

2017 Dr. Pedro Cossio Foundation Award

Premio Fundación Dr. Pedro Cossio 2017

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The Scientific Committee of the 43rd Argentine Congress of Cardiology selected 4 works to contend for the 2017 Dr. Pedro Cossio Foundation Award. Continuing with the tradition installed 31 years ago, we shall make brief comments about the works selected.

The winning work was:

"External Validation of Cardiovascular Risk Equations in the Southern Cone of Latin America: Which Predicts Better?", by Pablo E. Gulayin, Goodarz Danaei, Laura Gutierrez, Rosana Poggio, Jaqueline Ponzo, Fernando Lanas, Adolfo Rubinstein, Vilma Irazola. Institute for Clinical Effectiveness and Health Policy (IECS), Argentina; Chair of Public Health, School of Medicine, UNLP; Harvard T.H. Chan School of Public Health, United States; Universidad de la República, Uruguay; Universidad de la Frontera, Chile; National Ministry of Health, Argentina.

The Center of Excellence in Cardiovascular Health (CESCAS) conducts an important prospective population-based cohort study. Coordinated by the Institute for Clinical Effectiveness and Health Policy (IECS), the study is supported by the National Heart, Lung and Blood Institute (NHLBI, United States) and other important international institutions and universities. The study started in 2009 and included 7,524 men and women between 35 and 74 years. The population was recruited in 4 locations of the Southern Cone of Latin America: Marcos Paz and Bariloche (Argentina), Pando (Uruguay) and Temuco (Chile).

The aim of this study was to investigate the prevalence and incidence of risk factors for chronic non-communicable diseases as cardiovascular disease, chronic obstructive pulmonary disease and cancer in the general population and make a longitudinal record of events. Since the beginning of the project, this group has published numerous articles in international peer-reviewed journals. (1)

The estimation of global cardiovascular risk constitutes a crucial step in primary prevention, as it represents an adequate tool to decide the intensity of the measures to consider in each particular case. Several risk scores in different populations worldwide have been published in the last years. (2) Yet, none of them has been adapted to the population of the Southern Cone of America. The aim of this study was to evaluate

the external validity of cardiovascular risk prediction equations built in developed countries and compare the applicability of four known scores (Pooled Cohort Studies Equations, Framingham, CUORE and Globorisk) in the Argentine population. These scores were selected as they included the same variables used in the CESCAS cohort and considered the total number of coronary events as final endpoints.

The information was obtained during household visits and included socio-demographic data, anthropometric measurements and clinical variables. The following cardiovascular events were considered: angina, fatal and non-fatal myocardial infarction, fatal and non-fatal stroke, myocardial or peripheral revascularization, heart failure and sudden death.

The sensitivity, specificity, and prediction of occurrence or non-occurrence of events by means of the C-statistics (area under the ROC curve) was evaluated for each score, as well as the calibration analyzed through the comparison between predicted and observed events. After a median follow-up of 2.2 years, a total of 60 cardiovascular events were recorded (21 cases of angina and myocardial infarction, 15 cases of stroke, 10 of heart failure, 2 revascularizations and 12 cardiovascular deaths).

The Framingham risk score showed the highest sensitivity (81%) and the CUORE score presented the highest specificity (69%). All the curves in the CESCAS cohort had a C-statistic value >0.7. The calibration between predicted and observed values was higher for the CUORE, Globorisk and Framingham risk scores than for the Pooled Cohort Studies Equations.

There is evidence that risk equations developed in a given population are not adequately applicable to others with different genetic load, lifestyle or diet (3-4). The SAC Consensus on Cardiovascular Prevention recommends the use of WHO prediction risk charts for the sub-region America B as the most accurate tool at present. (2) CESCAS is the first longitudinal population-based study designed to evaluate the different cardiovascular risk prediction equations in the Southern Cone of America. Probably, it will allow in time to develop a specific model for our region, which may also include novel predictive variables such as atherogenic (lipoprotein A) or genetic biomarkers.

Despite the short follow-up period and the small number of events collected to make robust conclusions, the Jury of the 2017 Dr. Pedro Cossio Foundation Award unanimously considered that this work deserved to be the winner for its excellent design, meticulous development and originality of conclusions.

The other three works were:

"Increased Pulmonary Vascular Resistance in Heart Transplantation Candidates Predicts Postoperative Right Ventricular Failure: Is This Reason Strong Enough to Contraindicate Transplantation?", by Ezequiel Espinoza; Ignacio Martin Bluro; Santiago Sández Bustamente; Rodolfo Pizarro; Ricardo Marenchino; Marcela Proietto; Norberto Vulcano; Cesar Antonio Belzitti.

In this study, the investigators of the Instituto de Medicina Cardiovascular, Hospital Italiano de Buenos Aires, studied 93 patients undergoing heart transplantation between January 2012 and April 2017. The aim of this investigation was to determine the preoperative threshold value of pulmonary vascular resistance above which 30-day mortality (primary endpoint) or postoperative right ventricular (RV) dysfunction (secondary endpoint), defined as evidence of RV dysfunction on echocardiography associated with requirement of inotropic drugs or duration of inotropic support and mechanical ventilation, develop. The value of pulmonary artery pressures, pulmonary capillary wedge pressure and pulmonary vascular resistance expressed in Wood units (WU) were obtained during the last cardiac catheterization before transplantation. Mortality at 30 days was 5.3% and was only associated with inotropic requirement for >48 hours. The incidence of RV dysfunction in the immediate postoperative period was 22.6% and was associated with all the hemodynamic variables of pulmonary pressures and vascular resistance and with the echocardiographic variables of RV function.

Multivariate analysis revealed that tricuspid annulus plane systolic excursion (TAPSE)-to-pulmonary artery systolic pressure (PASP) ratio measured by Doppler echocardiography showed the best performance among all the hemodynamic and echocardiographic variables. A TAPSE/PASP ratio of 0.26 mm/mm Hg had an area under the ROC curve of 0.84 with very good calibration according to the Hosmer-Lemeshow test. Only this ratio presented an independent association with RV dysfunction (OR >10; 95% CI, 2.2->100; p=0.03). Pulmonary vascular resistance was the variable that best predicted postoperative RV dysfunction, and adequately classified 80% of the patients. Early mortality was 14.3% in patients with PVR >5.6 WU vs. 3.8% in those with PVR <5.6 WU (OR 4.2; 95% CI, 0.64-28; p=0.13).

Pulmonary hypertension is common in patients on the waiting list for heart transplantation and is sometimes a limiting condition for transplantation associated with adverse outcome, particularly due to acute RV dysfunction. The extensive waiting list and the dif-

ficulties related with organ procurement require allocation of the explanted hearts to candidates who are expected to benefit from the intervention. Thus, reliable criteria should be established for decision-making. Although the primary endpoint was not achieved, the authors of this paper suggest this cut-off value. This limitation could be explained by the retrospective design of this single-center study with a limited number of patients and few events.

"Prognostic Value of the Size of Necrosis in Patients with Ischemic Ventricular Dysfunction Undergoing Revascularization", by Santiago del Castillo, Diego Perez de Arenaza, Landy Rodriguez, Federico Marcos, Juan Benger, Mariano Falconi, Marcelo Petrani, Arturo Cagide, Ricardo Garcia Monaco, Cesar Belzitti.

In another study from Hospital Italiano de Buenos Aires, 35 patients with coronary artery disease with ischemic left ventricular dysfunction (ejection fraction $\leq 45\%$) undergoing myocardial revascularization (surgery or percutaneous coronary intervention) were studied. Before revascularization, myocardial viability was analyzed by cardiac magnetic resonance imaging (MRI) with quantification of the size of myocardial necrosis by late gadolinium enhancement (LGE). The aim of the study was to assess the prognostic value of quantifying the size of myocardial necrosis by LGE, and to compare it with viability criteria by cardiac MRI (necrosis involving <50% of wall thickness).

The primary endpoint was overall mortality or cardiac transplantation after a mean follow-up of 3 years. The median number of viable segments was 12 and mean necrotic mass was 46 ± 6 g. The primary endpoint was achieved in 28.5% of the cases. At univariate analysis, the number of viable segments and the size of myocardial necrosis in grams and indexed by body surface area was associated with the primary endpoint. However, the analysis of the ROC curve showed that a size of 28 g/m² had the best discrimination ability, with an area under the curve of 0.69 (95% CI, 0.45-0.92), with a sensitivity of 70% and a specificity of 84% for the primary endpoint. Multivariate Cox proportional hazard analysis demonstrated that age and indexed necrosis size were the only variables associated with the primary outcome (HR 1.16; 95% CI, 1.02-1.33 p=0.02 and HR 1.06; 95% CI 1.01-1.11 p=0.007, respectively).

Several observational studies and a meta-analysis published in the past decade suggested that patients with ischemic ventricular dysfunction and myocardial viability detected on functional stress imaging studies had better outcome and higher survival rate after revascularization. On the contrary, this benefit was not achieved by patients with necrotic dysfunction. (5) The pathophysiological basis of this hypothesis was that reperfusion of necrotic segments without viable contractile tissue would supply blood flow to areas without functional recovery. This would not happen if areas with viable myocardial tissue were revascularized. This statement was questioned by the

STICH (Surgical Treatment for Ischemic Heart Failure) study, which compared myocardial revascularization with medical treatment and did not identify patients with different survival rates. (6) Despite being conducted in a single center with a reduced number of cases, this paper presents a new hypothesis that highlights the importance of the total volume of the necrotic mass over the number of viable ischemic segments as a predictor of success achieved by revascularization. Yet, this hypothesis needs to be validated by additional larger prospective multicenter studies.

“Validation and Comparison of Two Simple Models of Risk Stratification in Patients with ST-Segment Elevation Acute Myocardial Infarction in Argentina”, by Lucrecia M. Burgos, Cristian M. Garmendia, Elián F. Giordanino, Casandra L. Godoy Armando, Ignacio M. Cigalini, Sebastián García Zamora. Ricardo Iglesias, Juan P. Costabel

This is a new publication of the fruitful production of the Argentine Council of Cardiology Residents (CONAREC). The aim of this study was to validate two international risk scores of patients hospitalized due to ST-segment elevation acute myocardial infarction in Argentina, included in the CONAREC XVII registry. (7) The scores mentioned were the Simple Risk Index (SRI) from the United States published in 2001 (8) and the Portuguese Registry of Acute Coronary Syndromes (ProACS) from Portugal, published in 2017. (9) Several scores have been developed for risk stratification of acute coronary syndrome patients with the goal of implementing diagnostic and therapeutic measures (medical treatment or invasive procedures) according to the risk calculated. Some scores are complex and include a great number of sophisticated variables, as biochemical, echocardiographic or angiographic parameters, and are therefore impractical for rapid bedside decision-making. These two scores were selected because they are simple and have adequate efficiency demonstrated by external validations. The SRI includes age, heart rate and systolic blood pressure. The ProACS risk score evaluates age, systolic blood pressure, ST-segment elevation and Killip and Kimball index.

A total of 694 patients from 45 centers were included. The primary endpoint, in-hospital mortality, occurred in 8.78% of patients. Both scores showed good discrimination to predict the primary endpoint (AUC 0.83; 95% CI, 0.78-0.88, $p=0.001$ for the SRI, and 0.78; 95% CI 0.71-0.86, $p=0.001$ for the ProACS risk score). In both cases, the calibration was satisfactory accord-

ing to the Hosmer-Lemeshow test. Although all the patients with ST-segment elevation acute myocardial infarction require urgent reperfusion with thrombolysis or percutaneous coronary intervention, the use of these tools would be useful for risk stratification as they include simple variables that can be quickly collected at the first contact with the patient in order to adjust the decision-making process.

The jury of the 2017 Dr. Pedro Cossio Foundation Award was formed by the former presidents of the Argentine Society of Cardiology, Dr. Hugo Grancelli and Dr. Alvaro Sosa Liprandi, to whom I am grateful for their skilled and responsible participation.

CONFLICTS OF INTEREST

None declared.

(See authors' conflicts of interest forms on the website/Supplementary material).

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