EDITORIAL

2022 Dr. Pedro Cossio Foundation Award

Premio Fundación Dr. Pedro Cossio 2022

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At last everything has returned to the long-awaited normality!

Although it is true that the prodigies of technology allowed our virtual congresses to be carried out successfully for two years, finally the 48th Argentine Congress of Cardiology could be enjoyed between October 20 and 22, 2022 with all our senses and in person.

The Scientific Committee of the Congress selected 4 works as candidates to obtain the Cossio Award corresponding to this year and the following work was the winner:

Effect of influenza vaccination in patients with cardiovascular disease: An updated meta-analysis of randomized controlled clinical trials. Authors: Lucrecia M. Burgos, Ezequiel J. Zaidel, Álvaro Sosa Liprandi, Adrián Baranchuk.

Influenza is an acute viral disease that predominates in autumn-winter, which according to estimates by the US Center for Disease Control affects 3 to 11% of the population each season, depending on age, comorbidities and the socio-cultural-economic condition of the population groups. (1) Although these proportions are estimates, there is no doubt that they represent a serious public health problem. Cardiovascular patients are one of the most vulnerable groups affected according to the incidence of complications or mortality. Several types and subtypes of influenza viruses have been identified, but one of the most common is influenza type A (influenza A) H1N1 based on encoding proteins present on its surface (H = hemagglutinin, N = neuraminidase).

During the 20th and 21st centuries, various influenza epidemics and pandemics occurred on the planet, but one of the most recent and resonant was that of the years 2009-2010. It affected the 5 continents and it is estimated that there were more than 1 600 000 affected and more than 19 000 registered deaths during the first 12 months. (2) Already in 2004, the well-remembered Enrique Gurfinkel and his collaborators had shown, in a pioneering work, a very significant reduction of cardiovascular death and coronary events in acute coronary patients who received the anti-influenza vaccine (AIV) randomly compared with a control group after 1-year follow-up. (3) But since the aforementioned pandemic, the World Health Organization and the main societies of cardiology in the US and Europe recommend annual vaccination against influenza in patients with cardiovascular disease, due to the afore-mentioned vulnerability, and because compelling benefits are achieved. The most recent recommendation was published in 2021 by the Inter-American Society of Cardiology through the authors of the work we are commenting on. (4) The 2009-2010 pandemic led to universal awareness about the usefulness of AIV with health and government campaigns to generalize its application in risk groups, but the ideal objectives have not yet been achieved, particularly in deprived population groups. (5)

Professionals from Instituto Cardiovascular de Buenos Aires, Sanatorio Güemes, and the Kingston Health Science Center in Ontario, Canada, carried out a meticulous systematic search of all the studies published in Pubmed, the Cochrane Library, and Clinical Trial Registries in relation to AIV in patients with heart failure (HF) or cardiovascular disease (CVD). (6) They also manually reviewed the reference list of all recent publications and presentations at international cardiovascular congresses by referencing keywords related to this topic, to ensure complete capture of relevant articles. This thorough search initially identified a total of 957 studies. Duplications were eliminated, the risk of bias was assessed and the existence of heterogeneity in the different works was quantified. From this extensive list, they selected those randomized clinical trials that compared the results of AIV vs. placebo or vs. no intervention, in patients with HF or CVD, and strict inclusion and exclusion criteria were applied. They followed the successive steps of the PRISMA protocol flowchart to analyze systematic reviews and finally selected 6 trials totaling 9316 patients for definitive analysis. The primary endpoint was all-cause mortality (ACM) and secondary endpoints were cardiovascular mortality (CM), myocardial infarction (MI), and major adverse cardiovascular events (MACE) among vaccinated and unvaccinated patients. After a mean follow-up of 16±9.7

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months, AIV was associated with a 33% reduction in ACM compared with control: RR 0.67 (95% CI 0.47 to 0.95) (p=0.03). It also reduced CM by 36% (p=0.02), MACE by 31% (p=0.007), and a non-significant trend of MI reduction of 18%.

This work has the enormous merit of the strict methodology used. It was a broad and meticulous search of all the available information, which was subjected to a detailed inclusion and exclusion process following a pre-established protocol, which concluded with the analysis of 6 publications. It is the most complete and updated meta-analysis existing, since it also included two studies published in the last year. Despite the overwhelming evidence available, the influenza vaccination rate in cardiovascular patients is far from ideal. A multicenter study demonstrated a wide variability of prescription (or acceptance) in patients with heart failure: between 70 and 80% in Europe, 52% in North America, and 2.6% in Asia. (7) In our setting there is also marked underutilization: 46% according to a study carried out in a high complex center. (8) Various barriers may be related to this behavior: among others, the lack of doctors' conviction, patients' myths and beliefs, economic limitations or the lack of provision by the public or private medical coverage systems. The results shown in this study should represent a stimulus for primary care physicians, clinicians, and cardiologists to extend the indication of influenza vaccination to cardiovascular patients and other high-risk groups.

The other candidate works to obtain the Cossío Award were:

Cardiogenic shock classification (SCAI) to predict in-hospital and long-term mortality in acute heart failure. Authors: Lucrecia M. Burgos, Rocío Baro Vila, Franco Ballari, Ana Spaccavento, Bianca M. Ricciardi, María L. Talavera, Fernando Botto, Mirta Diez

Cardiogenic shock (CS) is one of the most dramatic situations faced by the staff of an emergency room, intensive care or coronary care unit. Despite the number of highly efficient pharmacological and instrumental resources that have been incorporated in recent decades, mortality continues to be very high. On the other hand, the heterogeneity of patients with CS who attend the hospital at different stages of the disease is well known. They cover a wide spectrum of hemodynamic disorders ranging from isolated hypoperfusion that is reversed with initial therapies, to refractory shock with multiple organ failure and hemodynamic collapse. This implies the selection of different treatment modalities, from pharmacological to highly complex invasive ones, which will directly impact on clinical results and prognosis. Acknowledging the aforementioned heterogeneity of the groups of patients with CS, a multidisciplinary group led by the Society for Cardiovascular Angiography and Interventions (SCAI) recently designed a classification scheme for CS, with an adequate clinical basis for rapid evaluation at the patient's bedside. The purpose was to provide a simple and pragmatic tool to be used without delay in clinical practice in this group of patients. (9) This classification considers five stages, was widely validated in multiple publications and applied in practice. As a summary, stage A ("At risk") includes patients without signs or symptoms of CS, but who are at risk of developing it, for example, those with large acute myocardial infarction, previous acute infarction and/or symptoms of heart failure. Stage B ("Beginning") consists of patients who have clinical evidence of hypotension or tachycardia, but without hypoperfusion. Stage C ("Classic") comprises patients with hypoperfusion requiring an initial set of interventions (inotropes, vasopressors, mechanical support or extracorporeal membrane oxygenation, ECMO). Stage D ("Deteriorating") involves patients who have failed to stabilize despite intense initial efforts and require further escalation. Stage E ("Extremis") includes patients with circulatory collapse, often in refractory cardiac arrest with ongoing cardiopulmonary resuscitation or being supported by multiple simultaneous acute interventions, including ECMO.

This retrospective cohort analysis conducted at Instituto Cardiovascular de Buenos Aires aimed to validate the SCAI scheme in acute heart failure (AHF) and establish its in-hospital and long-term prognosis. A total of 856 consecutive patients with AHF admitted between 2015 and 2020 were included. Mean age was 74.7±13 years and 63.7% were male. The most frequent cause was coronary heart disease (35.6%), followed by valvular heart disease (27.5%). Median left ventricular ejection fraction (LVEF) was 42% (29-58), and 45.7% had LVEF <40%. The proportion of patients with shock, in SCAI stages A to E, was 39.8%, 39.4%, 14.1%, 4.1%, and 2.6%, respectively. Patients with more severe stages were younger; more frequently had reduced LVEF, were in functional class III-IV, and had had previous hospitalizations for AHF. There was a gradual increase of in-hospital mortality in each SCAI stage: A 0.6%, B 2.7%, C 21.5%, D 54.3%, and E 90.6% (Log Rank p <0.0001). After a follow-up of 16.8 months, mortality was: A 24.9%, B 24%, C 49.6%, D 62.9% and E 95.5% (Log Rank p <0.0001). After multivariate adjustment, each stage of SCAI shock remained associated with increased mortality (all with p <0.001 compared with stage A). But there was no difference between stages A and B for adjusted mortality (p = 0.1).

This work provides two important contributions: the applicability of the SCAI scheme in AHF and its remote prognosis. The limitation is that it was performed in a high complex center, and it is therefore difficult to reproduce these results in hospitals lacking advanced resources. There is no doubt that patients with CS or AHF in the severe stages of the SCAI scheme should be transferred in the short term to tertiary care centers with a 24/7 cardiac catheterization service and a specialized coronary care unit with mechanical circulatory support. Of course, that transfer will be conditioned

by the possibilities presented by the patient's situation and the resources available for transportation. One possible reason that would explain the paradox of the younger age of the cases in stages D and E that was observed in the work we are commenting on, is that in the selection of candidates to be referred to a reference center with the capacity for mechanical circulatory support and transplantation, they are usually younger and without comorbidities.

Presence of subclinical atheromatosis before 45 years of age. Analysis of a cohort study in Argentina. Authors: Gustavo A. Giunta, Lorena Helman, Pablo D. Cutine, Maria Florencia Aguiló, Daniel Antokoletz, Daniel Pirola, Maria Isabel Rodriguez Acuña, Laura Brandani

The ultrasound examination of the vascular bed (carotid arteries, aorta and femoral or iliac arteries) is a very valuable tool to diagnose subclinical atherosclerosis (ATS). It is particularly useful for the appropriate reclassification of persons at intermediate cardiovascular risk, as suggested by the main cardiovascular prevention guidelines with class IIb recommendation and level of evidence B. (10) Compared with other postulated methods (coronary calcium assessment) vascular ultrasound has the great advantage of its practicality, versatility, less sophisticated technology and lower cost.

This cross-sectional study of Fundación Favaloro analyzed 1788 patients between 18 and 45 years of age who spontaneously attended a cardiovascular prevention program between January 2017 and December 2018. Mean age was 30.1±8.6 years and 49.3% were women. Cases with clinical cardiovascular coronary, cerebrovascular or peripheral disease history were excluded from the study. Atherosclerosis was defined as the presence of atheromatous plaques evaluated by ultrasound at the level of the carotid arterial tree. These plaques were characterized by a focal protrusion towards the arterial lumen of ≥0.5 mm width, as more than 50 % increase of the adjacent intima-media thickness (IMT) or as a diffuse IMT increase of >1.5 mm measured between the media-adventitia and the intima-lumen. Its presence was considered as a binary variable: absence (No) and presence (Yes). Atherosclerosis was detected in 3.1% of cases. It was more prevalent in men and as expected, it was associated with age (<30 years=0.6%; 30 to <40 years=1.8% and ≥40 years=11.7%), hypertension (9% vs. 3%, p<0.01), total cholesterol (212.9±38.4 mg/dL vs. 182.5±35.8 mg/dL p<0.0001) and triglycerides (150±92 mg/dL vs. 105.3±65.3 mg/ dL, p <0.0001). HDL-cholesterol (HDL-C) was lower in patients with ATS (49.2±11mg/dL vs. 54.7±13.6 mg/dL p <0.0001) and the use of statins was higher in those with ATS (3.6% vs. 0.7%, p <0.05). Patients with ATS had a non-significant increase of the metabolic index (20% vs.10%; p=NS), but the prevalence of ATS was associated with the increase in the number of components present (p <0.005). The Framingham score evidenced a greater proportion of ATS patients at high or moderate risk, but 83.6% of subjects with ATS belonged to the lower risk category and 10.9% to that of moderate risk. The calculation of the vascular age among those over 40 years revealed an increase of 4.8 years in the absence of ATS and of 7.7 years in its presence (p<0.005).

There are few studies in our setting indicating that in young individuals, apparently healthy from a cardiovascular point of view, atherosclerotic lesions may be present, especially when there are risk factors, though this is infrequent. This work reflects this situation, demonstrating an exponential increase with age and its association with cardiovascular risk factors. The atherosclerotic vascular disease and its clinical consequences are generated by the interaction of LDL-C plasma concentration in the presence of an inflammatory state, but essentially as a function of time during which the endothelium was exposed to the deleterious effect of LDL-C. Consequently, it is important to detect at an early stage the existence of hypercholesterolemia and premature vascular lesions, with the purpose of aborting the damage that would ensue at the mid- or long-term. In the case of this study, it should be taken into account that its conclusions apply to a highly selected population, consisting of individuals who voluntarily attended a prevention program to know their health status, and cannot be directly extrapolated to the general population. Moreover, only the carotid territory was explored, excluding the iliofemoral and aortic territories. Recently, the examination of multiple vascular territories by ultrasound and computed tomography has demonstrated an increase of the diagnostic and predictive value. (11)

The cardiovascular exercise test contributes to an accurate risk assessment in patients with low-risk pulmonary hypertension. Authors: Ignacio Martín Bluro, Leandro Barbagelata, María Lorena Coronel, Luciano Melatini, Graciela Svetliza, Norberto Vulcano, Andrés Nicolás Atamañuk, Walter Mauricio Masson Juarez

Pulmonary hypertension is defined as mean arterial pressure of 20 to 25 mmHg or more (according to different criteria). It is a condition produced by numerous etiologies and it is formed by groups of diverse severity and prognosis. (12) According to its severity, patients can be classified into 3 risk groups: low (<5% estimated mortality risk at 1 year), intermediate (5-10% estimated mortality risk at 1 year) and high risk (>10% estimated mortality risk at 1 year). The following variables are recommended to define these groups: 1) functional capacity (FC) defined by the World Health Organization (WHO), 2) the 6-minute walk test (6MWT) and 3) oxygen consumption (VO_2) in a cardiopulmonary exercise test (CPET). (13)

Researchers from Hospital Italiano de Buenos Aires, the Cardiology Institute of Corrientes, the Southern Pneumonology Institute of Bahía Blanca and Hospital Juan A. Fernández of Buenos Aires carried out a cross-sectional multicenter study including 18 patients over 18 years old with pulmonary arterial

hypertension (PAH). Sixteen were women (89%), median age was 43.5 years and median time from diagnosis to evaluation was 4.7 years. In half of the cases (n=9) the etiology of PAH was considered idiopathic, in 6 cases associated with connective tissue disease, in 2 cases secondary to human immunodeficiency virus (HIV) and in 1 case to porto-pulmonary hypertension. The inclusion criteria involved belonging to a low-risk stratum according to the simplified risk evaluation of the French registry: 1) FC I-II, 2) NT-proBNP <300 pg./mL and 3) 6-minute walk test >440 meters. (14) Two patients (11%) were receiving a vasodilator drug, 12 (67%) 2 drugs and 4 (22%) 3 drugs. They all performed CPET on a treadmill following the Bruce or modified Bruce protocol, and the gas exchange was continuously analyzed. The recorded variables included heart rate, blood pressure, peripheral oxygen saturation (SpO_2), oxygen consumption (VO_2), rate of carbon dioxide production (VCO_2) and minute ventilation (VE). The respiratory quotient (RQ) or the respiratory exchange ratio (VCO_2/VO_2) were used as maximum exercise indicator. A RQ >1.1 was considered as maximum exertion. Peak $VO_2$was defined as average VO_2 during the last minute of exercise and was expressed in mL/min/kg, and was additionally reported as percentage of the predicted value (according to prespecified tables which consider sex, age and body surface area). Functional capacity was defined as normal when the VO_2 as percentage of predicted VO_2 was ≥85%. The three variables considered in risk evaluation were: peak VO_2, the percentage of the predicted value and the VE/VCO_2 slope. The proportion of patients presenting these abnormal parameters (peak VO_2 ≤15 ml/min/kg, the percentage of predicted value ≤65% and VE/VCO_2 slope ≥36) was examined. Despite all patients were considered at low risk when they entered the study, peak VO_2 was below the predicted 85% in all of them. Only one patient (6%) did not present any of the 3 high-risk variables, 8 (44%) presented one variable, 7 (39%) presented 2 and 2 (11%) presented the 3 variables. Therefore, 94% of PAH patients considered a priori as low risk, presented some high-risk factor when analyzed with the CPET. A message to consider with these results is the great accuracy presented by an objective, measurable and reproducible technique such as CPET instead of subjective estimations as FC. Moreover, CPET would be a potentially useful tool to identify "high-risk from low-risk"; in other words, to establish an "absolute low risk". However, these should be considered preliminary conclusions due to the low number of patients included and the sample heterogeneity. Finally, more extensive studies with a long-term follow-up should establish the prognosis and survival of the patients studied with the present protocol, to confirm its clinical utility.

The Jury of the 2022 Dr. Pedro Cossio Award was completed with the Argentine Society of Cardiology former presidents Dr Carlos Barrero and Dr. Carlos Tajer, to whom I thank their knowledgeable and responsible participation.

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