

2018 Dr. Pedro Cossio Foundation Award

Premio Fundación Dr. Pedro Cossio 2018

JORGE LERMAN

The Scientific Committee of the 44th Argentine Congress of Cardiology selected 5 works to contend for the 2018 Dr. Pedro Cossio Foundation Award. Proceeding with the tradition installed 32 years ago, we shall make brief comments about the selected works.

The winning study was:

“Alerts of cardiotoxicity during treatment with trastuzumab in breast cancer at four years of follow-up. First national report”. Authors: Daniel Alejandro Santos, María Estela Tettamanti, Carolina Chacón, Jorge Nadal, Victoria Costanzo, Adrián Nervo, Federico Losco, Reinaldo Chacón. Instituto Alexander Fleming. Buenos Aires, Argentina.

Breast cancer is the most common malignancy in women. Overexpression of human epidermal growth factor receptor 2 (HER2) occurs in approximately 25–30% of breast cancers and implies poor prognosis. Trastuzumab (Tr) is a humanized monoclonal antibody that targets the HER2 receptor, increasing survival by 33% at 3 years, (1) but is associated with left ventricular dysfunction in >20% of the cases, particularly in patients also receiving anthracycline or alkylating agents. (2) This drug produces structural changes in contractile proteins and mitochondria, but it rarely leads to cell death, explaining the potential for reversibility. Risk factors for anti-HER2 drug-induced cardiotoxicity include previous exposure to anthracyclines, low left ventricular ejection fraction and older age.

The authors of this paper studied 231 women with HER2-positive breast cancer, mean age 51 ± 11 years, treated with standard chemotherapy regimens (adriamycin, cyclophosphamide, paclitaxel) plus Tr during 12 months. The primary objective was to investigate Tr-induced cardiotoxicity after a mean follow-up of 48 months, comparing three definitions of cardiac injury. The American College of Cardiology defines cardiotoxicity as >10% fall in left ventricular ejection fraction (LVEF) compared with the baseline value. The NSABP B31 study considers >15% decline in LVEF while the MD Anderson Cancer Center defines cardiotoxicity as LVEF drop of up to 40%. In this prospective, longitudinal and open-label study, each patient

was a self-witness to define cardiotoxicity according to LVEF values before and after treatment. Before treatment, LVEF was $61 \pm 4.7\%$ and 65% of the patients presented >10% fall in LVEF with an average decline of 9.9% points. Left ventricular ejection fraction continued falling after treatment in 46% of the patients. In 45% of the cases LVEF recovered by the end of follow-up, 17% of the patients had to stop trastuzumab temporarily and 12% stopped treatment definitively. Eighty percent of the patients with a reduction in LVEF received cardiological medication. In the per-group analysis, cardiotoxicity criteria were met in 35% of cases when considering the ACC criteria, in 19% according to the NSABP B31 definition and in 11% assuming the MD Anderson Cancer Center conditions. The authors did not mention the use of biomarkers to identify myocardial injury. The consensus statement on diagnosis, prevention and treatment of anticancer therapy cardiotoxicity of the Argentine Society of Cardiology (SAC) recommends that biomarkers may be useful, but there is lack of indication in routine clinical practice (Class IIb, Level of evidence C) (3).

This work contributes to elevate the field of clinical cardiology to a new chapter: Cardio-oncology. Nowadays, as life expectancy of patients with cancer is longer due to the efficacy of new therapeutic agents, more new cases of cardiotoxicity occur. This was less evident in the past as life expectancy of cancer patients was short enough to prevent the development of long-term cardiovascular complications. For this reason, a new group of cardiac patients will be incorporated into the cardiologist usual practice, suggesting the need for the development of new work teams integrated by cardiologists, oncologists, clinicians, pharmacologists, radiotherapists and specialists in diagnostic imaging to manage this new subspecialty of Cardiology. (4)

The other studies were:

“Mechanisms of valvular dysfunction in bicuspid aortic valve disease. First Argentine study of prognostic markers in a cohort of patients with clinical

and electrocardiographic follow-up". Authors: María C, Carrero, Gonzalo R. Díaz Babio, Gerardo Masson Juárez, Iván Constantin, Facundo Verón, María D. Mezzadra, Gustavo L. Vera Janavel, Pablo Stutzbach. Instituto Cardiovascular de San Isidro.

Most patients with bicuspid aortic valve (BAV) disease will develop aortic stenosis or regurgitation, and many of them will present aortic root dilation. The aim of this study was to investigate clinical and echocardiographic variables to predict disease progression and development of moderate/severe aortic stenosis or regurgitation. The study included 243 patients (mean age: 43.14 years, 73.2% men) with BAV. Mild aortic regurgitation (AoR) was present in 45.6% of cases, moderate in 20.1% and severe in 4.1%, and moderate aortic stenosis (AoS) in 8.2% of patients and severe in 4.9%. Follow-up was achieved in 93% of cases; 2 patients died and 20 underwent valve surgery at 4.7 years. Surgery was decided in the presence of symptoms, left ventricular ejection fraction (LVEF) <55%, left ventricular diastolic dimension >75 mm or aortic diameter >55 mm. Compared with AoS, patients with AoR were more commonly men, younger, and with greater left ventricular, aortic valve annulus and aortic dilation. Male sex and valve prolapse were identified as independent predictors of significant AoR, while aortic valve calcification was an independent predictor of significant AoS. A progressive increase in left ventricular end-systolic dimension or a decline in LVEF are the most reliable signs of progression of AoR severity. Furthermore, valvular calcification and rapid increase in aortic-jet velocity are powerful predictors of the progression and aggravation of asymptomatic AoS. (5) Other experiences found that age and its association with moderate to severe AoR are main determinants of BAV disease aggravation. (6)

"Prevalence, awareness, treatment and control of hypertension in urban and rural communities of Latin America". Authors: Pablo Lamelas, Rafael Díaz, Andrés Orlandini, Álvaro Avezum, Fernando Lanás, Patricio López Jaramillo, Vilma Irazola, Salim Yusuf. The Population Health Research Institute (Hamilton, Ontario, Canadá), Estudios Clínicos Latinoamérica (Argentina), Dante Pazzanese Institute of Cardiology (Sao Paulo, Brazil), Universidad de la Frontera (Temuco, Chile), Fundación Oftalmológica de Santander (Floridablanca, Colombia), Institute for Clinical Effectiveness and Health Policy (Buenos Aires, Argentina).

This important cooperative study, carried out by 6 prestigious scientific institutions dedicated to epidemiological research, analyzed the current state of hypertension (HT) in 6 Latin American countries (Argentina, Brazil, Colombia, Chile, Peru and Uruguay). The study included 34,249 individuals with HT, defined as blood pressure (BP) values >140/90 mmHg. The prevalence of HT was 44.6% (from 19.3% in Peru to 52.5% in Brazil). Awareness of HT was 59.6%; 54.2% of these patients were treated and 37.6% of

them had adequate BP control. People living in urban areas and those with higher educational attainment were more aware of having HT, and the disease was better treated and controlled compared with people living in rural areas or with lower educational attainment, respectively. Two-thirds of the patients treated received only one antihypertensive drug and the rest of the patients were treated with 2 or more drugs. There were important differences in all the criteria analyzed among countries. This is the largest epidemiological survey with direct BP measurement conducted in Latin America. Direct BP measurement determined a greater prevalence of HT compared with other studies in which the participants were only interviewed. For example, the average prevalence of HT was 18% in the CARMELA study (7) and 29% in the INTERHEART Latin American study. (8) The conclusions of this study are discouraging: the prevalence of HT is high, while awareness, control and appropriate use of pharmacological agents and control of other cardiovascular risk factors are alarmingly low. Many factors contribute to this situation, including the socioeconomic status of patients, the indifference of physicians, and deficiencies in the health care system.

"Acute pulmonary embolism in Argentina. The XX CONAREC Registry". Authors: Ignacio M. Cigalini, Cristhian E. Scatularo, Juan C. Jáuregui, Maico I. Bernal, Sebastián García Zamora, José M. Bonorino, Jorge Thierer, Ezequiel J. Zaidel.

The aim of this new registry conducted by CONAREC was to know the reality of pulmonary embolism (PE) in Argentina. A total of 684 patients were included in 75 centers with cardiology residency programs. In 70.8% of cases, PE was the admission diagnosis; in the rest of the patients, PE occurred as a complication of other diseases. The most common predisposing factors were obesity, recent hospitalization, temporary bed rest, recent surgery and active cancer, in that order. Pulmonary computed tomography angiography was the most common diagnostic imaging technique used (81.4% of the cases) while ventilation/perfusion scintigraphy was used only in 13.4% of the cases. Ninety-one patients (13.3%) underwent reperfusion therapy. In-hospital mortality was 12.3% and was directly associated with PE in half of the cases. As with every CONAREC registry, the sample analyzed corresponds to centers with cardiology residency programs, representing moderate or high complexity academic institutions that may not be representative of the general population of Argentina.

"Pulmonary embolism reperfusion in Argentina. Analysis of the XX CONAREC Registry". Authors: Juan C. Jáuregui, Ignacio M. Cigalini, Cristhian E. Scatularo, Maico I. Bernal, Daniel Cornejo, Javier Ortego, José M. Bonorino, Ezequiel J. Zaidel.

In this sub-analysis of the previous study, 91 pa-

tients undergoing reperfusion therapy were analyzed. Systemic thrombolysis with streptokinase was used in 78 cases, 14 patients underwent endovascular procedures (thrombus fragmentation with or without aspiration) and 5 patients were treated with local thrombolysis. One patient underwent surgery. During hospitalization, PE recurred in 7% of the patients, 25% had kidney dysfunction, 15% presented bleeding, 45% required mechanical ventilation and 32% inotropic drugs. Only 49% of the patients with hemodynamic instability received reperfusion therapy despite the recommendation of SAC's acute thromboembolic disease consensus statement (Class I, level of evidence B) (9) and other international guidelines. In-hospital mortality among the patients reperfused was 27%, more than twice the mortality rate of non-reperfused patients (9.7%), as these patients constituted a subgroup in whom the disease was initially more severe, despite reperfusion therapy produces a significant absolute increase in pulmonary perfusion of 80% (14.6% vs. 1.5%) compared with treatment with heparin alone. (10) The main conclusion of these results is the low rate of reperfusion therapies used, either systemic or local thrombolysis, endovascular procedures with thrombus fragmentation or aspiration or surgical procedures in high risk patients with PE.

The jury of the 2018 Dr. Pedro Cossio Foundation Award was completed by the former presidents of the Argentine Society of Cardiology Dr. Daniel Piñero and Dr. Eduardo Mele, to whom I am grateful for their skilled and responsible participation.

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