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PROGNOSTIC VALUE OF CORONARY COMPUTED TOMOGRAPHY ANGIOGRAPHY PRIOR TO CARDIAC VALVE SURGERY.

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Berríos Bárcenas Enrique Alexander	MD, Msc, Outpatient care Department. Instituto Nacional de Cardiología Ignacio Chávez. Mexico City, Mexico; Cardiology Department. Hospital Español. Mexico City, Mexico.
Soto López, Maria Elena	MD, PhD, Inmunology Department. Instituto Nacional de Cardiología Ignacio Chávez. Mexico City, Mexico.
Rojas Serrano, Jorge	MD, PhD, Interstitial Lung Disease and Rheumatology Unit, Instituto Nacional de Enfermedades Respiratorias Ismael Cosio Villega. Mexico City, Mexico.
Meléndez Ramirez, Gabriela	MD, PhD, Magnetic Resonance Department. Instituto Nacional de Cardiología Ignacio Chávez. Mexico City, Mexico.
Castillo Castellón, Francisco	MD, Tomography Department. Instituto Nacional de Cardiología Ignacio Chávez. Mexico City, Mexico.
Estepa, Misael	MD, Msc, Research social service program. Instituto Nacional de Cardiología Ignacio Chávez. Mexico City, Mexico.
Lua Caro del Castillo, Fernanda	MD, Research social service program. Instituto Nacional de Cardiología Ignacio Chávez. Mexico City, Mexico.
Olguin Leyva, Marlenet	MD, Research social service program. Instituto Nacional de Cardiología Ignacio Chávez. Mexico City, Mexico.
Alexanderson Rosas, Erick*	MD, Nuclear Cardiology Department. Instituto Nacional de Cardiología Ignacio Chávez. Mexico City; Physiology Department, Faculty of Medicine, Universidad Nacional Autónoma de México, Mexico City, Mexico. *Corresponding Author

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ABSTRACT

BACKGROUND: International guidelines recommend a preoperative coronary angiography prior valve replacement. Coronary computed tomography angiography (CCTA) is a non-invasive study which has emerged as an alternative option. However, at the present time is not thae preferred imaging test for this purpose.

OBJECTIVE: The objective of the study is to evaluate the prognostic value of CCTA to predict death and / or myocardial infarction in the post-surgical period of valve replacement.

METHODS: This is a cohort study which included patients with valvular heart disease and low-intermediate pre-test probability of coronary artery disease (CAD), who underwent CCTA as part of their preoperative assessment, and who had not been previously diagnosed with CAD. Primary outcome included death and/or perioperative myocardial infarction.

RESULTS: A total of 319 patients were included, predominantly female, with an average age of 55±9.7 years. Only 4.7% presented obstructive CAD. The independent predictors of death and/or myocardial infarction were non-CAD in CCTA and high-risk EuroSCORE.

CONCLUSION: In low-intermediate pre-test probability of CAD, CCTA represents an important prognostic value to predict death and/or myocardial infarction in the postoperative period of valvular surgery, so it could be used as an initial screening method in this group of patients

1. INTRODUCTION:

Valvular heart disease (VHD) is a frequent cause of cardiac surgery worldwide [1,2]. The most frequent VHD is aortic stenosis (35%) followed by mitral valve disease (23%) [3]. Cardiac valvular replacement is the best treatment for these patients, the procedure can be done surgically or percutaneously. Surgical mortality risk is near to 7%, depending on the valve and the need for complementary procedures, such as multivalvular replacement, coronary artery bypass surgery, or valve repair [4]. Coronary artery disease (CAD) coexists in many patients with VHD [5-8].

At the present time invasive coronary angiography (ICA) with the subsequent surgical revascularization of obstructive CAD is recommended for all patients prior to cardiac surgery, mainly in men over 40 years of age, postmenopausal women or premenopausal women with cardiovascular risk factors [9]. Surgical revascularization has shown to reduce perioperative myocardial infarction, morbidity and mortality rates [10,11]. Coronary computed tomography angiography (CCTA) has emerged as a field of opportunity in this regard. Some studies with small populations have shown good diagnostic and prognostic performance in VHD [12-17]. CCTA is recommended as an alternative approach in people with low to intermediate risk of CAD [9], however little is known about its prognostic value, and many cardiologists prefer the use of ICA. The objective of the study is to evaluate the prognostic value of CCTA to predict death and/or perioperative myocardial infarction in the post-surgical period of VHD surgery.

1. METHODS

1.1. POPULATION:

This is a prospective cohort study and multivariate survival analysis

performed between 2012 and 2018 at the Instituto Nacional de Cardiologia Ignacio Chávez (Mexico City). We included patients over 40 years of age, of both sexes, with low to intermediate pre-test probability of CAD, and a recommendation from a medical-surgical team to undergo VHD surgery. Patients with a serum creatinine >2 mg/dL, a history of allergy to iodinated contrast medium or percutaneous coronary revascularization prior to surgery were excluded from the study. Patients who suffered a myocardial infarction, stroke or embolic complications in the period between the CCTA and surgery, as well as patients who had emergency surgery or a non-diagnostic CCTA were also excluded from the study. Pre-test probability of CAD was calculated by basic model of CAD consortium [18]. All patients were interrogated for traditional cardiovascular risk factors such as diabetes mellitus, high blood pressure, current or previous tobacco use or angina. Other factors associated with increased surgical risk such as previous stroke, chronic obstructive pulmonary disease, previous cardiac surgery and NYHA functional class were also assessed. The value of the left ventricular ejection fraction and the pulmonary artery systolic pressure (mmHg) were collected from the preoperative echocardiogram. The research protocol was evaluated and approved by the local research and ethics committees (number of approbation: 14-869). All included subjects signed informed consent.

1.2. CCTA PROCEDURE:

All patients had their serum creatinine checked prior to the CCTA. Basal heart rate was initially quantified. A beta-blocker (metoprolol 5-10 mg intravenously) was injected in patients with a heart rate greater than 70 bmp, until the heart rate fell below 70 bpm. The studies were performed with a 256- detector tomograph (SOMATOM Definition Flash; Siemens Medical Solutions, Florsheim, Germany). The cardiac examination area went from the carina to the diaphragm. Using a low radiation protocol (120 Kv, 50 to 80 mAs) and images of 3 mm thickness with an increase of 1.5 mm, simple images were acquired for the quantification of coronary calcium. Detection of coronary calcium was expressed in Agatson units (AU) [19]. Approximately 70 to 90 ml of iopamidol contrast (Iopamiron 370, 370 mg I / ml; Bayer Schering Pharma AG, Berlin, Germany) was used, followed by 40 ml of saline injected with a flow of 5 ml / sec. Contrast administration was performed using the bolus tracking technique. The images were acquired in the cranio-caudal direction with a collimation of 64 by 0.6, rotation time of 330 msec, pitch of 0.24, voltage of 120 kV and current of 500 to 750 mAs. The images were reconstructed in prospective synchronization with the electrocardiogram, with a thickness of 0.7 mm and an increment of 0.4 mm, using a medium filter (Kernel B30f) with a window for mediastinum. All images were transferred and reconstructed on a cardiac study workstation (Syngo.via Siemens). The minimum coronary vessel diameter to assess was 1.5 mm. Non-obstructive CAD was defined as a coronary stenosis <50% and obstructive CAD was considered present when the stenosis was quantified ≥50%. Patients with obstructive CAD underwent invasive coronary angiography (ICA) to address revascularization therapy. All the CCTA were interpreted by two cardiologists specialized in computed tomography with more than 5 years of experience.

1.3. SURGERY AND OUTCOMES:

EuroSCORE [20] was calculated for all patients prior to their surgery to identify those at high risk (score above 5 points). Patients underwent 3 types of VHD surgery: (1) isolated aortic valve replacement, (2) isolated mitral valve replacement, and high risk surgery: multiple valve replacement, concomitantly ascending aortic surgery or coronary by-pass revascularization. All surgeries followed standardized institutional protocols. Patients were evaluated in their postoperative period with an electrocardiogram and transthoracic echocardiogram looking for new pathological Q waves, or myocardial wall motion abnormalities in a pattern compatible with ischemic etiology. For patients who had abnormal electrocardiograms or echocardiograms, serum troponin levels were measured. Perioperative myocardial infarction was defined as the presence of the described electrocardiographic and echocardiographic alterations and a 10-fold elevation of the troponin level above the 99th percentile of the upper limit reported as normal [21].Finally, the mortality that occurred until the 30th day of hospitalization, regardless of the cause, was quantified. The primary outcome was death and / or perioperative myocardial infarction in the first 30 days after surgery. In addition, extracorporeal circulation time was measured as a surrogate for the complexity of the surgical procedure performed.

1.4. STATISTICAL ANALYSIS:

Sequential non-probability sampling was performed. Numerical data were summarized as mean and standard deviation or median and 95% confidence interval according to their distribution. The distribution was evaluated with the DÁgostino test for bias and kurtosis. Categorical data was summarized in frequency and percentage. Bivariate analysis was performed between subjects with or without outcome, with t-test, Mann Whitney's U test, Pearson's chi-square or linear trend, as appropriate. ROC curve was performed to identify the cutoff point of the significant numerical variables. Kaplan Meier graphs and log rank test were performed. The significant variables of the bivariate analysis, which do not present interaction, were introduced to the Cox proportional risk multivariate analysis. Two-tailed p <0.05 was considered significant. Previously, a sample of 316 subjects was calculated to obtain statistical power. All calculations were performed in the Statistical Package for the Social Sciences version (version 26, SPSS IBM Corp., Armonk, New York)

2. RESULTS

A total of 319 patients were included, predominantly females (60.8%), with an average age of 55 ± 9.7 years. The prevalence of coronary risk factors was low, with a predominance of hypertension (29%) and smoking (21%). Fifteen percent had a history of previous cardiac surgery. Eighteen percent had a NYHA functional class ≥ III. Most of patient (45.8%) had rheumatic valve disease, and 21% had degenerative etiology; 36% corresponded to aortic stenosis. Regarding the risk distribution by EuroSCORE, 50 patients (15.7%) had low risk, 177 (57.4%) had intermediate risk and 92 (28.8%) had high risk. Coronary calcium was <1 AU in 76% of the group, the majority did not have evidence of CAD (56%) and only 4.7% presented obstructive CAD. Calcium score was the best predictor of obstructive CAD (AUC = 0.958; 95% CI : 0.929-0.987, p<0.001). Isolated aortic valve replacement was done in 34% of patients, 26% had isolated mitral valve replacement, 39.5% had higher-risk surgeries (of these, 74% corresponded to Bentall surgery). The mean extracorporeal circulation time was 111 min (95%CI:64-236). The general characteristics are presented in Table 1.

Table 1. General Characteristics Of Population.

VARIABLES	VALUE (N=319)
Male sex	125 (39.2%)
Age (years)	55±9.7
Angina	88 (27.6%)
Diabetes	42 (13.2%)
Hypertension	92 (28.8%)
Tobacco use	68 (21.3%)
Chronic obstructive pulmonary disease	10 (3.1%)
Previous stroke	29 (9.1%)
Etiology: • Degenerative • Rheumatic • Bivalve • Congenital	 68 (21.3%) 146 (45.8%) 52 (16.3%) 27 (8.5%)
Aortic stenosis	116 (36.4%)
Previous cardiac surgery	50 (15.7%)
NYHA functional class: • Class I • Class II • Class III • Class IV	 75 (23.5%) 183 (57.4%) 49 (15.4%) 8 (2.5%)

Euroscore: • Low risk • Moderate risk • High risk	 50 (15.7%) 177 (55.5%) 92 (28.8%)
Left ventricular eyection fraction (%)	57±9.4
Pulmonary artery systolic pressure (mmHg)	45.4±16.9
Serum creatinin (mg/dL)	0.89 (0.6-1.28)
Calcium score (UA)	0 (0-230)
Coronary CT Angiography: • Non coronary lesions • Minimal lesions (1-25%) • Mild lesions(26-49%) • Significative lesions (≥50%)	 180 (56.4%) 87 (27.3%) 37 (11.6%) 15 (4.7%)
Cardiac surgery: • Isolated aortic valve replacement • Isolated mitral valve replacement • Two valves replacement • Three valves replacement and/or aortic surgery and/or coronary by-pass graft surgery	 108 (33.9%) 85 (26.6%) 94 (29.5%) 32 (10%)
Extracorporeal circulation time (min)	111 (64-236)
NYHA: New York Heart Association; AU: Agatston unit; CT: Computed tomography. Values are mean and standard desviation or median and 95% confidence interval.	

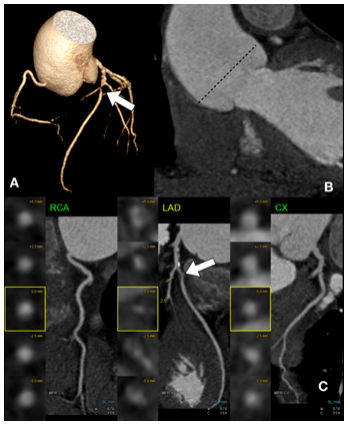
Table 2 shows the bivariate analysis between patients with or without a primary outcome.

Table 2. Bivariate Analysis Between Patients With And Without Adverse Events.

VARIABLE	No Outcome (n=298)	Death and/or myocardial infarction (n=21)	P value
Male sex	115 (38.6%)	10 (47.6%)	0.413
Age (years)	54.4±9.3	63.7±10.5	<0.001
Diabetes	38 (12.8%)	4 (19%)	0.499
Hypertension	83 (27.9%)	9 (42.9%)	0.142
Tobacco use	62 (20.8%)	6 (28.6%)	0.411
Chronic obstructive pulmonary disease	9 (3%)	1 (4.8%)	0.499
Previous stroke	29 (9.7%)	0	0.237
Left ventricular eyection fraction (%)	59.5 (36.9-70)	58 (26.5-68.6)	0.805
Pulmonary artery systolic pressure (mmHg)	45.4±17	45.2±15.9	0.953
Serum creatinin (mg/dL)	0.88 (0.6-1.27)	1 (0.66-1.71)	0.031
Previous cardiac surgery	40 (13.4%)	10 (47.6%)	<0.001
High risk Euroscore	78 (26.2%)	14 (66.7%)	<0.001
NYHA functional class ≥III	52 (17.4%)	5 (23.8%)	0.553
Aortic stenosis	106 (35.6%)	10 (47.6%)	0.267
Aortic root surgery	17 (5.7%)	6 (28.6%)	0.002
High-risk surgery	110 (36.9%)	16 (76.2%)	<0.001
Long extracorporeal circulation time (>133 min)	89 (30%)	18 (85.7%)	<0.001
Days of invasive mechanical ventilation	1 (0-3)	2 (0-19.5)	0.001
Calcium score (AU)	0 (0-184.7)	0 (0-1243.1)	0.153
Non-CAD (CCTA)	175 (58.7%)	5 (23.8%)	0.002
NYHA: New York Heart Association; AU: Agatston unit;CAD: Coronary artery disease; CCTA: Coronary computed tomography angiography.			

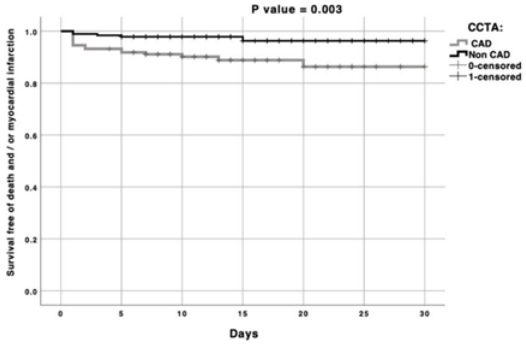
There were 20 deaths and 2 perioperative myocardial infarctions (one with both outcomes). The cause of death was low cardiac output syndrome in 15 patients, perioperative myocardial infarction in one patient, and 5 had post-operative bleeding. Sepsis coexist in four patients (Supplemental material) (Figure 1).

Fig 1. Coronary CTA from a 67 years old male. Volume rendering (A), coronal oblique (B) and curved planar reformation showing high grade stenosis of the LAD (arrows), RCA and LCX without significant stenosis and dilated aortic root with loss of sino-tubular junction in A and B. The patient also had severe aortic regurgitation (not shown). CTA: Computed tomography angiography, LAD: Left anterior descending, RCA: Right coronary artery, LCX: Left circumflex coronary artery.



Regarding the perioperative myocardial infarction, one of them presented obstructive CAD that was corroborated with coronary angiography and surgical revascularization was indicated; the other patient had no significant coronary lesions but underwent ascending aortic surgery with coronary artery reimplantation. Patients having the primary outcome were older (54 ± 9 vs 63 ± 10 years), with higher serum creatinine (0.88 vs 1.00 mg / dL) and had a history of previous cardiac surgery; these variables are included in EuroSCORE. In addition, the patients with primary outcome had high risk surgeries, longer extracorporeal circulation times and days of mechanical ventilation. Non-CAD in CCTA patients had a better survival free of events (Figure 2).

Fig 2. Kaplan Meier plot of survival free of death and/or periprocedural myocardial infarction. Patient without coronary artery disease in computed tomography angiography showed better survival (black line, p=0.003).



Different models were performed to predict event-free survival in the Cox proportional hazards analysis (Supplemental material). Independent predictors of the primary outcome were non-CAD in CCTA with HR of 0.25 (95%CI: 0.09 to 0.7) and high-risk EuroSCORE with HR of 4.56 (95%CI: 1.83 to 11.3) (See table 3). The type of surgery did not show statistical significance in any model.

Table 3. Cox Multivariate Analysis For Prediction Of Death And/or Myocardial Infarction.

VARIABLE	HR (95% Confidence interval)	P value
Non-CAD (CCTA)	0.25 (0.09-0.70)	0.008
High risk Euroscore	4.56 (1.83-11.33)	0.001
CAD: Coronary artery disease; CCTA: Coronary computed tomography angiography.		

3. DISCUSSION.

This study included elective patients considered by our cardiac team to be candidates for valvular heart surgery, the patients had no prior CAD documented. To our knowledge the sample number included is one of the largest reported in the medical literature.

Even though most countries report degenerative etiology as the main cause of valvular disease, our local reality still considers rheumatic etiology as a prevalent cause. In addition, being a highly specialized institution, our population includes bicuspid aortic valve, which is often accompanied by aortic root dilatation. All this translates into a population with a lower average age than expected, and with a lower prevalence of cardiovascular risk factors. In this scenario, CCTA diagnoses obstructive CAD in 4.7% of total cases, considering a stenosis cut-off value of 50%, which seems prudent for clinical decision-making in the context of valvular surgery. It should be noticed that although the main goal of the study was not to assess CCTA diagnostic accuracy, which would be impossible to quantify since only a minority of patient had ICA, we can assume that with a low prevalence of coronary calcifications, the stenosis degree is close to real.

Our low prevalence of CAD is different from other publications. A retrospective Lebanese study reported a prevalence of 27.75% in 1308 patients with VHD with an average age of 67±10 years [22]. On the other hand, an Indian retrospective study reported a lower prevalence (8.7%) in patients who were candidates for cardiac surgery, with an average age of 51.5 ± 9 years [23].Our opinion is that the prevalence of CAD in patients with VHD should be assessed in an individualized basis due to the heterogeneous population. Furthermore, it may be possible that age is the main predictor of CAD, and not VHD per se.

In populations with low prevalence and/or age below 65 years, CCTA may be the method of choice for initial screening for CAD, regardless of the type of VHD. However, most of cardiac teams continue to prefer ICA, possibly for fear of postoperative complications related to CAD. Previously, other studies have evaluated the CCTA prognosis in VHD surgery. Russo et al. published a retrospective study with 132 patients who underwent preoperative CCTA for non-coronary heart surgery, they reported no major cardiovascular events in patients with coronary obstructions <50% [16]. Cornily et al. [17] published a cohort of 215 patients who underwent CCTA prior to aortic valve replacement surgery: patients with a calcium score greater than 1000 AU were taken to ICA. From a total of 106 patients who underwent CCTA, only one presented a perioperative myocardial infarction. However, the infarction diagnosis was not standardized by the universal definition. Lee et al [23] reported an observational study based in an institutional surgical database and compared a group of CCTA versus ICA prior to VHD surgery. The 30-day mortality rate were similar between groups, however the CCTA group had more low cardiac output syndrome (2.3% vs 1.0%; p=0.008). Besides, the CCTA group had lower diagnosis of obstructive CAD and revascularization. Moreover, perioperative myocardial infarction was not reported and the high incidence of low cardiac output syndrome was not clarified.

Unlike the previous one, our study focused in mortality and perioperative myocardial infarction, the latter based on the 4th universal definition [21], diagnosing only two events, both with surgical manipulation of the coronary arteries. The absence of CAD on CCTA was a predictor of a good prognosis with a 75% lower risk of death from any cause and/or perioperative myocardial infarction. The other independent predictors were a high-risk EuroSCORE and prolonged surgical times, which are expected and consistent with other populations [20,25]. High risk surgery performed was not a predictor of outcomes, possibly due to the experience of our institution. Even more, a lower mortality than expected was observed (6.2%).

3.1. LIMITATIONS OF THE STUDY.

The limitations of our study are (1) the single-center character, which could make it difficult to extrapolate the results to other populations; (2) the low number of observed outcomes that can compromise the statistical significance of Cox analysis; and (3) the low age of our population that does not allow evaluating the impact of degenerative aortic stenosis on the prevalence of CAD.

3.2. NEW KNOWLEDGE GAINED:

In patients with severe valve disease who will undergo cardiac surgery, and who have a low to intermediate pretest probability of CAD, CCTA has an independent prognostic value of Euroscore, so it should be considered as the tool of choice.

4.CONCLUSION:

CCTA has important prognostic value to predict death and/or perioperative myocardial infarction in the post-surgical period of VHD surgery, and it could be used as the initial screening method in this population. In case of presenting CAD (≥50% of stenosis), our recommendation is to proceed with invasive coronary angiography to decide the need of a coronary revascularization therapy, however, this event happened in a very low proportion of our population (4.5%).

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