by its acronym in Spanish) World Cup to be held in Mexico in 2026 must have a structured program to deal with an SCD event expeditiously and efficiently. It is known that SCD events occur more frequently among the public and staff than among players in a stadium. Thus, in this article, the Asociación Nacional de Cardiólogos de México (ANCAM) proposes a cardioprotection protocol for the three Mexican stadiums that will host the 2026 FIFA World Cup.

RESUMEN

La muerte súbita cardiaca (MSC) en eventos deportivos ha creado conciencia por su impacto mediático, y el fútbol no está exento de ello. La próxima copa del Mundo de la Federación Internacional de Fútbol Asociación (FIFA) a realizarse en México en 2026 debe contar con un programa estructurado para poder atender un evento de MSC de manera expedita y eficiente. Se sabe que los eventos de MSC se presentan con mayor frecuencia entre el público y personal del mismo en comparación con los jugadores en un estadio. Con base en ello, en este artículo la Asociación Nacional de Cardiólogos de México (ANCAM) propone un protocolo para la cardioprotección de los tres estadios mexicanos, sedes de la Copa del Mundo de la FIFA 2026.

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Abbreviations:

AED = Automated External Defibrillator
ANCAM = National Association of Cardiologists of Mexico (Asociación Nacional de Cardiólogos de México for its Spanish meaning)
CPR = Cardiopulmonary Resuscitation
EMS = Emergency Medical Systems
ILCOR = International Liaison Committee on Resuscitation
SCA = Sudden Cardiac Arrest
SCD = Sudden Cardiac Death

INTRODUCTION

At the heart of every massive event beats the passion of thousands or even millions of people united by the same goal. The 2026 FIFA (by its acronym in Spanish, International Federation of Association Football) World Cup in Mexico promises to be more than a sporting spectacle: it will be a milestone for global connection and celebration. However, behind the euphoria, there is a vital challenge that we cannot ignore: the cardiovascular health of attendees, players, and staff involved. Although it does not happen frequently, Sudden Cardiac Arrest (SCA) during sporting events is an occurrence that can have fatal consequences for athletes and spectators who attend the stadiums and has a substantial impact on the players, teams, the community, the sport in general, and public health.[1,2]

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Several studies suggest that the incidence of SCA may be higher in athletes than in the general population, but spectators in the stadium are at a higher risk of Acute Coronary Syndrome (ACS) than those outside the stadium.[3,4]

International events of this magnitude present unique risk scenarios, where the high density of people gathered in a single setting, together with euphoria, emotional stress, and intense physical activity, can trigger cardiac emergencies among not only the competitors but also the spectators, merchants, and organizers.[5,6]

Cardioprotection, defined as implementing immediate response protocols for victims of Sudden Cardiac Death (SCD) that include high-quality cardiopulmonary resuscitation (CPR) and access to an Automated External Defibrillator (AED) in less than five minutes, has been established as a fundamental pillar to guarantee the safety and well-being of all, and it is a concept that must include massive sporting events.[7-10]

Strategic planning for adequate cardioprotection in the stadiums hosting the 2026 FIFA World Cup in Mexico can save lives and send a strong message: «Healthcare in sports must be prioritized as much as the sports events themselves».

This article is the result of a collective effort by cardiologists who are members of the National Association of Cardiologists of Mexico (ANCAM) and seeks to raise awareness about the urgency to integrate cardio-protective areas and cardiovascular care protocols in the soccer stadiums that will host the World Cup, highlighting the crucial role that authorities, organizers (including Mexican Soccer Federation), and health professionals will play in this global effort.

SOCCER UNITES THE WORLD

The «Football Unites the World» strategy, launched by FIFA, is a global initiative that uses football as a tool for unity and development in an international context marked by divisions and crises. In collaboration with the World Health Organization (WHO), this strategy promotes values such as health, equality, inclusion, and sustainability.

Formal collaboration between FIFA and the WHO began in 2019 with the signing of a memorandum of understanding. Since then, the partnership has grown stronger, leveraging the global reach of soccer to improve public health and foster social integration.

This campaign covers physical activity, promoting mental health, ensuring equitable access to health services, and addressing social issues, including online discrimination and hate. During the 2022 FIFA World Cup in Qatar, specific measures were implemented to turn stadiums into platforms for promoting healthy lifestyles and general well-being.

Cardioprotection at mass events, such as the 2026 FIFA World Cup, can become a natural extension of this WHO-FIFA strategy. Setting robust cardioprotection standards reflects this commitment in action; incorporating cardiovascular prevention and response measures as part of events protects attendees' lives and symbolizes a powerful message: sport must be a catalyst for health care at all levels. Just as football unites nations, a global network of cardio-protected stadiums can join efforts to save lives and build a legacy of safety and awareness for future generations.

RISK OF SCD IN STADIUMS

Most SCD events in athletes are caused by structural heart disease, presenting mainly with ventricular fibrillation or pulseless ventricular tachycardia.[5,11-15] The increased physical exertion of high-intensity activity can trigger an event of SCD, and this explains why these events occur mainly during training or within one hour after it.

The fact that not only athletes but also spectators are at high risk of suffering an SCD event in stadiums needs to be highlighted. The risk factors for this to happen include demographics, the stress of the moment, the emotional condition, the physical condition, substance and/or alcohol abuse, and weather conditions present in the game, such as high temperatures and humidity.

Crawford et al. report that 16.5% of victims of an SCA event at a football stadium in Glasgow, Scotland, were non-spectators, including staff.[5,6,16-20]

Another point to mention is that people who experience an acute coronary syndrome event in the stages are significantly more likely to be carriers of underlying heart disease compared to people who experience an SCD event outside the stages.[4,8,21]

The risk of an SCA event doubles in the areas around the stadium on game day, with an increase in the incidence of SCA in stadiums when the home team has an important match or against a good or famous rival team, possibly related to emotional stress and substance abuse before and during the game, as mentioned above.[22]

Therefore, compared to the general population, prevention of SCA events in the later stages requires special and different measures to ensure that this higher incidence will be successfully treated to prevent future complications.[8]

ROLE OF THE AED ON THE OUTCOMES OF SUDDEN CARDIAC ARREST

The survival rate of a patient who suffers SCA decreases between 7 and 10% per minute until defibrillation is administered. Probably the most critical determinant of survival to SCA is the delay between collapse and AED use in subjects with arrhythmias treatable by cardioversion or defibrillation. The highest success rates are achieved when electrical therapy is administered between three and five minutes after the arrest.[23-25]

Although many efforts have been made in SCA risk screening programs to identify a person with a risk factor or underlying disease, the risk of SCA remains high in athletes. Despite the implementation of these measures for multiple reasons, false negatives and hidden heart disease, this is one more reason for the placement of AEDs in stadiums.[26,27]

AEDs and early Cardiopulmonary Resuscitation (CPR) are the treatment of choice for patients with SCA. Data on football players with SCA receiving CPR showed an increase in survival rates from 23 to 50% compared to the general population when they receive CPR on time, and these numbers improve when the use of an AED is added to CPR maneuvers.[28-30]

Survival rates in stadiums are better than elsewhere due to greater availability and faster response of AEDs and CPR, including Emergency Medical Systems (EMS). Bystander CPR and AED use have also improved survival, which may apply to stadiums.[31,32]

ENOUGH AEDS IN NUMBER AND THEIR LOCATION

Despite evidence showing that the use of AEDs improves survival rates, many stadiums worldwide, including those in Mexico, do not have AEDs in their facilities. Borjesson et al. report that, across Europe, stadiums only have AEDs for matches and training, and 74% do not have personnel with advanced CPR training available.[33]

Malhotra et al. (2019) reported that all professional football stadiums in England had AEDs for their matches and training. Many of the stadiums that do not have AEDs may have local emergency action programs and protocols for community defibrillation when an SCD event occurs. However, as reported, this response takes more than 10 minutes in 33% of cases.[33,34]

To easily identify the location and number of available AEDs, the American Heart Association (AHA) recommends placing an AED within 1 to 1.5 minutes or approximately 160 m away from where an SCD event could potentially occur.[35]

The time required for a rescuer to grab the defibrillator, bring it to the scene, and place it on the patient should also be taken into account, giving a more accurate estimate of response time.

AED SIGNALING

The International Liaison Committee on Resuscitation (ILCOR) designed international symbols to indicate the locations of AEDs *(Figure 1)*. However, these symbols are not easily recognized by the general public: on average, 39% of travelers from 42 different countries recognize the symbology (range 29.4 to 47.9%).[36,37] The UK Resuscitation Council considered these data and changed the signs, obtaining 83.5% of the public's approval.[38]

In the context of an SCA event at a stadium, the rapid response of spectators, staff, and the

facility's EMS personnel must be able to find and locate an AED for its use quickly. Explicit signaling of the site where it is located is thus a priority.

Figure 2 shows the ANCAM's suggested signage to indicate the location of AEDs and their use.

Figure 1: International signal recognized by the ILCOR for the location of automatic external defibrillators.

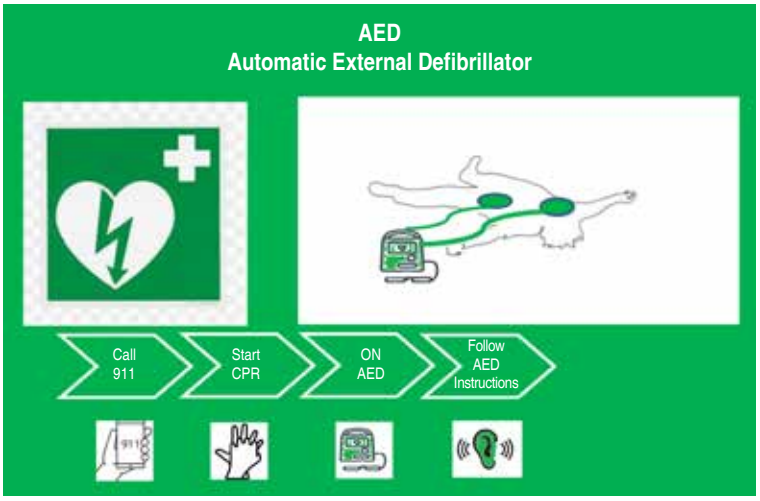

Figure 2: Signal for the AED in the stadium.
Modified from D Bassi M, Farina JM, Bombau J, Maurice MF, Bortman G, Nuñez E, et al. Sudden Cardiac Arrest in Basketball and Soccer stadiums, the role of Automated External Defibrillators: a review. For the BELTRAN Study (Basketball and Soccer stadiums: registry on Automatic external defibrillators). Arrhythmia & Electrophysiology Review 2023; 12: e03. doi: 10.15420/aer.2022.30.

IS A WORLD CUP POSSIBLE WITH CARDIO-PROTECTED STADIUMS?

The proposal for an immediate response protocol for an SCD seeks to be a comprehensive and multifaceted solution to achieve the goal of rescuing a victim in the event of an incident occurring at any of the 2026 FIFA World Cup football matches and not only on the field but in all facilities, both inside and outside the stadiums.

The protocol applies in general to the three World Cup Mexican stadiums: Azteca Banorte Stadium in Mexico City (CDMX), Akron Stadium in Zapopan, Jalisco, and the BBVA Bancomer Stadium in Monterrey, but it will have to be adapted to the peculiarities of each stadium according to its capacity, structure, map, and access.

The Azteca-Banorte Stadium

The Azteca Stadium, now called «Azteca Banorte», is an iconic venue, renowned for its rich history and capacity to accommodate over 87,000 spectators, serving as a prime example for implementing the cardioprotection protocol in locations hosting the 2026 FIFA World Cup.

This venue has demonstrated its commitment to the safety and well-being of attendees by adopting prevention and emergency response measures. Among the reasons that support her role as a model are:

1. Medical infrastructure: The Azteca Banorte Stadium has several nearby medical units strategically distributed, which guarantee rapid intervention in case of emergencies.
2. Established agreements with nearby hospitals with a Cardiovascular Intensive Care Unit and a hemodynamics room available, both with certified personnel, during the event (from one hour before and up to two hours after the event).
3. Integrated emergency protocols: This venue has implemented efficient communication systems that coordinate medical, security, and logistics personnel to optimize care at mass events, minimizing response times.

4. Staff training and public awareness: Through periodic training programs, the stadium team and volunteers receive training in medical emergencies, promoting attendees' awareness of the importance of acting in an emergency.
5. Operational tests: The Azteca Banorte Stadium has demonstrated its ability to respond effectively to high-demand massive events, such as international matches and concerts, making it a real laboratory for validating protocols.

Taking a similar approach at the stadiums hosting the 2026 FIFA World Cup will standardize safety measures and boost public confidence in the organizers' preparations. Cardioprotection must be a priority at events of this magnitude, and the Azteca Banorte Stadium shows us that it is possible to integrate health, technology, and logistics to save lives and protect those who make football the most exciting sport in the world.

Chivas Akron Stadium and Monterrey BBVA Stadium

The Chivas Akron Stadium has a capacity of 49,850, and the Monterrey BBVA Stadium has 53,500 spectators, respectively.

The maps of the three World Cup Mexican stadiums are represented in *Figures 3-5*.

The suggested locations for placing AEDs and their signage in each of the three stadiums are shown in *Figures 6 to 8*, respectively.

Implementation

This protocol seeks to ensure a rapid, coordinated, and effective response to any cardiovascular emergency, maximizing the chances of survival. To ensure that all personnel are fully prepared, the following must be taken into account:

1. Start of training (six months before the event):

    a) Begin training key staff (security, ushers, volunteers, and medical teams) in high-quality basic CPR and AED use.
    b) Conduct progressive training to ensure all rotating staff are covered.

2. Review and drills (three months before the event):

    a) Organize comprehensive drills at the stadium to measure response times. It helps fine-tune weak points in the protocol.
    b) Refresh training for staff who require it.
    c) Inform the public of the cardioprotection protocol that will be in effect during each match of the 2026 FIFA World Cup.

3. Final training (two weeks before the event):

    a) Refresher session with all personnel involved.
    b) Conduct a general drill under conditions similar to the event day (with attendees, real times, and specific roles assigned).

Protocol operation

The protocol must be fully operational seven days before the event, following the checklist:

- All medical equipment, AEDs, signage, and technology must be installed, tested, and ready to use.
- The command center and mobile emergency teams must communicate 72 hours before the event.

A checklist is suggested to ensure it is properly implemented:

- All medical equipment, AEDs, signaling, and technology must be installed, tested, and ready for use.
- The command center and mobile emergency teams must be in communication.

On the day of the event

First thing in the morning:

1. Mobile medical teams, security personnel, and volunteers are already in their assigned positions.
2. Confirm that all critical points (AED, communication, mobile application) are functional.

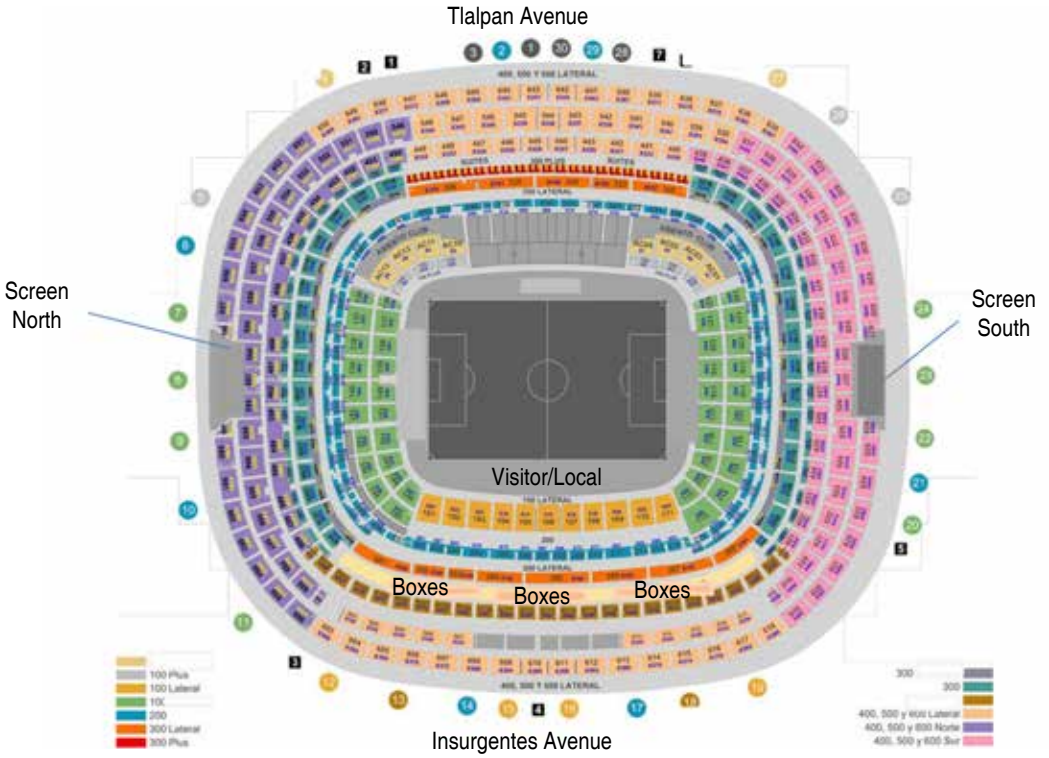

Figure 3:

Map of the Azteca Banorte Stadium in Mexico City, Mexico.

Figure 4:

Map of the Chivas Akron Stadium in Zapopan, Jalisco, Mexico.

Figure 5:

Map of the Monterrey BBVA Stadium in Monterrey, Nuevo León, Mexico.

3. Verify the ambulances' evacuation routes, which have the easiest and fastest access to the reference hospital with real-time updates. Assure cooperation with police authorities to help expedite ambulance mobilization.
4. Confirm with the hospitals that they agree on their availability for an SCA event that day.
5. It is suggested that event attendees receive free training in basic CPR and AED use, which ANCAM can provide.

On the day of the event, early in the morning:

- Keep staff on active alert from at least six hours before, throughout the match, and until the last person has left the stadium facilities, concourses, and parking lots.
- Conduct a dissemination campaign using visual advertisements to explain the cardioprotection protocol. When and how is it activated? What application should they have installed on their smartphones?
- Mobile medical teams, security personnel, and volunteers are already in their assigned positions.
- Confirm that all critical points (AED, communication, mobile application) are functional.
- Free training in basic CPR and AED use is suggested for event attendees.

During the Event:

- Keep staff on active alert from at least six hours before, throughout the match, and until the last person has left the stadium facilities, esplanades, and parking lots.
- Conduct a campaign to disseminate the cardioprotection protocol through visual advertisements, explaining what it entails. When and how is it activated? Which application should they install on their smartphones?

Closing of the event (debriefing):

- An executive report of the protocol must be made, as well as the incidents and/or medical care events that occurred during it.
- Improvement proposals based on the areas of opportunity and the threats detected during

Figure 6: Automatic external defibrillator location at Azteca Banorte Stadium in CDMX, Mexico.

Figure 7: Automatic external defibrillator location at Chivas Akron Stadium in Zapopan, Jalisco, Mexico.

Figure 8: Automatic external defibrillator location at BBVA Stadium in Monterrey Nuevo León, Mexico.

the application of the cardioprotection protocol at the end of the meeting.

– In the case of an SCA event, verify the care times, log records, follow up on the case with the reference hospital, and do not close the follow-up of this until the recovery and/or discharge from the hospital of the victim.

Transfer of the victim

Based on the family's decision, the victim will be transferred to the third-level hospital of their choice, having previously consulted the availability of cardiovascular equipment at the site where the victim will be transferred. An initial route by land ambulance must be drawn between the stadium and each hospital where the patient could be moved. In turn, an alternate route must be available in case of any unforeseen event, such as a car collision, closed streets, and demonstrations.

The hospitals closest to each of the three stadiums that have a 24/7 cath lab available are listed below:

Hospitals closest to Azteca Banorte Stadium in CDMX

1. National Institute of Cardiology «Ignacio Chávez». Distance: approximately 8.3 km. (20-30 minutes driving). Location: Juan Badiano No. 1, Col. Section XVI, Tlalpan, Mexico City.

2. National Institute of Medical Sciences and Nutrition «Salvador Zubirán». Distance: approximately 8.5 km. (25-35 minutes driving). Location: Vasco de Quiroga 15, Col. Belisario Domínguez Section XVI, Tlalpan, Mexico City.

3. Ángeles del Pedregal Hospital. Distance: approximately 8.3 km. (20-30 minutes driving). Location: Camino Sta. Teresa 1055-S, Heroes de Padierna, Héroes de Padierna, La Magdalena Contreras, 10700 Mexico City.

4. Ángeles Acoxpa Hospital. Distance: approximately 2.3 km (20 minutes

driving). Location: Calz Acoxpa 430, Coapa, Exhacienda Coapa, Tlalpan, 14308 Mexico City.

5. General Hospital of Mexico «Dr. Eduardo Liceaga». Distance: approximately 20 km. (40-50 minutes driving). Location: Dr. Balmis 148, Doctores, Cuauhtémoc, Mexico City.

6. Pemex Central South High Specialty Hospital. Distance: approximately 7.7 km (20-30 minutes driving). Location: Anillo Perif. 4091, Fuentes del Pedregal, Tlalpan, 14140 Mexico City.

7. Medica Sur Tlalpan Hospital. Distance: approximately 1.8 km (10 minutes driving). Location: Puente de Piedra 150. Col. Toriello Guerra Tlalpan. 14050 Mexico City.

Hospitals closest to Akron Stadium in Zapopan, Jalisco

1. New Civil Hospital of Guadalajara «Dr. Juan I. Menchaca». Distance: 16 km (25-30 minutes driving). Location: Salvador Quevedo and Zubieta 750, Independencia Oriente, Guadalajara.

2. General Hospital of the West (Zoquipan). Distance: 10 km (15-20 minutes driving). Location: Av. Zoquipan 1050, Zapopan, Jalisco.

3. Puerta de Hierro Andares Hospital (Zapopan). Distance: 11 km (15-25 minutes driving). Location: Blvd. Puerta de Hierro 5150, Zapopan, Jalisco.

4. Puerta de Hierro Sur Hospital. Distance: 18 km (25-35 minutes driving). Location: Av. López Mateos Sur 1710, Tlajomulco de Zúñiga, Jalisco.

Hospitals closest to Monterrey BBVA Stadium in Monterrey, Nuevo Leon

1. University Hospital «Dr. José Eleuterio González». Distance: approximately 12 km from the BBVA Stadium. (25-35 minutes driving). Location: Av. Dr. José Eleuterio González S/N, Mitras Centro, 64460 Monterrey, NL.

2. Zambrano Hellion Hospital. Distance: 16 kilometers from the BBVA Stadium (20 to 25 minutes driving). Location: Av. Batallón de San Patricio 112, Real San Agustín, 66260 San Pedro Garza García, N.L.

3. Christus Muguerza Alta Especialidad High Specialty Hospital. Distance: approximately 16 km. (20-25 minutes driving). Location: Miguel Hidalgo y Costilla 2525, Obispado, 64060 Monterrey, N.L.

4. Ángeles Monterrey Hospital. Distance: About 17 km (20 to 25 minutes driving). Location: Calz. del Valle 325, Del Valle, 66220 Monterrey, NL.

5. Doctors Hospital East. Distance: 7 Km (17 minutes driving). Location: Av. Prol. Francisco I. Madero 6060, Libertad, 67130 Guadalupe, N.L.

This planning will ensure the protocol is effective and operational from pre-event to conclusion.

CONCLUSIONS

1. Any stadium has a high incidence of SCA among athletes, spectators, and staff. The three World Cup Mexican stadiums are no exception. AEDs should be in sufficient numbers and placed strategically with easy access to the SCA event site.
2. Survival and complications of patients with SCD are significantly improved when CPR and AED are provided at the site of the SCA. The three World Cup Mexican stadiums should be equipped with AEDs and CPR-trained personnel on-site, without having to wait for EMS systems to come from outside the stadium to provide the service.
3. All three World Cup Mexican stadiums must have proper signage, and visualization of the AED location improves ease of use and facilitates rapid deployment. Visible signage, including bright colors, instructions, and additional directional signage > 5m

away, will allow for early deployment of defibrillation.

4. The three World Cup Mexican stadiums must have a dedicated program and an emergency action plan that includes the care of an SCA at any stage. The plan must be practiced at least once a year to improve, review, and care for the SCA.

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Uncertainty and probability are the basis of clinical epidemiology

La incertidumbre y la probabilidad son la base de la epidemiología clínica

José Luis Moragrega*

Keywords: complexity, Bayes theorem, probability, science.

Palabras clave: *complejidad, teorema de Bayes, probabilidad, ciencia.*

ABSTRACT

In science, including biology, complexity is the hallmark of the epoch. Statistics is the science of probability, and it is widely used since there is no certainty about the significance of the findings in an investigation, nor in a patient's data in the diagnosis or prognosis that we construct in clinical settings. The reductionism that medicine has employed to understand complex situations and construct the so-called «operative definition» to simplify complex problems must be revised to achieve a deeper understanding of the interactions among multiple factors influencing human bodily behavior.

RESUMEN

En la ciencia, incluyendo la biología, la complejidad es el sello distintivo de la época. La estadística es la ciencia de la probabilidad y es muy utilizada, ya que no hay certeza sobre la importancia de los hallazgos en la investigación ni en los datos de los pacientes en el diagnóstico o pronóstico que construimos en los entornos clínicos. El reduccionismo que la medicina ha elaborado para comprender muchas situaciones complejas y construir la llamada «definición operativa» para simplificar un problema que, de otro modo sería complejo, tiene que cambiarse por la comprensión profunda de las interacciones de muchos factores que influyen en el comportamiento del cuerpo humano.

INTRODUCTION

We know that statistics is the science of probability, and in relation to statistics and medicine, Sir William Osler wrote that, «Medicine is a science of uncertainty and an art of probability».[1]

In 2021, I published an article on how medicine is both a science and an art.[2] Now, as we define the role of statistics, we unveil another association between the two disciplines. In an era marked by complexity, as the late German physicist Hans-Peter Dürr[i] suggested, we must abandon reductionism and use statistics to comprehend natural phenomena. Albert Einstein held fast to his position on determinism, but Niels Bohr won out; Bohr's work confirmed Werner Heisenberg's uncertainty principle as the basis of quantum mechanics. You can read the beautiful book by Ian Stewart entitled «Does God Play Dice?»[3] and enjoy this beautiful dissertation.

Of course, in some moments it will rain if you are in the midst of a hurricane, and of course, you will die if you have rabies. However, in almost all other circumstances, events will occur with a certain probability. Medicine and meteorology are two fields where uncertainty is the norm. The simplest probabilistic statement will tell you the percentage probability of rain in the next 24 hours or the likelihood that pneumonia will resolve with a specific treatment. If it does not rain or the infection persists, this should not be surprising, given the probability of this occurrences.

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[i] https://frasesdedios.blogspot.com/2016/11/la-realidad-ya-no-permite-reduccionismo.html

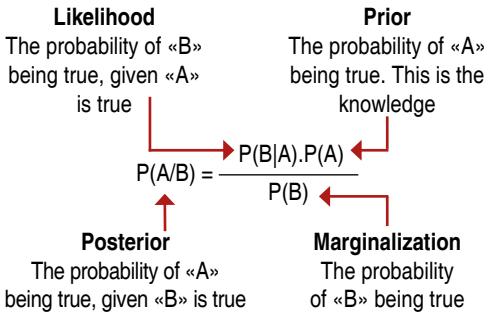
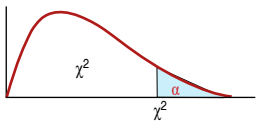


Figure 1: Conditional probability or Bayes' formula.

Table 1: Errors table. We can see that the concept is the same as accepting or rejecting the null hypothesis in scientific investigation.

	Reality	
Test	Sick	Healthy
	Accept alternative hypothesis H_1	Accept null hypothesis H_o
Sick		
Accept alternative hypothesis H_1	Correct ✓	Incorrect **Type I error** ✗
Healthy		
Accept null hypothesis H_o	Incorrect **Type I error** ✗	Correct ✓

Contingency table



Test	Reality	Sick	Healthy	Total
Positive		TP a	a FP	a + b
Negative		FN c	d TN	c + d
Total		a + c	b + d	N

TP: true positives
FP: false positives
TN: true negatives
FN: false negatives

a/a + c = sensitivity
d/b + d = specificity
a/a + b = predictive value of the positive test
d/c + d = predictive value of the negative test

Figure 2: We can visualize the sensitivity (a/[a + c]) and specificity (d/[b + d]), along with the false positives (FP) and false negatives (FN), as shown by the vertical arrows. However, to determine the predictive value of a single patient, we calculate the proportion of positive (a/a + b) or negative (d/c + d) test results, as indicated by the horizontal arrows.

In biostatistics, we express the probability that the calculated sample values accurately reflect the parameters of the universe from which the sample is drawn. The most commonly used calculations are presented as confidence intervals or «p» values, where the probability can range from 0 to 1.

Probability values can be expressed as fractions, where the numerator represents the number of cases of a disease and the denominator represents the exposed population. For instance, the number of diabetics among obese males is 10/100. Furthermore, this can be express as 10%. This is the simplest way to measure uncertainty. However, in biology, the effect of the independent variable (obesity) on the dependent variable (diabetes) is always influenced by other factors. In addition to body weight, we can calculate the impact of age, gender, physical activity, genetics, and many other factors. As you can see, we are entering a complex realm, one that is no longer bound by the reductionism that has plagued medicine thus far. Conditional probability is a statistical measure that indicates the probability of an event «A» occurring if another event «B» has happened. That is the conditional probability P(A|B) *(Figure 1)*. In clinical medicine, we encounter multifactorial events every day, and it remains a mystery how medical professionals evaluate the information and make decisions. For example, we can apply an algorithm to a patient with chest pain to categorize them by gender, age group, and type of pain. This helps us determine the probability that the pain is ischemic.

A situation where the concept of conditional probability is beneficial is in the evaluation of laboratory and imaging tests. Our example will help illustrate that the values of sensitivity and specificity are not sufficient to assess the usefulness of a test. We must calculate the predictive value of a positive or negative test and then estimate the prevalence of the disease in the group to which an individual patient belongs (the prior probability). We then use Bayes' theorem, which involves the proportion of probabilities (also known as the likelihood ratio), to calculate the posterior probability.

	Myocardial infarction		
Troponin	Sick	Healthy	
+	TP A 95 (0.95) SENS	B 20 (0.2) FP	C 115
–	D FN 5 (0.05)	SPEC E 80 (0.8) TN	F 85
	G 100	H 100	200

Figure 3: Shows the published sensitivity (SENS) (95%) and specificity (SPEC) (80%) of the troponin test for myocardial infarction in patients with acute chest pain.[8]

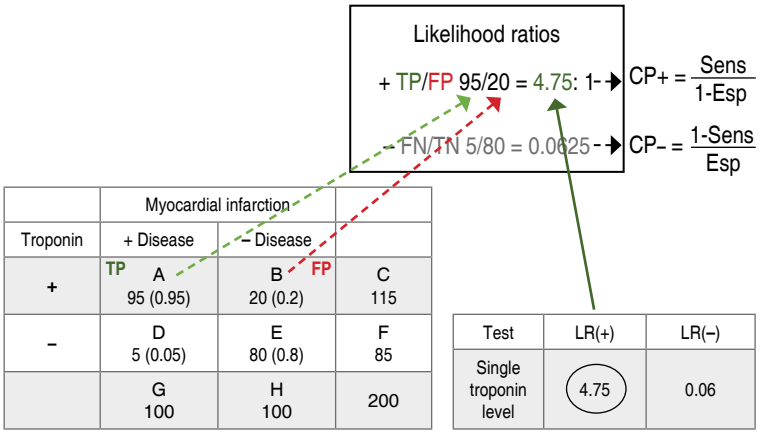


Figure 4: The proportion of true positives and false positives is the probability quotient of a positive test.

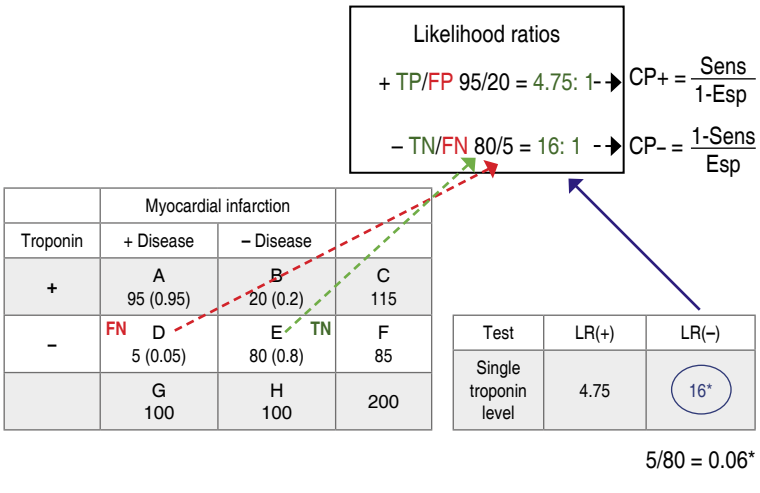


Figure 5: The proportion of true negatives and false negatives is the probability quotient of a negative test.

Let us begin by portraying in a contingency table, the test's results against the «reality» or the best estimation with the gold standard, accordingly to the state of the art *(Table 1)*.

A good test correctly identifies most sick individuals (sensitivity) and the healthy ones (specificity). Now, using the same table, we will calculate the sensitivity, specificity, and predictive values of a positive or negative test *(Figure 2)*. We will utilize the sensitivity and specificity of the troponin test, which is often used to evaluate patients with chest pain *(Figure 3)*. Then, we calculate the Bayes or likelihood ratio for a positive or negative test result. In *Figure 4*, we observe that the ratio of actual positives to false positives is 4.74 to 1. In *Figure 5*, we observe 16 cases of an actual negative test for every false negative, indicating that the test has better sensitivity than specificity and a better predictive value for ruling out the disease than for confirming it.

We will use these likelihood ratios in a nomogram published by Fagan,[4] but in order to illustrate the values for a negative or a positive test on the same graph, since the scale is exponential for the favorable ratio and logarithmic for the negative, we will calculate the negative likelihood ratio as FN/TN instead of TN/FN. In this case, the quotient will be the appropriate fraction (0.0625) for the nomogram *(Figure 6)*.

It has been demonstrated that, although precise numbers are not available because every disease has its own unique conditions, the utility of laboratory and imaging studies is greater in patients with an intermediate probability of having the disease *(Figure 7)*. The next step, as shown in *Table 2* from Diamond & Forrester,[5] is to calculate the prior probability of a disease. The score is built from the risk factors of gender, age, and type of chest pain, as published in the ESC guidelines.[6]

Some critics of Bayesian statistics argue that estimating pretest prevalence can be imprecise. Still, it is preferable to testing in the general population, where the number of false positives and negatives will be high, since no test is 100% accurate. It is easy to calculate that with a sensitivity and specificity of 98%,

clearly superior to the tests used in clinical medicine. If you study a population with a 5% prevalence of a disease, most positive and negative results will be false.

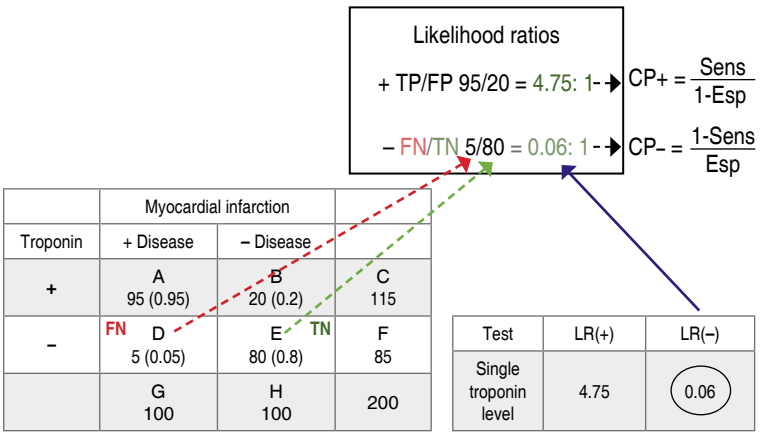


Figure 6: Here, we use the proportion of false negatives to true negatives to plot the predictive value of a positive or negative test in a single nomogram.

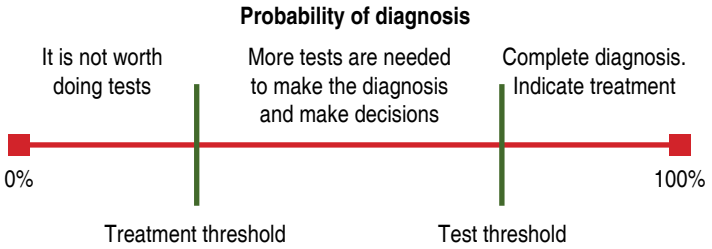


Figure 7: Usefulness of lab and imaging tests according to the prior disease probability.

Then, we will estimate the posterior probability of a disease using the combination of the pretest probability and the likelihood ratios of the test *(Figure 8)*. Using an intermediate probability of 50% for coronary artery disease, we can see that a positive troponin test increases the posterior probability to 80% and a negative one decreases the probability to 5%.[7]

With low and high probabilities, you gain very little from additional tests, as shown in *Figure 9*. Suppose you begin with a low pretest probability (0.1), as many diseases have in the general population. In that case, a positive test will at most put the probability in an intermediate score, not enough to confirm the diagnosis. The same applies to patients with a high pretest probability (0.9), such as those with typical symptoms and risk factors, for whom a negative test result will not necessarily rule out the disease. Therefore, studying patients with an intermediate probability of having a disease yields a larger benefit.

CONCLUSION

The era of reductionism in medicine must come to an end. Physics is the realm of complexity, and biology must be studied in the context of many factors. This results in a larger spectrum of functions than the sum of its parts. Consider the poem "The Blind Men and the Elephant" by John Godfrey Saxe:

Table 2: We can estimate the pretest probability with the Diamond and Forrester pretest probability data.

	High > 70% Typical angor		Intermediate 10-70% Atypical angor		Low < 10% Non angina pain	
Age (years)	M	F	M	F	M	F
30-39	59	28	29	10	18	5
40-49	69	37	38	14	25	8
50-59	77	47	49	20	34	12
60-69	84	58	59	28	44	17
70-79	89	68	69	37	54	24
> 80	93	76	78	47	65	32

It uses three variables: age, sex, and the type of pain, whether it is characteristic of angina pectoris. Numbers show the risk of coronary artery disease.

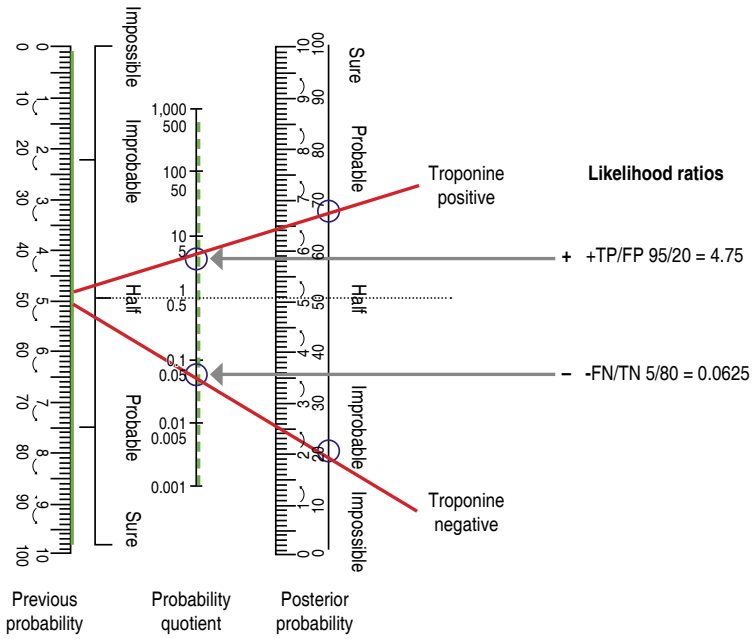


Figure 8: Nomogram to calculate the posterior probability of ischemic heart disease based on the pretest probability and the likelihood ratio of the positive or negative test.

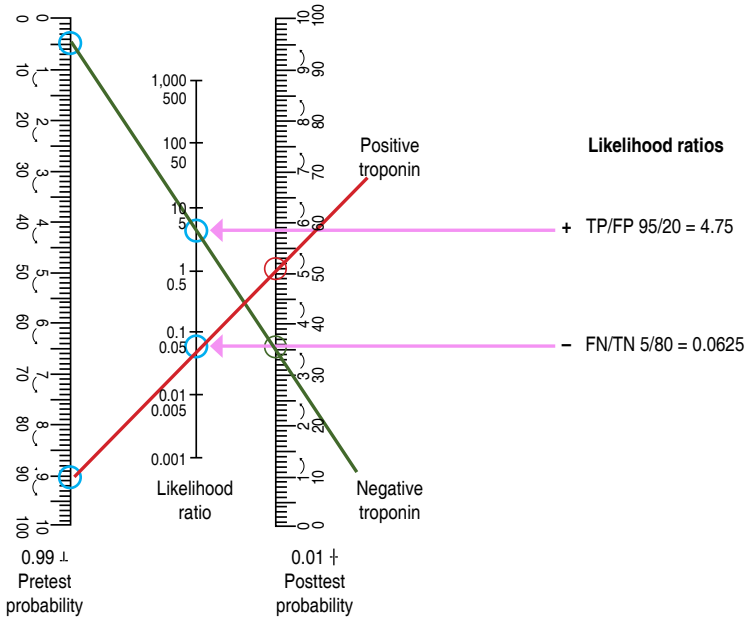


Figure 9: If you start with a low pretest probability (0.1), a positive test result will, at most, place the probability in the intermediate range (green line); similarly, a high pretest probability (0.9) will result in a negative test that does not entirely rule out the disease (red line). Therefore, studying patients with an intermediate probability of having a disease yields a larger benefit.

It was six men of Indostan
To learning much inclined,
Who went to see the Elephant
(Though all of them were blind),
That each by observation
Might satisfy his mind

And so these men of Indostan
Disputed loud and long,
Each in his own opinion
Exceeding stiff and strong,
Though each was partly in the right,
And all were in the wrong!

Each of the men describes what they feel, but no one is able to see the hole!

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