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Continuation of the Revista Mexicana de Cardiología

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- Optimal cut-off in blood pressure measurement
- Overcoming a problematic stent
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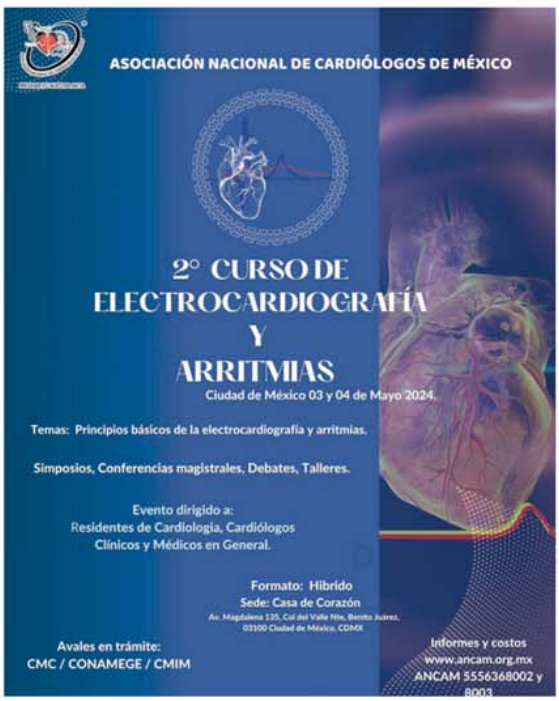

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Cardiovascular and Metabolic Science www.ancam.org.mx

Editorial

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What is the optimal cut-off threshold in blood pressure measurement? Who invented 140/90 mmHg?

¿Cuál es el umbral de corte óptimo en la medición de la presión arterial? ¿Quién inventó el 140/90 mmHg?

Martín Rosas-Peralta*

Nobody nowadays dares to doubt that high blood pressure is a cardiovascular risk factor and inexorably progressive and fatal. However, let's cite two experts on cardiovascular medicine in the 30th:

1. «The greatest danger to a man with high blood pressure lies in its discovery because then some fool is certain to try and reduce it» – JH Hay, 1931.[1]
2. «Hypertension may be an important compensatory mechanism which should not be tampered with, even where it is certain that we could control it» –Paul Dudley White, 1937.[2]

Thus, we have undoubtedly made remarkable progress in the last 85 years. After the death of USA President Franklin Delano Roosevelt, the evidence documented on his medical record that blood pressure progressively increased in the previous five years of life brought great concern. According to the thinking of that time, Ross McIntire, his family physician and a specialist in otorhinolaryngology, did not prescribe antihypertensive treatment. By 1944, pressures of more than 180/105 mmHg were documented, and he presented clear signs of heart failure. His doctor was treating him for bronchitis and sinusitis.[3]

Although 120/80 mmHg is often considered the standard upper threshold blood pressure for adults, its precise measure is an issue. Actual devices developed for blood pressure measurement come from the old mercury sphygmomanometers that allowed «standardized» measurement. Despite the high inter-observer variability, this vital sign has been accepted over decades as an extraordinary health marker of great importance. Thus, health staff and predominantly physicians were the only ones authorized to measure blood pressure for a long time. In 1905, Nikolai Korotkoff, a Russian military surgeon, wrote in a very brief report to the Imperial Military Medical Academy his auscultatory technique for obtaining systolic and diastolic blood pressure. This technique only requires a sphygmomanometer (blood pressure cuff) and stethoscope for listening to Korotkoff's sound.[4] The first sharp tapping sound defines the systolic pressure, and its disappearance defines the diastolic pressure.

Hypertension is a major risk factor for ischemic and hemorrhagic stroke, myocardial infarction, heart failure, chronic kidney disease, peripheral vascular disease (PVD), cognitive impairment, and premature death. So, what is the appropriate cut-off point for diagnosing a hypertension patient? Remember that blood pressure measurements give us systolic and diastolic values, respectively. The first reflects the blood impulse propagated in the arteries by the left ventricular contraction and the resistance of these arteries. On the other hand,

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diastole reflects the rebound distensibility of the arteries on the blood flow that attempts to return and is stopped by the closure of the aortic valve. However, many observational studies have found that both systolic and diastolic blood pressure exhibit a graded and independent relationship with mortality and morbidity (ESH-ESC 2013). Untreated hypertension can be associated with a gradual increase in blood pressure, potentially culminating in a state of resistance to treatment caused by associated vascular and renal damage.

The classic observational epidemiological research, elegantly analyzed by Macmahon and Peto, triggered a vital reflection. As diastolic and systolic pressures increase above 75 mm and 115 mmHg, respectively, the risk of a severe cardiovascular event (ischemic heart disease or cerebral vascular event) also increases significantly over the next 5 to 10 years.

Mathematical weightings and fittings had to be made with multiple rectilinear models to associate blood pressure levels with cardiovascular risk directly. So, one thing is clear: it is not a rectilinear phenomenon; no matter how many adjustments are made, biological phenomena always show some degree of internal variation. Generally, it is curvilinear, i.e., there is a first stage where the risk is 1.0 to 1.5 times greater with pressures of 115 to 135 mmHg in the systolic and 75 to 85 mmHg in the diastolic. Subsequently, generally, as of pressures of 140/90 mmHg for each 20 mmHg increase in systolic pressure and for each ten mmHg in diastolic pressure, the risk doubles. In the 70's- and 80's-decade, mathematical models of linear regression were introduced as predictors of events. However, it must be emphasized that many environmental, patient, and physician factors influence blood pressure measurement. For example, cuff size is crucial, and pressure values vary from 5 to 10 mmHg to the real one.

The recommended cuff sizes are: For an arm circumference of 22 to 26 cm, the cuff should be «small adult» size: 12 × 22 cm. For an arm circumference of 27 to 34 cm, the cuff should be «adult» size: 16 × 30 cm. For an arm circumference of 35 to 44 cm, the cuff should be «large adult» size: 16 × 36 cm. For an arm circumference of 45 to 52 cm, the cuff should be 16 × 42 cm. Now, being honest, how many physicians or health care staff who measure blood pressure have these standard cuffs?

HYPERTENSION IS NOT JUST A MATTER OF MMHG

However, reducing to «numbers» (mmHg) the cardiovascular risk in the patient living with arterial hypertension is to be unclear about the problem in a comprehensive manner. Blood pressure is a significant marker, but of course, a 40-year-old patient with 145/93 mmHg with no other cardiovascular risk factors will not be the same as another one with the same blood pressure level, of the same age and gender but with diabetes, obesity, and dyslipidemia. The latter will have a very high risk. Thus, we must understand the gradual elevation of blood pressure as a dynamic and progressive pathobiological and pathophysiological phenomenon. Intra- and intercellular signaling cascades are activated. This vasoreactivity also activates anti-inflammatory and vasorelaxant compensatory mechanisms. However, if the insult is perpetuated, the equilibrium towards biochemical and cellular mechanisms originates mechanisms of structural changes secondary to cellular proliferation, giving rise to arterial stiffness, atherosclerosis, and arteriolosclerosis.

WHO INTRODUCED 140/90 MMHG, AND HOW CAN WE ACHIEVE PREDICTIVE INDEPENDENCE OF A VARIABLE?

Multivariate linear regression models were introduced in the 70s and 80s as a robust strategy to elaborate mathematical predictive and association models where randomness would participate as little as possible. How do we compare several variables with each other? To rescue those that maintain their «independence» to be significantly associated with the target variable under study was the guideline that gave way to what was called «multivariate analysis».[5] The high risk of this method is the possibility of spurious variables leaking out and ruining the final interpretation. Removing confounding variables, such as collinearity, interference,

synergy, or antagonism, required statistical skills and full scientific knowledge of the area.

Thus, blood pressure levels went from observational studies to formal cohort research with robust mathematical analysis and modeling. The «sovereignty of blood pressure» was maintained as an «independent» continuous risk variable predictive of major cardiovascular events. However, later on, to make this knowledge practical (in its clinical use), it was necessary to search for cut-off points to turn continuous into categorical. Thus, the so-called ROC curves were used, where the «model» for defining cut-off points was found to have the best sensitivity and specificity *(Figure 1)*.

But stop and think about it: will there be a difference between 138/88, 140/90, or 143/93 mmHg on the risk continuum? If your answer is no, the objective of this editorial will have been achieved. Exactly! We can't get to reductionism in medical thinking. The number of violations and assumptions that are made when trying to make the inaccuracy of a biological phenomenon, which per se, is variable, oscillatory, and dependent on several biological, biochemical, and environmental circumstances, is to want to «tear away» from the physician the most valuable thing he has, his clinical judgment. There is no mathematical model that outperforms it, even artificial intelligence.

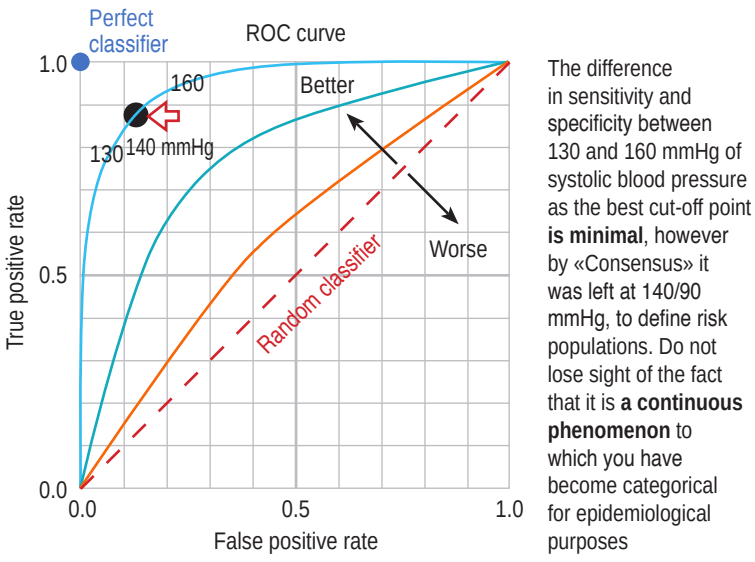

Figure 1: Receiver operating characteristic curves are the graphic representation that allows visualization of the best value as a classificatory cut-off point for a continuous phenomenon that one wishes to make categorical. What is sought is the point with the best sensitivity and predictive specificity.
ROC = Receiver Operating Characteristic.

GOOD CLINICAL JUDGMENT

What happened once we accepted that 140/90 mmHg is a mathematical construct to define risk population classification? Once the value was agreed upon, many studies on arterial hypertension were conducted, both clinical and basic. It was possible to integrate follow-up cohorts to evaluate the impact of pharmacological and non-pharmacological strategies in short-, medium- and long-term follow-up.

The impact was such that 140/90 mmHg was popularized worldwide and emerged as a goal or treatment objective in all the guidelines and directives in the world. The efficacy and safety of all antihypertensive drugs are based on their ability to reduce blood pressure to < 140/90 mmHg. The dispute to find the best drug is «confined» to differences as small as 3-5 mmHg.

And that's not all. Since many drugs achieved the goal of reducing to < 140/90 mmHg, competition arose in other areas such as half-life, adverse effects, pleiotropic effects, costs, and adherence. Thus, the physician returns to the essence of his raison d'être and stops seeing the patient as a number to realize that there are multiple factors involved in cardiovascular risk in the real world. Syndrome X, or metabolic syndrome, appeared in the 80s to try to connect different risk factors that are frequently associated. Today, attempts are being made to popularize the cardio-reno-metabolic syndrome, which is not a syndrome at all but a new construct to draw attention to a pathophysiological situation shared by obesity, diabetes, hypertension, and dyslipidemia.

For this reason, in the practice of medicine, clinical judgment is insuperable. The same patient with 145/95 mmHg can be «low» risk or very high risk, depending on the context.

So, it means that we should ignore 140/90 mmHg. Nothing is false other than that; the importance is to take it for what it is, «a frame

of reference», and the context of the patient should draw your attention. Thus, step 1, the figure per se, should draw my attention because it is already a point to consider in the pathological blood pressure elevation continuum. Step 2: make sure that the measurement is accurate and that it was made under optimal conditions. Step 3: make sure it is not a white coat phenomenon.

For this reason, taking and recording blood pressure outside the doctor's office is essential. A good log of home measurements or an ABPM will be of considerable diagnostic help. Step 4: define your patient's context to the possibility of other related risk factors. Step 5: Stratify your patient's risk by determining whether they are low, intermediate, high, or very high risk depending on the number of associated factors, presence or absence of target organ damage, structural damage, or history of a significant cardiovascular event, as well as blood pressure level. It will even help you decide which type of combination drug therapy is best for your patient.

WHAT IS THE GOAL < 140/90 MMHG OR LESS THAN 130/80 MMHG?

Last but not least, a plan of therapeutic goals must be drawn up. Again, do not get bogged down in an exact amount. The accumulated evidence indicates that it should be maintained at < 140/90 mmHg to reduce cardiovascular risk. However, ideally, it is to achieve < 130/80 mmHg without reaching values below 110/70 mmHg. Attaining this range of reduction has been associated with greater protection from cardiovascular risk. However, to achieve these blood pressure ranges without taking into account the goals of the other associated risk factors is to consign the patient to continue to be at cardiovascular risk. Therefore, spare no effort to achieve comprehensive control of your patient.

Another grave mistake is not focusing on long-term strategies. It will be in vain for the patient to maintain optimal pressures for six months if they then abandon the treatment. It is common for the patient to change or modify it for «not feeling anything», whether they take it or not. The primary failures to change the natural history of arterial hypertension in Mexico and the world are due to underdiagnosis, inappropriate treatment, non-adherence, medical inertia, and lack of physician-patient communication. A work plan should be established in which the patient is an active and co-responsible co-participant.

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CLINICAL CASE

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Overcoming an under-expanded and undilatable stent

Cómo superar un stent poco expandido y no dilatable

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Arsis Ahmedieh,* Melisa Uçar,‡ Mehdi Zoghi¶

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under-expanded, balloon uncrossable, chronic total occlusion.

Palabras clave:
subexpandido, globo incruzable, oclusión total crónica.

ABSTRACT

Underexpansion is an important issue for interventional cardiologists in terms of long term results. Herein we report a successful rotablation of an under-expended stent struts. The patient was a 75 years old female with a history of Percutaneous Coronary Intervention (PCI) on Left Anterior Descending Artery (LAD) with 2 overlapping drug eluting stents a week ago in another center. Unfortunately, the stents were deployed without proper lesion preparation in heavily calcified lesions and hence the stents couldn't be dilated properly after deployment. The stent struts were successfully rotablated with 1.5 and 1.75 burrs respectively followed by subsequent stenting. The patient was discharged uneventfully. Under-expansion of a stent generally arises from inadequate lesion preparation. Impaired healing secondary to under-expanded stent struts is the main cause of re-stenosis in the short term. Hence adequate pre-dilatation especially in heavily calcified lesions is of quite importance. More sophisticated techniques such as Non-Compliant balloon (OPN), rotablation, shock wave balloon and laser should be used for adequate pre-dilatation when conventional balloon pre-dilatation methods fail. These methods can also be used for dilatation of an under-expanded stent. Consequently, under-expansion of a stent is one of the leading causes of stent restenosis. Rota-ablation can be used to debulk the under-expanded stent struts and hence prevent possible short term restenosis.

RESUMEN

La subexpansión es una cuestión importante para los cardiólogos intervencionistas en términos de resultados a largo plazo. En este documento informamos una rotación exitosa de puntales de stent subutilizados. Mujer de 75 años con antecedentes de Intervención Coronaria Percutánea (ICP) sobre Arteria Descendente Anterior (ADA) izquierda con dos stents farmacoactivos superpuestos hace una semana en otro centro. Desafortunadamente los stents se desplegaron sin una preparación adecuada de la lesión en lesiones muy calcificadas y por lo tanto, no se pudieron dilatar adecuadamente después del despliegue. Los struts de la endoprótesis se rotaablizaron con éxito con fresas de 1.5 y 1.75 respectivamente y a continuación se implantó la endoprótesis. El paciente fue dado de alta sin incidentes. La expansión insuficiente de un stent generalmente se debe a una preparación inadecuada de la lesión. El deterioro de la cicatrización secundario a puntales del stent poco expandidos es la principal causa de reestenosis a corto plazo. Por lo tanto, es de gran importancia una predilatación adecuada, especialmente en lesiones muy calcificadas. Se deben utilizar técnicas más sofisticadas como balón Non-Compliant Balloon (OPN), rotablación, balón de ondas de choque y láser para una predilatación adecuada cuando los métodos convencionales de predilatación con balón fallan. Estos métodos también se pueden utilizar para la dilatación de un stent poco expandido. En consecuencia, la expansión insuficiente de un stent es una de las principales causas de reestenosis del stent. La rotaablación se puede utilizar para reducir el tamaño de los puntales del stent poco expandidos y por lo tanto, prevenir una posible reestenosis a corto plazo.

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INTRODUCTION

An under expended stent is a nightmare for an interventional cardiologist. A malapposed stent is the main cause of short time re-stenosis. Hence implanting the stent after adequate pre-dilatation is of great importance. Especially in heavily calcified lesions, more sophisticated techniques such as OPN balloon, rotablation, shock wave balloon and laser should be used for adequate pre-dilatation when conventional balloon

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pre-dilatation methods fail. Herein we report a case of successful rotablation of an under-expended stent struts.

CASE PRESENTATION

The patient was a 75 years old female with a history of Percutaneous Coronary Intervention (PCI) on Left Anterior Descendent (LAD) coronary artery with two overlapping drug eluting stents a week ago in another center. Unfortunately, the stents were deployed without proper lesion preparation in heavily calcified lesions and hence the stents couldn't be dilated properly after deployment. The first operator implanted a 2.75 stent via insufficient pre-dilatation in LAD which was severely under expanded and post dilation with a 3.0 × 12 mm Non-Compliant (NC) balloon up to 35 atm had failed. The stents were malapposed and under-expanded so the patient was referred to our clinic for bailout management.

In our center, first NC balloon with 40 atm and then OPN balloon with 42 atm were performed but both failed. Since shock wave and laser system were unavailable rotablation of the under-expanded stent struts was our next approach. At first the wire was exchanged with a soft rota wire and then the rotablation was performed with 1.5 burr. After multiple rota runs and aggressive NC balloon post dilatation, the rota burr was upgraded to 1.75 *(Figure 1)*. The rotawire was exchanged with an extrasupport rotawire over the microcatheter to gain more support for different rota burr and change the contact points of the burr.

After multiple rota and balloon post dilatation IVUS was performed to evaluate the lesion and fracture in the previous stent, ablated previous stent struts and relative debulcking in calcium burden were detected *(Figure 2)*. Hence stenting over ablated and fractured previous stent was decided. A 3.5 × 38 mm drug eluting stent was deployed at 20 atm *(Figure 3)*.

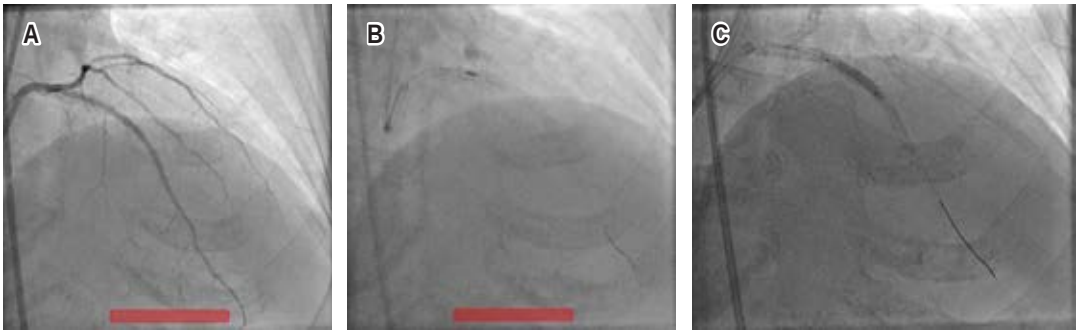

Figure 1: A) Angiographic appearance of underexpanded stent struts. **B)** Rotablation of underexpanded stent struts. **C)** Non-compliant balloon dilatation after rota runs.

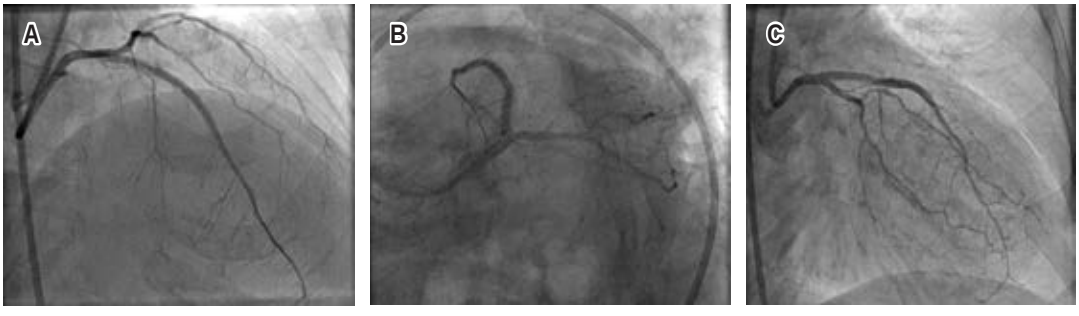

Figure 2: A) Angiographic appearance after multiple rota runs and balloon dilatations. **B)** A 3.5 × 38 mm drug eluting stent was deployed inside the first under-expanded stent at 20 atm. **C)** Final angiographic appearance.

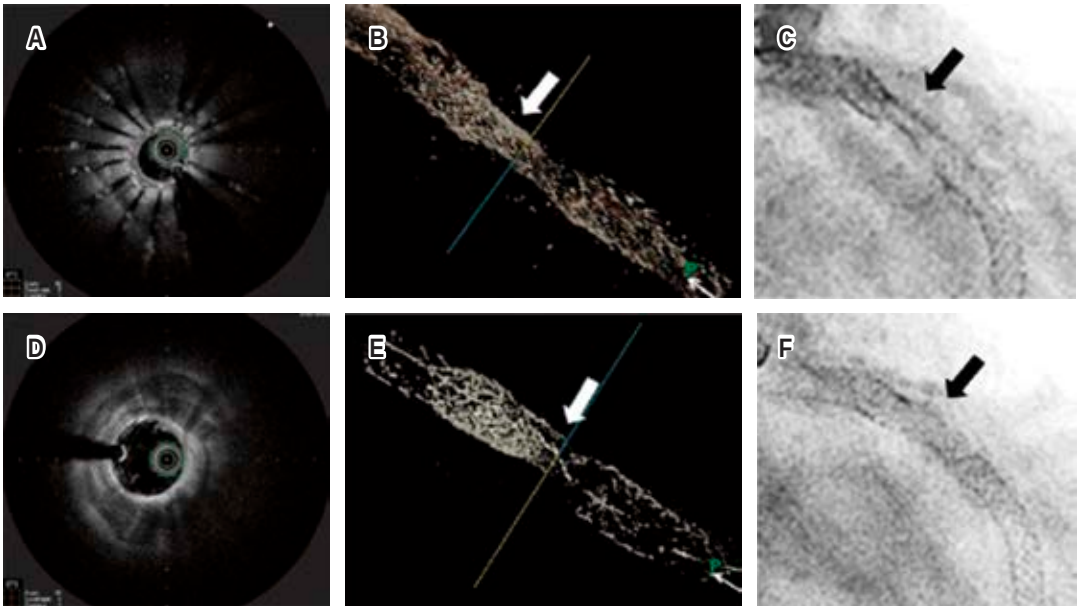

Figure 3: A) Intravascular ultrasound showing under-expanded stent. **B)** Optic coherence tomography optical coherence tomography appearance before rotablation of under-expanded stent struts. **C)** Clear stent appearance showing the under-expanded part of the stent. **D)** Intravascular ultrasound shows destruction of the under-expanded stent struts after rotablation. **E)** Absence of under-expanded stent struts in optical coherence tomography. **F)** Appearance in clear stent function after rotablation.

DISCUSSION

This paper reveals that rotablation of under-expanded stent struts can be performed as a bail-out option when the first choice maneuvers such as high pressure Non-Compliant (NC) and OPN balloon inflations fail.

Under-expansion of a stent due to inadequate lesion preparation poses a great challenge for the interventional cardiologist and generally there are a few strategies to fix this problem. The possible maneuvers are leaving the under-expanded stent as it is, prolonged high pressure NC balloon inflation, OPN balloon, rota-ablation of the under-expended stent, shock wave balloon and laser or surgery as a last resource.[1-4]

In this case, due to absence of laser and shock wave, our choice was rotablation of the under-expended stent struts. The greatest concern with longitudinal stent ablation is to slip through the under expanded stent without ablating the metal and leaving the burr immovable. Hence in this case the burr advanced more gradually and more carefully than our usual approach. During the procedure, multiple runs and NC balloon dilatations were performed. Changing distal wire position and exchange between soft and extra support rota wire facilitated the contact between the burr and the stent. The other concern is slow flow and no reflow due to metallic debris and stent thrombosis due to heat generation so short runs were preferred in our case. Thankfully, none of these complications happened in our case probably due to our particular attention about keeping the rota runs as short as possible. In line with our current case, recent Optical Coherence Tomography (OCT), Intravascular Ultrasound (IVUS) and also electron microscopy studies have also shown that stent ablation by rotablation can remove under-expanded stent struts.[5-7]

CONCLUSIONS

Consequently, under-expansion of a stent is one of the leading causes of stent restenosis.

Under-expansion of a stent has a challenging consequences for the interventional cardiologists. It could cause of stent restenosis. There are some options to maintain stent restenosis and rotablation is one of them. Rotablation can be used to debulk the under-expanded stent struts and hence prevent possible short term restenosis.

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Double cardiac stress in the postpartum period. Case report of sepsis-induced cardiomyopathy complicated by acute pulmonary embolism

Doble estrés cardiaco en el periodo postparto. Reporte de un caso de cardiomiopatía inducida por sepsis complicada con embolismo pulmonar agudo

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Keywords: cardiomyopathy, myocardial dysfunction, septic cardiomyopathy, sepsis-induced cardiomyopathy, puerperium, echocardiography.

Palabras clave: *cardiomiopatía, disfunción miocárdica, cardiomiopatía séptica, cardiomiopatía inducida por sepsis, puerperio, ecocardiografía.*

ABSTRACT

Sepsis-induced cardiomyopathy is a clinical entity rarely reported in the literature. It lacked an objective and agreed-upon definition, and although there are clinical criteria, there are no diagnostic guidelines or specific treatment; its identification, approach, and management imply a challenge for the clinician. Its presence increases mortality by up to 70%. It is considered an acute onset complication that manifests with alterations in systolic and diastolic function, finally showing reversibility in a period of seven to ten days. When this entity is suspected, the gold standard for diagnosis is the echocardiogram. Infection control, life support, and hemodynamic measures associated with the use of vasopressors and inotropes are the main therapeutic tools that have shown a decrease in mortality. However, this entity usually requires advanced organic support, even requiring ventricular assistance devices such as an intra-aortic balloon pump (IABP) or extra corporeal membrane oxygenation (ECMO), which have shown promising results in the treatment of this pathology. Despite this, mortality is high, and the prognosis continues to be unfavorable without early identification, hence the importance of unifying criteria, establishing risk factors, validated diagnostic tools as well as differentiating it from other clinical entities, thereby improving its outcome and prognosis.

RESUMEN

La cardiomiopatía inducida por sepsis es una entidad clínica escasamente reportada en la literatura, carece de una definición objetiva y consensuada y aunque existen criterios clínicos, no existen guías diagnósticas ni tratamiento específico, su identificación, abordaje y manejo implican un reto para el clínico. Su presencia incrementa la mortalidad hasta 70%. Es considerada una complicación de inicio agudo que se manifiesta con alteraciones en la función sistólica y diastólica, finalmente muestra reversibilidad en un periodo de 7 a 10 días. Ante la sospecha de dicha entidad, el estándar de oro para el diagnóstico es el ecocardiograma. El control de la infección, medidas de soporte vital y hemodinámico asociados al uso de vasopresores e inotrópicos son las principales herramientas terapéuticas que han mostrado disminución en la mortalidad. Sin embargo, esta entidad suele requerir de soporte orgánico avanzado, siendo necesarios incluso dispositivos de asistencia ventricular como balón de contrapulsación intraaórtico o membrana de oxigenación extracorpórea que han mostrado resultados prometedores en el tratamiento de esta patología. A pesar de esto la mortalidad es elevada y el pronóstico continúa siendo desfavorable sin una identificación temprana, he ahí la importancia de unificar criterios, establecer factores de riesgo, herramientas diagnósticas validadas, así como diferenciarla de otras entidades clínicas y con ello mejorar su desenlace y pronóstico. Presentamos el caso de una mujer en puerperio inmediato quien desarrolló sepsis secundaria a retención de restos placentarios, enseguida desarrolló choque séptico complicado con miocardiopatía inducida por sepsis y hacia el final de su hospitalización manifestó embolismo pulmonar agudo. Finalmente describimos su evolución desde el inicio hasta la reversibilidad del cuadro mediante ecocar-

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diografía, también dimos seguimiento posterior, a siete meses y un año mostrando su evolución a lo largo del tiempo sin el desarrollo de complicaciones o eventos adversos. Destacamos que el abordaje temprano y el seguimiento ecocardiográfico fueron clave para la buena evolución.

INTRODUCTION

Since the first case of septic cardiomyopathy was reported in 2010, multiple reviews highlighted the importance of ultrasound evaluation of patients with sepsis. The data remain ambiguous; there is no objective definition of septic cardiomyopathy, and it remains a challenge to establish well-defined criteria. For its correct approach, a new standardized definition is necessary, as well as guidelines for the diagnostic approach.[1] Derived from the findings of different hemodynamic profiles in septic shock, it is necessary to standardize the measurement and use of ultrasound variables to monitor myocardial function in these patients. Its importance lies in the fact that standardization, dissemination, and knowledge of the entity favor its identification, reducing mortality due to complications of sepsis.[2]

CASE PRESENTATION

A 25-year-old woman, originally from Campeche, Mexico, with no relevant clinical antecedent and a history of two pregnancies, at the time was carrying a full-term pregnancy, which before the onset of symptoms was resolved by delivery without complications. Twenty-four hours after her discharge, the patient had a fever for four days. On the fifth day, she experienced severe acute chest pain, dyspnea, diaphoresis, and palpitations. The patient received medical attention at a local hospital unit and was subsequently referred to the next level of care. The patient was treated in the emergency department with signs of acute respiratory failure; she was admitted to the intensive care unit, where non-invasive mechanical ventilation was started. The condition was associated with arterial hypotension, tissue hypoperfusion, and fever. Biochemical blood studies at the time showed leukocyte count of 16.570 × 10^3/µL, neutrophils 88.00 × 10^3/µL, lymphocytes 8.0 × 10^3/µL, hemoglobin of 12.44 g/dL. Hematocrit 38.95%, mean globular volume 83.96 fL, mean Hemoglobin concentration of 26.68 pg, mean concentration of corpuscular hemoglobin 31.94 g/dL, distribution index of erythrocytes (RDW) 14.37%, platelets 167,200 × 10^3/µL, mean platelet volume 11.11 fL. Serum urea level of 40.88 mg/dL, blood urea nitrogen (BUN) 19.00 mg/dL, serum creatinine 0.66 mg/dL, uric acid 3.20 mg/dL. Serum sodium 151.34 mEq /L, potassium 3.40 mEq /L, chlorine 119.49 mEq /L, magnesium 1.85 mg/dL, phosphorus 4.45 mg/dL, calcium 7.58 mg/dL. Total bilirubin 0.92 mg/dL, conjugated bilirubin 0.67 mg/dL, unconjugated bilirubin 0.25 mg/dL, aspartate amino transferase (AST) 51.31 U/L, alanine amino transferase (ALT) 28.96 U/L, gammaglutamyl transpeptidase (GGT) 131.58 U/L, alkaline phosphatase (FA) 120.63 U/L, total proteins 4.70 g/dL, serum albumin 4.90 g/dL, globulin 3.50 g/dL, activated partial thromboplastin time (aPTT) 24.80 sec. Prothrombin time (PT) 16.10 sec. International Normalized Index (INR) 1.31 and procalcitonin 1.89 ng/mL. The electrocardiograms performed initially only showed sinus tachycardia of up to 130 beats per minute. Later, the patient presented atrial fibrillation-type arrhythmias that reverted to the therapeutic approach.

With the clinical suspicion of septic shock, broad-spectrum antimicrobial and vasopressors were started, and invasive mechanical ventilation, sedation, and analgesia were needed. Initial laboratory studies highlighted leukocytosis and anemia, a hyperdynamic hemodynamic pattern in gas analysis, and the transthoracic echocardiogram showed a decrease in the left ventricular ejection fraction (LVEF) at 36%, left ventricular dilation, and compromised global motility with moderately

depressed systolic function and suspected peripartum cardiomyopathy.

As part of the study protocol, cultures of blood, urine, and bronchial secretions were obtained, all without the development of microorganisms, also serological tests for COVID-19, influenza, and human immunodeficiency virus (HIV) with negative results, the initial procalcitonin was 2,580 ng/mL. An abdominal ultrasound revealed widespread free fluid and uterine alterations suggestive of endometritis. Due to the poor response to the initial fluid resuscitation and persistence of hemodynamic instability, it was decided to perform exploratory laparotomy, finding purulent fluid in the abdominal cavity and placental remains during uterine curettage.

After surgery, there was significant clinical improvement, a decrease in acute phase reactants, and remission of the hemodynamic pattern; withdrawal of hemodynamic support and invasive mechanical ventilation was achieved. At this point biochemical blood test performed showed a reduction in leukocyte count with 13.310 $\times$ 10^3/µL, neutrophils 79.00 $\times$ 10^3/µL, hemoglobin 9.59 g/dL, hematocrit 26.13%, medium globular volume 93.12 fL, concentration mean hemoglobin 30.56 pg, mean corpuscular hemoglobin concentration 32.81 g/dL, RDW 13.51%, platelets 382,500 $\times$ 10^3/µL, mean platelet volume 9.0 fL. Serum urea 17.12 mg/dL. BUN 8.0 mg/dL, serum creatinine 0.38 mg/dL. Uric acid 2.70 mg/dL, serum sodium 142.20 mEq/L, potassium 4.40 mEq/L, chlorine 108.75 mEq/L, magnesium 1.99 mg/dL, phosphorus 2.88 mg/dL, calcium 7.09 mg/dL. Total bilirubin 0.84 mg/dL, conjugated bilirubin 0.58 mg/dL. Unconjugated bilirubin 0.26 mg/dL, AST 26.96 U/L. ALT 20.07 U/L. Lactic deydrogenase (DHL) 288.09 U/L, aPTT 33.40 sec. PT 22.20 sec. INR 1.79, and procalcitonin 0.20 ng/mL. Erythrocyte sedimentation rate (ESR) 50.00 mm/h, D-dimer 9.34 µg/mL and creatine phosphokinase (CPK) 68.36 U/L. Troponin curve couldn't be obtained. After 48 hours, an echocardiographic control was performed, which reported improvement in the LVEF with 46%, left ventricular dilation, generalized hypokinesia, and decreased systolic function, changes suggestive of sepsis-induced cardiomyopathy.

The antimicrobial regimen was followed, and she was discharged to the general ward. During initial mobilization, the patient presented with a sudden intense onset of retrosternal chest pain, tachycardia, dyspnea, tachypnea, and hypotension associated with a decrease in oxygen saturation, with suspicion of acute pulmonary embolism. A new echocardiogram showed right ventricular pressure overload with a dicrotic notch on pulmonary valve Doppler. Pulmonary angiography (CTPA) reported a filling defect in branches of the right pulmonary artery and amputation of the circulation in the left pulmonary artery and some areas in the right circulation, bilateral atelectasis, and images that suggested probable thrombosis of the iliac veins, the study confirmed the diagnosis, classifying it as high risk. The electrocardiogram recorded elevation of the ST segment in precordial leads v1 to v4 and D-dimer 9,340 ng/mL. The therapy used was oxygen and unfractionated heparin, showing improvement in less than 24 hours.

An echocardiogram performed on the tenth day showed an increase in the contractile function of the left ventricle. LVEF of 63%, showing reversibility of the morphological alterations and contractility, concluding that it was septic cardiomyopathy and acute pulmonary embolism. In a control CTPA, reversibility of the previously described filling defects was observed. Also, serum procalcitonin in normal ranges, anticardiolipin, and anti-beta 2 glycoprotein antibodies were negative; also, the presence of lupus anticoagulant and protein S deficiency with overactivity of anti-thrombin III antibodies were found.

DISCUSSION

Sepsis is an organic dysfunction caused by a deregulated host response to an infection, and septic shock occurs when important circulatory, metabolic, and cellular abnormalities occur, necessitating the use of vasopressors. Sepsis is the most important cause of morbidity and mortality in patients admitted to intensive care units, with 48.9 million cases occurring worldwide each year.[3] The high mortality is due to its most common complications, septic shock, multiple organ dysfunction

syndrome, and sepsis-induced cardiomyopathy or septic cardiomyopathy (SCM), of which the prevalence varies widely from 10 to 70% in inpatients with sepsis, developing it implies a 1.4-fold increase in the risk of death during hospitalization compared to patients who do not develop it. Among the risk factors for presenting it are being a man, a young adult, having high lactate levels and high severity scores, as well as patients with pre-existing heart disease or diabetes.[4,5]

Although most infections that occur during pregnancy and the postpartum period are mild, the physiological and immunological adaptations present during pregnancy make women more susceptible to sepsis. The period of greatest vulnerability is postpartum; sepsis during this period causes up to 75,000 deaths a year.[6] Its presence in pregnant patients is rare; it is estimated that one case in every 8,338 births, and the association between SCM and postpartum sepsis is an even rarer presenting entity and implies high mortality.[7]

In 1975, myocardial dysfunction in sepsis was described for the first time by Heyndrickx and collaborators, who documented the phenomenon in experiments with animal models. By 1982, it was observed that this had a self-limiting nature, and in 1996, Clowes, through hemodynamic monitoring and invasive measurements in the pulmonary artery, confirmed the development of myocardial depression in patients with septic shock.[8] In 1984, Parker introduced the concept of sepsis-induced cardiomyopathy. In his study, patients with septic shock were subjected to ventriculography with simultaneous use of radionucleotide and subsequently to catheterization of the right ventricle, finding that in some of them, the ejection fraction of the right ventricle was less than 38% both in patients with high cardiac output and with normal or low cardiac output. Its importance was such that in 2005, Annan and collaborators proposed sepsis-induced cardiomyopathy as a diagnostic criterion for severe sepsis.[9]

Despite there being no formal definition, all authors agree that it shares characteristics such as having an acute onset, a poor response to initial resuscitation and catecholamines, being reversible in a period of seven to 10 days after the onset of the condition, and after resolving the septic state, also having ruled out coronary ischemia as a triggering cause.[10,11] All the clinical data on cardiac dysfunction is manifested, elevation of biomarkers of damage, decrease in the LVEF, structural alterations, and changes in the conduction system and hemodynamics.[12]

Septic cardiomyopathy is characterized by alterations in left and right ventricular function with the following proposed ultrasound criteria: decrease in LVEF of less than 45%, S' wave < 7.5 cm/s, global longitudinal strain (GLS) < -20%. Lateral E' wave values < 7 cm/sec and lateral E'/e ratio > 13 cm/sec. Right ventricular dysfunction characterized by right and left ventricular dilatation > 0.6, Tricuspid annular plane systolic excursion (TAPSE) < 16 mm, Tissue Doppler imaging (TDI) Str' wave < 10 cm/s and right ventricular fractional area change < 35%. Finally, there is a decrease in cardiac output as well as dilation of the left ventricle.[1,13,14]

Multiple secondary pathways to the host's already known deregulated immune response towards the infection have been proposed, which seek to explain how these are associated with changes in myocardial contractility and generate the changes found in septic cardiomyopathy to try to explain the pathophysiological mechanism. The trigger is sympathetic activation, which generates changes and alterations in myocardial performance and contractility. When tachycardia exists, diastolic filling time is reduced, the lusiotropic effect is lost, deficiencies in filling are generated, and myocardial contractility is worsened. The state of hyperinflammation present leads to immunoparesis, causing the deregulated response. To date, there is no complete understanding of how all the changes in the immune system and the release of inflammatory mediators are related to cardiomyopathy due to sepsis. What is known is that these mechanisms have consequences on the short- and long-term prognosis, increasing mortality and the risk of presenting future cardiovascular events.[15]

During the infection process, pathogens enter the bloodstream, stimulating the immune system through pathogen-associated molecular patterns (PAMPs), damage-associated molecular

patterns (DAMPs) and by activation of the complement system via toll-like receptors (TLRs), giving initiation to an excessive inflammatory response and cytokine storm, which compromises contractility, affects cardiac output, reduces coronary perfusion, generates local disturbances to microcirculation, triggering compensatory responses and shutdown of cellular metabolic pathways, causing regional tissue hypoperfusion and damage to the endothelium.

At the mitochondria in septic cardiomyocytes, the morphology is altered, which causes loss of the barrier function, and through metabolic and structural changes, DNA is damaged, compromising cellular function and increasing membrane permeability, which activates apoptosis signaling pathways dependent on caspases, mainly pyroptosis and other forms of cell death such as necroptosis, ferroptosis, and autophagy, triggered by different substances such as endotoxins, exotoxins, lipids, and RNA or DNA sequences, this through signaling pathways activated during injury to cardiomyocytes such as the MAPK, PI3K/AKT/mTOR and TLR/NF-kB pathways. MAPK is involved in a variety of cellular processes, including mitosis, apoptosis itself, differentiation, and cell proliferation.[15] Other signaling pathways confer future therapeutic importance, such as PI3K/protein kinase B AKT, which can suppress cardiomyocyte apoptosis and mitigate sepsis-induced myocardial damage by improving cardiomyocyte function. All of the aforementioned pathways activate pattern recognition receptors (PRRs), initiating a massive inflammatory response and establishing a phase of immunosuppression.[16,17]

Mitochondrial damage generated by oxidative stress reduces antioxidant capacity and thus generates an imbalance in metabolic processes, causing mitochondrial respiratory dysfunction. Inadequate adenosine triphosphate (ATP) production and imbalance results in direct damage and death of the cardiomyocyte. In some cases, the impairment of mitochondrial functions in damaged cells causes them to reach a state of apparent «mitochondrial hibernation», which favors energy saving in response to ischemia and promoting mitochondrial synthesis, helping to maintain the long-term viability of the mitochondria; this process could be involved in the reversibility of damage in septic cardiomyopathy.[16]

In 1985, myocardial depressant factors also intervened in the pathophysiology; studies in animal models reported that there was a reduction in the amplitude and speed of contraction of myocardial cells that were infiltrated with serum from animals with sepsis. It was then confirmed that there are different inhibitory factors directly related to cardiac contractility that are increased during sepsis and septic cardiomyopathy. These myocardial depressant factors act as direct inhibitors and intervene in two ways: in the downregulation of beta receptors and in reducing the adrenergic response through the action of inflammatory cytokines and nitric oxide (NO).[18]

Various substances involved in the inflammatory response have been considered myocardial depressants, including tumor necrosis factor alpha (TNF-α), interleukine-1 (IL-1), interleukine-6 (IL-6), complement-activated C3, C5a or membrane attack complex, anaphylatoxin and lipopolysaccharide (LPS), among other cytokines, LPS, high mobility group band-1 (HMGB-1), extracellular histones, and metalloproteinases of the extracellular matrix such as matrix metalloproteinase-9, all these increase their values and generate a depressant effect during the first phases of sepsis, normalizing their levels at 48 hours of the onset of the inflammatory response. In conclusion, the pathophysiological mechanism is complex, from the activation of the sympathetic nervous system that results in metabolic changes, an excessive inflammatory response, mitochondrial damage and oxidative stress, autophagy, and apoptosis mechanisms, and the imbalance in calcium homeostasis in cardiomyocytes, the downregulation of beta-adrenergic receptors, vasoplegia that compromises circulation are what finally produces myocardial depression with the clinical manifestations typical of the entity.[12,19]

The gold standard for diagnosis of SCM is the echocardiogram. In addition to the existing clinical characteristics, we used different echocardiographic variables for the analysis of the case. Echocardiograms were performed on day one of the onset of symptoms, at 48

hours, on day 10, and subsequently at seven months and one year. Initial echocardiograms show dilation of the left ventricle, accompanied by alterations in segmental motility. The left ventricle recovered its normal size without alterations in motility after 10 days.[20,21]

The initial LVEF was 36%, and 48 hours later, it was 47% *(Figure 1)*. The echocardiogram showed important dilation of the left ventricle *(Figure 2)*. The echocardiographic controls performed on the tenth day, at seven and 12 months, showed recovery and normal LVEF,

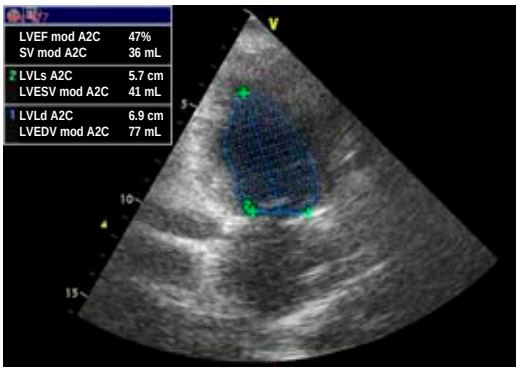

Figure 1: A two-chamber view showing the dilation of the left ventricle and the ejection fraction in the echocardiogram was performed 48 hours after the onset of the condition.
LVEF = left ventricular ejection fraction. A2C = apical two-chamber (view). SV = stroke volume. LVLs = left ventricular length at end-systole. LVESV = left ventricular end-systole volume. LVLd = left ventricular length at end-diastole. LVEDV = left ventricular end-diastole volume.

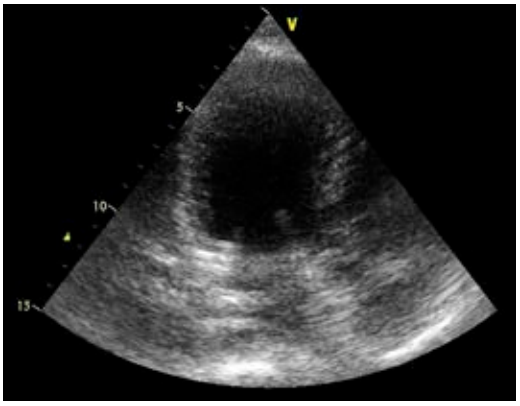

Figure 2: An apical 3-chamber view of the echocardiogram was performed after 48 hours, where spherical dilation of the left ventricle was observed.

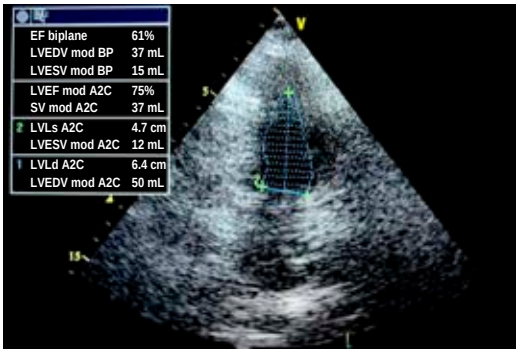

Figure 3: A two-chamber view showing the reversibility of the changes in the morphology of the left ventricle and the recovery of the ejection fraction in the echocardiogram performed one year later.
EF = ejection fraction (biplane). A2C = apical two-chamber (view). SV = stroke volume. LVEDV BP = left ventricular end-diastole volume (biplane). LVESV BP = left ventricular end-systole volume (biplane). LVEF = left ventricular ejection fraction. LVEDV = left ventricular end-diastole volume. LVESV = left ventricular end-systole volume. LVLs = left ventricular length at end-systole. LVLd = left ventricular length at end-diastole.

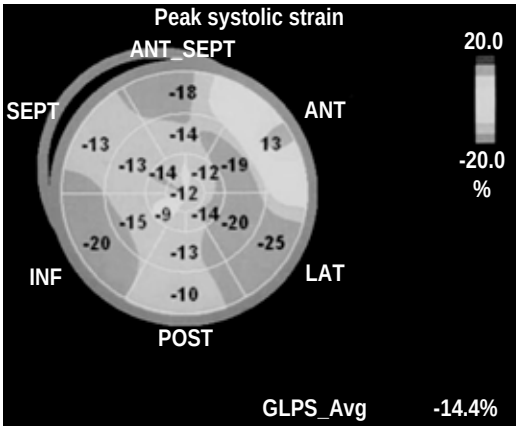

Figure 4: The global longitudinal strain was obtained, and an echocardiogram performed in the first 24 hours of the onset of the condition.
ANT_SEPT = anteroseptal (view). ANT = anterior (view). LAT = lateral (view). POST = posterior (view). INF = inferior (view). SEPT = septal (view). GLPS_Avg = global longitudinal peak strain average.

demonstrating complete reversibility at 10 days that continues up to one year *(Figure 3)*. There was no compromise in cardiac output according to measurements in the five echocardiograms performed. The cardiac

index was calculated using the Dubois cardiac index estimation formula; the cardiac index was not altered during the development of the pathology.[22] GLS is also used to assess left ventricular systolic function in patients with septic shock. It detects subtle changes in myocardial contractility and is more sensitive and accurate in evaluating systolic ventricular function compared to LVEF. We obtained a GLS of -14% initially *(Figure 4)*; in the 12th month of echocardiographic control, normalization of the values was found with a GLS of -20.6% *(Figure 5)*, therefore recovery of systolic function, which is considered normal at values of -18% to -20%. Measurement of variables through direct methods was not possible.

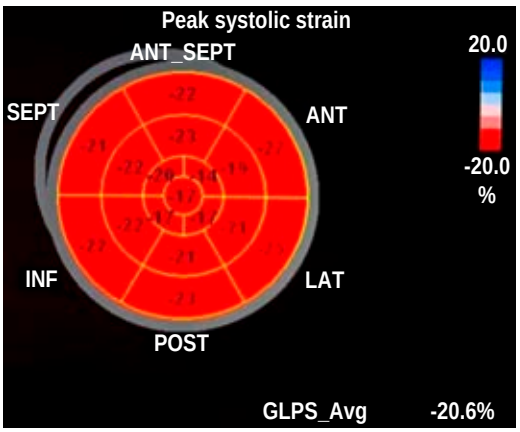

Figure 5: The global longitudinal strain was obtained in an echocardiogram performed after one year with normal values.
ANT_SEPT = anteroseptal (view). ANT = anterior (view). LAT = lateral (view). POST = posterior (view). INF = inferior (view). SEPT = septal (view). GLPS_Avg = global longitudinal peak strain average.

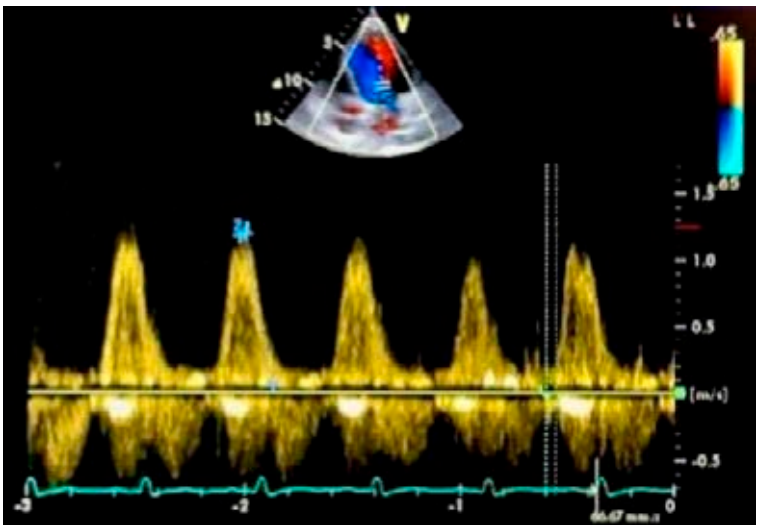

Figure 6: Diastolic dysfunction in echocardiogram performed after 48 hours.

In the echocardiographic assessment of the diastolic function of the left ventricle, dilation of the left atrium was found. In the echocardiogram performed at 10 days, at seven, and at 12 months, measurements that establish reversibility of the atrial dimensions were found. The filling pattern was normal during the evolution of the pathology, and the E/A ratio was reported to be 1.03, with the normal range of said value being 0.75 up to 1.5. The assessment of systolic function using tissue Doppler was abnormal, manifesting alterations in the contractility of the right ventricle. The right atrium showed dilation until reaching reversibility of its structure; the maximum velocity of the tricuspid valve maintained average values of 2.6 m/sec, in addition to the presence of a dicrotic notch when measuring pulmonary artery flow using Doppler. Concluding that the patient had systolic and diastolic dysfunction *(Figure 6)* with preserved cardiac output during the acute stage of the condition, subsequent changes suggestive of acute pulmonary embolism that would be corroborated by CTPA *(Table 1)*.

Women have a four to five times greater risk of presenting acute pulmonary embolism during pregnancy compared to women who are not pregnant. Its prevalence is one to 1.72 in every 1,000-3,000 births. The most severe form is acute pulmonary embolism of high risk, which causes hemodynamic instability due to extensive pulmonary arterial obstruction and requires the use of aggressive reperfusion therapies with systemic thrombolysis as the first line of treatment. The risk increases in the peripartum period and early postpartum, where there is a very high risk of bleeding. Cases of pulmonary embolism associated with pregnancy are responsible for 10 to 15% of maternal deaths in Europe and North America.[23,24] The high thrombotic risk is attributed to the physiological hypercoagulable state induced by pregnancy, as well as the decrease in

Table 1: Echocardiograms performed.

	Echocardiogram performed				
	On day one	After 48 hours from the initial symptoms	On day 10	After 7 months	After one year
Septum (mm)	11	14	8.0	8.0	9.0
Posterior wall (mm)	11	9.0	9.0	0.6	0.7
End-diastolic volume (mL)	111	118	144	135	106
End-systolic volume (mL)	54	56	144	45	37
Stroke volume (mL)	57	62	81	91	69
Fractional shortening (%)	27	27	30	37	36
Left ventricular ejection fraction (%)	36	47	63	64	61
End diastolic diameter (mm)	49	50	54	53	48
End systolic diameter (mm)	36	36	38	33	31
Cardiac output (mL)	5,586	6,944	6,075	6,370	3,136
Cardiac index (L/min/m^2)	3.6	4.48	3.92	4.11	3.13
Left atrium	48 × 42 mm, dilated, without thrombi	48 × 44 mm, dilated without thrombi	47 × 43 mm slightly dilated without thrombi	50 × 40 mm normal	58 × 32 mm normal
Right atrium	45 × 52 mm, dilated without thrombi	45 × 53 mm, dilated without thrombi	45 × 37 mm normal and without thrombi	44 × 33 mm normal	43 × 34 mm normal
Left ventricle	Dilated, adequate thickness of its walls	Dilated, adequate thickness of its walls	Normal size, adequate wall thickness	Normal size, adequate wall thickness	Normal size, adequate wall thickness
Eccentricity index	Not reported	1.58	1.9	Not reported	1.81
Mitral annular plane systolic excursion (cm/sec)	6.0	9.0	11	7.0	7.0
Tricuspid valve E/A wave ratio	–	1.03	–	–	1.3
Isovolumetric relaxation time (msec)	44	59	59	67	67
Global longitudinal peak strain (%)	-14.4	Not reported	Not reported	Not reported	-20.6
Tricuspid annular plane systolic excursion by tissue Doppler (cm/sec)	13	15	15	12	8.1
Systolic pulmonary artery pressure (mmHg)	38.8	32.5	28.7	21.7	21.8
Maximum speed of the tricuspid valve (m/sec)	2.8	3.4	2.4	2.1	2.2

venous return in the lower extremities due to mechanical obstruction by the uterus.

There are no specific biomarkers for SCM, but during early septic shock, N-terminal prohormone of brain natriuretic peptide (NT-proBNP) and troponin I are elevated. These are related to greater mortality due to septic shock. However, their presence is not related to the induced myocardial dysfunction due to sepsis. Some recently proposed potential biomarkers are eotaxin-1/CCL11, lipocalin 10 (Lcn10), and sestrin. Eotaxin-1/CCL11 was identified as a potential biomarker to predict 30-day mortality in patients with SCM, and the

rest are being investigated for their relationship with the pathology.[25] There are also no specific electrocardiographic manifestations; changes similar to those observed during an acute coronary syndrome usually occur, including depression or elevation of the ST segment, Q wave, left bundle branch block, changes in the T wave, prolongation of the QT interval, in addition, an increase on the risk of presenting cardiac arrhythmias.[26]

Treatment and therapy should be directed to the cause of sepsis in accordance with what is established by international guidelines. New treatments studied at the molecular level focus on the prevention of SCM, with objectives directed at the inflammatory cytokines TNF-α and IL-6. In addition to seeking to block the production of NO, these strategies have not been demonstrated to be effective.[27] Molecules such as mirR 187a-3p are proposed to be involved in the activation of inflammation and ventricular remodeling.[28] Drugs such as levosimendan have been used with promising results, and ventricular assistance devices such as IABP have been used to improve cardiac output and reduce the need for vasopressors. At least 12 cases have been reported in the literature from inpatients with SCM with left ventricular dysfunction who did not respond to conventional treatment and in whom this device was used with favorable results.[29] ECMO has also been used successfully as a last-ditch therapy in patients with cardiogenic shock and sepsis who develop septic cardiomyopathy.

Other molecules under study are enzymes such as Sirtuin 6 (SIRT6), which has demonstrated a protective effect against endotoxins in SCM.[30] Pellino 1 (Peli 1), a ubiquitin ligase that causes inhibition of apoptosis and oxidative stress and preserves cardiac function in models with myocardial infarction.[31] Sivelestat, an inhibitor of the human neutrophil elastase protein, has shown improvement in viability and suppresses apoptosis of stimulated cells. *In vivo*, it has been associated with an improvement in survival rate and reduces serum levels of cardiac troponin, TNF-α, and IL-1B, improving cardiac function and reducing cardiomyocyte apoptosis, among other beneficial molecular effects. In conclusion, sivelestat can play a protective role against sepsis-induced myocardial dysfunction by activating the PI3K/AKT/mTOR signaling pathway.[32]

In the context of the case, initially, with the clinical signs obtained and the echocardiographic data, we consider other entities, such as peripartum cardiomyopathy, as a differential diagnosis. This is defined as non-ischemic idiopathic cardiomyopathy, manifested with heart failure secondary to diastolic dysfunction of the left ventricle present towards the last month of pregnancy and in the first five months after birth in women without a history of cardiovascular disease or any other clinical explanation for heart disease. Therefore, the clinical picture of acute heart failure that is complicated by arrhythmias and thromboembolic events added to an infectious origin as the cause of cardiac dysfunction excludes this variable as a diagnosis.[33,34]

As part of the study protocol and thinking about long-term anticoagulation treatment, immunological studies were requested in search of autoimmune diseases that could complicate the evolution, obtaining negative results in screenings for antiphospholipid syndrome (APS), systemic lupus erythematosus (SLE) as well as determination of protein S, protein C and antithrombin III. We found protein S deficiency, in addition to the increase in antithrombin III, changes typical of the hypercoagulable state of pregnancy, which consists of an increase in the concentrations of coagulation factors VII, factor VIII, as well as Von Willebrand factor, fibrinogen, and plasminogen inhibitor activating factor, while protein S levels decrease.[35]

CONCLUSIONS

We conclude that it is important to make the condition known so that it can be suspected and treated in time. We highlight the importance of using ultrasonographic monitoring in critical areas without replacing classic hemodynamic monitoring systems and establishing standardized echocardiographic indices for its proper approach. Defining and unifying criteria, as well as standardizing echocardiographic measurement parameters, will provide them with prognostic value and improve their approach. Recently, research

has been progressing to find useful biomarkers and potential treatments, improving survival. However, these are not yet reproducible or applicable to the large population of existing patients with sepsis.

Currently, there is no reference to this entity in management guidelines, which means that it could be unknown to many if it is not suspected. Therefore, it is not adequately addressed; this increases short- and long-term mortality in all patients who develop septic cardiomyopathy during sepsis. As it is an entity related to serious infectious processes, it is usually outside the daily management of some doctors, internists, cardiologists, and emergency physicians, with the approach being carried out by intensive care doctors. We consider that every inpatient with hemodynamic instability should be approached with critical care echocardiography. Its use has recently become relevant and is already considered a pillar of diagnostic support in emergency and intensive therapy areas.

At present, there are no studies that describe the long-term follow-up of sepsis survivors who develop septic cardiomyopathy. With the case presented, we demonstrate that early intervention with the help of current tools such as ultrasound makes a big difference, targeted treatment and Echocardiographic monitoring at key moments in the development of the pathophysiology of septic cardiomyopathy was key to guiding management, medium-term follow-up demonstrates a favorable evolution, and finally the 1-year control verifies the reversibility of the entity, the good prognosis and the absence of the development of long-term cardiovascular events.

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Cardiopulmonary resuscitation: beyond just giving chest compressions, ethical considerations

Resucitación cardiopulmonar: consideraciones éticas más allá de las compresiones torácicas

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Keywords: cardiopulmonary resuscitation, sudden cardiac death, cardiac arrest, bioethics.

Palabras clave: *resucitación cardiopulmonar, muerte súbita cardiaca, paro cardiorrespiratorio, bioética.*

ABSTRACT

Sudden cardiac death (SCD) is a global health problem that requires, in many cases, cardiopulmonary resuscitation (CPR) and automatic external defibrillation (AED). Generally, it is initiated by a witness and continued by trained personnel. Many of the patients who suffer from SCD have a history of cardiac problems, and the decision to start CPR bystander must be made in seconds, which entails medical and bioethical decisions. Some of these decisions involve not only the initial rescuer but also health personnel and the family, and everyone must be conscious that a patient's death is possible. The objective of this paper is to mention the main bioethical considerations that are directly related to CPR, both the people who receive it and those who administer it in the context of SCD.

RESUMEN

La muerte súbita cardiaca (SCD por sus siglas en inglés) es un problema de salud mundial, que requiere para su tratamiento, en muchas ocasiones la reanimación cardiopulmonar (RCP) y el uso de desfibrilador automático externo (DAE por sus siglas en inglés); generalmente es iniciada por un testigo y posteriormente continuado por un equipo entrenado en el terreno de la atención médica. Muchos de estos pacientes tienen antecedentes de problemas cardiacos y la decisión de iniciar la RCP debe realizarse en segundos, lo que conlleva decisiones médicas y bioéticas, algunas de las cuales involucran no solo al rescatador inicial sino también al personal de salud y la familia y todos ellos deben estar conscientes que la muerte del paciente es probable. El objetivo de este escrito es mencionar las principales consideraciones bioéticas que se encuentran en relación directa con la RCP tanto de las personas que reciben la intervención como los que la proporcionan.

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INTRODUCTION

The need for immediate action in the presence of a sudden cardiac death (SCD) event and the need to start cardiopulmonary resuscitation (CPR) can be the difference between life and death. This difference in concept can cause some dilemmas when acting logically; CPR will require therapeutic activity without delay to try to abort SCD. In contrast, death requires NO initiation or cessation of all therapeutic activity. Given the importance of the decision about the attitude to take or not (remember that the patient is dead or on the verge of death with the possibility of living), the diversity of ways in which the problem and need for speed in treatment can be interpreted beforehand. The decision creates dilemmas and has bioethical aspects to be defined. Considering this point of view, we will develop the main bioethical aspects related to CPR.

Cardiac arrest (CA) is the sudden cessation of cardiac activity with a loss of consciousness state with an unresponsive victim without normal breathing and no signs of circulation.[1] Without immediate treatment, this condition

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progresses to SCD and could be treated and potentially reversed by CPR and defibrillation. Annually in the USA, approx., 400,000 people are victims of SCD.[2] Most of them are unexpected and commonly occurring in populations with a previous diagnosis of heart disease. Bystander CPR (B-CPR) and advances within emergency medical services (EMS) have proven successful interventions. Nonetheless, only approximately 10% of the patients with CA events leave the hospital alive, with a high incidence of neurologically impaired functions.[3]

Even if CA and SCD are used in the same context, this should not happen because SCD has an epidemiological impact, and CA should be considered in clinical practice. This difference should be linked because CA treatment aims to offer a guideline to the personnel who assist the victim in the implementation of CPR.[4]

CA in the context of SCD has multiple causes but shares in the pathophysiology, cessation of mechanical activity of the heart with circulatory collapse, loss of respiration, systemic hypo perfusion, and finally, death. The treatment with CPR initially substitutes those lost functions, trying to restore breathing and circulation in order to avoid death secondary to irreversible injury to vital organs.[5]

In the context of an SDC, the decision to start CPR with any rescuer (ideally B-CPR) should be made in seconds, and sometimes different types of conflicts may arise. Some bioethics in the decision-making during CPR include beneficence, non-harmful autonomy, and justice, related to integrity, efficiency, confidentiality, and fidelity, autonomy directly related to the patient, beneficence with the doctor-patient relationship, and the good samaritan law and justice with the society. These principles seem to be generally well accepted but may differ between cultures, religions, personal convictions, etcetera.[6]

A wide variety of ethical questions arise during and after caring for a patient who receives CPR, generally related to how much sense it makes to receive care and for how long for a patient with a limited life expectancy. These questions generally arise among medical personnel, nursing, paramedics, friends, and family of patients, mainly regarding what is the best treatment that the person receiving CPR should have, especially when the time of death is close.[4]

These four principles that govern medical ethics are known under the name of principlism, after the four guiding principles in medical ethics.[7]

1. Respect for autonomy: also known as self-determination, the actions are their own and independent of the will of others. That means they are free to reach their own conclusions. An autonomous person must be free to avoid being influenced or controlled by others who may interfere in making responsible decisions. It is the right of every patient to be informed and participate in making medical decisions regarding their case, and it is considered an essential piece in current medical bioethics.
2. Beneficence: perform acts that (are intended to) generate something good for the one who receives them, where doctors are required to act in patients' best interests. The doctors must offer options to our patients that, in our professional judgment, will further improve the patient's values and goals.
3. Non-maleficence: *Primum non nocere* (The first thing is not to harm). This maxim has accompanied the medical profession since its beginnings. Doctors are obliged to avoid causing harm or suffering to their patients.
4. Justice: consideration of the interests of all those involved in the result of an action. This is how to guarantee fair access to health resources and their use; in other words, doctors must promote systematic solutions to address the inequalities present in health systems, require all people to receive good, fair, and equitable treatment, propose that all social values should be distributed equally unless and be beneficial to all stakeholders.

ALTERNATIVE MORAL FRAMEWORKS

Using of a single theoretical framework on ethical issues can create difficult conflicts to resolve between doctors, their patients, and

their families. Thus, it has been suggested that different ethical frameworks be in the face of a complex clinical situation such as SCD that gives rise to difficult ethical questions.

These are:

1. Utilitarian/consequentialist view. Highlights the way to act in a way that obtains the greatest balance between the risks and benefits of the patient. For example, a utilitarian approach is used to decide whether or not to initiate CPR on a patient. What is the probability of survival, quality, and quantity of life compared to the suffering, consequences potential, and costs?
2. Deontological view. This view holds that some actions may exceed net profit calculations. A clear example is when a physician suggests the withdrawal or suppression of some treatment based on a utilitarian evaluation of futility, but on the other hand, the family members favor continuing the treatment out of a sense of family duty.
3. The doctrine of double effect. It is based on the idea that although an action or fact can have more than one result (intentional or unintentional), it is ethically justified as long as the intended benefit significantly outweighs the unintended harm. For example, giving painkillers to a dying person is justified, even if an unintended could be that death is hastened.
4. Communitarian view. This vision emphasizes the values of the common good and the majority, social objectives, traditional practices, and trying to help. For example, be in favor of universal access to health care with the idea of improving the quality of life of an entire community.
5. Rights-based approaches. This view emphasizes the legal rights of individuals. For example, patients near the end of their lives are extremely people who also have the right to participate in and benefit from appropriate research on their condition.
6. Social contractarian view. Try to find a balance or intermediate point of view between the social responsibilities of an individual and the responsibilities of society towards him. An example is the carrying out of pharmaceutical research studies in poor countries where their citizens could not afford the treatment. It violates this social principle by putting pressure on one population so that another can obtain the benefit.
7. Ethics of caring (or feminist ethics): Under this statement, caring for others is the basis of people's moral behavior, emphasizing that relationships with others should not be based on the universality of individual rights but rather on a sense of responsibility.[8]
8. Virtue ethics. While utilitarians focus on benefits and burdens, and deontologists focus on duty, virtue ethicists focus on the moral character that informs behavior, emphasizing the practice of compassion/empathy, fidelity, justice/advocacy, and practical wisdom.[9]

Decisional capacity

This is the patient's ability to receive, understand, and process the information regarding the benefits, possible risks, and alternatives of treatment and to deliberate and make his own choices. A doctor determines it, but competence itself is a legal determination that must be determined by a judge.

Patient rights

Patients have the right to decide about the life-sustaining medical treatments they receive as long as they have decision-making capacity. They also have the right to be informed of their diagnosis, prognosis, and treatment and may accept, reject, or stop any treatment even if it could hasten their death. Also, patients do not have the absolute right to expect or demand that their doctor apply treatments that are not clinically indicated.[10-14]

Futility

Condition in which the doctor considers that the patient when applying a treatment or procedure, does not have a reasonable possibility of improving the patient's condition or, where appropriate, that the patient himself,

or his responsible person at that moment, concludes the same treatment offered, is NOT in accordance with the patient's own goals and values. An example of a futile intervention is when a CPR maneuver does not seek the recovery of spontaneous circulation (ROSC) but rather its application alone, only prolongs the dying process and will not prolong the patient's life in any case. They can value-based futility (or the futility of quality of life) that defines that a treatment or intervention such as CPR maneuvers in a patient with SCD conflicts with the patient's values and objectives, that is, the patient DO NOT agree to receive it; but if the objectives of the procedure, or treatment, are NOT known: the values, and objectives of care will also be unknown.[15]

If a treatment is unlikely to have a result compatible with the objective values, quality of life, etc., desired by the patient, the doctor should consider that treatment as No acceptable based on the principle of non-maleficence. This makes the patient the one who defines what is futile for him based on his own values. It is then when the doctor must be empathetic and respectfully take the decisions that the patient has made based on his own goals and values, and should then give therapeutic recommendations that are consistent, as much as possible, with what the patient wants or needs.[16,17]

LIVING WILLS AND ADVANCE DIRECTIVES

Advance application directive: it is any form of expression of a patient's thoughts, desires, or even preferences about the care to receive during the end of life. These typically provide advance instructions about limiting care, which frequently include CPR in CA situations. Advance directives can be based on conversations, written directives, living wills, or legal attorney papers for health care. While still competent, the patient's conversations with relatives, friends, or physicians are the most common form of advance directives. Written advance directives are generally considered legally more reliable than conversations held between patients and other people, including family. In this way, a patient who has lost his decision-making capacity but who has written advanced directives, ensures that his autonomy right is respected. The legal aspects of these advance directives vary according to the different legislations in the world.

APPLICATION OF DO NOT RESUSCITATE ORDERS (DNR)

There are some international recommendations for patients in CA and SCD to receive CPR unless there is a (DNR) order or in cases where CPR is futile (e.g., signs of irreversible death).[18] CPR is a unique condition in the context of medicine because it is the only medical intervention in which the patient is presumed to accept treatment (based on implied consent for emergency treatment that endangers life), and not carrying it out requires an explicit medical or legal order. It is not unusual to find cases in which resuscitation may be possible from the theoretical and physiological point of view but medically useless.[19] In other words, while a doctor believes that a patient under CPR, patient circulation can be physiologically restored, at the same time, the doctor also believes that it is very unlikely that the patient will survive hospital discharge for those patients with severe advanced or terminal illnesses, without an indication DNR, requiring CPR in the event of CA, places physicians in a difficult position, with the patients and families to not to start CPR and not provide treatment when they believe it is not indicated. In turn, patients and families are in a difficult and sometimes unacceptable position to make a decision that will shorten their lives, even if this is very brief.

An example is that stopping CPR is appropriately accepted when the only possible outcomes are extremely high morbidity, premature or imminent death as expressed by the American Heart Association, only extremely preterm infants less than 23 weeks, or birth weight < 400 g, and anencephaly. There is a lack of training and guidance for doctors to suspend CPR in adults, and there is often the question in hospital settings whether, at some point, the doctor may decide unilaterally to suspend CPR resuscitation in those cases where they believe it is medically useless. The point of view of patients in

intensive care units cannot be ignored since it often requires multiple interventions or treatments from different points of view, sometimes useless who will potentially end up receiving CPR in a futile manner, defining medical l futility as all the excessive medical interventions (both in terms of effort required and economic resources) that have little chance of changing the patient's final clinical outcome.[20] Although it could be appealing to the medical personnel to be able to refuse to provide potentially useless or futile therapies on the basis that doing so would preserve valuable resources for other patients, it is «rationing» that does not contribute at all to granting improvement in health care that is fair to the person or to the population.[21] We can say that if a patient does not agree to receive CPR maneuvers, this decision must be respected based on the principle of the patient's autonomy. On the other hand, if the patient agrees to receive CPR maneuvers, then he should receive the maneuvers only if the professional medical judgment of the doctor who will order the CPR on the patient results in a possible favorable outcome for the patient and it is in accordance with his principles, needs, and, goals. However, if, on the contrary, the doctor decides based on that same judgment that CPR maneuvers will not have a favorable outcome for the patient then CPR maneuvers should be considered medically unbeneficial and should not be carried out. This is the way to honor the principle of beneficence and, at the same time, that of non-maleficence, which, apparently, could be useful but, in truth, NOT beneficial for patients. It must be taken into account that ethically tense situations, such as the case of a patient with SCD receiving CPR maneuvers. The tension must be communicated clearly and precisely to all those involved, especially to patients and their families. Helping to reduce pain in situations like these and relying on palliative care medicine can be of great help and should be considered more frequently in emergency rooms. Likewise, one must act with complete transparency and a good communication chain, transparency and communication must be frequent about the patient's condition at all moments.

CONCLUSIONS

There are numerous clinical and ethical issues and difficult problems that involve CPR. Basic principles of bioethics can be valuable in assessing and concluding ethical dilemmas. An uncontroversial principle is that CPR should be given when indicated, avoided when it is not or was not accepted by the patient previously, and suspended when efforts are ineffective.

It is mandatory not only to increase teaching CPR in the medical field but also in the general population, and not less important to teach the ethical principles of CPR in all medical fields, including paramedics, in teaching programs that currently are not widely diffused.

Education of patients regarding resuscitation is crucial to improving physicians' abilities to comply with individual patients' wishes. Communication with patients and families is an essential skill that should be taught in medical education and practice with competence throughout the career.

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