ORIGINAL ARTICLE

Long-term Outcomes of Coronary Artery Bypass Surgery According to the Presence or Absence of Left Main Coronary Artery Disease

Resultados a largo plazo de la cirugía de revascularización coronaria según la presencia o no de enfermedad del tronco de la arteria coronaria izquierda

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ABSTRACT

Background: Coronary artery bypass grafting (CABG) has modified the natural evolution of patients with left main coronary artery (LMCA) disease. There is little information in our setting regarding the mid- and long-term follow-up of operated patients.
Objective: The aim of this study was to evaluate the implication of LMCA disease in the long-term evolution of patients operated on with CABG, and to assess the mortality and incidence of myocardial infarction (AMI) and/or stroke.
Results: Follow-up was completed in 438 patients (95.6%) with a median of 58 months [interquartile range (IQR) 35-88 months]. Actuarial survival at 10 years was 91.8% for the entire population, with no significant differences between the LMCA group (91.57%) vs. the non-LMCA group (91.86%), HR 1,008 95% CI 0.38-2.65, p=0.98. In multivariate analysis, preoperative left ventricular ejection fraction (HR = 0.95; 95% CI 0.93-0.97; p < 0.001), age (HR 1.1, 95% CI 1.04-1.13, p<0.001) and non-elective priority of surgery (HR=3.71; 95% CI 1.3-10.35; p=0.01) were independent predictors of long-term mortality. AMI-free survival was 96.8% (LMCA 94% vs. non-LMCA 97.4%, p=0.8) and freedom from stroke was 98% (LMCA 97.8% vs. non-LMCA 98.1 %, p=0.8).
Conclusion: In patients undergoing CABG, the presence of LMCA disease did not increase the rate of hard events (death, AMI, and stroke) at the long-term follow-up. The results obtained in this series of patients are similar to those published in the international literature used to develop myocardial revascularization guidelines.

Key words: Myocardial Revascularization - Follow-Up Studies - Coronary Artery Bypass - Left Main Coronary Artery Disease

RESUMEN

Introducción: La cirugía de revascularización miocárdica (CRM) ha modificado la evolución natural de los pacientes con enfermedad de tronco de la arteria coronaria izquierda (TCI). En nuestro medio es escasa la información relacionada con el seguimiento a mediano y largo plazo de los pacientes intervenidos.
Objetivo: Evaluar la implicancia de la enfermedad del TCI en la evolución alejada de los pacientes intervenidos con CRM, y conocer la mortalidad e incidencia de infarto de miocardio (IAM) y/o accidente cerebrovascular (ACV).
Resultados: El seguimiento se completó en 438 pacientes (95,6%) con una mediana de 58 meses [Rango intercuartilo (RIC) 35-88 meses]. La sobrevida actuarial fue a 10 años del 91,8% para toda la población, sin diferencias significativas entre el grupo TCI (91,57%) vs grupo no TCI (91,86%), HR 1,008, IC 95% 0,38-2,65, p=0,98. En el análisis multivariado se encontraron como predictores de mortalidad alejada la fracción de eyección ventricular izquierda preoperatoria (HR = 0,95; IC 95% 0,93-0,97; p < 0,001), la edad (HR 1,1, IC 95% 1,04 - 1,13, p< 0,001) y la prioridad no electiva de la cirugía (HR = 3,71; IC 95% 1,3-10,35; p = 0,01). La sobrevida libre de IAM fue del 96,8% (TCI 94% vs no TCI 97,4%, p= 0,8) y la libertad de ACV fue del 98% (TCI 97,8% vs no TCI 98,1%, p= 0,8).
Conclusión: En los pacientes sometidos a CRM, la presencia de enfermedad del TCI no incrementó la tasa de eventos duros (muerte, IAM y ACV) en el seguimiento alejado. Los resultados obtenidos en esta serie de pacientes son similares a los publicados en la bibliografía internacional utilizada para desarrollar las guías de revascularización miocárdica.

Palabras clave: Revascularización miocárdica - Estudios de Seguimiento - Puente de Arteria Coronaria - Enfermedad de tronco de arteria coronaria izquierda

INTRODUCTION

The results of coronary artery bypass grafting (CABG) in patients with multivessel disease have been previously documented, and the presence or absence of left main coronary artery (LMCA) disease in the preoperative coronary angiography has been analyzed. Moreover, the development of the surgical technique and changes in anesthetic and postoperative management have contributed to reduce the morbidity and mortality of the procedure. In our patients, the LMCA disease group did not have a higher incidence of isolated death, myocardial infarction (AMI) and/or stroke; however, when these hard events were combined there was a higher incidence of the composite endpoint com-

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pared with the non-LMCA disease group. (1) Knowing the immediate perioperative results of LMCA disease, evaluating the long-term follow-up is the next step to assess its quality. The evidence shows the advantages of this strategy and we should have reference information to compare it with new revascularization procedures. (2,3) The objective of our work was to evaluate mortality and the incidence of AMI and stroke at 10 years in patients treated with CABG, analyzed according to the presence or absence of LMCA disease.

METHODS

This was a retrospective cohort study of consecutive patients undergoing isolated CABG (single procedure) from January 1, 2011 to March 31,2020 at Hospital Universitario Austral (HUA). Patients included were over 18 years of age, and the presence of significant coronary artery disease was defined in the LMCA by an obstruction greater than 50%, and in the rest of the coronary arteries by an obstructive lesion ≥70%. Patients who received an additional procedure to CABG were excluded from the analysis.

Data from the electronic medical records of HUA were collected and an exclusive database was created for this study. The registry was approved by the independent Evaluation and Ethics Committee of the institution which waived the need for individual consent since the patients were not identified, nor was sensitive data required (according to Law 25,326 of Habeas Data on the Protection of Personal Data).

Mid-term survival and events were evaluated from the follow-up carried out and documented in the medical records of our institution and epicrisis in case of hospitalization outside HUA, as well as from communication with the patient, family, and treating physicians. Data on death, AMI, and stroke at follow-up were collected.

Statistical analysis

Continuous variables are described as mean ± standard deviation or median and interquartile range according to their distribution, and categorical variables are expressed as numbers and percentages. For the bivariate analysis, Student's t test or the Mann Whitney U test was used to compare continuous variables, as appropriate, and the chi square test or Fischer's exact test with Yates' correction, for dichotomous variables. A survival analysis was performed using Kaplan-Meier curves to assess the occurrence of death during follow-up between both groups, evaluating the difference between curves with the log-rank test. A Cox model was created to evaluate the relationship between age, preoperative ventricular function, diabetes and elective status of surgery with the incidence of mortality. The proportional hazards assumption was verified by means of graphs and statistical tests (Schoenfeld test). The discrimination capacity of the model was evaluated using the C index. The same analysis was repeated for the occurrence of AMI and stroke during follow-up. Significant differences between variables were considered for $p < 0.05$.

Final endpoint

The endpoint was defined as the occurrence of isolated events and the composite of death, stroke and/or AMI in the long-term follow-up of CABG, including results within 30 days after surgery.

The following definitions were used:

Perioperative AMI: Development of new persistent Q waves of at least 0.04 s duration in two or more consecutive leads and/or a decrease in the precordial R wave voltage >25%, with >10-fold increase in troponin and/or wall abnormalities on the echocardiogram consistent with electrocardiographic disorders.

AMI during follow-up: The criteria of the fourth definition of infarction or the diagnosis referred to in the epicrisis of the patient when he/she had been admitted to another institution were considered. (4)

Stroke: Focal and/or diffuse brain injury confirmed by clinical findings and computed tomography with sequelae at patient discharge.

RESULTS

Among a total of 458 consecutive patients operated on for isolated CABG between January 2011 and March 2020, 187 (40.82%) had LMCA disease and 271 (59.18%) did not. As previously reported, overall hospital results were as follows: mortality 1.96%, stroke 0.65%, AMI 1.74%, with no statistically significant differences between the two groups analyzed depending on the presence or not of LMCA disease. However, in the univariate analysis, patients in the LMCA disease group had a higher incidence of major adverse cardiovascular events (MACE): 3.93% vs. 2.2%, p=0.022. (1)

Long-term follow-up was completed in 438 patients (95.6%) with a median of 58 months (IQR 35-88 months). The overall survival of the LMCA disease group at 120 months was 91.57%, with no significant difference with the non LMCA disease population (91.86%) (HR 1,008 95% CI 0,38-2,65, p= 0,98) (Figure 1). Independent predictors of death were evaluated in a multivariate analysis, including impaired ventricular function, age, diabetes, and non-elective surgery status as covariates. Impairment of ventricular function (HR 0.95, 95% CI 0.93-0.97, $p < 0.001$), age (HR 1.1, 95% CI 1.04 - 1.13, $p < 0.001$) and the non-elective priority of surgery (HR = 3.71; 95% CI 1.3-10.35; p = 0.01) were significantly associated with mortality, but not diabetes. The proportional hazards assumption was verified by graphical and statistical methods (Schoenfeld test) (Table 1).

AMI-free overall survival in the LMCA disease group was 96%, with no significant difference compared with 97.4% in the non-LMCA disease group (Log-rank p=0.8) (Figure 2). Neither ventricular function nor age or diabetes were significantly associated with AMI occurrence. Stroke-free survival at 120 months was 97.8% for the LMCA disease group vs. 98.1% for the non-LMCA disease group, with no statistically significant difference. (Log-rank p= 0.86) (Figure 3). Also in this case, the variables mentioned were not significantly associated with the incidence of this outcome.

When analyzing the composite endpoint events, no worse outcome was observed in patients with preoperative LMCA disease (table 2).

DISCUSSION

There is solid evidence to indicate CABG in multivessel coronary and LMCA disease. This is summarized

in the meta-analysis by Yusuf et al. published in 1994, which considered 7 randomized trials of CABG vs. medical treatment, involving 2650 patients followed up for 10 years (5). Although these works are now obsolete compared with better current surgical techniques and medical therapy, they established certain principles that are still valid today. Studies showed that there was longer survival and improved symptom relief in patients undergoing CABG who had three-vessel disease or LMCA disease, especially when the proximal anterior descending artery was mainly affected

Clearly, CABG has been improving from that time to the present with the use of arterial conduits, the advent of surgery without cardiopulmonary bypass (CPB), improvement of the perioperative process, and use of optimized medical treatment during follow-up according to the comorbidities of each patient, as well as the management of secondary prevention of cardiovascular disease with drugs tested for this purpose.

In the multicenter ART study (Arterial Revascularization Trial), by Taggart et al., with random assignment to the use of one or two internal thoracic artery arteries, two groups including 1260 patients each were generated, divided by the use or not of CPB for CABG (6). Mortality recorded at 30 days was comparable between CABG without and with CPB (1% vs. 1.2%; p=0.7). All-cause mortality at 5 years was 8.9% vs. 8.3%, respectively, with no significant differences (HR 1.14; 95% CI, 0.86-1.52; p=0.35), and cardiovascular mortality 4.1% vs. 3.1%, respectively (HR 1.39; 95% CI 0.90-2.13; p=0.13). There were no statistically significant differences in long-term AMI between CABG without CPB, 3%, and with CPB, 4.1% (HR 0.66; 95% CI 0.43-1.02; p=0.06), nor in the occurrence of late stroke 3.3% vs. 2.6%, respectively (HR 1.32; 95% CI 0.83-2.11; p=0.24).

These ART results are of great value since they demonstrate that CABG without CPB is a safe treatment with a 5-year follow-up comparable to CABG with CPB, similar to those reported in our current experience (1).

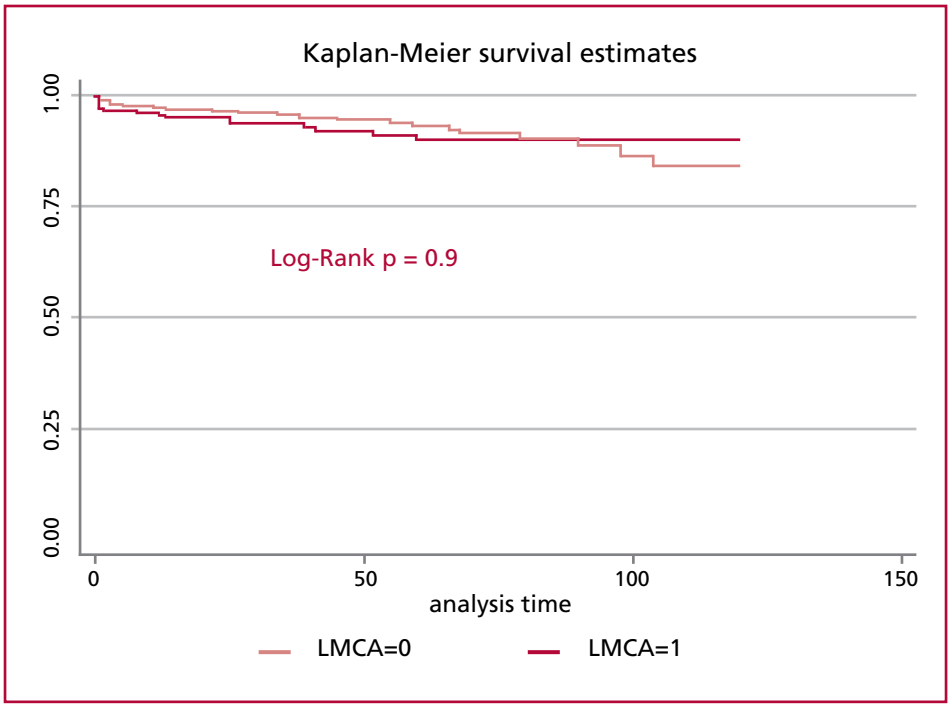
In a subsequent ART analysis, it was concluded that low-volume CABG centers without CPB are asso-

Table 1. Multivariate analysis of long-term mortality predictors

Variables	HR	95% CI	*p* value
Age	1.1	1.04-1.13	<0.001
Diabetes	1.28	0.85-1.94	0.228
LVEF	0.95	0.93-0.97	<0.001
Status			
Elective	Reference		
Non elective	3.71	1.30-10.35	0.01

LVEF: Left ventricular ejection fraction

Fig. 1. Actuarial survival at 10 years. Kaplan-Meier curve. Comparison in coronary patients operated on with coronary artery bypass grafting with and without left main coronary artery (LMCA) disease (LMCA=1 and LMCA=0, respectively)



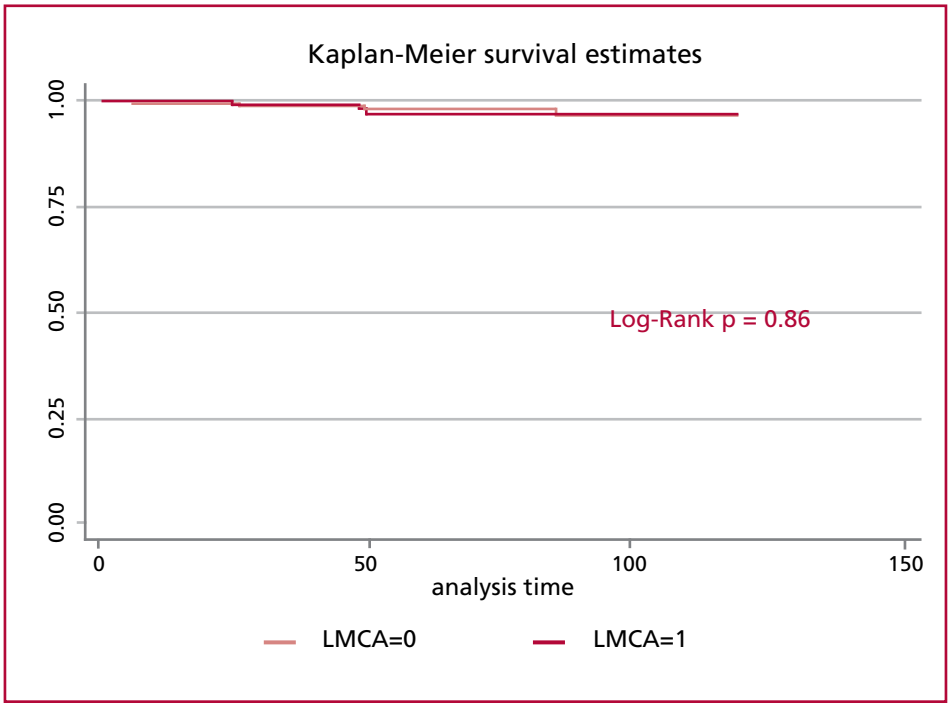


Fig. 2. AMI-free survival. Kaplan-Meier curve. Comparison in coronary patients undergoing coronary artery bypass grafting with and without left main coronary artery (LMCA) disease (LMCA=1 and LMCA=0, respectively).

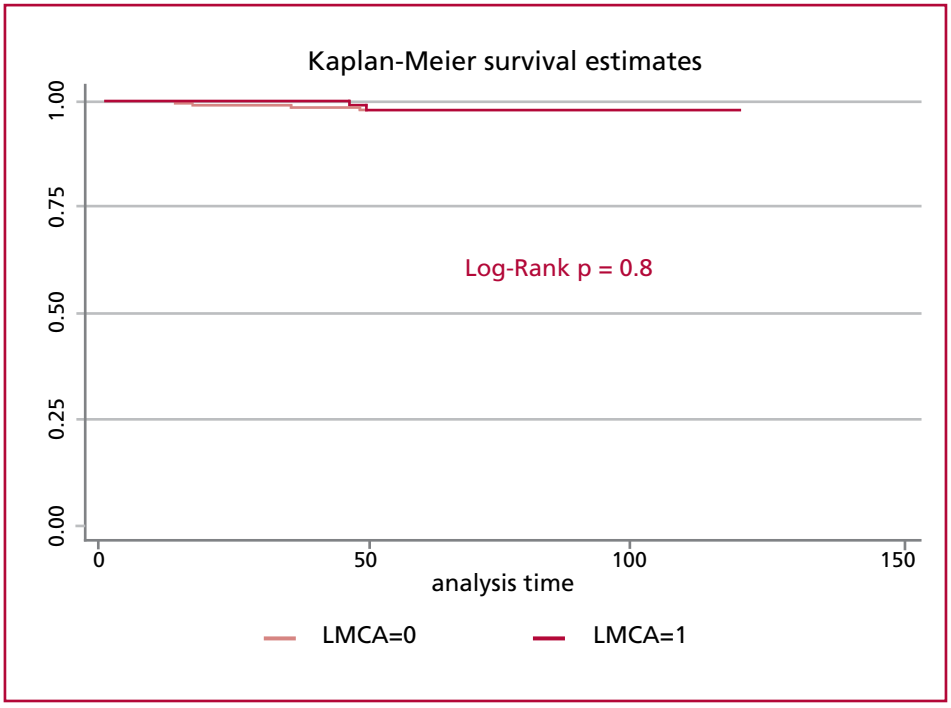


Fig. 3. Stroke-free survival. Kaplan-Meier curve. Comparison in coronary patients undergoing coronary artery bypass grafting with and without left main coronary artery (LMCA) disease (LMCA=1 and LMCA=0, respectively).

ciated with fewer bridges, a higher rate of conversion to surgery with CPB, and increased cardiovascular risk (7). Moreover, Benedetto refers that CABG without CPB is as safe as with CPB in the short. and long-term in highly experienced surgical teams. (8)

In the EXCEL percutaneous coronary intervention (PCI) vs. CABG in LMCA disease study, randomization was stopped prematurely with 1900 instead of the 2600 patients initially planned. (9) Patients included should have a low to moderate coronary anatomy complexity. The 5-year results showed no difference in the composite endpoint of death, AMI, and stroke (PCI 22% vs. CABG 19.2%; OR 1.19; 95% CI 0.9-1.5; p=0.13). All-cause mortality occurred more frequently in the PCI group (13% vs. 9.9%; (OR 1.38, 95% CI 1.03–1.85); however, cardiovascular mortality was similar in both groups (5% and 4.5%, respectively; OR 1.26, 95% CI 0.85-1.85), and AMI rate was also similar (10.6% and 9.1%, respectively; OR 1.14; 95% CI 0.84–1.55). There was also no difference in the in-

Table 2. Baseline characteristics of the population

	LMCA group	Non-LMCA group	Total	*p* value
Patients	175	263	438	
AMI	7 (4%)	7 (2.6%)	14 (3.2%)	NS
Stroke	4 (2.2%)	5 (1.9%)	9 (2%)	NS
Death	15 (8.5%)	21 (8%)	36 (8.2%)	NS
MACE	26 (15.8%)	33 (12.5%)	59 (13.5%)	NS

LMCA: Left main coronary artery. AMI: Acute myocardial infarction. MACE: Major adverse cardiovascular events.

cidence of stroke (CABG 3.7% vs. PCI 2.9%, OR 0.78; 95% CI 0.46-1.31). Ischemia-driven revascularization was more common after PCI than after CABG (16.9% vs. 10.0%; OR 1.84; 95% CI 1.39-2.44; p <0.001).

The SYNTAX study included 1800 patients with three-vessel lesion or LMCA randomly assigned to PCI (n=903) or CABG (n=897). Coronary artery bypass grafting treatment showed lower rates of death and AMI at 5 years in patients with three-vessel disease; therefore, CABG should continue to be the standard of care for three-vessel coronary lesions. (10) It would seem that patients with more complex coronary artery disease would benefit from CABG while PCI would be a valid treatment option in patients with less complex disease, although with a higher rate of subsequent re-intervention.

In this study, a follow-up greater than 93% was achieved at 10 years, (11) with long-term mortality of 248 patients (28%) after PCI and 212 (24%) after CABG (OR 1.19; CI 95 % 0.99–1.43, p=0.06). Among patients with three-vessel disease, 153 (28%) out of 546 had died after PCI vs. 114 (21%) out of 549 after CABG (OR 1.42, 95% CI 1.11–1.81); however, there were no differences in mortality among patients with LMCA disease: 27% with PCI and 28% with CABG (OR 0.92, 95% CI 0.69–1.22; p for interaction=0.023).

The long-term evolution of patients undergoing CABG clearly depends on the type of grafts used. In this case, the great contribution of the work by Lytle et al., in which superiority in long-term survival was observed in those patients with bilateral vs. single internal thoracic artery bypass grafts for CABG, was having promoted a change in the revascularization strategy with a greater tendency to use more than one arterial conduit for revascularization. (12) Taggart in the editorial comment about our publication in Rev Argent Cardiol, precisely highlights the need to investigate and publish the surgical results of both the perioperative and the follow-up periods to analyze the surgical strategies used. (13)

Gaudino et al. carried out a meta-analysis including 35 studies with 149 902 patients in which venous and arterial conduits were used. (14) Mean follow-up time was 6.9 years. The use of arterial conduits (internal thoracic and radial) was associated with a decrease in operative mortality (OR 0.68; 95% CI 0.55–0.83), perioperative AMI (OR 0.77; 95% CI 0.64–0.92) and perioperative stroke (OR 0.80; 95% CI 0.65–0.98) with respect to the use of venous conduits. They also observed lower long-term mortality in CABG with arterial conduits (OR 0.80; 95% CI 0.75–0.85).

The evidence obtained in this meta-analysis did not reveal statistically significant differences between the use of the radial artery or the right internal thoracic artery as the second conduit (the left internal thoracic artery in situ is the first conduit) regarding operative mortality (OR 0.96; CI 95% 0.83– 1.11), perioperative stroke (OR 0.87; 95% CI 0.45–1.68) or perioperative AMI (OR 0.32; 95% CI 0.03–3.13). Moreover, they observed that using the internal thoracic artery skeletonization technique did not increase the risk of mediastinitis.

These data show that surgical groups should increasingly perform CABG, preferably using arterial grafts. In our study population, 82.5% of patients underwent CABG exclusively with arterial grafts, with an average of 3 per patient. This type of surgical technique obviously has an impact and would help reduce cardiovascular risks in the immediate perioperative period and long-term follow-up. We believe that the satisfactory results obtained in our series are comparable to international reference centers with higher volume of surgeries per year. The performance of CABG without CPB with preferably multiple arterial conduits (internal thoracic and radial arteries) should be the background to compare new revascularization procedures. It should be noted that at the beginning of the experience, the learning curve by the surgical group performing CABG without CPB should be considered, perhaps with a selection bias for this surgical modality.

Furthermore, it is important to clarify that there has been no selection of patients for CABG according to the distribution of coronary disease, an aspect that should be taken into account in the analysis of results of other comparative treatment strategy studies for LMCA disease in selected anatomies. In this sense, not all the cases are the same.

Limitations

The greatest limitation of this analysis is its single-center, observational, and retrospective design. Most patients were directed to CABG according to the current recommendations of the American and European revascularization guidelines, as well as according to the consensus reached between the cardiology, endo-

vascular therapy and cardiac surgery services of our hospital. For this reason, strict considerations cannot be made regarding the indication of the therapy indicated due to prior selection bias.

CONCLUSIONS

In our experience, in patients with multivessel coronary artery disease operated on with CABG, the presence of LMCA disease did not increase the rate of serious events (death, infarction and stroke) both in the immediate perioperative period as in the long-term follow-up. The results obtained in this series of patients are similar to those published in the literature used to develop cardiovascular practice guidelines and constitute a local reference to evaluate long-term results.

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