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Cardiovascular and Metabolic Science

Continuation of the Revista Mexicana de Cardiología

2022

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- Code infarction initiative during COVID-19 pandemic
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Editorial

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Cardiovascular medicine and gender equity

Medicina cardiovascular y equidad de género

Eduardo Meaney*

The future of humanity will be stamped and guided by the principle of gender equity. Of course, this engine of the combat for the dignity and equality of women is part of the broadest conception of *all rights for all*, including the respect and protection for our close relatives, the non-human animals, and the entire natural world, the beloved garden we inherited, our planet Earth. Only significantly older adults, like the author of this editorial, can be aware of the enormous progress achieved by women in the last decades. However, it is clear that the accomplishments are not enough and that we have not yet founded the entire reign of justice and equity. There are still lags, prejudices, harassment of all kinds, and abuses of the patriarchal power, which, as it sees its near end, sometimes adopt insane and criminal conduct against women in general and liberated women in particular.

Cardiology has been and still is a male fiefdom. However, there have been renowned cardiological figures such as Drs. Maude Abbott (classification of congenital heart diseases), Helen B. Taussig (developing with Dr. Alfred Blalock and his brilliant assistant, Dr. Vivien Theodore Thomas, the systemic-pulmonary shunt operation), my admired professor in the Albert B. Chandler University Hospital at Lexington, Ky., Jacqueline Anne Noonan (discoverer of the genetic disorder that bears her name), among many others. Moreover, in Mexico, many of us were gratified by the teachings and the example of the iron temper of Dr. Victoria de la Cruz, the distinguished founder of the Mexican school of embryology and one of the glories of our national cardiology.

Nonetheless, more than others, our discipline in Mexico and the rest of the world is mainly reserved for men. We do not have specific representative national data, except for a commendable but small survey on five Latin American countries, whose data are insufficient to reveal our national situation.[1] In the US, for example, as it happens in our country, half of the enrollment in medical schools is women. Despite this, less than 15% of cardiology practitioners and less than 5% of cardiology interventionists are women.[2] An analogous situation is seen in the United Kingdom and Australia.[2] Surprisingly, a recent survey in continental China showed that 41.5% of cardiologists were female.[3]

There are numerous explanations for this low representation of women in our specialty. Nevertheless, there is one that deserves to be more detailed. It is often heard, even from male colleagues re-educated in gender equality as the author of these lines, the argument that feminine biology plays a trick on the vocation of many of our female medical colleagues. The inconveniences associated with menstruation and premenstrual syndrome can affect a certain proportion of women during their youth and early adulthood. Besides, the long pregnancy, the duties of nursing, and the meticulous care that helpless human babies require dictate an extraordinary effort to professional women who also want to be mothers. All this seems to militate against being a specialist in a particularly demanding medical branch, cardiology, without schedules or predictable agenda. Nonetheless, the same barriers are faced by women who decide to be commercial

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or military jet pilots, mountain climbers, nuclear physicists, operators of complex heavy industrial machines, or high-performance athletes, among other stressful activities. Furthermore, despite their biological «predicaments» (which are not), women have proven to be as effective as men in any human activity, mainly if the latter help with housework and parental care, shoulder to shoulder with their life partners.

Our Association and all our sister societies already practice an attempt at gender equity. Even when the number still is low, the situation is positively evolving. For example, Dr. Gabriela Borrayo is our present president, and Dr. Adriana Puente, some time ago, led the National Association of Cardiologists at the Service of State Workers (ANCISSSTE). We now have special study groups, formed chiefly by female cardiologists, focused on the peculiarities and problems of heart diseases in women. We have built a fraternal spirit and profound respect for our female companions in our professional activities. However, it is not enough. In addition to the lower number of women in our specialty, most senior management and decision-making positions continue to be held primarily by men. Then, we must support that promotion to direction positions in cardiology and research departments be just motivated by issues of talent and capacity and not by gender. At the same time, we must continue furthering equity by attracting more young female doctors to our residency programs. Finally, of course, we must instill, especially in young cardiologists, a culture of non-harassment and unrestricted respect for the dignity and safety of our female colleagues. We must join the national re-education effort to permanently banish the toxic patriarchal prejudices and behaviors that limit and difficult women's free flourishing in our country.

The future cardiology will be egalitarian, or it will not be.

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ORIGINAL RESEARCH

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Code infarction initiative of Bajio region, during the pandemic by COVID-19 in a reconversion hospital

Iniciativa código infarto en la región Bajío, durante la pandemia por COVID-19 en un hospital de reconversión

Keywords: acute myocardial infarction, COVID-19, code infarction initiative.

Palabras clave: *infarto agudo al miocardio, COVID-19, iniciativa código infarto.*

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ABSTRACT

Introduction: acute myocardial infarction has a high prevalence and possibility of death if timely care is not given. It is possible that treatment could be delayed during a health crisis such as the COVID-19 pandemic. **Objective:** the objective of this study was to evaluate the impact of the COVID-19 pandemic on the function of the infarction code in the High Specialty Medical Unit of our institution. The medical indicators of acute coronary ischemic syndrome

RESUMEN

Introducción: *el infarto agudo de miocardio es una entidad de alta prevalencia y posibilidad de muerte en caso de que no se cuente con una atención oportuna, incluso durante la pandemia por el virus SARS-CoV-2.* ***Objetivo:*** *demostrar el impacto de la pandemia por SARS-CoV-2 en el funcionamiento del código infarto, en nuestra Unidad Médica de Alta Especialidad, al comparar los indicadores médicos del síndrome isquémico coronario agudo con elevación del segmento ST, antes y después*

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with ST-segment elevation were compared at two times: before the COVID-19 pandemic and during it. **Material and methods:** an ambispective, analytical, comparative cohort study was conducted, comparing the periods of February-September 2019 and February-September 2020, in the High Specialty Medical Unit, Centro Médico del Bajío number 1, *Instituto Mexicano del Seguro Social*, Leon, Guanajuato, Mexico. All patients older than 18 years with clinical, electrocardiographic, and enzymatic data of acute coronary ischemic syndrome, accepted in the medical network as infarction code registered in the National Registry of Acute Coronary Ischemic Syndromes (RENASCA) electronic case report form were included in the study. **Results:** the independent samples t-test was used to determine the impact of the infarction code initiative based on the reperfusion therapies performed, the door-to-needle, the door-to-balloon time, and the ischemia time. There was a significant difference in the reperfusion strategy, with greater thrombolysis during the COVID-19 pandemic (57.4% versus 72.6%, odds ratio [OR] 1.97, 95% confidence interval [CI] 0.49-0.82, p < 0.001), as well as reperfusion criteria (21.03% versus 35.37%, OR 2.05, 95% CI 0.53-0.80, p < 0.0001). Mortality was not different between the time periods. **Conclusions:** the COVID-19 pandemic has not impacted operation of the infarction code in the High Specialty Medical Unit Centro Médico del Bajío number 1 because the medical indicators of acute coronary ischemic syndrome with ST-segment elevation did not change.

de ésta, durante el mismo lapso de tiempo. ***Material y métodos:*** *se realizó un estudio ambispectivo de cohortes comparativas, analítico, que incluye los periodos de febrero a septiembre del 2019 y febrero a septiembre de 2020, en la Unidad Médica de Alta Especialidad del Centro Médico del Bajío No. 1, Instituto Mexicano del Seguro Social en León, Guanajuato, México. Se incluyeron en el estudio todos los pacientes mayores de 18 años con datos clínicos, electrocardiográficos y enzimáticos de síndrome isquémico coronario agudo, aceptados en la red médica como «Código Infarto» registrados en la plataforma electrónica RENASCA (Registro Nacional de Síndromes Isquémicos Coronarios Agudos).* ***Resultados:*** *se realizó una comparación con prueba t para muestras independientes, para determinar el impacto del funcionamiento de la iniciativa «Código Infarto» con base en las terapias de reperfusión realizadas, los tiempos puerta-aguja, puerta-balón y tiempo de isquemia. Encontrándose diferencia en la estrategia de reperfusión, siendo mayor la trombólisis durante la pandemia por COVID-19 (57.4% frente a 72.6% OR 1.97 IC 95% 0.49-0.82, p < 0.001), así como criterios de reperfusión (21.03% frente a 35.37% OR 2.05 IC 95% 0.527-806, p < 0.0001). No se evidencio diferencia en mortalidad entre ambos grupos.* ***Conclusiones:*** *la pandemia por SARS-CoV-2 no impacta en el funcionamiento del «Código Infarto» en la Unidad Médica de Alta Especialidad del Centro Médico del Bajío No. 1 ya que no se modifican los indicadores médicos del síndrome isquémico coronario agudo con elevación del segmento ST durante el mismo lapso de tiempo.*

INTRODUCTION

According to the World Health Organization (WHO), cardiovascular diseases (CVs) continue to be the leading cause of non-transmissible diseases. CVs are the cause of 30% of the deaths reported in the world. Moreover, 68% of these deaths are due to ischemic heart disease of atherothrombotic etiology. Therefore, the main objective in patients with acute ST-segment elevation myocardial infarction (STEMI) is reperfusion of the responsible artery. Primary percutaneous angioplasty has shown superior benefit compared with thrombolysis.[1] However, experimentally, the extent of rescued myocardial tissue has an inverse relationship with the time of evolution; hence, time is critical to preserve cardiac function.[2]

The CAPTIM study demonstrated that vessel patency improves the quicker the intervention occurs. The authors reported a lower incidence of cardiogenic shock and death within 30 days after the ischemic event when percutaneous coronary intervention (PCI) is performed within 2 hours of symptom onset.[3] Developed countries have instituted initiatives focused on building governmental systems for comprehensive care in an acute myocardial infarction scenario because up to 30% of patients with the acute coronary ischemic syndrome do not receive a reperfusion strategy.[4]

By the end of 2019, local health care institutions in Wuhan city, Hubei province, China, had reported several clusters of an atypical, highly contagious pneumonia caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Given the rapid spread and severity, on January 30, 2020, the WHO declared that the COVID-19 outbreak an international public health emergency.[5-7] The COVID-19 pandemic has placed international health systems in a serious overload situation, and with this, there has been inattention to other diseases, including those of cardiovascular origin. Given

the urgent need for reperfusion treatment during acute coronary syndromes, be it pharmacological or invasive, in patients with and without COVID-19, various care protocols have been established and adapted to the capacities of hospitals around the world.[8-12]

The hospital where this research was carried out was converted to care for COVID-19 patients because it is a tertiary care setting. To guarantee the care of infarction code patients in the Bajío region, in addition to the hemodynamics room for patients with infarction code without respiratory symptoms, a hemodynamics room was set up for the exclusive care of patients with respiratory symptoms and suspected COVID-19 *(Figure 1)*. This room included trained personnel equipped with personal protective equipment as well as a special path to transfer these patients from the emergency department to the hemodynamics room.

One year after the hospital had reopened all care services due to the significant decrease in the number COVID-19 cases, we wanted

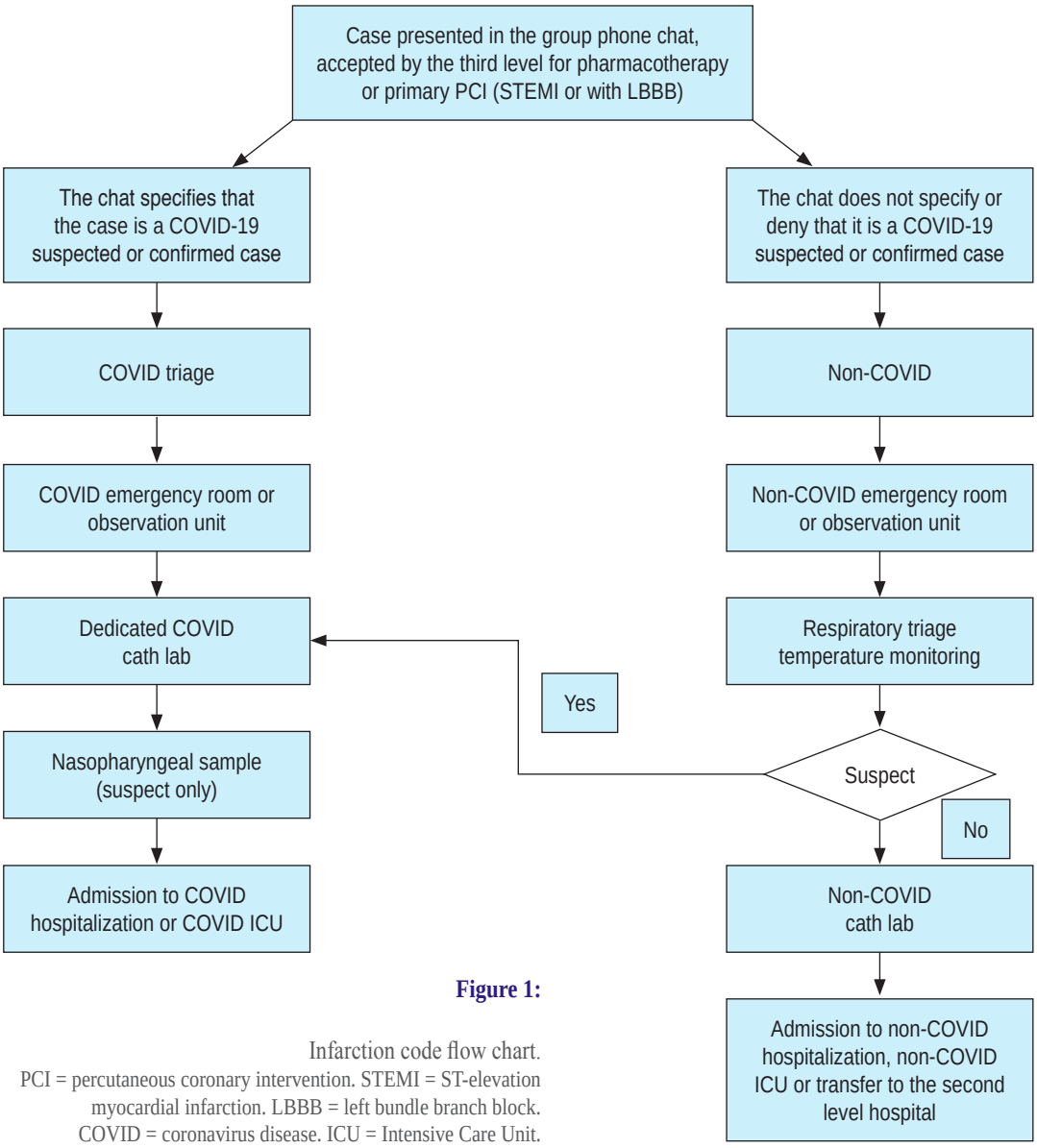

Figure 1:

Infarction code flow chart.
PCI = percutaneous coronary intervention. STEMI = ST-elevation myocardial infarction. LBBB = left bundle branch block. COVID = coronavirus disease. ICU = Intensive Care Unit.

to evaluate the impact of the COVID-19 pandemic on infarction code functionality by comparing medical indicators of acute coronary syndrome with ST-segment elevation before and during the pandemic. We quantified the number of patients with ST-segment elevation acute coronary syndrome and the reperfusion strategies employed (fibrinolysis, primary angioplasty, and pharmacoinvasive angioplasty) during these periods.

MATERIAL AND METHODS

An ambispective, analytical, comparative cohort study was performed, including the period from February to September 2019 (before the COVID-19 pandemic) and February to September 2020 (during the COVID-19 pandemic), for the High Specialty Medical Unit, *Centro Médico del Bajío No. 1, Instituto Mexicano del Seguro Social* (IMSS), Leon, Guanajuato, Mexico. Once approved by the local ethics and research committee with registration number R-2020-1001-086, all patients over 18 years old; of both genders; with clinical, electrocardiographic, and enzymatic data of acute coronary syndrome; accepted in the medical network as infarction code; and registered in the electronic case report form (eCRF) called *Registro Nacional de Síndromes Isquémicos Coronarios Agudos* (RENASCA) were included in the study. Patients with acute ischemic coronary syndrome without ST-segment elevation and patients who had not received tertiary medical care for any reason were not included. In addition, patients with incomplete records in RENASCA were eliminated.

The primary variables in this study were the number of patients with acute coronary syndrome, the reperfusion strategy, the needle-to-gate time, the balloon-to-gate time, and mortality. Other variables such as age, gender, body mass index (BMI), diabetes mellitus, systemic arterial hypertension, dyslipidemia, smoking, and the cardiac wall affected by infarction were also analyzed.

The Kolmogorov-Smirnov test was used to determine whether the continuous variables were normally distributed. Continuous variables are reported as mean ± standard deviation (SD) or median and interquartile range (IQR), as appropriate. Categorical values are presented as absolute values or percentages. The χ^2 test and Fisher's exact test were used to compare categorical variables, and Student's t-test for independent samples was used to compare quantitative variables between groups. A p-value < 0.05 was considered significant. SPSS Version 23 software was used.

RESULTS

A total of 212 patients were treated during the period of the COVID-19 pandemic, while 366 individuals were treated at the same time in previous year, representing a 42.1% reduction in the need for STEMI care. The characteristics of the patients were similar at both time points: a predominance of the male gender in 2019 (76.8%, 281) and 2020 (78.8%, 167), and a mean ± SD age of 62.34 ± 12.67 years in 2019 and 62.45 ± 11.73 years in 2020. The most predominant cardiovascular risk factors for 2019 and 2020 were systemic arterial hypertension at 65.57% and 62.7%, respectively; smoking at 55.2% and 51.9%, respectively; and diabetes mellitus at 46.2% and 49.1%, respectively. There were no significant differences between the two time periods regarding demographic variables, the presence of chronic degenerative diseases, and cardiovascular history *(Table 1)*.

Concerning the acute coronary event, there were more patients with right ventricular extension in 2020 than in 2019 (24 vs 13, p = 0.01). More patients received the benefit of thrombolysis in 2020 (210 vs 154, p = 0.01), although there were no differences with respect to the presence of clinical symptoms or infarct location *(Table 2)*.

During the COVID-19 pandemic, the time from symptom onset to hospital admission for medical care was longer (10.92 ± 16.57 h vs 6.95 ± 13.81 h, p = 0.02) as well as the door-to-electrocardiogram time (19.42 ± 30.75 h vs 15.25 ± 9.75 h, p = 0.01). However, there were no differences in relation to the other care indicators such as the door-to-needle, the door-to-balloon, and ischemia times *(Table 3)*.

For 2019 and 2020, the most commonly affected segment of the heart wall during these events was the inferior wall at 40.7% and 49.5%, respectively; followed by the anterior wall at 37.2% and 39.2%, respectively; the

Table 1: Population characteristics.

	2019	2020	p
Population	366	212	
Age (years)*	62.34 ± 12.67	62.45 ± 11.73	0.072
Male	281	167	0.607
Female	85	45	
Body mass index (kg/m^2)*	27.37 ± 4.07	27.48 ± 3.88	0.892
Smoking	202	110	0.489
Diabetes mellitus	169	104	0.545
High blood pressure	240	133	0.528
Dyslipidemia	92	49	0.616
Previous heart attack	58	25	0.218

* Mean ± standard deviation.
Note: none of the p-values are significant.

Table 2: Location of the infarction.

	2019	2020	p
Anterior wall	136	83	0.657
Inferior wall	149	105	0.045
Lateral wall	53	35	0.549
Right ventricle	13	24	0.005

The data were analyzed with the χ^2 test; $p < 0.05$ is significant.

lateral wall at 14.5% and 16.5%, respectively; and finally, the involvement of the right ventricle at 3.6% and 11.3%, respectively *(Table 2)*.

The decision to perform thrombolysis as the initial reperfusion therapy was made in 210 patients (57.4%) patients in 2019 and 154 patients (72.6%) patients in 2020 (p = 0.001), achieving reperfusion criteria in 77 patients (21.0%) in 2019 and 75 patients (35.4%) in 2020 (p = 0.001). There were no significant differences between the time periods when the approach was invasive.

There were no significant differences regarding the time when reperfusion treatment was established. The average door-to-needle time was 17.55 minutes in 2019 and 25.95 minutes in 2020 (p = 0.131). The average gate-to-balloon time was 18.45 minutes in 2019 and 30.19 minutes in 2020 (p = 0.086). The ischemia time was also not different: 1377.96 minutes in 2019 and 1320.99 minutes in 2020 (p = 0.914) *(Table 3)*.

DISCUSSION

Acute myocardial infarction continues to be one of the main causes of morbidity and mortality worldwide. Hence, its timely and accurate diagnosis with the application of appropriate therapeutic management is vital.[13]

The benefits of the infarction code protocol have already been demonstrated in Spain, and this approach has been adapted to institutional medicine in Mexico, with a focus on emergency services. It complements the IMSS regulations, organizes the emergency and continuous admission services, and assigns specific activities to the personnel involved in patient care to guarantee the diagnosis and treatment of a patient who requires urgent care in an acute myocardial infarction scenario. With this protocol, patients receive reperfusion treatment with primary angioplasty in the first 90 minutes, or fibrinolytic therapy in the first 30 minutes after admission to the IMSS emergency services. Based on the most recent results for this national initiative, involving more than 21,827 cases, 71.4% of patients with the coronary ischemic syndrome were offered timely impact therapy,

compared with 34.9% before the code had been instituted ($p \leq 0.0001$), with a decrease in mortality from 21.1% to 9.4% ($p \leq 0.0001$). The heart attack code initiative began formally in the High Specialty Medical Unit, *Centro Médico del Bajío No. 1*, IMSS, in December 2016. By 2018, mortality had decreased from 9.1 to 4%.[14-17]

By the end of 2019, local health care institutions in Wuhan city, Hubei province, China, had reported several clusters of an atypical, highly contagious pneumonia caused by a virus; it was suspected to be an airborne disease.[18] The novel virus was first identified in January 2020, when Chinese scientists isolated it from patient samples. Its origin was suspected to be a local market for wild animals and seafood. On February 11, 2020, the virus was officially named SARS-CoV-2.[5] In a matter of weeks, SARS-CoV-2 had reached pandemic proportions, affecting more than 100 countries.[6,7] In Mexico, the first case was reported on February 27, 2020. Regarding the clinical manifestations of the disease, although they are predominantly respiratory, up to 19.7% of hospitalized patients develop some serious cardiovascular complication during their hospitalization.[9] These complications include arrhythmias, myocarditis, pericarditis, heart failure, myocardial ischemia, and type 1 and type 2 acute myocardial infarction, or the exacerbation of an underlying cardiac disease, leading to higher mortality in hospitalized patients.[19]

In Western countries, in the presence of ST-segment elevation acute coronary syndrome, a rapid diagnostic test for SARS-CoV-2 should be performed and fibrinolytic therapy should be indicated as the first choice provided there are no contraindications,[10] even in unstable patients. Only when there have been two negative COVID-19 tests should the necessary actions be taken.[11] However, this approach is controversial because primary PCI is considered the standard of care for patients with STEMI in Europe, Canada, and the United States.[20] On the other hand, access to rapid testing for COVID-19 is limited and in some countries such as Mexico it is not a procedure considered within the first line of screening to confirm or exclude SARS-CoV-2 infection.

The approach to a patient with COVID-19 and acute coronary ischemic syndrome with ST-segment elevation must be individualized, based on resources, exposure of health personnel, and the benefit of primary PCI. Therefore, during the COVID-19 pandemic, fibrinolysis in stable patients has been considered the best treatment option in most countries.[8] In patients with STEMI and suspected COVID-19, which is defined as fever; respiratory symptoms; headache; cough; and some minor symptoms such as general discomfort, myalgias, arthralgias, and anosmia, primary or facilitated PCI is reserved for patients with clinical deterioration despite maximized treatment.[21,22] In these patients, in addition to completing the protocol for the procedure, it is necessary to exclude the presence of SARS-CoV-2 by nasopharyngeal swab nucleic acid test and chest tomography, among other screening tests.

Contrary to conventional pharmacoinvasive approach, stable patients with confirmed COVID-19 infection who have undergone successful pharmacological thrombolysis should not be moved and scheduled for non-urgent cardiac catheterization. These patients should undergo appropriate follow-up and subsequent risk stratification and be relocated when they

Table 3: Reperfusion time.

	2019	2020	p
Door-to-needle time (minutes)	17.55	25.95	0.131
Door-to-balloon time (minutes)	18.45	30.19	0.086
Ischemia time (minutes)	1377.96	1320.99	0.914

The data were analyzed with the independent samples t-test. None of the p-values are significant.

have defective fibrinolysis, especially if they are hemodynamically unstable.[12] Given the changes implemented because of the overload of the hospital system, it is necessary to evaluate the effectiveness of the infarction code program as a viable initiative despite the limitations generated during this global event.

To provide timely care to patients with acute coronary syndrome with and without COVID-19, a care protocol was established to ensure the safety of health personnel and patients, with special care routes and a hemodynamics room exclusively for patients with severe respiratory symptoms.

The initial findings of our study agree with those reported in the international literature, with a reduction in patients treated for STEMI. Our 42.1% reduction is higher compared to reports of 22.7% in Spain and 38% in the United States.[23,24]

The duration of the ischemia is a major determinant of the size of the affected area in patients with STEMI, and timely recognition and early management are critical to reduce morbidity and mortality.[25-27] Despite the logistic challenges associated with the COVID-19 pandemic, there was no significant difference in the delay in initiating reperfusion therapy. This demonstrates an excellent adaptation of the infarction code to the current crisis. The nonsignificant increase in the door-to-balloon time was likely due to protective measures required to carry out interventional procedures.

Some possible behavioral explanations for these findings could be the avoidance of seeking medical treatment due to social distancing measures, as well as concern about the risk of contracting SARS-CoV-2 in hospitals. The pandemic has received massive coverage in the media, with particular emphasis on the forms of infection and the most common places where SARS-CoV-2 is most easily spread.[28,29] Fear is a well-known determinant of avoiding health care, and avoiding contact with the hospital environment is linked to a pandemic.[30]

The scientific community has developed recommendations for reperfusion strategies during the COVID-19 pandemic, with advice that may appear complex to apply, depending on the socio-economic status of each country. The Interventional Council of the American College of Cardiology and the Society for Angiography and Cardiovascular Interventions state that fibrinolysis should be considered for relatively stable patients with STEMI and active COVID-19 to prevent exposure of personnel. In Mexico, medical centers with catheterization rooms should favor primary PCI over justified fibrinolysis due to the high success rate, the lower risk of complications, and the shorter hospital stay. Fibrinolysis is the therapy of choice in centers that do not have a catheterization room available and/or in patients with pneumonia or severe COVID-19. It has been proposed to defer the conventional drug-invasive strategy to avoid transferring stable patients with confirmed COVID-19 who have had successful drug thrombolysis results.[12]

Previous publications have shown an increase in in-hospital mortality during the COVID-19 pandemic that is not explained by adjusting the data for COVID-19, age, gender, Killip class, and time from the onset of symptoms to the onset of reperfusion therapy.[31] In the current context, patients avoid or delay going to the emergency room, a factor that could explain the increase in mortality in the out-of-hospital setting. This phenomenon has been described in Italy.[31-35] Finally, in the long term, suboptimal revascularization and larger affected heart wall territories would increase the rate of complications related to worse ventricular remodeling, such as heart failure and the incidence of ventricular arrhythmias.

Limitations. This is an observational study, and our results reflect patients who arrived at the hospital alive. We do not have information of patients who died before or after hospitalization.

CONCLUSIONS

Although patients took longer to request medical care after they started having chest pain during the pandemic, medical indicators of care such as the door-to-needle and balloon-to-gate times were similar in both time periods, with similar mortality. These data reflect the proper functioning of the infarction code initiative during the COVID-19 pandemic in our hospital.

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Right atrial heart myxoma, two different presentations of the same entity and histopathological findings

Mixoma cardiaco auricular derecho, dos presentaciones diferentes de una misma entidad y hallazgos histopatológicos

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Keywords:
myxoma, atrial mass, cutaneous T cell lymphoma, embolism and histopathological findings.

Palabras clave:
mixoma, masa auricular, linfoma cutáneo de células T, embolia y hallazgos histopatológicos.

ABSTRACT

Introduction: cardiac myxomas are the most common primary neoplasms of the heart. The most common location is the left atrium (75%), followed by the right atrium (15-18%) and left ventricle. They may present with the triad of obstructive, embolic and constitutional symptoms. *Case 1:* a 59-year-old man under follow up for non-Hodgkin cutaneous T cell lymphoma, suffering from progressive dyspnea, was found to have a mass located on the right atrium. Resection of the tumor was performed, and replacement of the mitral valve due to severe mitral regurgitation. Histopathology confirmed the diagnosis of myxoma. *Case 2:* a 61-year-old woman presented with thrombosis in the basilic, cephalic and right jugular veins. An echocardiogram showed an 80 × 40 mm cardiac mass in the right atrium. On the histopathological report, a cardiac myxoma with the greatest diameter of 7.5 cm was reported. The patient was discharged nine days after surgery. **Conclusion:** there could be an unusual presentation of atrial myxoma occurring simultaneously with a neoplasm of different lineage. Atrial myxoma should be suspected even in unusual locations and regardless of concomitant neoplastic disease. Embolic phenomena, as the first presentation, may be misleading, although some parameters and scores might be useful predictors.

RESUMEN

Introducción: *los mixomas cardiacos son las neoplasias primarias más frecuentes del corazón. La ubicación más común es la aurícula izquierda (75%), seguido de la aurícula derecha (15-18%) y ventrículo izquierdo. Pueden presentarse con la tríada de síntomas obstructivos, embólicos y constitucionales. Caso 1: varón de 59 años en seguimiento por linfoma cutáneo no Hodgkin de linfocitos T, que padecía disnea progresiva y presentaba una masa localizada en la aurícula derecha. Se realizó resección del tumor y reemplazo de la válvula mitral debido a insuficiencia mitral severa. La histopatología confirmó el diagnóstico de mixoma. Caso 2: mujer de 61 años que consulta por trombosis en vena basílica, cefálica y yugular derecha. Un ecocardiograma mostró una masa cardiaca de 80 × 40 mm en la aurícula derecha. En el informe histopatológico se informó un mixoma cardiaco con el diámetro mayor de 7.5 cm. Fue dada de alta nueve días después de la cirugía.* ***Conclusión:*** *podría haber una presentación inusual de mixoma auricular que ocurra simultáneamente con una neoplasia de diferente linaje. Debe sospecharse mixoma auricular, incluso en ubicaciones inusuales e independientemente de la enfermedad neoplásica concomitante. Los fenómenos embólicos, como la primera presentación, pueden inducir a error; aunque algunos parámetros y puntuaciones pueden ser predictores útiles.*

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INTRODUCTION

Cardiac tumors can be conceptualized as primary simple, primary complex and secondary. Primary neoplasms of the heart are uncommon; they occur at an incidence rate of 30 per 100,000 people per year, of which 80 to 90% are benign.[1,2] Being cardiac myxomas

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the most common of them, accounting for 50% of all benign cardiac tumors in adults. Finally, secondary tumors are 30 times more common than primary cardiac tumors. Myxoma is derived from its appearance as a cell poor myxoid neoplasm with a mucopolysaccharide rich extracellular matrix. They may present with the triad of obstructive cardiac symptoms including dyspnea, presyncope and sudden cardiac death;[1] embolic and constitutional symptoms. However, some studies report dyspnea as the most common symptom of cardiac tumors.[2]

The most common location is the left atrium (75%), then the right atrium (15%), with the remaining cases equally distributed between the right and left ventricle.[1] Tumors of the right side grow suspicion of metastatic disease.

There is a possible association between reports of lymphoproliferative neoplasms within a cardiac myxoma with Epstein-Barr virus (EBV) infection and inflammatory cytokines. We present two different cases of right atrial myxoma.

CASE PRESENTATION

Case 1: a 59-year-old man, without a positive family history, under ten years follow up for cutaneous T cell Lymphoma, presented with progressive dyspnea of nine months of evolution. A physical exam revealed a mitral regurgitation murmur.

The electrocardiogram showed sinus rhythm, p-mitral and non-significant ST-segment depression.

A transthoracic echocardiogram (TTE) reported a mobile right atrial mass *(Figure 1)* with right lateral pedicle anchored to the right atrial wall near the origin of the inferior vena cava without compromise of venous drainage. No vascularization evidence by color Doppler was found, neither obstruction nor infiltration to the right ventricle.

A trans-esophageal echocardiogram reported severe mitral regurgitation with P3 segment prolapse and a regurgitant jet area of 5.6 cm^2. The coronary angiography showed a tumor nutrient artery emerging from the posterolateral branch of the right coronary artery *(Figure 2)*. The patient underwent right atrial tumor resection through right atriotomy and mechanical mitral valve replacement of 31 mm through a transeptal approach. The right atrial pedicle tumor of 25 × 30 mm was infiltrated into two different locations: the inferior vena cava outflow tract and the right atrium wall *(Figure 3)*. The pathologic study reported atrial myxoma and fibromyxoid degeneration of the mitral valve *(Figure 4)*. Surgery was carried out without complications, and post -operative care was unremarkable. He was discharged satisfactorily after anticoagulant adjustment, staying free from recurrences.

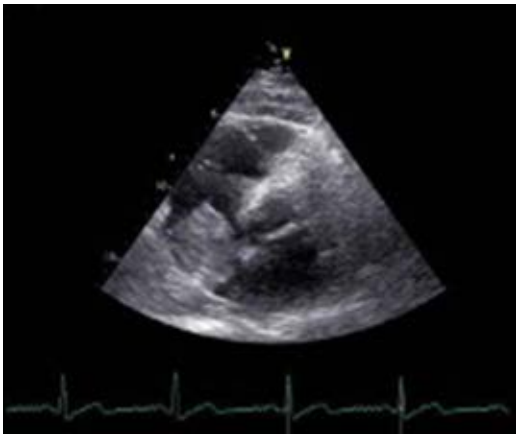

Figure 1: Transthoracic echocardiogram showing a right atrial mass of 42 × 49 mm of diameter with heterogeneous echogenicity and areas of calcification.

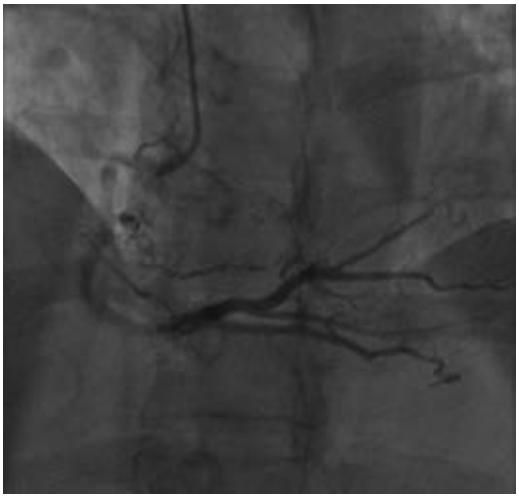

Figure 2: Coronary angiography showing the nutrient artery towards the right atrial mass.

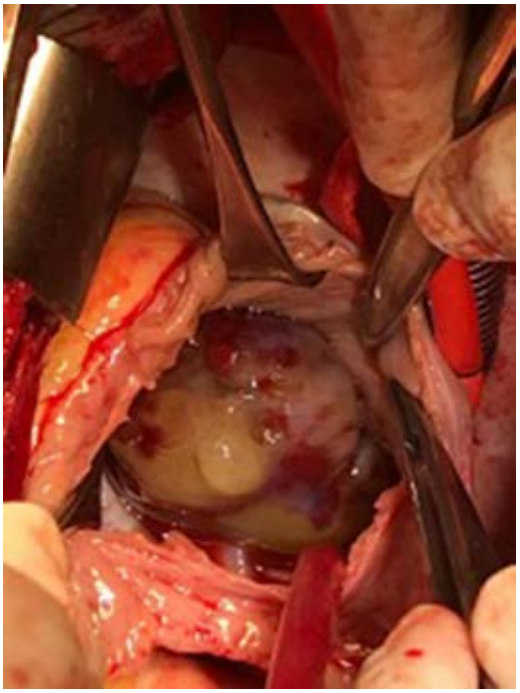

Figure 3: *In situ*, operative view of right atrial, multilobulated mass with bleed areas, consistent with atrial myxoma.

The patient did not go into remission of cutaneous lymphoma. Two months after surgery, he developed reactivation of dermatological lesions in the left pelvic limb. However, a contrast abdominal CT showed no evidence of lymphoproliferative activity. He continued management with pegylated interferon, deflazacort, hydrocortisone, topic fluocinolone and symptomatic management with hydroxyzine and ursodeoxycholic acid.

Case 2: a 61-year-old woman without any history of chronic degenerative diseases developed one month before admission left internal jugular vein and subclavian vein thrombosis. The patient was started on anticoagulation with rivaroxaban for six months.

Ten days before her admission, the patient presented sudden dyspnea. Pulmonary thromboembolism was initially suspected, and pulmonary angiography was performed, which revealed an apparent intracavitary thrombus in the right ventricle. The patient was sent to our unit for further evaluation.

On admission, a hypoechoic thrombus in the basilic vein, cephalic vein and right jugular vein with collateral venous vessels that flow into the left jugular vein was confirmed with a new ultrasound.

A transthoracic echocardiogram was performed, which showed an 80 × 40 mm cardiac mass in the right atrium, with insertion

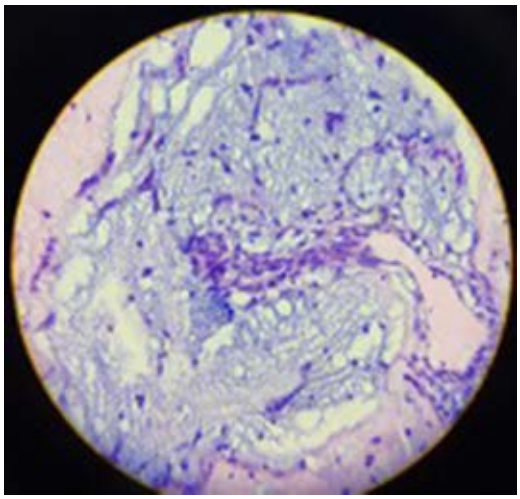

Figure 4: 40× H&E staining showing myxoid matrix. There is typical ring structure infiltration by chronic inflammatory cells. No mature vessels are seen, and neither are interconnecting anastomosing channels. No evidence of cutaneous T cell lymphoma was found.

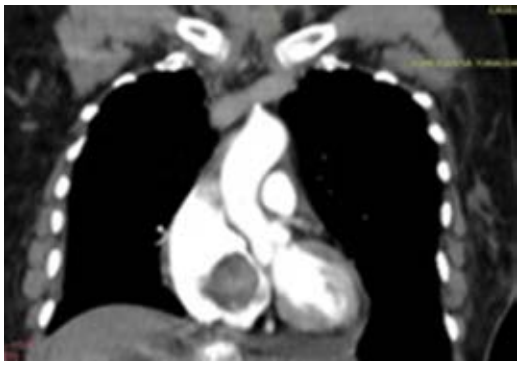

Figure 5: Contrast CT scan showing a mass in the RA and RV, predominantly hypodense, heterogeneous, with no significant enhancement after contrast. Seated on the interventricular septum, occupying the tricuspid entry point and partial extension to the RV outflow tract. No calcifications.

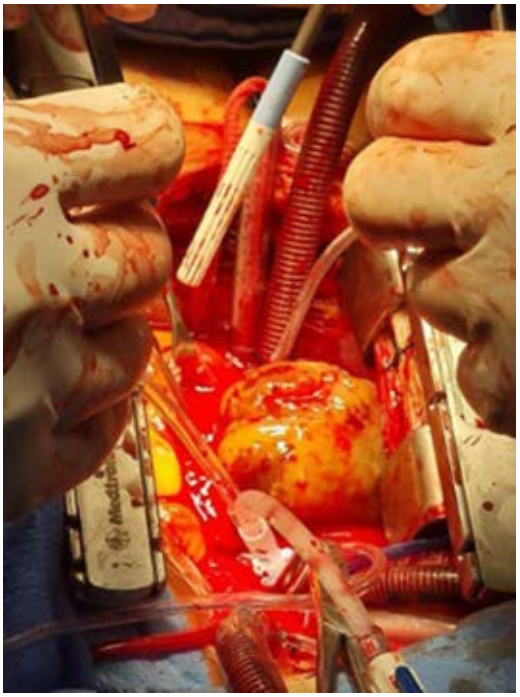

Figure 6: A 7.5 × 5 × 3.5 cm polypoid mass with areas of hemorrhage and gelatinous consistency.

at the interatrial septum, heterogeneous, with mobile calcifications that protrude into the right ventricle occupying it entirely. The left ventricle had normal global and segmental mobility with LVEF of 75%.

A contrast CT of the thorax and abdomen *(Figure 5)* revealed a heterogeneous mass measuring 55 × 44 mm, with partial extension to the RV outflow tract. Pretracheal and aortopulmonary adenomegaly was present. However, no data of a primary tumor was found. Our principal differential diagnoses were myxoma and angiosarcoma.

The patient underwent resection of the mass *(Figure 6)*. In the histopathological report, a cardiac myxoma with the greatest diameter of 7.5 cm was reported *(Figures 7 and 8)*. The surgical border was free of the lesion. The patient was weaned off mechanical ventilation without complications but presented a hypertensive emergency at admission to the post-surgical unit that was successfully treated with nitroprusside. Prerenal acute kidney injury improved with crystalloids. The patient was discharged nine days after surgery.

DISCUSSION

Primary heart tumors are rare, found in 0.001 to 0.3% of unselected patients at autopsy.[1] About 75% of primary tumors are benign, and 50% of these are myxomas, which most commonly arise from the left atrium.[3,4] Only 15-20% of myxomas arise from the right atrium, in the interatrial septum close to the border of the fossa ovalis.[5] Sporadic cases arise as isolated and solitary left atrial tumors, whereas familial myxoma can occur in any cardiac chambers as a multicentric neoplasia.[6] Myxomas range in size from 1 to 15 cm and are oval or lobulated with a smooth surface.

Atrial myxomas occur predominantly in females, between the fourth and sixth decade of life,[7] with a 2:1 female preponderance.

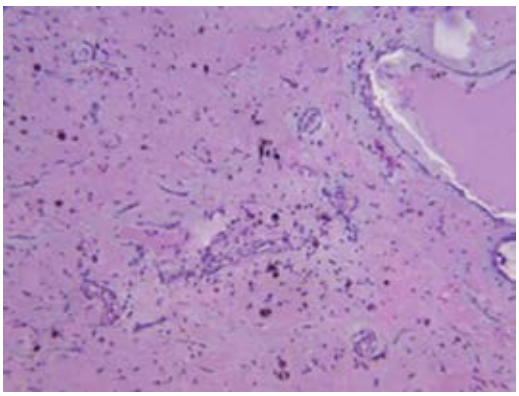

Figure 7: 20× H&E staining, polygonal stellate cells incorporated into the amorphous myxoid matrix.

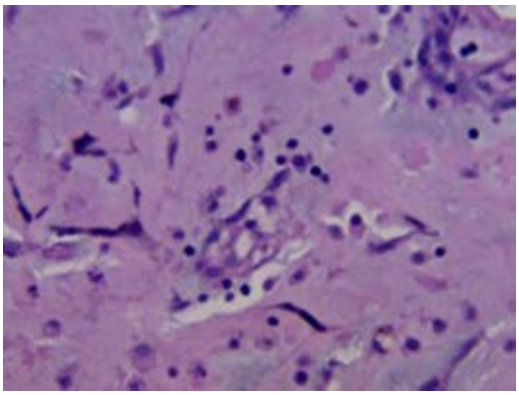

Figure 8: 40× H&E staining syncytial multinuclear giant tumor cell.

Approximately 10% of myxomas follow an autosomal dominant genetic pattern, as in Carney's complex, which presents as atrial, cutaneous and mammary myxomas, lentigines, blue nevi, endocrine disorders and testicular tumors. Other myxoma syndromes include LAMB (lentigines, atrial myxomas, mucocutaneus myxomas and blue nevi), NAME (nevi, atrial myxomas, myxoid neurofibroma, and ephelides).[8]

Most tumors of the right side are metastatic: in order of frequency, primary lung cancer, breast cancer and hematologic malignancies.[4] In the first case, metastasis was the first diagnostic impression, although no systemic manifestations such as fever, anemia, leukocytosis and weight loss were reported.

Most patients present with one or more symptoms of the triad of embolic events, intracardiac flow obstruction and constitutional symptoms.[9] Obstruction and dyspnea are the most common manifestations.[2,5] Small myxomas may go asymptomatic (about 10%),[5] as symptoms depend on size, location, mobility, physical activity and body position. Functional tricuspid stenosis may be found and, a «tumor plop» early in diastole has been reported.[7] Concomitant signs of mitral or tricuspid valve insufficiency are described.[6]

The tumor's long stalk may obstruct the orifice of the tricuspid valve resulting in syncope or sudden death.[4]

Up to 90% may develop systemic symptoms and occur independently of tumor size and location and include physical weakness, lethargy, fatigue, loss of appetite, anorexia, recent and progressive decrease in body weight and persistent and unexplained low grade fever. Arthralgia, myalgia, facial edema, hyperhidrosis and nocturnal hemoptysis and chronic anemia are less common. Paraneoplastic manifestations may occur, such as vasculitis, Raynaud phenomenon, amyloidosis, livedo reticularis, depletion of factor VII and others.[6,10,11]

As was shown by the second case, embolism may be a presenting sign in up to 30% of patients. The contour of the tumor is most often lobular and smooth but can be villiform in appearance, which is believed to be associated with thromboembolism.[2] They are caused by tissue fragmentation, detachment of tumor as a whole and dissemination of overlaying thrombi. It should be clear that venous thrombosis has no relation to arterial thrombosis.

Embolism is an important complication occurring in 30-50% of patients with cardiac myxomas and is associated with cardiac mortality, especially preoperative. Irregular surface contributes to tumor fragmentation and this was found to be an important risk factor contributing to embolism (HR 2.7); also, a high platelet count has been associated with an elevated risk of thrombosis. Inflammatory cytokine levels increased in patients with cardiac myxomas, which may be related to a high platelet count.[12,13] Prompt surgical excision of myxomas is indicated for patients at increased risk of embolism. Venous thrombosis associations with atrial myxomas are very broad. Indeed, an association between atrial myxoma, Budd Chiari syndrome and portal vein thrombosis has been described.[14]

Predictors of embolism are tumor size. Tumor size above 4.6 cm predicted embolism with a sensitivity of 77% and specificity of 73%, with an area under the curve of 0.858. Left atrium diameter and irregular villous surface morphology were significantly higher in the embolic group.[15] Higher BMI, E/e' ratio and older age were reported in other studies, with a similar ROC of 0.83. Interestingly, patients who developed postoperative atrial fibrillation, stroke or embolism related events in the perioperative period had significant higher CHAD2DS2 VASC scores (≥ 4 points) than those without embolism. However, it is debatable whether embolism occurred due to atrial fibrillation or tumor embolism.[16,17]

Obstructive heart failure is associated with solid, polypoid tumors, while neurologic and other embolic events represent the most common clinical feature of fragile papillary myxoma.

TTE is useful for detecting the insertion site, morphology, calcifications, cysts, necrotic foci and hemorrhage. Calcification of the tumor is suggestive of myxoma, particularly in the right atrium.[3] On echocardiography, a myxoma may be heterogeneous or homogeneous and may have calcifications. Typical findings on contrast-enhanced CT are a spherical or ovoid mass lower in attenuation than surrounding myocardium.[2] On CT, heterogeneity is a

common imaging feature with areas of hemorrhage, necrosis, cyst formation, fibrosis or calcification. However, the most helpful feature is the narrow base of attachment which is not seen with other neoplasms.[15]

One of the most difficult differential diagnoses is a thrombus. Axial late gadolinium enhancement magnetic resonance may show small foci of internal enhancement, a useful differentiating feature from thrombus since thrombi do not show enhancement.[8]

Microbubble contrast agents delineate the myocardium blood interface and may aid in the differential diagnosis. Contrast enhanced ultrasonography is based on microcirculation imaging which can display the blood flow of the mass, which can help differentiate benign and malignant tumors from thrombi. There is no enhancement inside a simple thrombus. Benign tumors have greater enhancement than the myocardial tissue with a mean value of peak enhancement of 0.63; on the other hand, malignant tumors are more inhomogeneous and more strongly enhanced with a mean value of 1.49.[18]

The study by Kirkpatrick, J et al. demonstrated that enhancement with echocardiographic contrast is useful to differentiate the neovascularization of malignancy or vascular tumor from the avascularity of a thrombus. Vascular tumors are hyper-enhanced, while stromal tumors and thrombi are hypo-enhanced. The thrombi failed to enhance.

Continuous infusion of contrast assesses dynamically whether a mass is filled by microbubbles. This intravascular tracer raises the possibility of malignancy.[19]

There is a possible association between Epstein-Barr virus (EBV) infection, inflammatory cytokines and lymphoproliferative neoplasms with atrial myxomas. A series of 18 cases of primary lymphomas arising within cardiac myxoma have been reported;[9] however, none of them is associated with cutaneous T cell lymphoma as in the first case.

It is believed that IL-6 plays a role in the immune-inflammatory response and is a key factor in the B-cell maturation process. IL-6 in atrial myxomas may be associated with the selection of a population of EBV-infected B cells.[9]

We found the coexistence of mitral insufficiency due to fibromyxoid degeneration and atrial myxoma. This association is not entirely understood.

The treatment of choice is resection, which can be curative. Resection must be performed promptly because of the risk of embolism and sudden death. If pedunculated, it can be easily removed. Resection must be completed with wide margins. Careful manipulation is important to prevent intracardiac implants and recurrence,[4] which has been reported in 1-3%. Septal defects due to resection must be repaired; also, adhesion to the leaflets may require valve repair, annuloplasty or valve replacement with a prosthesis. In the first case, we chose a bicaval drainage looking for better exposure of the right atrial chamber, taking advantage of performing a transseptal approach for the implantation of the mitral prosthesis.

There is a survival rate after resection of 92.7% at ten years. However, multicentric myxomas are independently associated with recurrence with an OR = 9.45. In one series of 95 patients, there was only a single recurrence over five years following excision. Patients must be followed with transthoracic echo one year following excision and then every five years.[2] After surgical resection of primary lesions, recurrence has been observed in 1-4% of sporadic and 12-22% of familial cases.[6]

The most common residual effects seen in a small series were neurologic deficits in nine patients. There were four cases of arrhythmias and two cases of mitral regurgitation.[16] Both of our patients underwent an uneventful recovery.

CONCLUSIONS

Atrial myxoma should be suspected even in unusual locations and regardless of concomitant neoplastic disease. As shown by the first case, there is a possible association with Epstein-Barr virus (EBV) infection, IL-6 and lymphoproliferative neoplasms within the setting of cardiac myxoma. As shown in the first case with severe mitral regurgitation, associated valve disease may be present. The treatment of choice is resection, which can be curative, with a survival rate of 10 years in more than 90%. The second case illustrates

the association with embolic events that can be predicted by findings such as left atrium diameter and tumor surface. However, embolic phenomena, as the first presentation, may be misleading. Previously validated scales such as the CHAD2DS2 VASC score may help identify the patients with the highest risk of embolism and post-operative complications.

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Clinical case

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Penetrating cardiac trauma in a second-level hospital. Presentation of two cases

Traumatismos cardiacos penetrantes en un hospital de segundo nivel. Presentación de dos casos

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Keywords:
cardiac trauma, cardiac tamponade, cardiac suture.

Palabras clave:
traumatismo cardiaco, taponamiento cardiaco, sutura cardiaca.

ABSTRACT

Introduction: cardiac injuries represent a group of pathologies within thoracic trauma that often result in fatal hemorrhage. These types of injuries can be contained by the membrane surrounding the heart, allowing enough time for the patient to receive emergency treatment. **Case report:** we present two patients with stab wounds to the thorax. The first patient presented wounds to the anterior and posterior wall of the right ventricle and an injury to the diaphragm and liver. The second patient was admitted with a left ventricle wound very close to the anterior descending artery and a left lung laceration. Both cases underwent emergency surgery, and sutures were performed both in cardiac cavities and injured structures with favorable evolution. At the present date, they are still alive with no cardiovascular complications.

RESUMEN

Introducción: *las lesiones cardiacas constituyen un grupo de patologías dentro del trauma torácico que muchas veces resultan en hemorragia fatal. Este tipo de lesiones pueden ser contenidas por la membrana que rodea el corazón, lo que genera suficiente tiempo para que el paciente reciba tratamiento de emergencia.* ***Presentación de caso:*** *presentamos dos pacientes con heridas de arma blanca en el tórax. El primer paciente presentó heridas en la pared anterior y posterior del ventrículo derecho, además de lesión en el diafragma y el hígado. El segundo paciente ingresó con una herida en el ventrículo izquierdo muy cerca de la arteria descendente anterior y también presentó una laceración del pulmón izquierdo. Ambos casos fueron intervenidos de urgencia, realizándose suturas tanto en cavidades cardiacas como en estructuras lesionadas con evolución favorable. En la actualidad, siguen vivos sin complicaciones cardiovasculares.*

INTRODUCTION

Penetrating cardiac trauma (PCT) has been well defined over time. It was first described in Homer's famous Iliad, where exsanguination is described as a cause of death due to foreign objects penetrating the heart.[1]

Penetrating cardiac injuries are devastating injuries that currently represent a 40-90% mortality rate. Its short therapeutic window implies a surgical challenge where treatment depends on the patient's mechanism of injury and hemodynamic status.[2-6] The most affected cavity in this type of lesion is the right ventricle due to its anterior location.[7] Surgical repair in PCT has improved notably in recent decades, with successful surgical results.[8]

CASE PRESENTATION

Case 1: a 27-year-old male was brought by relatives with a stab wound in the anterior precordial region. During the physical examination, the patient was drowsy, hypotensive (80/50 mmHg), with tachycardia (110 beats/min), jugular vein distention and muffled heart sounds.

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Initial laboratory tests showed a hemoglobin of 10.6 g/L with a normal white blood cell count and normal platelet count.

The surgery was performed in supine decubitus. The patient experienced a cardiac arrest during general anesthesia induction and was provided with rapid stabilization. Then a left thoracotomy with transverse sternotomy was performed via the fourth intercostal space following vascular control of the mammary arteries.

A large hematoma was found opening the pericardium in the anterior wall of the right ventricle (RV). A clot was extracted, and an internal cardiac massage was performed.

After sinus rhythm was recovered, a 1 cm wound was found in the anterior wall of the RV, near the lower margin of the heart. The wound was irrigated and closed with a 3-0 nylon suture. A 1 cm laceration was also found in the inferior wall of the RV and was closed with a 3-0 nylon suture.

The left margin of the heart was lifted with no signs of bleeding *(Figure 1)*, and we then performed ligation of the internal mammary arteries. Subsequently, the thoracic cavity was explored with no findings of pleuropulmonary lesions *(Figure 2)*. A 2 cm laceration in the diaphragmatic side of the liver was repaired with a 3-0 nylon suture by performing a 10 cm longitudinal incision in the epigastrium. The surgery was finished with no other complications.

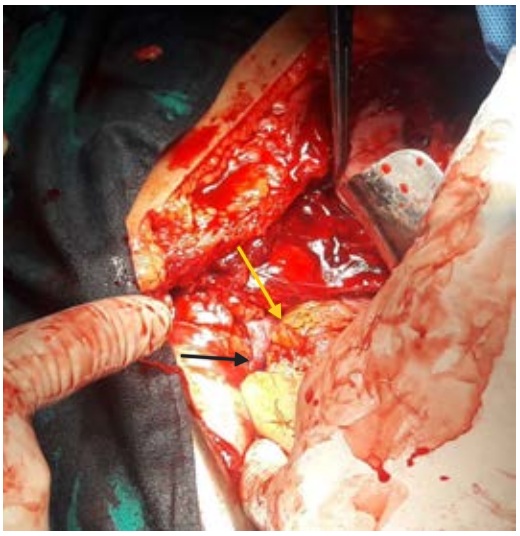

Figure 1: Exposure to cardiac sutures. Suture on the anterior wall of the right ventricle (yellow arrow). Inferior wall suture (black arrow).

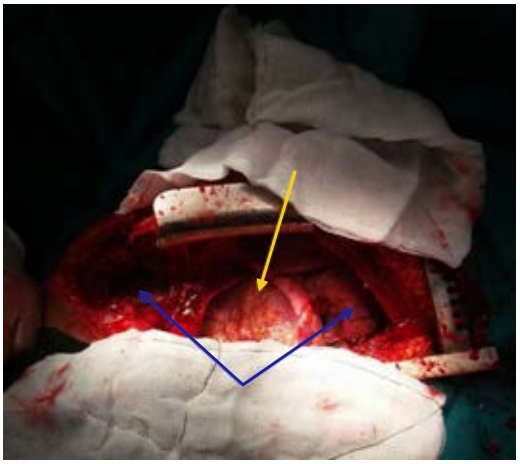

Figure 2: Left anterolateral thoracotomy with a transverse section of the sternum. Opening of the pericardium with cardiac visualization (yellow arrow) and opening of both pleurae with the observation of both lungs (blue arrows).

During the postoperative period, three units of red blood cells were transfused, and 1 gram of ceftriaxone every eight hours was administered. Days later, an exploratory laparotomy was performed because of severe persistent abdominal distension. Nevertheless, we did not find any alterations. The patient was referred to the Intensive Care Unit (ICU) of a private clinic by agreement with the ministry of health, where he evolved favorably.

Follow-up visits were made for a total period of one year after surgery, and no cardiovascular sequelae were reported.

Case 2: a 38-year-old male was admitted to the emergency department with a stab wound in the lateral region of the thorax. On admission, the patient was dyspneic, hypotensive (80/50 mmHg), with tachycardia (130 beats/min), jugular vein distention and muffled heart sounds.

Initial laboratory tests showed a hemoglobin of 8.7 g/L with a normal white blood cell count and normal platelet count.

A life-saving pericardiocentesis was performed in the emergency room and resulted in an immediate improvement of the patient's

hemodynamic status. Five units of red blood cells were transfused, and 2 grams of cefazolin and an intravenous norepinephrine infusion were administered.

The patient was rapidly taken to the operating room (OR), where a left thoracotomy was performed via the fourth intercostal space. We immediately found a cardiac tamponade that improved with the opening of the pericardium.

After blood aspiration was performed, we identified a 2 cm longitudinal laceration in the left ventricle (LV), approximately half a centimeter from the left anterior descending artery (LAD). A cross stitch was made to control bleeding, using a 3-0 nylon suture that bordered the LAD artery in the epicardium, deepening the incision below the artery and returning to the other edge of the ventricular wound to avoid kinking of the vessel and prevent the occurrence of perioperative infarction. An additional stitch was placed due to residual bleeding, and both stitches were reinforced with a pericardial patch *(Figures 3 and 4)*.

A nylon 3-0 suture was used to close a 3 cm laceration located in the lower lobe of the left lung, and we then performed ligation of the internal mammary arteries. Other structures of the thorax were checked without any abnormal findings, and a 24 cm thoracostomy tube was placed. The surgery was finished with no other complications.

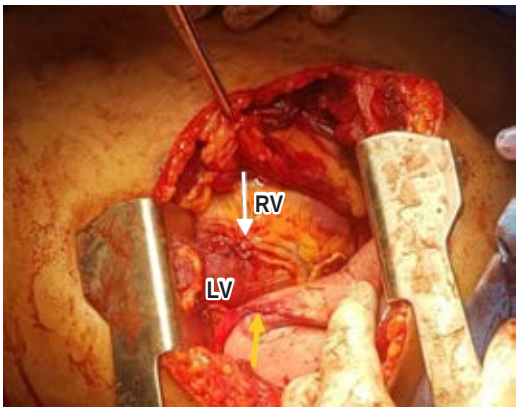

Figure 3: View of left heart and lung: lung suture (yellow arrow), cardiac suture with a pericardial patch (white arrow).
RV = right ventricle. LV = left ventricle.

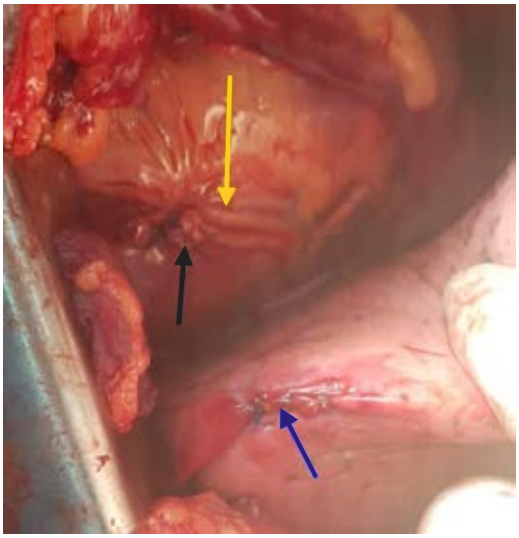

Figure 4: View of left heart and lung: pericardial patch (black arrow), lung suture (blue arrow), anterior interventricular groove, course of the anterior descending artery (yellow arrow).

During the postoperative period, the patient remained in the ICU with a thoracostomy tube for four days and an intravenous treatment of meropenem 500 mg every eight hours for seven days. The patient was discharged three days later and continued to be evaluated for one year without cardiovascular complications.

DISCUSSION

Historically, cardiac injuries had fatal outcomes and were considered untreatable; currently, around 90% of patients die before reaching the emergency room.[9] Some authors have found associations between mortality and hemodynamic status of the patient on admission, type of weapon, surgical findings, and complexity of the repair.[10] In our case, the role played by the medical emergency team was crucial for the survival of these patients.

A cardiac injury should be suspected in any patient with penetrating wounds in the thorax, especially in the anterior face of the thorax, mainly on the left side, upper abdomen, and neck.[11]

The presence of agitation, cold extremities, venous distension of the neck, paradoxical pulses and muffled cardiac sounds in patients

with penetrating wounds suggest cardiac injury with tamponade.[6] Some authors consider cardiac tamponade as a protective factor for patient survival.[12] The resolution of tamponade increases cardiac output, restores normal circulation, and improves anoxia.[13] Cardiac tamponade was present in both our patients, where a life-saving pericardiocentesis was performed in one of them before the patient was rapidly taken to the OR.

The RV is affected more frequently than the LV due to its location and anterior extension.[2] Bamous et al. showed similar results, with greater involvement of the RV (56%), 52% of which was associated with PCT.[14]

There are several types of approaches to dealing with PCT, including left anterior thoracotomy, right anterior thoracotomy, pericardial window, and median sternotomy. The latter is widely used due to its exposure,[10] although it is not as fast as other approaches. In our cases, left thoracotomy with transverse sternotomy was performed in one patient, where a classic sternotomy would have delayed vascular control.

Several authors recognize that the survival rate after suffering a penetrating cardiac injury probably depends on the time of attention.[12] Stranch et al. found a highly significant association between delay in reaching the hospital, clinical condition on admission, mechanism of injury, and aggressive surgical treatment with survival rates.[15]

CONCLUSIONS

Emergency thoracotomy, which is characterized by relief of tamponade and control of bleeding, is an important pillar that increases survival in patients with PCT. The left anterior thoracotomy is the fastest cardiac approach and, with its extension to a transverse sternotomy, offers wider exposure to right chambers and caval veins. After surgical intervention, the patient should undergo a thorough cardiological study to rule out intracardiac lesions.

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Clinical case

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Acute myocarditis after administering the BNT162b2 (Pfizer-BioNTech) vaccine against COVID-19 in an adolescent patient

Miocarditis aguda tras la administración de la vacuna BNT162b2 (Pfizer-BioNTech) contra COVID-19 en un paciente adolescente

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Keywords:
COVID-19, SARS-CoV-2, vaccine, magnetic resonance, myocarditis, Pfizer-BioNTech.

Palabras clave:
COVID-19, SARS-CoV-2, vacuna, resonancia magnética, miocarditis, Pfizer-BioNTech.

ABSTRACT

Myocarditis is a multifactorial inflammatory condition of the myocardium. Recently myocarditis has been recognized as an adverse event in patients vaccinated against COVID-19 with Pfizer-BioNTech and Moderna (mRNA vaccines), mainly in adolescents and young adults. Cardiac magnetic resonance (CMR) allows the characterization of myocardial tissue and cardiac function and has become the non-invasive diagnostic gold standard in patients with suspected acute myocarditis. The authors present a 16-year-old male case with stabbing chest pain after the second dose of immunization against SARS-CoV-2 with the BNT162B2 (Pfizer-BioNTech) vaccine. The electrocardiogram (ECG) showed disclosed ST-segment elevation, and increased myocardial injury markers were also observed. Angio tomography (AngioCT) showed subtle signs of myocardial hypoperfusion and left ventricular dysfunction. Gadolinium CMR was performed, identifying global hypokinesis of the left ventricle (LV), myocardial edema hyperemia and late gadolinium enhancement (LGE) as evidence of myocardial injury, and markers of non-ischemic intramyocardial inflammatory lesion. Having excluded other etiologies, this presentation of acute myocarditis is proposed to be an adverse reaction associated with the BNT162b2 vaccine against COVID-19. The long-term risks of the COVID-19 vaccine in children, adolescents and young adults are still unknown, and further investigation will be needed.

RESUMEN

La miocarditis es una condición inflamatoria multifactorial del miocardio. La miocarditis ha sido reconocida recientemente como un evento adverso, en pacientes vacunados contra COVID-19 con Pfizer-BioNTech y Moderna (vacunas de ARNm), principalmente en adolescentes y adultos jóvenes. La resonancia magnética cardiaca (RMC) permite caracterizar el tejido miocárdico y la función cardiaca y se ha convertido en el estándar de oro no-invasivo en pacientes con sospecha de miocarditis aguda. Los autores presentan a un paciente masculino de 16 años con dolor torácico punzante tras la segunda dosis de inmunización contra el SARS-CoV-2 con la vacuna BNT162B2 (Pfizer-BioNTech). El electrocardiograma (ECG) mostró elevación del segmento ST y aumento de los biomarcadores de lesión miocárdica. La angiotomografía (AngioTC) mostró signos sutiles de hipoperfusión miocárdica y disfunción ventricular izquierda. Se realizó RMC con gadolinio, identificando hipocinesia global del ventrículo izquierdo (VI), hiperemia por edema miocárdico y realce tardío de gadolinio (RTG) como evidencia de lesión miocárdica y marcadores de lesión inflamatoria intramiocárdica no-isquémica. Habiendo excluido otras etiologías, se propone que esta presentación de miocarditis aguda sea una reacción adversa asociada a la vacuna BNT162b2 contra COVID-19. Los riesgos a largo plazo de la vacuna contra la COVID-19 en niños, adolescentes y adultos jóvenes aún se desconocen, por lo que será necesario seguir investigando.

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INTRODUCTION

Myocarditis is an inflammatory disease of the myocardium diagnosed by histological, immunological and immunohistochemical criteria. The World Health Organization and the working group of the Society and International Federation of Cardiology on the definition and classification of cardiomyopathies histologically define myocarditis as the presence of inflammatory infiltrates in the myocardium with degeneration and necrosis of myocytes of non-ischemic origin (Dallas criteria). Regarding immunohistochemical criteria the diagnosis would be made in the presence in the myocardium of ≥ 14 leukocytes/mm^2, including up to 4 monocytes/mm^2 and ≥ 7 CD3-positive T lymphocytes/mm^2. The working group defines inflammatory dilated cardiomyopathy (DCM) as myocarditis associated with cardiac dysfunction.[1,2] Myocardial damage leads to humoral and cellular response initiated in an attempt to eliminate the causal agent accompanied by edema, necrosis and regional or global alterations of myocardial contractility. Complete recovery of tissue and function can be seen in uncomplicated cases, whereas in severe cases an autoimmune reaction is triggered in the heart with myocardial necrosis and the release of antigens that perpetuate the damage. Progression to DCM occurs predominantly in patients with persistent inflammation who cannot eliminate the causal agent or develop antibodies against myocardial structures.[3-6]

Myocarditis has several different etiologies as infections, immune disorders, toxic agents, etc. The most common viruses implicated in myocarditis are coxsackie B, adenovirus, hepatitis C, cytomegalovirus (CMV), echovirus, influenza, Epstein-Barr, parvovirus B19 and herpes virus. In the past few years, myocarditis has been recognized as a complication of severe COVID-19.[2,4-6] With the emerging use of the vaccine against COVID-19, post-vaccination-related acute myocarditis has been described.[7-9] COVID-19 vaccine related myocarditis diagnosis is based on an appropriate clinical data scenario, cardiac biomarkers, and imaging studies, including echocardiogram, AngioCT and CMR. CMR allows the characterization of tissue and cardiac function and has become the non-invasive diagnostic gold standard in patients with suspected acute myocarditis.[10-12]

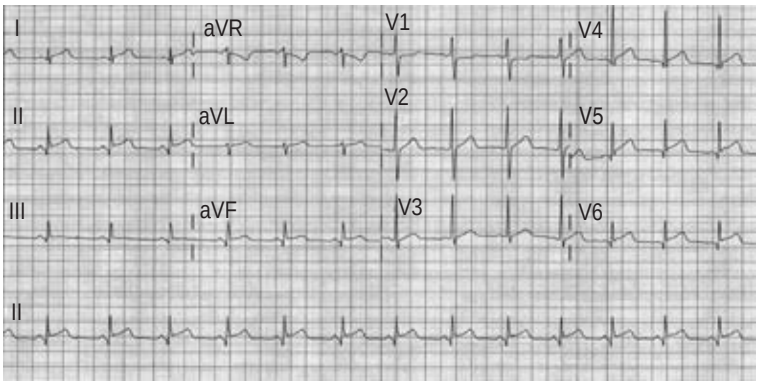

Figure 1: The ECG showed elevation of the ST-segment.

CASE PRESENTATION

The authors describe a 16-year-old male case with no past relevant medical history. The patient had full immunization against SARS-CoV-2 with the BNT162B2 (Pfizer-BioNTech) vaccine; the second dose was administered in May 2021. On July 7, 2021, the patient complained of stabbing chest pain and was evaluated at another institution. A transthoracic echocardiogram was performed with global and segmental hypokinesia of the posteroinferior and mid-apical region. Left ventricular ejection fraction (LVEF) was normal with no pericardial effusion. Anti-inflammatory treatment was prescribed. The patient was admitted to our institution on July 10, 2021, with an improvement in symptoms. On emergency physical examination, vital signs were normal. An electrocardiogram (ECG) showed sinus rhythm, 81 bpm, normal QRS and elevation of ST-segment *(Figure 1)*. Chest-X Ray was normal. Blood tests revealed elevated myocardial injury biomarkers: ultrasensitive troponin T 2123 ng /L, creatine phosphokinase (CPK) 1297 IU /L, MB fraction of creatine phosphokinase (CPK-MB) 105 ng /mL, brain natriuretic peptide (proBNP) 493 pg /mL, D-dimer 618 ng /mL and C-reactive protein (CRP) of 14.97 mg /L. Coronary AngioCT was performed on July 11, 2021 with normal coronary arteries *(Figure 2A)*. Slightly depressed left ventricular function with an ejection fraction of 47%, hypokinesia in non-

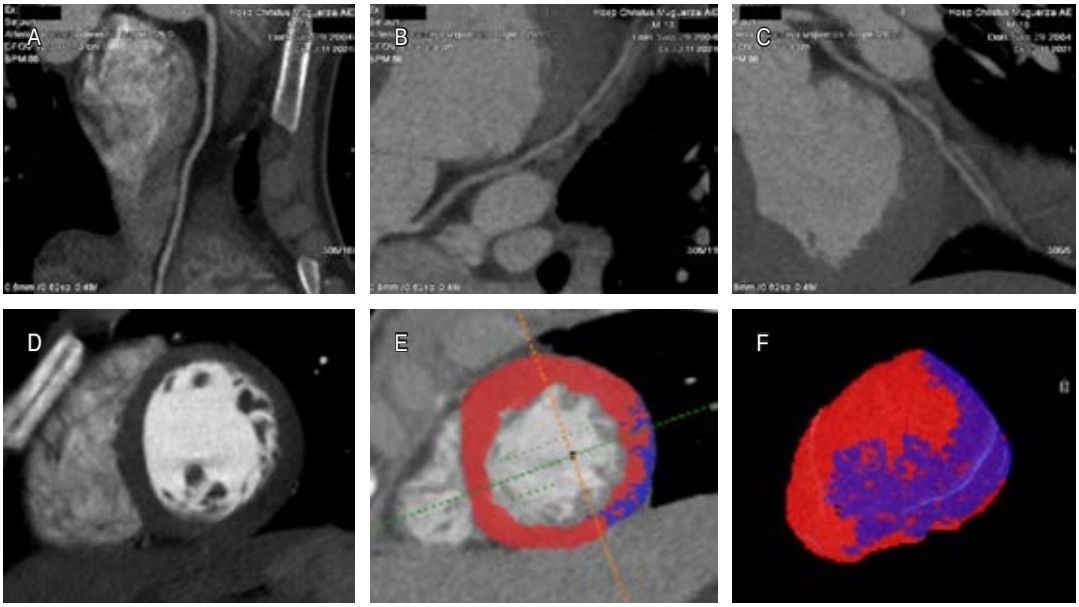

Figure 2: AngioCT with normal coronary arteries **(A, B and C)**. Inferolateral hypodensity of myocardial wall **(D)** with hypoperfusion demonstrated after the post-process **(E and F)**.

contiguous segments and lower attenuation of inferolateral myocardium were observed *(Figure 2B and 2C)*. Post-process was made, and inferolateral wall hypoperfusion was demonstrated *(Figure 2D to 2F)*.

CMR (Optima™ MR450W GEM 1.5T, GE Healthcare, Chicago, IL, USA) with endovenous gadobutrol (Gadovist®) (0.1 mmol / kg) was performed to identify global hypokinesis of the LV with LVEF of 41%. The STIR sequence showed areas of increased myocardial signal intensity in the inferolateral, basal and medial, lateral-apical and anterior-apical segments, compatible with edema *(Figure 3A)*. After administration of gadolinium, areas of the myocardium with early enhancement were identified in the anteroseptal basal, inferolateral basal, inferolateral medial, lateral-apical and anterior-apical segments compatible with hyperemia *(Figure 3B)*. Non-ischemic pattern LGE in lateral subepicardial and midwall at the apical septal level was observed *(Figure 3C)*. Pericardium was normal. The findings represent markers of non-ischemic intramyocardial inflammatory lesion. The viral serology was negative (Cytomegalovirus, Epstein Barr, Coxsackie A and B, Echovirus, as well as anti-Salmonella typhi and paratyphi, Brucella and Proteus). Due to the temporal relationship between vaccination and the development of signs and symptoms and having excluded other etiologies, this presentation of acute myocarditis is proposed to be an adverse reaction associated with the BNT162b2 vaccine against COVID-19. Beta-blocker, antihypertensive and anti-inflammatory treatment was prescribed. Due to the low-risk profile and favorable clinical evolution, an endomyocardial biopsy was not considered. The patient was discharged after five days without complications.

DISCUSSION

Acute myocarditis has been recognized as an adverse event in patients vaccinated with Pfizer-BioNTech and Moderna (mRNA vaccines), mainly in adolescents and young adults. The Vaccine Adverse Event Reporting System (VAERS) had received 1,783 reports of myocarditis or pericarditis in the 12 and 29-year-old age group who received COVID-19 vaccines (November 4, 2021). Most cases in adolescents or young men after the second dose. The Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA) confirmed 1,031 reports

of myocarditis or pericarditis. The Clalit Health Services database in Israel reports its highest incidence in male patients aged 16-29 years, up to 10.69 cases per 100,000 persons.[7-9,13]

The Pfizer-BioNTech vaccine has been shown to be 94% to 95% effective in preventing COVID-19 infection in the 16- to 55-year-old population and 100% effective in the 12-to-15-year age group. To date, the FDA has authorized its emergent use in the population aged 5 to 15 years and full approval in 16 years and older. The long-term risks are still unknown. The adverse reactions described in different vaccines within the cardiovascular sphere are isolated cases of the acute coronary syndrome, atrial fibrillation, ventricular extrasystole and cardiac arrest.[14-17]

Under the clinical suspicion of acute myocarditis, the diagnostic approach includes a 12-lead ECG (changes in ST-segment, T wave, Q waves, AV and bundle branch block, arrhythmias; limited use), biomarkers of cardiac injury (high sensitivity, although low specificity), transthoracic echocardiography, CMR and endomyocardial biopsy in selected cases. Echocardiography helps to rule out other entities and to monitor changes in cavity size, myocardial thickness, ventricular function and pericardial effusion. Some alterations such as global ventricular dysfunction, alterations in segmental contractility or diastolic dysfunction are nonspecific. Myocardial deformation analysis by speckle tracking shows greater sensitivity for the detection of myocardial damage in patients with preserved LVEF and its prognostic evaluation.[18,19]

In patients who undergo AngioCT, hypodensity of the myocardium has been described. Post-process demonstrated hypoperfusion could be an indicator of edema, although further investigation on this topic is needed.[20]

CMR modified Lake Louise criteria (sensitivity 87.5%, specificity 96.2%) consists in identifying three diagnostic targets for myocarditis: edema, hyperemia and LGE. A positive case is defined as the presence of at least one T2 criterion (sensitivity 84.6%, specificity 88.5, precision 86.2%) with at least one additional T1 criterion (sensitivity 90.0%, specificity 76.9%, accuracy 84.8%). Pericardial effusion and LV wall abnormality are considered supporting criteria.[10-12]

CONCLUSIONS

Acute myocarditis is a multifactorial inflammatory condition of the heart that can be assessed non-invasively by using CMR-modified Lake Louise criteria. Post COVID-19 vaccine related myocarditis is a rare adverse event most likely seen in children, adolescents and young

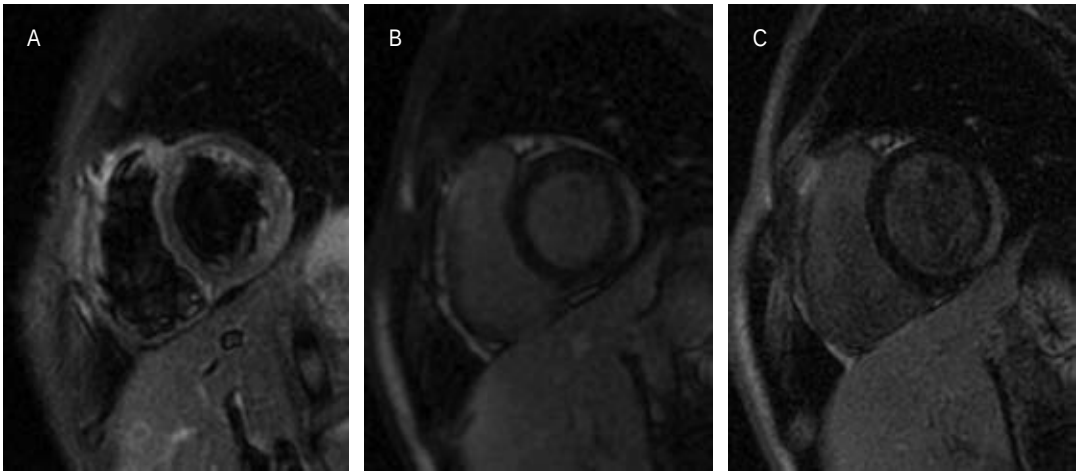

Figure 3: The CMR short axis STIR sequence showed increased myocardium signal (edema) in the inferolateral, basal and medial, lateral-apical, and anterior-apical segments **(A)**. Early gadolinium enhancement **(B)** is compatible with hyperemia. Non-ischemic pattern late enhancement in lateral subepicardial and midwall is shown **(C)**.

male adults. However, the authors believe that future research is needed to provide more evidence that can establish recommendations for immunization based on the well-known benefits of SARS-CoV-2 vaccination and better identification of patients with increased vaccine-related risk of adverse effects.

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Clinical case

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Persistent angina without persistent ST-segment elevation: do not forget a myocardial infarction with acute occlusion of a coronary artery

Angina persistente sin elevación persistente del segmento ST: que no se te olvide el infarto de miocardio con oclusión aguda de una arteria coronaria

Albina Aldomà-Balasch,* Pedro Kristian Rivera-Aguilar,* Marta Zofia Zielonka*

Keywords:
transmural acute myocardial infarction, right bundle branch block, repolarization abnormalities, coronary collateral circulation.

Palabras clave:
infarto agudo de miocardio transmural, bloqueo de rama derecha, alteraciones de la repolarización, circulación colateral coronaria.

ABSTRACT

Case report: a 57-year-old man consulted for chest pain suggestive of angina. The electrocardiogram (ECG) showed a right bundle branch block (RBBB), not present in previous ECGs, with secondary abnormalities of repolarization without meeting the criteria for ischemia. Due to persistent angina despite treatment, an emergent coronary angiography was performed, which showed an acute thrombotic occlusion of the right coronary artery (RCA) with good collateral circulation (CC) from the left coronary tree, which did not present significant stenosis. After reperfusion, angina progressively disappeared, and RBBB resolved. The infarct size was smaller than expected, as well as the poor electrocardiographic expressiveness, due to the good heterocoronary CC that was observed in the infarcted territory. **Conclusion:** myocardial infarction with acute occlusion of a coronary artery must be kept in mind in patients with persistent angina despite treatment, and the ECG does not show the typical abnormalities.

RESUMEN

Caso clínico: *paciente de 57 años que consultó por dolor torácico sugestivo de angina, con un electrocardiograma (ECG) que mostraba un bloqueo de rama derecha (BRD) no presente previamente, con las correspondientes alteraciones de la repolarización en contexto de bloqueo de rama sin cumplir criterios de isquemia. Por persistencia de angina a pesar del tratamiento se decidió realizar coronariografía emergente objetivando una oclusión trombótica aguda de la arteria coronaria derecha con buena circulación colateral (CC) heterocoronaria desde el árbol coronario izquierdo, el cual no presentaba lesiones significativas. Después de la revascularización, la angina desapareció progresivamente y se resolvió el BRD. Dada la buena CC heterocoronaria del territorio infartado, el tamaño del infarto fue menor de lo esperado y esto justificaría la escasa expresividad del ECG.* ***Conclusión:*** *el infarto de miocardio con oclusión aguda de una arteria coronaria debe tenerse en cuenta en pacientes con angina persistente a pesar del tratamiento y que el ECG no muestre las anomalías típicas.*

INTRODUCTION

When a patient consults for chest pain with anginal characteristics, a 12-lead electrocardiogram (ECG) should be performed immediately to rule out an acute coronary syndrome (ACS) with persistent ST-segment elevation that requires urgent reperfusion. We present a case of a patient who came to the emergency room for progressive angina despite treatment, with pathological ECG but without persistent ST-segment elevation.

CASE PRESENTATION

A 57-year-old man with obesity, hypertension and former smoker as cardiovascular risk factors, and previous history of Sjögren's syndrome and gastroesophageal reflux, consulted his general practitioner for chest pain compatible with angina on moderate exertion. The ECG

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showed a right bundle branch block (RBBB) not present in previous ECGs *(Figures 1 and 2)*. Treatment with ASA 100 mg od, statin and beta-blocker were started, and the patient was referred preferentially to cardiology for further evaluation. A conventional stress test was performed two weeks later. However it was stopped in the middle of the second stage of the Bruce protocol (6.8 METs and 88% of maximum heart rate) due to angina, without presenting electrocardiographic repolarization changes suggestive of ischemia. Progressive angina persisted despite treatment, so the patient consulted the emergency room four days later due to persistent chest pain at rest. The ECG did not show changes compared to the previous one, however biomarkers of myocardial necrosis were elevated (peak Tn I-hs 5140 pg/mL and CK 411 U/L), so the patient was admitted to the coronary care unit with the diagnosis of non-ST-segment elevation myocardial infarction (NSTEMI). On admission, an echocardiogram showed akinesia of the inferior basal and inferolateral basal segments with preserved parietal thickness, and normal biventricular ejection fraction, without significant valve disease or other notable findings. Antithrombotic therapy was started with ASA 100 mg, clopidogrel 300 mg, fondaparinux 2.5 mg sc, and intravenous nitroglycerin, with slight improvement, but without complete resolution of angina, so an emergent coronary angiography was decided to perform. Acute thrombotic occlusion of the right coronary artery (RCA) was observed, with collateral circulation (CC) from the left coronary tree, which did not present significant stenosis *(Figure 3)*. Angioplasty was performed with implantation of a drug-eluting stent, with subsequent resolution of angina and disappearance of the RBBB. The patient presented a favorable clinical evolution, being discharged on the fourth day of admission.

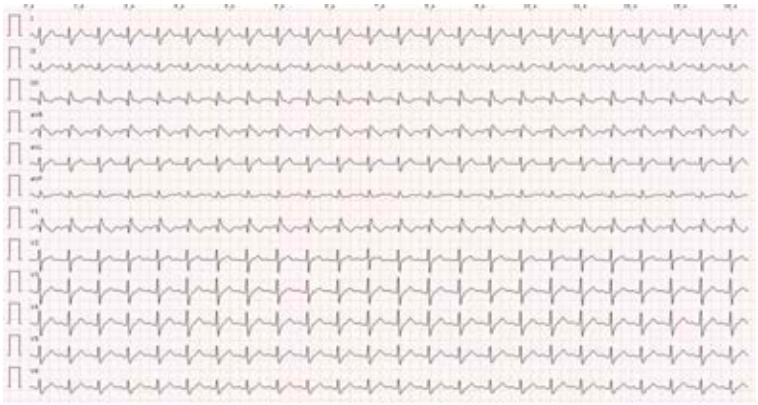

Figure 1: ECG at initial evaluation shows an RBBB with secondary repolarization abnormalities.

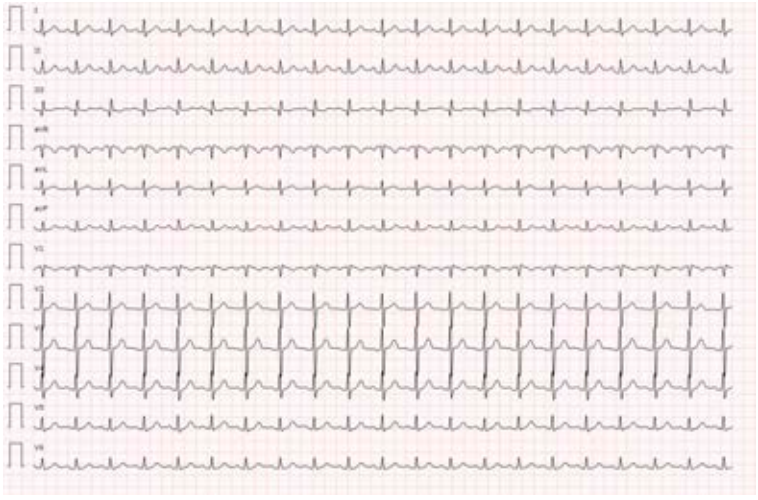

Figure 2: Previous ECG with narrow QRS complex without repolarization abnormalities.

DISCUSSION

When a patient presents with symptoms suggestive of angina, a 12-lead resting ECG should be performed immediately to assess repolarization changes suggestive of ischemia, especially to identify early persistent ST-segment elevation, which requires emergent reperfusion.[1] Characteristic ECG abnormalities in ACS without persistent ST-segment elevation include ST-segment depression, transient ST-segment elevation, and T-wave changes. Even though the ECG in this setting may be normal in more than 30% of patients,[2] If the patient has signs or symptoms suggestive of ongoing myocardial ischemia and the standard leads are inconclusive, additional leads should be recorded. The left circumflex artery occlusion may be detected only in posterior leads (V7-V9) or right ventricular MI only in V3R and V4R.[3] In case of persistent or recurrent

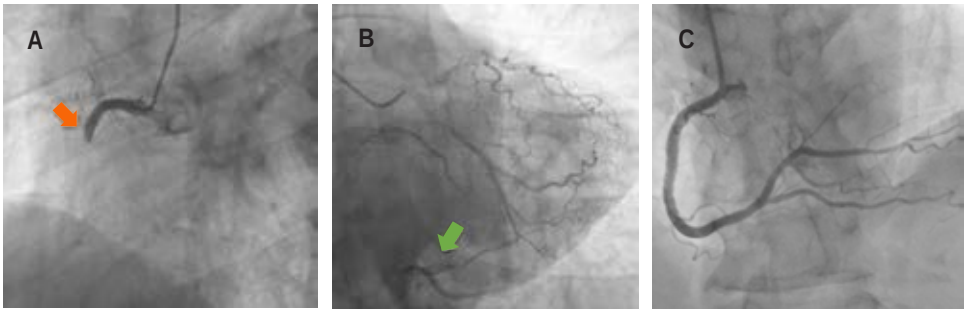

Figure 3:

Coronary angiography shows **A)** total occlusion of RCA (orange arrow) with **B)** good heterocoronary collateral circulation from the left coronary tree (green arrow). **C)** RCA after stent implantation.

symptoms or diagnostic uncertainty, it is also recommended to obtain additional 12-lead ECGs. In patients with a preexisting left bundle branch block (LBBB), specific ECG criteria (Sgarbossa's criteria) help detect candidates for immediate coronary angiography.[4] Patients with high clinical suspicion of ongoing myocardial ischemia and LBBB, regardless of whether it was previously known, should be treated similar to those with STEMI.[1] In patients with RBBB, ST-elevation indicated of STEMI, while ST-segment depression in the leads I, aVL, and V5-6 is indicative of NSTE-ACS.[5] Our patient did not strictly meet ECG criteria for persistent ST-segment elevation. However the patient persisted with symptoms of ongoing angina despite treatment and presented with a recent RBBB, so it was decided to perform emergent coronary angiography. Given the good heterocoronary CC observed in the infarcted territory, the infarct size was smaller than expected, as well as the poor electrocardiographic expressiveness. Therefore, it is important to always keep in mind the possibility of a MI with acute occlusion of a coronary artery in the presence of persistent angina despite adequate treatment and few repolarization abnormalities (even with a normal ECG) or new bundle branch block.

CONCLUSIONS

Myocardial infarction with acute occlusion of a coronary artery must be kept in mind in patients with persistent angina despite treatment, and the ECG does not show the typical abnormalities.

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Review

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Reducing radiation exposure in an electrophysiology lab with the CARTO-UNIVU™ module

Reducción de la exposición a la radiación en un laboratorio de electrofisiología con el módulo CARTO-UNIVU™

Mariana Tinoco,*,‡ Filipa Cardoso,* Sérgio Leite,* Lucy Calvo,* Victor Sanfins,* Sílvia Ribeiro,* António Lourenço*

Keywords:
fluoroscopy, radiation, CARTO-UNIVU™, radiofrequency ablation, electroanatomic mapping.

Palabras clave:
fluoroscopia, radiación, CARTO-UNIVU™, ablación por radiofrecuencia, mapeo electroanatómico.

ABSTRACT

Radiofrequency ablation is an effective and safe technique for the treatment of different types of arrhythmias. Radiofrequency ablation is performed using fluoroscopy, a standard navigation guide, which is related to radiation exposure and its well-known harmful effects on patients and laboratory staff. In the last decade, electroanatomic mapping systems have noted a steep development. Despite their indisputable advantages, they do not include information obtained by real-time fluoroscopy. This important limitation is tackled by the new CARTO-UNIVU™ module as it seamlessly combines fluoroscopy images with three-dimensional (3D) electroanatomic mapping into a single accurate 3D view, enabling a pronounced reduction in radiation exposure. We report four cases of our single center first experience of the new CARTO-UNIVU™ module.

RESUMEN

La ablación por radiofrecuencia es una técnica eficaz y segura para el tratamiento de diferentes tipos de arritmias. La ablación por radiofrecuencia se realiza mediante fluoroscopia, una guía de navegación estándar, que está asociada con la exposición a la radiación y sus efectos nocivos bien reconocidos para los pacientes y para el personal de laboratorio. En la última década, los sistemas de mapeo electroanatómico han experimentado un fuerte desarrollo. A pesar de sus indiscutibles ventajas, no incluyen información obtenida por fluoroscopia en tiempo real. El módulo CARTO-UNIVU™ aborda esta importante limitación, ya que combina imágenes de fluoroscopia con el mapeo eletroanatómico tridimensional (3D) en una sola vista 3D, lo que permite una reducción pronunciada de la exposición a la radiación. Presentamos cuatro casos de nuestra primera experiencia en un solo centro con el nuevo módulo CARTO-UNIVU™.

INTRODUCTION

Radiofrequency (RF) ablation is an effective and safe technique that has become the standard treatment for various arrhythmias. Since ablation results are improving and the incidence of complex arrhythmias is increasing, the issue of radiation exposure has become increasingly important.[1]

Fluoroscopy is a standard navigation guide used to perform RF ablation and is associated with exposure to ionizing radiation. The increasing complexity of electrophysiology (EP) procedures requires detailed mapping and extensive ablation therapy. Thus, procedural and, more notably, fluoroscopic times (FT) have progressively lengthened.[2]

Radiations are odorless and invisible, so becoming complacent about their dangers is easy. Operators are so caught up in performing procedures that they overlook the tools that help reduce radiation exposure. Consequently, patients and operators can be exposed to higher radiation levels than necessary.[3]

There are two main deleterious effects of radiation: deterministic and stochastic effects. The first ones occur once a threshold of exposure has been exceeded, and their severity increases with increasing doses, becoming evident days to months after exposure. On the other hand, stochastic

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effects are related to the potential future harm to the tissue and the body. Deterministic effects of most concerns for patients and operators include skin injuries (which may occur when FT exceed 20 min, using high-contrast fluoroscopy mode, or 60 min in low-level fluoroscopy) and cataract (present in one-third to half of the interventional cardiologists, whose dose threshold was 2 Gy for a single dose or 5 Gy for fractionated dose). The stochastic effect of most concern is a carcinogenic effect in exposed patients and physicians. In this effect, the cell is modified by DNA damage but remains viable, the harm expressed through cell proliferation. The cancer risk is highest in children, higher in women than in men, and reduced by one-half in the elderly. The tissues with a higher risk of radiation-induced cancer were the breast, colon, lung, stomach and bone marrow.[4,5]

The best model to estimate radiation risk is the linear-no-threshold model, which supports the concept that no radiation dose, even the smallest, can be considered completely safe. The risk is dose-related, with higher radiation levels related to higher risks. Based on this rationale, using non-standard fluoroscopy settings or implementing the ALARA principle (as low as reasonably achievable) for EP procedures seem insufficient to provide complete protection for the patient and laboratory staff.[6,7]

Therefore, significant efforts have been made in the past few years to reduce radiation exposure among patients and operators. For instance, incorporating advanced imaging modalities such as real-time ultrasonography, intracardiac echocardiography (ICE), and three-dimensional electroanatomic mapping (3D-EAM) systems have greatly reduced the requirements for fluoroscopy in EP laboratories without any significant difference observed in the safety and efficacy of the procedures.[2]

In the last decade, EAM systems have noted a steep development. Currently, they enable the generation of 3D reconstruction of any part of the heart without the need for fluoroscopic navigation. Despite these indisputable advantages, they do not include information obtained by real-time fluoroscopy. This important limitation is tackled by the new CARTO-UNIVU™ module as it seamlessly combines fluoroscopy images with 3D-EAM into a single accurate 3D view. It helps reduce the procedural time (PT) and fluoroscopy dose (FD) to as low as reasonably achievable. It helps reduce radiation exposure for physicians, staff, and patients, allowing navigation, with confidence, from an integrated view with just one fluoroscopic image or cine sequence needed for continuous anatomical orientation, making it possible to perform an equally precise ablation.[8-10]

This article aims to share our single center first experience with the CARTO-UNIVU™ module.

The CARTO-3® system uses hybrid electromagnetic and current-based navigation to allow precise catheter location. A locator sensor in the distal end of the ablation catheter interacts with three electromagnetic fields generated by a location pad positioned underneath the patient table, providing a map of any heart chamber. Six electrode patches positioned at the patient's front and back screen a unique current emitted from different catheter electrodes, providing additional information for catheter electrode localization.

In addition, 3D-EAM displays the voltage of the recorded electrograms, low voltage or scar region defined by the voltage map is known to be correlated with the arrhythmogenic substrate. The anatomic shell thereby constructed is, in some cases, integrated with the 3D anatomic dataset or generated by previous computed tomography or magnetic resonance imaging (MRI) scans to optimize the use of such a system.

The CARTO-UNIVU™ module integrates the CARTO-3® system with the fluoroscopic image or cine. This system consists of a registration plate mounted onto the location pad positioned under the patient table, which aligns the CARTO-3® system to the conventional fluoroscopy, and a software module. It has a very simple and efficient workflow consisting of a small registration step at the beginning of the procedure with a single snapshot of the fluoroscopic incidences of interest.

In all procedures, a quadripolar diagnostic catheter was positioned into the right ventricular apex or right atrium and a decapolar catheter into the coronary sinus under fluoroscopic guidance. The locator sensor determined catheter position, then the CARTO-UNIVU™ module was registered, and cine loops were recorded in anteroposterior, right, and left anterior oblique projections. Subsequently, the EAM was created under active catheter tracking in pre-recorded

cine loops. Consequently, the operator can handle the catheters, mimicking the use of fluoroscopy but without the use of further radiation exposure. Lesion formation parameters such as ablation time, contact force, impedance, and RF energy are disclosed to illustrate the lesions. Catheter ablation (CA) procedures were performed with the EAM using the pre-recorded cine loops and only, if necessary, with active fluoroscopy.

Without this technology, operators must rely on 3D-EAM and fluoroscopic images for catheter positioning.[1,11,12]

Here, we report four cases of our single center first experience of the CARTO-UNIVU™ module.

Patient 1. An 86-year-old female was admitted to the emergency room with signs and symptoms of acute heart failure (HF). She had type 2 diabetes, Parkinson's disease, and atrial fibrillation (AF).

The ECG revealed a pre-excited AF with a rapid ventricular response. Transesophageal echocardiography (TEE) showed a thrombus in the left atrial appendage. After clinical stabilization, the patient was discharged with warfarin for four weeks. Shortly before the end of the four-week treatment, the patient was again hospitalized for acute HF. During hospitalization, a TEE was performed that excluded thrombus. The patient was then submitted to electrical cardioversion with reversion to sinus rhythm. Later, an electrophysiological study (EPS) was performed. An electrical programmed ventricular stimulation showed concentric and decremental retrograde conduction. The tricuspid annulus was mapped during atrial pacing, locating the accessory pathway (AP) in the right posteroseptal region. An application of RF energy was performed with the immediate disappearance of ventricular preexcitation.

The PT was 50 minutes, fluoroscopy time (FT) was 2.3 minutes, and FD was seven mSv *(Figures 1 and 2)*.

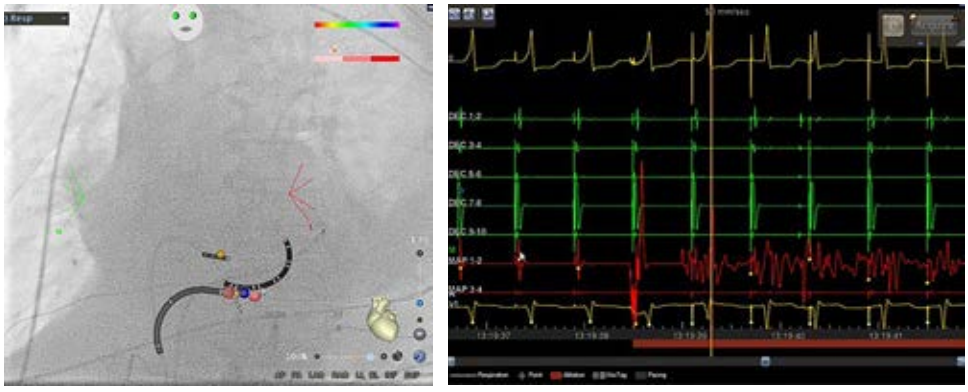

Figure 1:

Left anterior oblique projection. His bundle signal (orange dot). An application of RF energy was delivered with the immediate disappearance of ventricular pre-excitation.

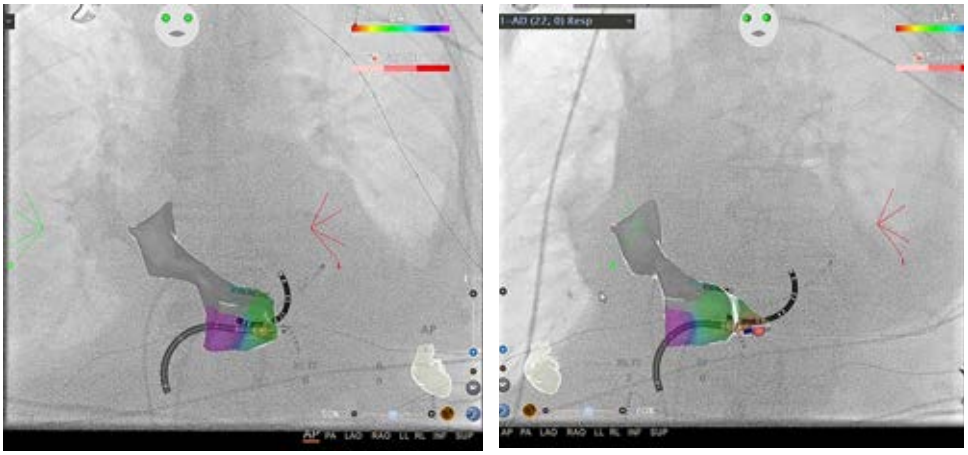

Figure 2:

Anteroposterior and left anterior oblique projection. The activation mapping identified the hotspot on the right posteroseptal region of the tricuspid annulus.

Figure 3:

Right anterior oblique and antero-posterior projection. The activation map revealed the earlier activation focus on the upper and lateral region of the RVOT, just below the pulmonary valve.

Patient 2. A 33-year-old woman with a medical history of lymphocytic colitis and symptoms of fatigue and palpitations underwent an EPS in 2018 due to premature ventricular complexes (PVC) arising from the right ventricular outflow tract (RVOT). A cardiac MRI showed no structural cardiac abnormality. An ablation was successfully performed without complications.

In 2020, the patient presented with similar symptoms and underwent a 24-hour Holter monitoring that revealed > 22,500 (19.4%) interpolated PVCs with a predominant focus on the RVOT. Transthoracic echocardiography (TTE) showed a left ventricular ejection fraction (LVEF) in the lower limit of normal (54%).

A second EPS was performed, and activation mapping revealed the earlier activation focus on the upper and lateral region of the RVOT, just below the pulmonary valve. Pace-mapping found a 12/12 correlation with the PVCs. Eight RF applications were performed in that location with the complete cessation of extrasystoles. Isoprenaline was administered, and extrasystoles were not induced.

The PT was 90 minutes, FT was 1.8 minutes, and FD was 21 mSv *(Figures 3 and 4)*.

Patient 3. A 59-year-old female with a past medical history of obesity, arterial hypertension, and dyslipidemia was admitted to the emergency room with a 1-month history of irregular and intermittent palpitations associated with dyspnea for progressively lesser efforts, orthopnea, and peripheral edema. Lab

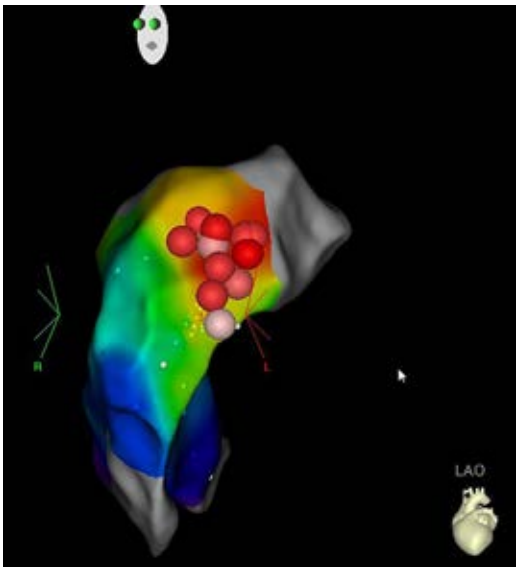

Figure 4: Left anterior oblique projection. Eight ablation lesions on the upper and lateral region of the RVOT, which corresponds to the hotspot (red dots).

results were unremarkable. The ECG revealed supraventricular tachycardia with a heart rate of 170 bpm. TTE revealed biventricular systolic dysfunction. Adenosine bolus was administered (6 + 12 mg), resulting in auriculoventricular node slowing. Atrial tachycardia was revealed as the supraventricular rhythm.

A bolus dose of amiodarone followed by infusion was administered with reversion to sinus rhythm. Amiodarone was discontinued

due to QT interval prolongation. During hospitalization, atrial tachycardia recurred frequently. The patient also presented with typical atrial flutter (AFL).

The patient was submitted to an EPS. At the beginning of the procedure, the ECG showed typical AFL. An activation map of the cavotricuspid isthmus (CTI) was performed, and a point-by-point ablation line at the medium CTI was carried out with reversion to sinus rhythm. Programmed ventricular electrical stimulation showed concentric and decremental conduction through the AV node. Programmed atrial electrical stimulation was performed with rapid induction of focal atrial tachycardia.

An activation mapping was performed with a multipolar catheter. An area of highest precocity at the level of the interatrial septum was located. A patent foramen oval (PFO) was detected, a mapping-ablation catheter progressed through the PFO, and the left atrium was mapped. In the right anteroseptal region, the highest precocity was located. An RF application was performed at this level, with immediate interruption of the tachycardia. Additional ablation lesions were delivered.

Programmed electrical stimulation was performed again under isoprenaline without tachycardia induction. Bidirectional conduction block in CTI was confirmed by pacing maneuvers.

The PT was 110 minutes, FT was 3 minutes, and FD was 17.1 mSv *(Figure 5)*.

Patient 4. A 54-year-old woman, with a medical history of arthropathic psoriasis and some episodes of paroxysmal supraventricular tachycardia (PST) was submitted to an EPS. The programmed ventricular electrical stimulation documented a concentric and decremental retrograde conduction through the AV node. Then, programmed atrial electrical stimulation revealed a dual physiology nodal conduction without tachycardia induction. The programmed atrial stimulation was repeated, under isoprenaline, with an AV nodal re-entry tachycardia induction. An RF pulse was applied in the slow conduction pathway in sinus rhythm. Programmed electrical stimulation was performed again, under isoprenaline, without evidence of dual nodal conduction and, consequently, without induction of AV nodal re-entry tachycardia.

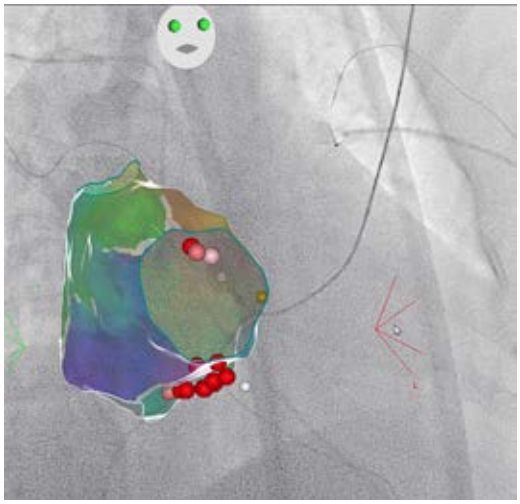

Figure 5: Right anterior oblique projection. His bundle signal (orange dot). A point-by-point ablation line at the medium CTI was carried out, and RF applications were performed in the right anteroseptal region.

The PT was 60 minutes, FT was 2.5 minutes, and FD was ten mSv *(Figure 6)*.

DISCUSSION

3D-EAM was developed to support the mapping and ablation of arrhythmic substrates by providing a more useful image of heart chamber size and catheter positioning than fluoroscopy alone. Long-standing concerns about the effects of ionizing radiation exposure on laboratory staff and patients led researchers to explore the ability of these systems to effectively and safely minimize radiation exposure. Currently, the goal is to attempt the elimination of fluoroscopy, even for more complex CA procedures. Operators rely on this traditional imaging modality and usually generate several fluoroscopic images during a CA procedure. The integrated view provided by the CARTO-UNIVU™ module in conjunction with the CARTO-3® system, enables operators to obtain several sources of visual information using different imaging modalities, helping navigation during CA procedures. This approach increases confidence and decreases the necessity of repeated fluoroscopic images.[11-13]

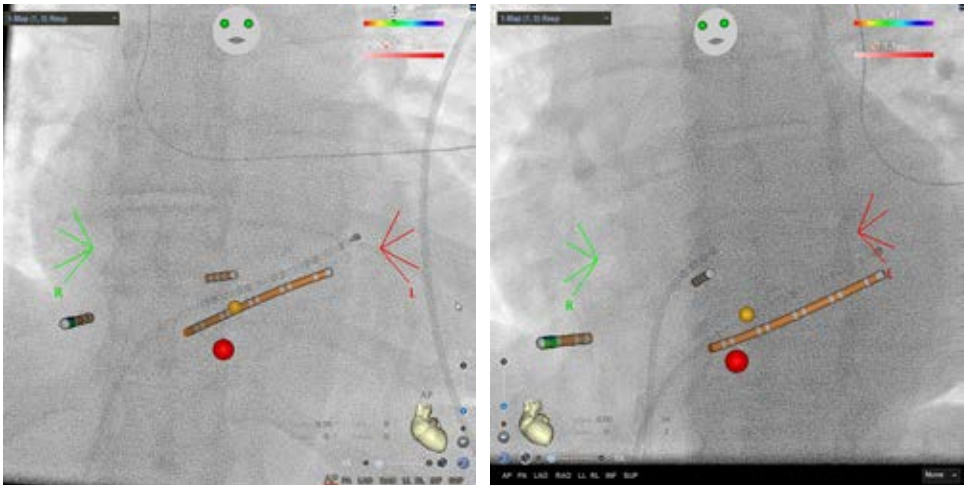

Figure 6:

Anteroposterior and left anterior oblique projection. His bundle signal (orange dot). An RF dot (red dot) in the slow conduction pathway.

CA procedures can be subdivided into four stages: vascular access, positioning the catheter inside the heart chambers, EPS, and ablation. The EAM can markedly decrease radiation exposure in the last two stages and lesser in the previous two, mostly if the operator is less skilled. «Near-zero» or «zero» fluoroscopic procedures can be achieved only after appropriate training and experience.[11-13]

Specifically, a diagnostic EPS is associated with a mean effective dose of 3.2 mSv, comparable to 160 chest radiographs (each one has approximately 0.02 mSv) or 1.2 years of background radiation. In contrast, a CA procedure is associated with 15.2 mSv, equivalent to 760 chest radiographs or 5.7 years of background radiation.[5] The overall risk of fatal malignancy caused by radiation increases by 0.05% for every ten mSv of exposure. Therefore, a CA procedure with mean radiation exposure of 15 mSv is related to a higher cancer risk of 1 in 750 men aged 50. There is strong evidence linking radiation exposure and cancer for doses > 50 mSv. This cumulative radiation exposure can be reached with a single examination but more frequently by repeated diagnostic or interventional procedures.[14]

Several studies have examined FD in patients during CA procedures and estimated excess fatal malignancies of 0.3 and 2.3 per 1,000 patients per hour of fluoroscopy.[11]

Although the total PT was unaffected, several studies found a statistically significant reduction in FT and FD during CA procedures using the CARTO-UNIVU™ module. Sporton et al. compared 3D-EAM (CARTO) and conventional fluoroscopically guided activation. The authors found that 3D-EAM is viable and associated with a drastic reduction in FD (one-fifth) compared with the conventional approach (6.2 ± 6.1 vs 20.8 ± 32.7 Gray, $p = 0.003$). The mean FT in the CARTO group was 20 minutes less than that in the conventional group (9.3 ± 7.6 vs 28.8 ± 19.5 min, $p < 0.001$). The use of EAM was associated with similar PT, success, and complication rates.[11] Separate series by Akbulak et al. and Huo et al. demonstrated that the use of the CARTO-UNIVU™ module (compared to the CARTO-3® system) for AF ablation procedures was associated with a significant decrease in FD: by 50% in Akbulak et al. series (883 vs 476 cGy × cm^2; $p < 0.001$) and by 75% in Huo et al. series (2,440 vs 652 cGy × cm^2; $p < 0.001$) without affecting PT, complications, or jeopardizing long-term success.[15,16] Expanding on this information, Christoph et al. examined the use of the CARTO-UNIVU™ module for a wide spectrum of arrhythmias. The authors revealed a significant reduction in FD: 60% for AFL ablation (1,641 vs 657 cGy × cm^2, $p = 0.002$), 49% for AF (7,369 vs 3,726 cGy × cm^2, $p < 0.001$), 68% for atrial tachycardia (5,088 vs 1,620 cGy × cm^2, $p < 0.001$), and 41% for VT ablation (12,550 cGy × cm^2 vs 7,391 cGy × cm^2, $p = 0.017$).[1] Cano et al. demonstrated an 82% reduction in FT and 65% reduction in FD with the CARTO-UNIVU™ module in AF

procedures.[10] Sakama et al. studied CTI ablation in patients with AFL using ablation under the guidance of the CARTO-UNIVU™ module and demonstrated a shorter FT (0.2 ± 0.4 vs 1.7 ± 2.0 min, $p < 0.001$) and shorter RF time (4.2 ± 2.4 vs 5.1 ± 2.5 min, $p = 0.011$).[17] Moreover, Sommer et al. demonstrated a significant learning effect associated with using this technology and reported a significant decrease in FT and FD with the operator's familiarity with the technology. Concretely, when comparing the first 50 cases with the last 50 cases, the FT reduced from 6.0 to 1.1 minutes, and FD reduced from 2,363 to 490 ($p < 0.001$ for both).[18]

In our series, in contrast to a CARTO-3® group of Christoph et al. study, there was a lower FT during ablation of AP (case 1) (2.3 vs 7.1 ± 1.2 min), PVC (case 2) (1.8 vs 17.6 ± 2.3 min), AFL (case 3) (3 vs 8.6 ± 0.8 min) and PST (case 4) (2.5 vs 23.4 ± 3.1 min). The FD was also reduced during ablation of AP (case 1) (2,536 [7 mSv] vs 3,823 ± 868 cGy × cm^2), PVC (case 2) (7,609 [21 mSv] vs 4,688 ± 838 cGy × cm^2) and PST (case 4) (3,623 [10 mSv] vs 5,088 ± 969 cGy × cm^2), with no reduction in the AFL ablation (case 3).[1]

This article describes our first experience with the CARTO-UNIVU™ module and includes our learning curve. As our experience of the system has grown, we have used less fluoroscopy to confirm catheter position, which is already available from the CARTO map. We recently acquired a DecaNav® decapolar catheter that allows its placement in the coronary sinus without fluoroscopy, which will further decrease FD.

When considering implementing new technology, cost-effectiveness is an important consideration. Nonetheless, this increased cost is likely compensated by the decrease over the years of radiation-induced malignancies.[11]

In our experience, the use of the CARTO-UNIVU™ module promoted a marked reduction in radiation exposure during RF ablation of a wide range of arrhythmias without prolonging PT and compromising patient safety. Achieving a low level of radiation exposition is imperative in clinical practice. «Near-zero» or «zero» fluoroscopic procedures are as safe and effective as the traditional fluoroscopy-guided approach. The possibility of broader access at a reasonable cost, mainly in developing countries, would bring this benefit even closer to a large number of patients.

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Dyslipidemia corner

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Dyslipidemias, fatty liver, and cardiovascular disease

Dislipidemias, hígado graso y enfermedad cardiovascular

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Eduardo Meaney,‡ Nayelli Nájera‡

Keywords:
non-alcoholic hepatic steatosis, metabolic syndrome, insulin resistance, obesity, cardiovascular disease.

Palabras clave:
esteatosis hepática no-alcohólica, síndrome metabólico, resistencia a la insulina, obesidad, enfermedad cardiovascular.

ABSTRACT

Non-alcoholic fatty liver disease (NAFLD) results from an unhealthy lifestyle (including a hypercaloric diet and sedentary lifestyle) and metabolic diseases such as obesity, insulin resistance, dyslipidemia, hypertension, and metabolic syndrome. The accumulation of free fatty acids (FFA) and lipid metabolites in hepatocytes, causes the disturbance of insulin-triggered cell signaling and the development of hepatic insulin resistance, and the consequent development of hyperglycemia and hyperinsulinemia. Also, increased lipogenesis and abnormalities in lipid metabolism trigger atherogenic dyslipidemia with release of adipokines that favor the development and progression of NAFLD. In addition, pro-inflammatory cytokines are released into the circulation, promoting chronic inflammation and thrombotic susceptibility with systemic microvascular damage, leading to cardiovascular disease. This short review addresses the association between NAFLD, metabolic syndrome, and cardiovascular disease.

RESUMEN

La enfermedad del hígado graso no-alcohólico (NAFLD, por sus siglas en inglés) es el resultado de un estilo de vida poco saludable (que incluye una dieta hipercalórica y un estilo de vida sedentario) y enfermedades metabólicas como la obesidad, la resistencia a la insulina, la dislipidemia, la hipertensión y el síndrome metabólico. La acumulación de ácidos grasos libres (FFA, por sus siglas en inglés) y metabolitos lipídicos en los hepatocitos, provoca la alteración de la señalización celular desencadenada por la insulina y el desarrollo de resistencia a la insulina hepática, con el consecuente desarrollo de hiperglucemia e hiperinsulinemia. Además, el aumento de la lipogénesis y las anomalías en el metabolismo de los lípidos desencadenan una dislipidemia aterogénica con liberación de adipocinas que favorecen el desarrollo y la progresión de la NAFLD. Adicionalmente, las citocinas proinflamatorias se liberan en la circulación, lo que promueve inflamación crónica y susceptibilidad trombótica con daño microvascular sistémico, lo que lleva al desarrollo de enfermedad cardiovascular. Esta breve revisión aborda la asociación entre NAFLD, síndrome metabólico y enfermedad cardiovascular.

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INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is a spectrum of conditions that usually start as a reversibly benign simple hepatic steatosis.

However, it can progress to non-alcoholic steatohepatitis (NASH), cirrhosis, and finally hepatocellular carcinoma.[1,2]

NAFLD development is associated with risk factors such as diet (high in saturated fat and processed meat), altered metabolism, metabolic liver disease, and metabolic syndrome.[3-5]

It is clear that with population aging and the current metabolic syndrome epidemy NAFLD's clinical and economic burden will undoubtedly be overwhelming in the coming decades worldwide.[6]

This article will address the association between NAFLD, metabolic syndrome, and cardiovascular disease.

NAFLD, a silent pandemic. The global prevalence of NAFLD is 25.4%, being higher in South America (30.45%) and the Middle East (31.79%) and lower in Africa (13.48%). In Asia and the Pacific, NAFLD numbers are also increasing, mainly due to changes in diet and urbanization, and the adoption of the Western lifestyle.[1]

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The growth of metabolic diseases such as obesity and type 2 diabetes mellitus (DM2) parallels the increase in NAFLD. The prevalence of NAFLD is between 50% and 75% in people with DM2 and between 80% and 90% in obese subjects; while in patients who have more than one risk factor, the incidence is almost total (80-100%); Similar figures have been observed in the population waiting for a bariatric surgery procedure.[4,7]

Pathogenesis of NAFLD. The exact mechanism(s) establishing fat accumulation in the hepatocyte, especially those that set the development of inflammation, fibrosis, and the evolution of the disease, are not precisely known. The pathology is complex and multifactorial since it involves multiple genetic, metabolic, environmental, and nutritional factors.[7] Various theories have emerged to describe the pathophysiology of NAFLD. The first was the two-hit hypothesis. The first hit is caused by an excessive accumulation of lipids in the liver, produced by multiple factors, such as hypercaloric diets, sedentary lifestyle, obesity, and insulin resistance (IR). This first blow sensitizes the liver. The second hit is secondary to various metabolic insults that lead to inflammation and fibrogenesis. This theory was considered too simple to explain the pathogenesis of NAFLD and, as a consequence of the multiple hit impact hypothesis was developed; this hypothesis states that environmental factors such as excessive high-calorie diets and low physical activity, and genetic factors can favor the development of insulin resistance, obesity, adipose tissue dysfunction, and alterations in the intestinal microbiota. Intercellular crosstalk between hepatocytes, Kupffer cells, and hepatic stellate cells is also involved in the pathogenesis of NAFLD.[8] All together are involved in the development and progression of the disease.

Interrelation of NAFLD and metabolic syndrome. **Insulin resistance and NAFLD.** Insulin resistance (IR) is a weak or altered biological response to insulin, decreasing insulin-mediated glucose uptake, despite normal or elevated insulin concentrations. In states of IR, the pancreas releases more insulin to solve the defects in peripheral glucose uptake and eliminate hepatic glucose production. In hepatocytes, insulin promotes glycogenesis, inhibits gluconeogenesis, and activates *de novo* lipogenesis (DNL), that is, the formation of triglycerides (TG) from glycerol and three molecules of free fatty acids (FFA). Contrariwise, IR increases lipolysis (the catabolic release of FFA from TG), raising their blood concentration. The accumulation of FFA and lipid metabolites in hepatocytes activates kinases, which phosphorylate serine or threonine residues of the receptor, altering the normal phosphorylation of tyrosine residues and leading to deficient insulin signaling pathway and causing the phenomenon known as IR. The altered signaling cascade interferes with the translocation of the GLUT-4 glucose transporter to the cell membrane, impeding the glucose inflow from the blood and increasing the level of glycemia. Furthermore, IR causes a decrease in glycogenesis and stimulates gluconeogenesis. Probably, the hyperinsulinemia that accompanies IR, while the pancreas can secrete insulin, is a primary defect more than a compensation mechanism of IR.[9] Although insulin promotes DNL in hepatocytes, hepatic IR does not lead to suppression of DNL but to an increase through mechanisms that are not completely clear.[10-13]

Association between NAFLD, obesity, dyslipidemias, and adipose tissue dysfunction. In obesity, the excessive accumulation of lipids in adipocytes increases the size of fat cells and the entire mass of adipose tissue (AT). Not in all, but in most obesity cases, adipocyte function is impaired. The activation of c-JNK and lkKbeta-dependent inflammation pathways causes reduced insulin sensitivity. Obesity is a risk factor for IR and NAFLD. IR in adipose tissue alters the antilipolytic effect of insulin, increasing lipolysis. The hyperinsulinemia and hepatic IR induced increases in hepatic DNL and a more significant release of TG from the liver, which translates into a high load of circulating lipids delivered to the AT, aggravating the adipocyte's functional deficiency. The AT plays an essential endocrine role in the body. It secretes hormones and adipokines such as adiponectin and leptin, critical metabolic regulators. AT functional alterations are related to the development and progression of NAFLD and NASH. Adiponectin improves

hepatic IR since it suppresses glycogenolysis and lipogenesis, improving glucose utilization. Its deficiency could intervene in mitochondrial dysfunction, IR, and obesity. Adiponectin levels decrease as adipocyte size and IR increase and relate to the low plasma concentrations found in subjects with NAFLD, which predicts the risk of NASH. On the other hand, leptin acts centrally, reducing food intake and increasing energy use, preventing the accumulation of lipids in organs other than the AT, such as the liver. Obese subjects and those with NASH develop leptin resistance, increasing plasma concentrations. The increase in leptin relates to decreased glucose uptake and increased gluconeogenesis, generating hyperglycemia, and therefore participating in the development of IR.[14-16] Finally, increased lipogenesis, resulting from an increased fat mass that is responsible for the high levels of circulating FFA, overproduction of VLDL, and other abnormalities in lipid metabolism, can lead to significant lipid anomaly characterized by an increase in the population of small and dense LDL, the concentration of TG and a decrease in HDL (hypoalphalipoproteinemia).[8] This atherogenic dyslipidemia or lipid triad is seen mainly in dysmetabolic, diabetic or not, obese or overweighed patients and seems to be the primary lipid abnormality causing myocardial infarction in Mexicans.[17]

Relationship between NAFLD, cardiovascular diseases, and hypertension. There is diverse evidence suggesting that patients with NAFLD have a high cardiovascular risk, representing the leading cause of death in these patients.[18,19] Several epidemiological and clinical studies have suggested a role for NAFLD in the progression of different cardiovascular manifestations, such as endothelial dysfunction, left ventricular dysfunction, atherosclerotic cerebrovascular disease (CVD), abnormalities of the cardiac conduction system, and ischemic stroke.[20,21] There are multiple pieces of evidence that NAFLD is a promoter risk factor for the occurrence of high blood pressure (HBP), and at the same time, HBP can aggravate the fibrotic reaction in fatty livers. The mechanisms of this back-and-forth relationship are not entirely elucidated. Still, everything indicates that inflammation, endothelial dysfunction, increased oxidative stress, gut microbiota abnormalities, and overexpression of the renin-angiotensin-aldosterone system, among many other phenomena, can intertwine both clinical conditions.[22,23] The mechanisms by which NAFLD increases CVD risk are complex and involve various pathways at different functional and structural levels, such as metabolism, the cardiovascular system, and liver function.[24-26] The liver has the most significant number of resident macrophages and an increase in pro-inflammatory cytokines (TNF-α, IL-6, CRP) that can be chronically released into the circulation and promote chronic inflammation and thrombotic susceptibility.[27,28] Therefore, it is considered that liver damage and the release of proinflammatory cytokines result in systemic microvascular damage, abnormalities of the coagulation system, altered endothelial dysfunction, and the generation of oxidative stress. It is also suggested that NAFLD and CVD share a common hereditary predisposition. The endothelial damage induces an increase in arterial stiffness, which promotes the development of hypertension and CVD.[25,26] High serum concentrations of vascular endothelial growth factor (VEGF) and high levels of prothrombotic factors (factors VIII, IX, XI, and XII) have been reported in patients with NAFLD, and they correlate with hepatic fat content. Therefore, they may be related to an increased cardiovascular risk. Recently, it has been reported that there is a systemic role for liver tissue-specific molecules (hepatokines), which appear to affect multiple metabolic pathways. These molecules play a relevant role in developing cardiovascular complications in patients with NAFLD. For example, the fibroblast growth factor 21 (FGF-21), a peptide secreted by the liver, negatively affects the cardiovascular system. Increased serum concentrations of FGF-21 are associated with thickening of the carotid intima-media and coronary atherosclerosis.[29-32] Therefore, NAFLD stimulates pro-inflammatory and prothrombotic factors, contributing to several chronic diseases, including ischemic heart disease, cardiomyopathy, cardiac arrhythmias, and chronic kidney disease.[2]

Metabolic syndrome and NAFLD. Metabolic syndrome (MS) or dysmetabolic

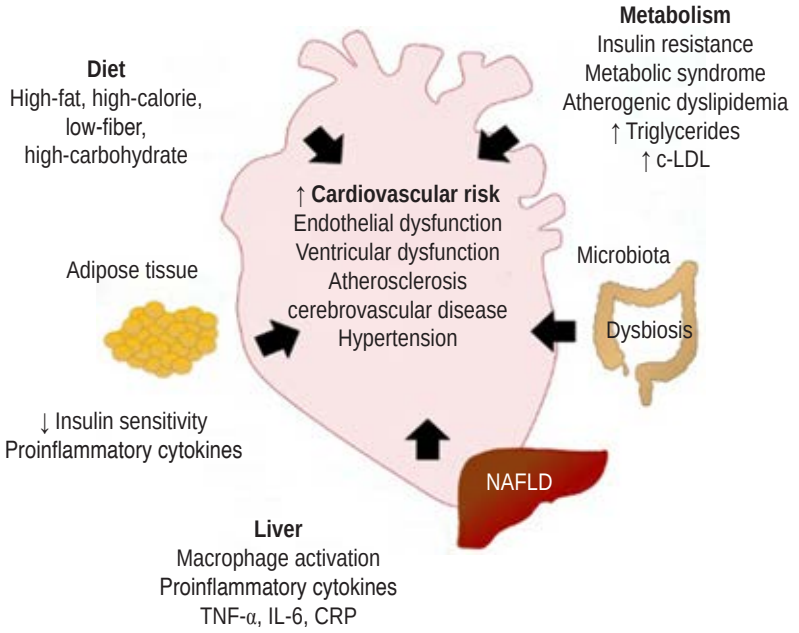

Figure 1:

Representation of the multiple factors involved in the increase in cardiovascular risk, in which the liver is significantly involved.

obesity is a set of metabolic disorders consisting of centrally distributed obesity, decreased concentrations of cholesterol bound to high-density lipoproteins (HDL), elevated concentrations of TG, high blood pressure arterial hypertension, and hyperglycemia. All these alterations are present in patients with NAFLD. The prevalence of MS in obese patients with NAFLD is 67%. Furthermore, the presence of MS was associated with an increased risk of NASH and severe fibrosis. However, not all patients with NAFLD exhibit the typical features of MS. Approximately 30% of NAFLD patients suffer from metabolic abnormalities.[33,34] In many patients, both clinical conditions, NAFLD and MS, are early, almost simultaneous manifestations of IR. The current concept signals that NAFLD is the hepatic expression of MS, but frequently, hepatic abnormalities can worsen IR. On the contrary, the lipid abnormalities were seen in MS; for example, the so-called lipid triad can aggravate the lipid liver storage.[35]

Microbiota and NAFLD. Alterations in the microbiota (dysbiosis) have recently been associated as part of the origin of the pathogenesis of NAFLD; for example, a greater abundance of *Escherichia coli* and *Bacteroides vulgatus* has been found in the fecal microbiota of patients with NAFLD. An increase in the intestinal barrier permeability has also been found with hypercaloric diets high in saturated fat, low in fiber, rich in refined carbohydrates, and high in fructose in patients with NAFLD. Dysfunction of the intestinal barrier allows the activation of receptors that trigger the production of proinflammatory cytokines, such as TNF-α. Also, it will enable the passage of lipopolysaccharides (LPS) into the circulation, activating the immune system, including Kupffer cells (hepatic macrophages), triggering more inflammatory processes, oxidative stress, and liver damage.[36]

CONCLUSION

NAFLD is a growing problem for public health in most countries worldwide. Uncertain diagnosis without specific treatment is one of the significant challenges of basic science and clinical science today. Considering the risk factors for the development of NAFLD *(Figure 1)*, we can justify the need for comprehensive management of the patient from the early stages, from identifying and controlling overweight or obesity to preventing dyslipidemia, metabolic syndrome, and other complications. The central pillar in public health continues to be promoting a healthier lifestyle, including a diet with a low content of simple carbohydrates and

saturated fat, rich in polyunsaturated omega-3 fat acids, fiber, prebiotics, probiotics, and nutraceuticals such as epicatechin from cocoa. In addition, an increase in physical activity reduces the impact of Western life on the liver and cardiovascular health.

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Consensus Statement

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COMECITE post-percutaneous cardiovascular intervention care

Cuidados postintervención cardiovascular percutánea. COMECITE

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Keywords:
fasting, hydration, ultra-low contrast, early discharge, ward and intensive care unit monitoring, vascular complications.

Palabras clave:
ayuno, hidratación, medio de contraste ultra-bajo, egreso temprano, monitoreo en hospitalización terapia intensiva, complicaciones vasculares.

ABSTRACT

Introduction: medical literature has huge information on studies and guidelines for patients with coronary, peripheral, or structural interventional procedures; nonetheless, a few papers focused on optimal fasting time, hydration, contrast dye used, post-intervention discharge monitoring in-home, ward, or intensive care unit as vascular complications. This paper review aims to provide achievable facts that aid physicians in protecting patients' integrity in hospitals and homes.

RESUMEN

Introducción: *existe una vasta información en la literatura médica de los procedimientos coronarios, estructurales y periféricos en diversos estudios y guías, sin embargo, pocos documentos abordan temas como tiempo óptimo de ayuno, hidratación, cantidad de medio de contraste, monitoreo del paciente después del procedimiento; cuándo puede ir a casa, al área de hospitalización, a terapia intensiva o unidad coronaria y las posibles complicaciones vasculares. Este manuscrito de revisión contiene datos que ayudarán a los médicos a ser vigilantes de la integridad de los pacientes en hospitales y sus hogares.*

INTRODUCTION

The Mexican College of Interventional Cardiology and Endovascular Therapy (COMECITE for the name in Spanish: *Colegio Mexicano de Cardiología Intervencionista y Terapia Endovascular*) formed the consensus group with a designated chairman and co-chairman; that later distributed functions to the rest of the members. Every member searched and analyzed relevant publications about fasting, hydration, early discharge, low contrast in percutaneous interventions, monitoring patients in intensive care unit and ward post interventional procedures, and vascular complications settings. The authors used the Cochrane Handbook[1] for systematic reviews of interventions and AMSTAR 2 (A MeaSurement Tool to Assess Systematic Reviews): a critical appraisal tool for systematic reviews that included randomized or non-randomized study trials of healthcare interventions.[2] The members also reviewed single papers regarding special anatomical conditions. The consensus group discussed each paper in an expert panel format, nominal group technique, and anonymous Dolphy survey.[3]

The consensus timing process took from Dec 1/2021 through April 2022.

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FASTING

The catastrophic event of pulmonary aspiration of gastric contents justifies the usual indication for fasting before general anesthesia to prevent several respiratory syndromes, such as aspiration pneumonitis due to chemical injury after inhalation of gastric contents, aspiration pneumonia for inhalation of oropharyngeal secretions, and pathogenic bacteria colonization, airway obstruction, lung abscess, exogenous lipoid pneumonia, and chronic interstitial fibrosis.[5,6]

Death or permanent severe injury may result from pulmonary aspiration during general anesthesia, and the major risk factors are, in order of frequency.[7]

1. Emergency procedures.
2. Acute intraabdominal processes.
3. Morbid obesity.
4. Gastroesophageal reflux disease.
5. Diabetes mellitus.
6. Recent oral intake.
7. Recent opioid administration.
8. Major trauma.
9. Previous gastric bypass or sleeve.
10. Neurological disease.
11. Pregnancy.

The American and Canadian Anesthesiologists recommend eight hours of fasting from fatty food or meats, six hours for non-human milk or a light meal, four hours for breast milk, and two hours for clear liquids before the anesthesia. However, the Canadian Pediatric Anesthesia Society and the European Society of Anaesthesiology preoperative guidelines are more permissive for less prolonged fasting times, especially encouraging liquids intake.

Anesthesiologists have enough imaging skills to incorporate gastric ultrasound, which is feasible in obese, pregnant, and pediatric patients, especially during the uncertainty of prandial status and gastric emptying. <1.5 mL/kg of clear fluid is consistent with a state of fasting, in contrast with ≥1.5 mL/kg of clear fluid or solids.[8]

Interestingly, doctors indicated caloric liquids three hours before surgery during the early 19th century to prevent aspiration during anesthesia; one hundred years after, practice switched towards fasting from midnight under the misconception to reduce such risk.[9]

Anxiety, dehydration, postoperative nausea, hypoglycemia, hypovolemia, and vomiting may result from prolonged fluid fasting indeed, free fluids before anesthesia may reduce postoperative nausea and vomiting, considering no more than 3.5-hour clearance for both clear and non-clear liquids and less than two hours when not exceeding 220 kcal; the same applies for pediatrics.[10] Stress response to trauma induces insulin resistance, which associates with a poor prognosis.[11]

Prolonged fasting causes undesirable effects and does not guarantee stomach emptying; hence the currently preferred indication for liquids by mouth 2 hours before surgery and one hour in pediatrics.[12]

There is no evidence-based support for fasting before cardiac catheterization, especially for local anesthesia and mild sedation, and there is a lack of supportive evidence for lung aspiration in emergencies, such as percutaneous coronary intervention or brain interventions.[13-15] Heart disease patients may also receive poor hydration and diuretics, thereby increasing the risk of contrast dye kidney damage.[16,17]

The contemporary indication for free feeding before percutaneous endovascular intervention recently received supporting concepts from leaders of the Society for Cardiac Angiography & Interventions (SCAI), perhaps leaving some restrictions for large catheter size-based and valvular procedures.[18]

Highlighting fasting at any age and gender:

1. Results from customs, not science.
2. Usually results in uncontrolled and prolonged periods without meals and liquids.
3. Associates to morbidity and mortality.
4. May aggravate poor hydration and exposure to contrast dye kidney damage.

5. It does not prevent efficiently pulmonary aspiration.

Short-term calorie-liquids:

1. May prevent nausea and vomit.
2. Causes faster gastric emptying.
3. It does not relate to pulmonary aspiration.

Finally, free-feeding before cardiac catheterization (not general anesthesia, large catheter size, and valvular intervention) may be better than fasting.

Patients must have a fasting protocol based on individualized needs under personal schemes or institutional program centers for the best patient comfort and safety. Nonetheless, the Consensus group decided on the following recommendations, applied to all ages, genders, and procedure complexity:

1. Indications for fasting do not apply to immediate urgency for cardiac catheterization and rescue interventions that proceed without any delay.
2. Encourage the anesthesiologist to perform ultrasound identification of the contents of the antrum; this helps not to delay the procedure when the fasting time is uncertain.
3. Avoid more than twelve hours of fasting. The usual indication for «nothing by mouth (NPO)» since dinner, for institutional schedule, forces at least twelve hours fasting for the first-time procedure chart and increases on the second time and so on with the rest of the patients, being up to more than 20 hours for the afternoon procedures. Overcome the problem with the following:
   a. Indicate NPO since dinner on all patients.
   b. Indicate at 08:00 AM.
   c. Indicate at 08:00 a liquid diet with glucose for the rest of the morning patients.
   d. Indicate complete breakfast and liquid diet at noon for all scheduled afternoon patients *(Table 1)*.
   e. Assess every patient's hydration status for additional parenteral fluids.
   f. Consider shorter fasting periods before low catheter-sized procedures under local anesthesia and mild sedation.
4. Above recommendation improves significantly on individualized care and indication for fasting.
5. Pediatrics must avoid more than six hours of fasting and consider two-hour clear liquids before the procedure.
6. Consider the patient's consciousness condition for the next meal after the procedure, which should be sooner.

HYDRATION

Hydration is essential for metabolism, substrate transport across membranes, cellular homeostasis, temperature regulation, and circulatory function. Normal plasma osmolality ranges 266-301 mOsm/kg may be considered normal but is age-dependent. Inter-individual differences and comorbidities are the primary reasons why widespread consensus regarding the daily water requirements has not been reached to this date.[19]

Table 1: Fasting summary.

Coronary, structural or peripheral	Fasting hours	Previous diet	Recommendations	Post-intervention meal
Emergency	None	No matters	Gastric ultrasound	As soon as possible
Morning 1st time	8	No restricted dinner	—	As soon as possible
Morning 2nd time	8	No restricted dinner	≤ 200 clear liquids at 08:00	As soon as possible
Morning 3rd time	8	No restricted dinner	≤ 200 liquids with ≤ 220 kcal at 08:00	As soon as possible
Afternoon 1st time	6	No restricted breakfast	—	As soon as possible
Afternoon 2nd time	6	No restricted breakfast	≤ 200 clear liquids at noon	As soon as possible
Afternoon 3rd time	6	No restricted breakfast	≤ 200 liquids with ≤ 220 kcal at noon	As soon as possible

The 2004 US National Academy of Medicine (NAM) publication, which presented dietary reference intakes for water, this report concluded that: (a) individual water requirements can vary greatly on a day-to-day basis because of differences in physical activity, climates, and dietary contents; and (b) there is no single daily water requirement for a given person.[20]

Optimal hydration must be a premise to avoid complications in interventional procedures. Pre- and post-intervention hydration balance is the best method to prevent contrast-induced nephropathy (CIN) plus low contrast volume. Patients with dehydration or low cardiac output need a high fluid volume infusion but are restricted for congestive heart failure or high cardiac output and must individualize hydration.

Initial hydration evaluation starts with clinical symptoms and signs of dehydration like thirst, dry mouth, low volume of urine or sweat, dark-colored urine, dry skin, feeling tired, and dizziness in adults; dry mouth and tongue, crying without tears, no wet diapers for three hours or more, high fever, sleepy or drowsy, irritability, eyes sunken in infants and young children. Upgrade dehydration includes confusion, fainting, lack of urination, tachycardia, tachypnea, and shock.

Methods for assessing hydration include hematocrit, plasma, urine, saliva or tear osmolarity, serum sodium, bioimpedance, body mass, vital signs, and hormone variables. Precision, reliability, cost, invasiveness, and required time rates from low to high and often impractical. Ultrasound is a useful tool for evaluating inferior vena cava diameter with a normal value of 50%, suggesting a normal mean right atrial pressure (RAP) of 0 to 5 mmHg. Lack of vena cava collapse suggests elevated mean RAP 10-20 mmHg. It is worth the invasive central venous pressure monitoring or Swan Ganz catheterization and lactic acid test.

Optimal hydration in percutaneous endovascular intervention is essential to maintain homeostasis and reduce risk complications in widespread scenarios and structures (coronary, structural, and peripheral).[21-23]

Intravenous hydration with 0.9% saline solution 1 to 1.5 mL/kg/min infusion rate is a conventional hydration technique that should be applied pre, peri, and post-procedure, starting 12 hours before the intervention and continuing for up to 12 hours after completion of the hemodynamic procedure achieving the goal of a urinary flow of 150 mL/h.[24,25]

Central venous pressure (CVP) using a venous catheter at a superior cava level provides records to guide the liquids handling; consider that pericardial, intra-abdominal, and intrathoracic pressure may modify the CVP. The normal value of CVP is 8 to 12 cmH_2O or 1 to 8 mmHg, 1 cmH_2O is equal to 0.735591 mmHg. Values below the lowest normal ranges indicate volume needs[26] and values greater than the highest range indicate fluid overload.

Swan Ganz catheter provides useful information on body hemodynamics in unstable patients and should be the gold standard for hydration monitoring, yields pulmonary artery pressure, CVP, pulmonary capillary wedge pressure, cardiac output, mixed venous oxygen saturation (SvO_2), systemic vascular resistance, pulmonary vascular resistance, and cardiac index.[27,28] POSEIDON trial concludes that left ventricular end-diastolic pressure (LVEDP) guides hydration in patients with GFR < 60 mL/min/1.73 m^2 by MDRD equation and diabetes, age > 77, hypertension, and history of CHF, reducing major adverse event, death, and dialysis in contrast nephropathy status. Scale protocol recommends a pre-procedure saline infusion rate of 3 mL/kg/h, during the procedure with LVEDP 18 infusion rate of 1.5 mL/kg/h. Post-procedure infusion rate continued for 4 hours at least.[29] Hydration governed by urinary volume (RenalGuard) has a console with software that measures the urinary volume excreted hourly and replaces intravenously the same amount per hour.[30]

Recommendation

1. With comorbidities, always estimate hydration status in pre-and post-percutaneous endovascular procedures.
2. Clinical examination findings and urinary flow may be a hydration guide in stable patients.
3. Parenteral solutions and rates could be evaluated based on serum or urinary

osmolality, by ultrasound assessing inferior vena cava collapse index, and invasive through central venous pressure, or Swan-Ganz catheterization.
4. In patients with contrast nephropathy risk, LVEDP guides hydration solutions rate.
5. Indicate invasive monitoring tailored hydration.

ULTRA-LOW CONTRAST IN PERCUTANEOUS INTERVENTION

Percutaneous intervention procedures use intravascular iodinated contrast media injections. The maximum allowable volume of iodine contrast in healthy adult individuals is ≤ 300 mL with a 300 mg I/mL concentration. In patients with renal insufficiency, the contrast volume should be as low as possible, not exceeding 5 × weight (kg) / creatinine (mg/dL) with a 300 mg I/mL concentration.[31]

Acute renal failure is a common complication in interventional procedures; it may increase morbidity, mortality, and healthcare cost.[32] Contrast-induced nephropathy (CIN) may appear after 48-72 hours from exposure to a contrast agent with an increase of serum creatinine values ≥ 0.5 mg/dL or at least ≥ 25% elevation compared to baseline.[33] It particularly affects subjects with chronic kidney diseases (CKD), diabetes, heart failure, acute coronary syndromes, and cardiogenic shock. Intra-arterial vs intravenous contrast media administration has a greater risk of CIN, although the mechanism of this phenomenon is not clear.[34]

Ultra-low contrast coronary angiography is a technique performed using less than 15 mL of nonionic, iso-osmolar contrast agent volume per estimated glomerular filtration rate (eGFR), a ratio should be less than 1 (e.g. if the patient's eGFR equals 15 mL/min/1.73 m^2, the CV should be less than 15 mL). Consider using 5-6F catheters without side holes, and small syringes (e.g., 3 or 5 mL); 3 mL is sufficient to visualize the left coronary artery, whereas 2 mL is enough for the right coronary artery. Remove contrast dye before any drug administration (e.g., nitroglycerine) or when exchanging catheters to avoid pushing it into the patient.

Acquisition time with a high frame rate (i.e., 30 frames/s) helps. Spider view and cranial right anterior oblique projection may be enough to visualize the left coronary artery lesion location, and cranial left anterior oblique projection are usually sufficient for right coronary angiography anatomy. If more projections are necessary, contrast dilution with saline 2:1 may limit the overall contrast amount. Biplane angiography limits the number of acquisitions.[35] Patients with renal disease usually have calcified lesions in proximal coronary artery segments which may help to identify the ostial and facilitate catheter engagement. To confirm the proper engagement, inject 10-20 mL of saline through the catheter and observed temporal changes in the electrocardiogram like T-wave inversions or ST-segment depression or elevation.[36] This method requires heparin administration and has some risk of coronary dissection.

Hydration remains the cornerstone of CIN prevention; in the POSEIDON trial, left ventricular end-diastolic pressure (LVEDP) guided fluid administration in patients undergoing cardiac catheterization. According to this study, each patient should receive a saline infusion of 3 mL/kg one hour before the procedure. Then, the fluid rate administration adjusts to LVEDP, i.e., 5 mL/kg/h for LVEDP lower than 13 mmHg, 3 mL/kg/h for LVEDP 13-18 mmHg, and 1.5 mL/kg/h for LVEDP higher 18 mmHg. The fluid rate starts at the beginning of the procedure and continues during the procedure and for the next four hours.[37]

Invasive physiological assessment of coronary lesions with fractional flow reserve (FFR), instant wave-free ratio (iFR), or another interchangeable method should tailor the intervention. Image evaluation with intravascular ultrasound imaging (IVUS) or optical coherence tomography (OCT) which use a mixture of saline and colloid or dextran-40 highlights the feasibility of interventional procedure success.

Pre-dilatation of the lesion is permitted if the imaging catheter does not cross the evaluated lesion. The use dynamic coronary Roadmap system (DCR) with Azurion (Phillips Healthcare), is a novel technology that creates dynamic motion-compensated real-time coronary arteries, which reduce the fluoroscopy

time and contrast volume; this novel system is safe and effective.[38]

Recommendations

1. Use ultra-low or low-contrast methods in high-risk patients to avoid CIN.
2. Hydration using the POSEIDON protocol.
3. Use physiological and image methods to evaluate and justify interventional procedures.

EARLY DISCHARGE AFTER PERCUTANEOUS CORONARY INTERVENTIONS

Early discharge is a service physicians and healthcare professionals provide for patients' home care, including treatment and supervision after percutaneous interventions (PCI). It could be feasible and safe.

There are two types of early discharge, 1. Same-day discharge[39-42] or 2. early discharge (24 to 72 hours).[43,44] For the first group, the hospital would have lounge facilities or a similar hospital area. For the second group, the hospital ward is enough *(Figure 1)*.

The lounge is a dedicated facility area able to host patients with individual cubicles, comfortable seats with or without massage, monitor TV and entertainment devices, fast Wi-Fi, restrooms, and shower facilities; should have vital signs monitors (ECG, blood pressure, temperature, oxygen saturation) and adjacent resuscitation room. The staff team includes nurses and physicians trained in standard and emergency procedures. 12-lead ECG and laboratory are also available. Fed and drinks were allowed 30 minutes after the patient's arrival. Open working hours of the lounge starts at 08:00 and closed at 20:00; the patient long monitoring stay would be less than 6 hours.[45]

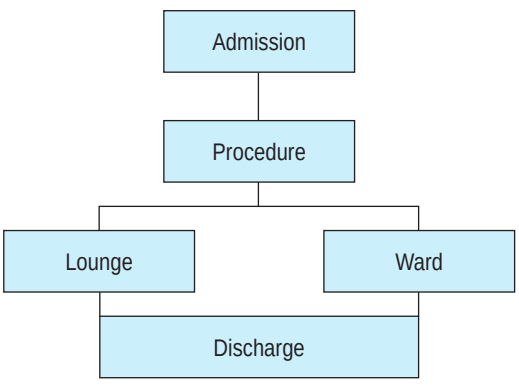

Figure 1: Admission flow.

Diagnostic or interventional procedures such as radial or femoral vascular approaches[46] are suitable for early discharge, but a stable patient is essential.

There are two main types of active arterial closure devices: 1. **collagen plug** (e.g., AngioSeal or Exoseal), which uses suture cinches or/and collagen plug, and the anchor breaks down over months. 2. **Suture-mediated** (e.g., Perclose), uses a suture not absorbable on each side, tied using a preloaded knot, the suture is cut close to the arterial wall, and active closure method involving surgical staple/clip technology (e.g., StarClose) which uses not absorbable clip deployed through the peel-away sheath.[47]

The exclusion criteria for early and same-day discharge are: cardiac arrest, shock, complicated acute myocardial infarction, congestive heart failure, urgent or emergent procedure, left main intervention, complex lesions, large volume contrast dye (> 500 mL), decreased renal function (eGFR 80, > 30 km from PCI facility,[48] left ventricular ejection fraction < 45% or right ventricular fractional area change < 35%, and use of GP IIb/IIIa inhibitors.

Early discharge 24-72 hours, exclusion criteria are unstable patients, cardiac arrest, shock, acute myocardial infarction complications, congestive heart failure, and acute renal failure.

Candidates for early discharge checklist *(Table 2)*.

After discharge patient, relatives or caregiver informs to hospital medical staff or Cardiologist in charge of any clinical change or complaints to a 24 hours phone number.

Goals

1. Patient safety.
2. Patient comfort and satisfaction.
3. Patient or hospital cost savings.

Recommendations

1. Same-day discharge is safe and effective in the management of uncomplicated elective PCI.

Table 2: Discharge checklist.

Parameter	Normal
Alert status	✓
Vital signs	✓
Capillary refill	✓
Oral tolerance	✓
Urinary flow	✓
Hydration	✓
No vascular sheaths or catheters	✓
No bleed or bleeding risk	✓
No hematoma	✓
No pain, distal pulse, and temperature	✓
No side effects	✓
No interaction medication	✓
No arrhythmias	✓
No significant abnormal lab test	✓
No significant electrocardiogram baseline changes	✓
Normal walking tolerance	✓

2. Same-day discharge is an option for hospital and patient cost savings.
3. Early discharge is feasible for all non complicated postprocedural interventions.

POST-INTERVENTIONAL PROCEDURE MONITORING IN THE HOSPITAL WARD

Hospital Ward is a screening or recovering area where patients should be monitored and studied closely.

The inclusion criteria are diagnostic, peripheral, coronary, or structural percutaneous interventions without serious complications or arterial or venous sheaths at the site.

The hospital ward staff must have the medical records and complete procedure information after every intervention.

Initial evaluation encompasses AVPU score (alert, verbal response, painful response, or unresponsive)[49] vital signs (heart rate, respiratory rate, systolic and diastolic pressure, temperature, oxygen saturation), capillary refill, appetite, urinary flow, hydration, and bleeding, which would be recording every 4 hours.

Monitoring issues from initial admission to discharge:

1. Bleeding with compression devices or conventional compressive dress supervision and hypovolemic shock evaluation.[50]
2. Evaluate local pain, distal pulse, and temperature.
3. Supervise hydration (clinical and urinary flow) with an intravenous solution.
4. Monitor acute and chronic arrhythmia.
5. Confirm oral tolerance and appetite.
6. Side effects evaluation and classification (serious or not) inherent to the procedure, medications, or allergic reactions.
7. Medication interaction checker.
8. Supervise walking tolerance after the procedure.
9. Consider laboratory, electrocardiogram, X-ray, echocardiogram, computed tomography scan, or magnetic resonance as required.

Percutaneous post-interventions in hospital ward discharge must be limited to a checklist *(Table 2)*.

POST-INTERVENTIONAL PROCEDURE MONITORING IN THE INTENSIVE CARE UNIT

The Intensive Care Unit (ICU) is a department of a hospital in which unstable patients are kept under constant observation and support for failing vital functions.[51]

Inclusion criteria are diagnostic, peripheral, coronary, or structural percutaneous interventions with pre or post-procedure complications such as cardiac arrest, shock, complicated acute myocardial infarction, congestive heart failure, pulmonary embolism or edema, life-threatening cardiac arrhythmias, urgent or emergent procedure, left main intervention, complex lesions or procedure, large volume contrast medium > 500 mL, decreased renal function (eGFR <60 mL/min) or acute renal insufficiency, left ventricular ejection fraction < 45% or right ventricular fractional area change < 35%, and use of GP IIb/IIIa inhibitors.[52]

After the intervention, the medical record of the patient and complete procedure information should be provided to the ICU staff.

Initial evaluation encompasses AVPU score (alert, verbal response, painful response, or unresponsive),[50] airway, vital signs (heart rate, respiratory rate, systolic and diastolic pressure, temperature, oxygen saturation), capillary refill, bleeding with compression devices or conventional compressive dress, vascular sheaths, catheters or leads. Local pain with distal pulse and temperature or organ site pain, hydration (clinical and urinary flow), intravenous solution, oral tolerance, and appetite. Arrhythmias with acute or chronic onset, side effects, and classification (serious or not) inherent to the procedure, medications, allergic reactions, and medication interaction checker, would be assessed and recorded every hour.

Central venous pressure (CVP) and Swan Ganz catheter provide useful information on body hemodynamics in unstable patients and should not be withdrawn until the patient is stable.

Lab tests, electrocardiograms, X-ray, echocardiograms, computed tomography scans, or magnetic resonance would be individualized and performed as required.

Anaphylaxis score[53] and cardiac shock classification[54] should be evaluated constantly from initial admission to discharge.

Shock treatment was established as the etiology was identified.[55] The hemodynamics type shock parameters must guide the specific treatment *(Table 3)*.

Post-interventional percutaneous procedure discharge ICU criteria have been established when the patient at the time is stable with no serious complications nor arterial or venous sheaths at the site. Avoid discharging patients from ICU after 19:00.[56]

Recommendations

1. ICU admission is indicated for patients with post intervention procedures unstable or complex intervention.
2. ICU discharge is limited for stable patients (hemodynamic, respiratory, neurological, and metabolic).
3. Avoid ICU discharge after 19:00.

VASCULAR ACCESS COMPLICATIONS

The increased use of arterial radial access diminished vascular complications compared to the femoral approach,[57] even so, femoral access is necessary for structural, peripheral, and coronary high-risk patient procedures.

Bleeding, ecchymosis, hematoma, pseudoaneurysm, infection, distal ischemia due to embolic occlusion, on-site or distal dissection, arteriovenous fistula, compartment syndrome, and perforation are common complications with any vascular intervention. Compartment syndrome is the most serious complication, frequently related to trauma with the guidewire

Table 3: Hemodynamics type shock parameters.

Type of shock	mPAP echo	CVP	MAP	PCWP	CO/SV	SVR	DO_2I
Normal range	< 25 mmHg	8-12 cmH_2O 1-8 mmHg	> 60 mmHg	4-12 mmHg	2.5-4.0 L/min/m^2 33-47 mL/m^2/beat	700-1,500 dynes/s/cm-5	500-600 mL/min/m^2
Hypovolemic	↓	↓	↓	↓	↓	↑	↓
Cardiogenic	↑	↑	↓	↑	↓	↑	↓
Obstructive	↑	↑	↓	↑	↓	↑	↓
Distributive	↓	↓	↓	↓	↑	↓	↑

mPAP = mean pulmonary artery pressure. CVP = central venous pressure. MAP = mean arterial pressure. PCWP = pulmonary capillary wedge pressure. CO/SV = cardiac output/stroke volume. SVR = systemic vascular resistance. DO_2I = global oxygen delivery index. mPAP echo = tricuspid regurgitation peak velocity^2 × 4 (0.61) + 2. DO□I = Q × (Hb × SaO_2 × 1.34 + (PaO_2 × 0.003)/m^2SC.

accompanied by a forearm, leg, or pectoral hematoma, which increases pressure in the compartment area and potentially damages the muscle and nearby nerves.

Radial and ulnar artery

Spasm is their more frequent complication, conditioning catheter/sheath entrapment, and eversion endarterectomy; obey to small vessel diameter, insufficient sedation/analgesia, and repeated punctures. Topical, subcutaneous, or sublingual nitroglycerin, reactive hyperemia with blood pressure cuff inflated to 30 mmHg above-average systolic pressure for 3 minutes, forearm heating (i.e., Balbay maneuver)[58] for 3 minutes, hydrophilic sheaths or sheathless guide catheters, excessive catheter manipulation avoidance, telescopic technique use, intraarterial verapamil 2.5 mg, diltiazem 2.5-5 mg or nicardipine and nitroglycerin 10-200 mcg and sedation/analgesia, may prevent spasm.[59]

Femoral artery

The inguinal hematoma is the most frequent complication that may happen sooner or later, imposes a potential risk for the patient, and increases cost due to delays in discharge and ambulation. Over-anticoagulation, large-diameter sheaths, obesity, and female gender are the more common risk factors for hematoma, mostly prevented with refined puncture techniques and vascular closure devices; conservative treatment is the best initial option.

Retroperitoneal hematoma is one of the most serious complications, usually after the iliac or femoral vessels lesion with bleeding into the retroperitoneal space that may hold a large amount before detection. Repeat puncture attempts, over-anticoagulation, large introducer diameters, concomitant venous sheaths, obesity, low body weight, peripheral vascular disease, renal failure or elevated creatinine, hypotension or shock, low platelet count, prolonged procedure duration, repeat PCI, arterial puncture site, and female gender, low body surface, and older age are the more common risk factors, better prevented with a single arterial wall puncture, micropuncture technique,[60] fluoroscopic and or ultrasound guidance, reverse over-anticoagulation, arterial closure device, adequate vessel hemostasis, and supervised compression.[61]

Venous access

Cannulation of antecubital, internal jugular, subclavian or femoral vein is feasible for catheters or leads and allows for high fluid administration, monitoring, or pacing. Ultrasound guidance and or landmark techniques facilitate structure identification. Trendelenburg's position may prevent air embolization. Complications are arterial puncture, hematoma, hemorrhage, embolism (air or catheter fragment), erosion or perforation, infection, phlebitis, and thrombosis.[62]

Recommendations to prevent and treat complications:

1. Master the technique.
2. Try a single wall puncture.
3. Use ultrasound guidance puncture in difficult cases.
4. Be cautious and get enough material, including hydrophilic wires and use the smallest sheath diameter.
5. Perform a checklist before the procedure with available materials and medications.
6. Verify for enough gadgets to manage possible complications.
7. Stay calm and, if necessary, ask for help from more experienced staff.

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Location and date:

Rofucal®

Hidroclorotiazida

Información para prescribir (versión reducida)

1. Denominación distintiva: ROFUCAL®

2. Denominación genérica: Hidroclorotiazida

3. Forma farmacéutica y formulación: Tabletas

Cada tableta contiene:

Hidroclorotiazida ..... 12.5 mg o 25 mg

Excipiente cbp. ..... 1 tableta

4. Indicaciones terapéuticas: ROFUCAL® es un diurético de la familia de las tiazidas que está indicado en: Hipertensión arterial. Como monoterapia o combinado, para incrementar el efecto de otros antihipertensivos cuando se trata de formas más severas de hipertensión. En Edema, cuando está asociado a insuficiencia cardiaca congestiva, cirrosis hepática y en terapia con corticoesteroides y estrógenos. ROFUCAL® es útil también en el tratamiento de edemas relacionados con disfunción renal, como el síndrome nefrótico, la glomerulonefritis y la insuficiencia renal crónica. **5. Contraindicaciones:** el uso de ROFUCAL® está contraindicado en pacientes con anuria e hipersensibles al principio activo o componentes de la formulación, así como a otros fármacos derivados de las sulfonamidas. **6. Precauciones generales:** en pacientes que reciben tratamiento con dosis mayores de tiazidas, se pueden presentar casos de hiperuricemia o franca gota. Una diabetes latente puede hacerse manifiesta con el tratamiento a base de tiazidas. Los diuréticos pueden en dosis mayores precipitar una azoemia en pacientes con insuficiencia renal. **7. Restricciones de uso durante el embarazo y la lactancia:** no se recomienda su uso en embarazadas sanas o con edema pues se expone a la madre y al feto a un riesgo innecesario. Los diuréticos no previenen el desarrollo de toxemias del embarazo y no hay evidencia concluyente de que sean útiles en su tratamiento. Las tiazidas cruzan la barrera placentaria y aparecen en la sangre del cordón umbilical existiendo un riesgo de ictericia neonatal, trombocitopenia y otros posibles efectos adversos. **8. Reacciones secundarias y adversas:** Sistema gastrointestinal: Anorexia, irritación gástrica, náuseas, vómito, diarrea y muy ocasionalmente pancreatitis y sialoadenitis. Sistema Nervioso Central: Mareos, vértigo, parestesias y cefaleas. Hematológicos: Leucopenia, neutropenia/agranulocitosis, trombocitopenia, anemia aplásica y anemia hemolítica. Cardiovasculares: Hipotensión ortostática, vasculitis. Hipersensibilidad: Púrpura, fotosensibilidad, erupción cutánea, urticaria, fiebre y reacciones anafilácticas. Renales y urinarias: Disfunción renal y nefritis intersticial. Otros: Hiperglucemia, glucosuria, hiperuricemia, espasmo muscular, debilidad, inquietud, visión borrosa transitoria, calambres. **9. Interacciones medicamentosas y de otro género:** cuando se administran en forma conjunta otros fármacos puede ocurrir interacción con diuréticos tiazídicos como ROFUCAL®. **Alcohol, barbitúricos o narcóticos:** Puede haber aumento de la presión ortostática. **Aminas presoras:** Puede disminuir la respuesta a las aminas presoras, pero no lo suficiente como para no utilizarlas. **Anfotericina B, corticoesteroides o corticotropina:** Pueden intensificar el desequilibrio hidroelectrolítico, hipocalemia especialmente. **Anticoagulantes orales:** Pueden disminuir los efectos anticoagulantes. **Agentes antiinflamatorios no esteroideos:** Éstos pueden disminuir el efecto diurético. **Colestiramina y colestipol:** Retardan la absorción de ROFUCAL®. **Glucósidos digitálicos:** La hipopotasemia o la hipomagnesemia inducida por tiazidas favorece la aparición de arritmias cardiacas inducidas por digital. **Hipoglucemiantes orales e insulina:** Puede requerirse ajuste de la dosis de antidiabéticos. **Litio:** Los diuréticos disminuyen la depuración renal de litio y aumentan el riesgo de toxicidad. **Medicamentos para la gota:** La hidroclorotiazida puede aumentar el nivel de ácido úrico sérico. **Otros antihipertensivos:** Efecto aditivo o potencializante de sus efectos. **Sales de calcio:** Los diuréticos tiazídicos pueden incrementar los niveles séricos de calcio debido a la reducción de la excreción. **Probenecid o sulfinpirazona:** Se recomienda aumentar su dosis ya que la hidroclorotiazida puede tener efectos hiperuricémicos. **Relajantes no despolarizantes del músculo esquelético (ej. tubocurarina):** la hidroclorotiazida puede potenciar el efecto. **Ciclofosfamida, metotrexato:** Las tiazidas pueden reducir la excreción renal de los fármacos citotóxicos y potenciar su efecto mielosupresor. **10. Precauciones en relación con efectos de carcinogénesis, mutagénesis, teratogénesis y sobre la fertilidad:** estudios conducidos en animales no reportaron efectos carcinogénicos, mutagénicos así como tampoco alteraciones sobre la fertilidad a dosis terapéuticas. **11. Dosis y vía de administración:** ROFUCAL® se administra por vía oral. La dosis aplicada debe ser individual y acorde a la respuesta del paciente. ESQUEMA POSOLÓGICO DE ROFUCAL®. **Pacientes adultos con hipertensión arterial:** Inicio: 25 mg/día dosis única o repartida en varias tomas.*Ajustar la dosis según las cifras de tensión arterial. Máx: 50 mg diarios. **Pacientes adultos con edema:** 25 a 100 mg/día en una o dos tomas. Máx: 100 mg diarios.**

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*Algunos pacientes responden con una dosis inicial de 12.5 mg/día sola o combinada con otros antihipertensivos.

**Algunos pacientes responden al tratamiento intermitente (en días alternos o de tres a cinco días/semana).

Pacientes pediátricos con hipertensión arterial: Dosis pediátrica usual: 2.5 mg/kg/día en dos tomas. Lactantes <6 meses: hasta 3.5 mg/kg/día en dos tomas. Niños hasta 2 años: 12.5-37.5 mg/día en dos tomas. Niños 2-12 años: 37.5-100 mg/día en dos tomas. Muy pocos pacientes requieren de dosis altas sostenidas. **12. Manifestaciones y manejo de la sobredosificación o ingesta accidental:** además de la diuresis esperada, la sobredosis de ROFUCAL® puede producir grados variables de letargia, la cual puede progresar al coma en pocas horas con mínima depresión de las funciones respiratorias y cardiovasculares y sin evidencia de cambios en los electrolitos séricos o deshidratación. Además del lavado gástrico y del tratamiento de apoyo para el estupor o coma, puede ser necesario tratamiento de los efectos gastrointestinales. No se ha establecido claramente el grado en que la hidroclorotiazida es eliminada por hemodiálisis. Se debe mantener la hidratación y el equilibrio hidroelectrolítico, la respiración, las funciones cardiovascular y renal. **13. Presentaciones:** Caja de cartón con 15, 30 o 60 tabletas de 12.5 mg en envase de burbuja. Caja de cartón con 20 o 30 tabletas de 25 mg en envase de burbuja. **14. Leyendas de protección:** su venta requiere receta médica. No se deje al alcance de los niños. No se use durante el embarazo ni en mujeres en periodo de lactancia. Literatura exclusiva para médicos. Reporte las sospechas de reacción adversas al correo: farmacovigilancia@cofepris.gob.mx Para mayor información del producto o para reportar eventos adversos comuníquese al teléfono en la ciudad de México 4040-7671 0 LADA nacional sin costo al 01800-200-0170 o correo electrónico: farmacovigilancia@probiomed.com.mx **15. Nombre y domicilio del laboratorio:** PROBIOMED S.A. DE C.V. Yácatas No 307, Colonia Narvarte, Delegación Benito Juárez 03020 México, D.F. **16. Número de registro del medicamento ante la secretaría:** Reg. No. 74276 SSA IV.

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Edema: 25 a 100 mg/día en una o dos tomas. **Dosis máxima:** 100 mg diarios.

***HTA:** Hipertensión Arterial.

Referencias: 1. Bell K, *et al.* Hypertension: the silent killer: Updated JNC-8 Guideline Recommendations (2015). Alabama Pharmacy Association; 1:1-8. **2.** Información para prescribir amplia. Rofucal®. **3.** Uchiwa, H., Kai, H., Iwamoto, Y., Anegawa, T., Kajimoto, H., ... Fukuda, K. (2017). Losartan/hydrochlorothiazide combination is safe and effective for morning hypertension in Very-Elderly patients. Clinical and Experimental Hypertension, 40(3), 267–273.

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