

# Comparative Study of the Results of Coronary Artery Bypass Grafting and Angioplasty for Myocardial Revascularization in Patients with Equivalent Multivessel Disease

Paulo Roberto Dutra da Silva, Whady Armindo Hueb, Luiz Antônio Machado Cesar, Sérgio Almeida de Oliveira, José Antônio Franchini Ramires  
Rio de Janeiro, RJ / São Paulo, SP - Brazil

## Objective

To investigate the relative efficacy of different therapeutic strategies in patients with symptomatic multivessel coronary artery disease with preserved ventricular function. The primary objectives were defined as a combination of death of cardiac origin, acute myocardial infarction (AMI), and refractory angina that required revascularization, and the secondary objectives were defined as anginal state and exercise-induced ischemia.

## Methods

Of the 20,769 patients assessed on cine coronary angiography at InCor, 210 were chosen for this study and were randomized either for coronary artery bypass grafting (CABG,  $n=105$ ) or transluminal coronary angioplasty (TCA,  $n=105$ ).

## Results

A mean of  $3.2 \pm 0.8$  vessels received anastomoses and  $2.1 \pm 0.8$  were successfully dilated in the CABG and TCA groups, respectively. In a 5-year follow-up, the rates of events in the CABG and TCA groups were, respectively: mortality, 9.52% and 12.38%; acute myocardial infarction, 2.85% and 8.57% ( $P = 0.0668$ ); and additional intervention, 2.85% and 24.76% ( $P < 0.001$ ). The survival rate was 88.39% for CABG and 84.93% for TCA; the respective AMI-free percentages were 84.40% and 77.40%. In the CABG and TCA groups, 62% and 60% of the patients had no angina, respectively. The exercise tests were considered nonischemic in 62.5% and 62.1% of the patients in the CABG and TCA groups, respectively.

## Conclusion

In multivessel patients, compared with angioplasty, coronary artery bypass grafting was associated with a lower incidence of long-term events and a reduced need for new interventions ( $P=0.001$ ).

## Key words

transluminal coronary angioplasty, coronary artery bypass grafting, coronary artery disease

The impact of the relief of anginal symptoms, the reduction in the incidence of acute myocardial infarction, and the improvement in survival in some subgroups of patients with impaired ventricular function support the use of coronary artery bypass surgery (CABG) as an effective treatment for ischemic heart disease<sup>1,2</sup>. The observation of the development of intimal hyperplasia, atherosclerosis, and the occurrence of thrombosis and occlusion in the grafts, mainly the venous<sup>3</sup>, motivated a progressive increase in the use of arterial grafts, in an attempt to decrease the indices of occlusion of venous grafts, which ranged from 5% to 15% in the first month, and 15% to 25% in the first year, and reached up to 50% in the first 10 years<sup>4-6</sup>. Therefore, based on the Coronary Artery Surgery Study<sup>7</sup>, which was carried out in the 1970s and used the left internal thoracic artery (LITA) as a graft for the anterior interventricular branch (AIVB)<sup>8</sup> in up to 20% of the patients, the arterial graft became increasingly more used, reaching, at the end of the 1980s and beginning of the 1990s, 37% to 90% of the patients<sup>9-14</sup>.

The advance in the techniques of myocardial revascularization in the 1990s stimulated the use of other arterial grafts, such as the double graft of the right and left internal thoracic arteries (RITA and LITA), whose results showed a lower recurrence of anginal symptoms, a decrease in reoperations, and a tendency to longer survival<sup>15,16</sup>.

Comparative studies of patients undergoing myocardial revascularization through either surgery or angioplasty have not reported statistically significant differences in regard to immediate or late survival rates between the 2 types of treatment. These results did not consider the existence of variations in the samples regarding the number of arteries impaired or the number of arteries effectively treated in each type of intervention. These variations, however, have been observed in recent studies comparing the results of surgery and angioplasty<sup>9</sup>, including 45% of patients with single-vessel disease, while the samples of other studies<sup>14,17</sup> had 60% of patients with 2-vessel stenoses.

When the number of arteries that effectively underwent intervention through the 2 methods is compared, variations are observed in the mean number of arteries treated with angioplasty and those receiving distal anastomoses. In our sample, the mean number of arteries treated with transluminal coronary angioplasty (TCA) was smaller than the number of grafts per patient (2.4 vs 3.1)<sup>14</sup>.

Another relevant aspect is the initial number of arteries con-

sidered adequate for TCA and the number of arteries successfully treated and effectively cleared. This condition characterizes an incomplete revascularization, frequent in the major studies<sup>9-14</sup>. Therefore, the final result of myocardial revascularization obtained with TCA is different from that expected in all the studies performed, regardless of whether they were planned to obtain complete anatomical revascularization<sup>10</sup>, complete or equivalent functional revascularization<sup>9,11</sup>, or even the allowed incomplete myocardial revascularization<sup>12,13</sup>.

Therefore, when analyzing the revascularization indices of the 2 types of intervention, greater indices of complete myocardial revascularization have been frequently observed with CABG than with TCA, ie, 88% vs 51%<sup>11</sup>, 91% vs 57%<sup>14</sup>.

The initial data from the NHLBI-PTCA Registry (1985-86), showing results of long-term follow-up, have contributed to validate incomplete anatomical revascularization as compared with complete anatomical revascularization<sup>18</sup>.

That report showed no difference between the 2 forms of revascularization regarding the analysis of major cardiac events (death, Q-wave infarction, and recurring angina).

The results of the BARI study regarding the comparative strategy between anatomically incomplete and complete TCA showed no differences in the medium-term survival, confirming the initial studies of the 1980s<sup>19,20</sup>. It is worth mentioning that the functional results of the 2 myocardial revascularization methods (TCA and CABG) are rarely discussed.

On the other hand, few studies are available about the success of patent grafts and corresponding arteries or about the late results of percutaneous transluminal coronary angioplasty.

Therefore, despite all benefits achieved with those 2 therapeutic methods for myocardial revascularization, several clinical, angiographic, and prognostic conditions of the patients still remain questionable. The randomized and controlled clinical studies involving CABG and TCA in patients with multivessel coronary artery disease discussed previously could not establish a consensus regarding the procedure with better long-term clinical results. Most of those studies have valued the evolution aspects and the clinical events secondary to the procedures, lacking information on the myocardial ischemic load. Because the final objective of both procedures is to improve myocardial ischemia, the analysis of the procedures under that viewpoint is pertinent, and, therefore, our results should be compared with those reported in the major studies<sup>19,20</sup>. Perhaps the aimed-for complete myocardial revascularization may have been excessively over-rated compared with the functionally adequate myocardial revascularization.

This study aimed at assessing the efficacy of each intervention in protecting ischemic myocardium and in the long-term survival of patients with chronic obstructive coronary artery disease and at establishing the condition of myocardial ischemia at the end of the study in patients indicated for one of the 2 therapeutic myocardial revascularization options.

## Methods

This study assessed and followed up a subgroup of 210 patients selected based on 20,769 cine coronary angiographies performed at the Instituto do Coração of the Hospital das Clínicas of the Medical School of the University of São Paulo. This is a single-

center randomized, prospective, multidisciplinary study that compares the therapeutic options, CABG and TCA, in patients with multivessel coronary artery disease, stable angina, and preserved ventricular function. The scientific committee on ethics at our institution approved the study.

The study comprised patients with multivessel coronary artery disease and stable angina or exercise-induced myocardial ischemia, or both, diagnosed through cine coronary angiography, which revealed significant coronary stenoses (> 70%) in 2 or more vessels, representing the patients with multivessel coronary artery disease treated for angina or myocardial ischemia. The criteria of eligibility were as follows: Canadian Cardiovascular Society FC II or III stable angina<sup>21</sup> or evidence of exercise-induced myocardial ischemia requiring myocardial revascularization. The exercise test was considered positive when the patients developed angina during exercise or when abnormal depressions (horizontal or descending) in the ST segment of 1mm were observed in men and of 2mm in women, analyzed 80 ms from the J point. Multivessel coronary artery disease was angiographically defined as stenosis  $\geq$  70% in vessels with a diameter > 1.5 mm, affecting one of the major arteries or their branches amenable to treatment through TCA or CABG. For randomization, a triple concordance between the clinical cardiologist, interventional cardiologist, and the cardiovascular surgeon was required. The patient's informed consent was required for randomization.

Patients with the following findings were excluded: congenital heart diseases; orovalvular heart diseases; cardiomyopathies; unstable angina or AMI requiring emergency revascularization; left ventricular aneurysm; previous history of TCA or CABG; single-vessel coronary artery disease; and patients aged < 35 years or > 75 years.

The patients were randomized for CABG or TCA and underwent the respective procedures of revascularization of the ischemic myocardium at an interval, when possible, of up to 4 weeks after randomization.

Therefore, patients were selected in an equivalent and consecutive manner, according to the number of arteries involved and the location of the coronary lesions. The indications for both myocardial revascularization procedures were similar.

Angina was classified according to the functional classification of the Canadian Cardiovascular Society<sup>21</sup> and was considered refractory when the triple anti-ischemic therapy (beta-blocker or calcium channel blocker, or both, nitrate, and aspirin) did not succeed.

Acute myocardial infarction was defined as follows: 1) appearance of new Q waves in at least 2 contiguous electrocardiographic leads; or 2) symptoms compatible with acute myocardial infarction associated with an elevation in the creatine phosphokinase (CPK) MB fraction greater than 3 times the upper limit of normality. In the TCA group, if that elevation occurred within 96 hours after the revascularization procedure, it was not considered diagnostic of acute myocardial infarction<sup>22,23</sup>.

Anatomically complete myocardial revascularization was angiographically defined as the absence of residual coronary lesion (>70%) in all epicardial branches considered amenable to treatment with TCA, or according to the number of distal anastomoses performed in all vessels considered impaired in the same condition<sup>18</sup>. The cardiac events were analyzed after the patients who survived the myocardial revascularization procedures were discharged.



Clinical assessment was performed every 3 months during the first 5 years after intervention. Functional assessment was performed by use of treadmill exercise testing (ET) according to the modified Bruce protocol at baseline and at the end of every year of follow-up until completing the fifth year after the intervention.

Except when contraindicated, all patients received aspirin, nitrates, HMG-CoA reductase inhibitors, ACE inhibitors, and beta-blockers, or calcium channel blockers, or both. The routine tests included rest electrocardiography, echocardiography, and routine laboratory tests every 6 months.

All patients underwent cine coronary angiography in a Philips device, Integris 3000 model, which included coronary angiography and left ventriculography according to the Sones or Seldinger technique<sup>24</sup>. At least 4 orthogonal projections were recorded for assessing the left coronary artery, and 2 projections for the right coronary artery, as well as for assessing the arterial or venous grafts, when present in the CABG group undergoing control cine coronary angiography. The ejection fraction was calculated according to the formula proposed by Dodge et al<sup>25</sup>.

Two experienced observers visually quantified the obstructions (those = 50% were considered significant), as well as the presence of collateral circulation. The coronary lesions were classified according to their location, severity, extension, and angulation<sup>26</sup>.

Multivessel coronary atherosclerotic disease was defined as the disease found in more than one coronary artery or its branches, with stenosis  $\geq$  50%, considering only vessels whose luminal diameter was  $>$  1.5mm.

Coronary artery bypass grafting was performed according to the standardized surgical technique using hypothermia and a cardioplegic solution<sup>27</sup>. The cardiovascular surgeon was encouraged to treat all approachable arteries, including those with stenosis  $\leq$  50%. Thus, the surgical strategy was determined by the surgeon with the objective of obtaining complete myocardial revascularization, using venous grafts or arterial segments, whenever possible. The patients underwent the procedure after the definition of the therapeutic strategy and were medicated with beta-blockers and antiplatelet drugs, whenever possible, both in the pre- and postoperative period.

Transluminal coronary angioplasty was performed according to the conventional technique, including the oral administration of aspirin or ticlopidine in the preceding 24 hours<sup>27</sup>. Intravenous heparin (10,000 IU) and nitroglycerin were administered immediately before and during the procedure<sup>28</sup>.

The interventional cardiologists were encouraged to treat all arteries that could be contributing to myocardial ischemia, or that showed an obstruction  $\geq$  70%, or both. In addition, all types of techniques based on catheters were available, such as balloon catheter, stent, laser, either directional or rotational atherectomy, or both. The strategy was planned to allow complete functional revascularization, beginning with the treatment of the culprit lesion, followed by the treatment of other vessels. When necessary, TCA was planned and performed in more than one session.

In the case of acute occlusion of the vessel treated during TCA, the interventional and clinical cardiologists could indicate emergency coronary artery bypass grafting.

The result was considered successful when the residual obstruction was lower than 50% or was reduced by at least 20% of its initial value<sup>22,27</sup>.

All variables were analyzed descriptively. The quantitative variables were analyzed through observation of the minimum and maximum values and the calculation of the means and standard deviations. The qualitative variables were analyzed through calculation of the absolute and relative frequencies.

The hypothesis of the equality of the means of the groups was tested using the Student t test for independent samples<sup>29</sup>. The proportions were compared by using the chi-square test or the Fisher exact test, when expected frequencies below 5 occurred<sup>29</sup>. For assessing the time elapsed until the occurrence of events, Kaplan-Meier curves were adjusted and tested by using the log-rank test. The significance level used in the tests was 5%. The statistical analyses were performed by using the Statistical Analysis System (SAS).

## Results

The present study consecutively analyzed the first 105 patients in the TCA group and the first 105 patients in the CABG group, who survived their respective invasive procedures and were discharged from the hospital. In the TCA group, 45 (42.9%) patients had stenosis in 2 arteries and 60 (57.1%) in 3 arteries, and were treated with TCA. In the other group, 34 (32.4%) patients had stenosis in 2 arteries and 71 (67.6%) in 3 arteries, and were treated surgically.

The groups were randomized from 06/26/1995 to 12/15/1998, allowing the assessment of cardiac events during a 5-year follow-up in each group.

The distribution of the demographic, clinical, and angiographic characteristics of the patients undergoing TCA and CABG are shown in table I. No significant differences were observed in regard to mean age, sex, dyslipidemia, diabetes mellitus, systemic arterial hypertension, smoking, and anginal state. The groups differed regarding previous acute myocardial infarction ( $P = 0.004$ ); the TCA group had a significantly greater percentage than that in the CABG group (60%).

Concerning the administration of beta-blockers and calcium channel blockers, the CABG group received a significantly greater percentage of those drugs than did the TCA group. However, the percentage of the previous use of aspirin, ACE inhibitors, statins, insulin, and oral antidiabetic drugs was similar in both groups (tab. II).

Concerning cine coronary angiographic characteristics, 3-vessel coronary disease predominated over 2-vessel coronary disease in both groups ( $P = 0.117$ ). In the TCA group, 60 (57.1%) patients had 3-vessel stenoses, and, in the CABG group, 71 (67.6%) patients did.

In the CABG group, 332 vessels were treated, revealing a mean of 3.16 grafted vessels per patient as follows: 98 (93.33%) received at least one anastomosis using arterial grafting, which resulted in an anatomical revascularization considered complete in 71.4% of the patients. At least one of the internal thoracic arteries (ITA) was used in 71 (67.61%) patients; 2 thoracic arteries and the radial artery were used in 13 (12.38%) patients; and the gastroepiploic artery was used in 3 (2.85%) patients.

During the 5-year follow-up, 10 deaths of cardiac origin and 3 nonfatal AMIs occurred; of the latter, one required new coronary artery bypass grafting, and 2 required coronary angioplasty.

In the TCA group, 260 vessels were treated. The mean number of vessels treated per patient was 2.47 and the success rate was 85% (221 in 260). Revascularization was considered complete in 53 (50.47%) patients. The percentages of technical resources used to clear the vessels by the interventional cardiologist were: 74 (70%) stents; 65 (61.9%) balloons; 9 (8.57%) interventions using isolated rotational atherectomy; 2 (7.9%) interventions using the association of atherectomy and stent; and only 2 (1.9%) patients underwent the laser technique.

During the 5-year follow-up, 13 (12.38%) deaths of cardiac origin occurred, 9 (8.57%) patients experienced nonfatal AMI, 20 (19.04%) patients required a new coronary angioplasty, and 6 (5.71%) underwent coronary artery bypass grafting.

The combined event-free survival rate was significantly different

between the groups studied. Patients in the TCA group had a greater number of combined events, defined as the need for revascularization, AMI or death of cardiac origin, when compared with the patients treated with the surgical therapy – CABG ( $P < 0.001$ ) (fig. 1).

No significant difference in death of cardiac origin was observed in the 2 therapeutic strategies. Thirteen deaths occurred in the TCA group and 10 in the CABG group. The cumulative survival rate in 5 years was 95 (88.39%) and 92 (84.93%) patients in the CABG and TCA groups, respectively (fig. 2).

During the 5-year follow-up, 3 (2.85%) patients in the CABG group and 9 (8.57%) patients in the TCA group had acute myocardial infarction ( $P = 0.0668$ ) (fig. 3).

Only 1 (0.95%) patient in the CABG group and 6 (5.71%) in the TCA group required additional coronary artery bypass grafting ( $P = 0.0872$ ).

During the same period, 2 (1.90%) patients in the CABG group and 20 (19.04%) in the TCA group required reintervention through coronary angioplasty ( $P < 0.003$ ).

One important difference between the 2 groups related to the frequency of interventions required during the 5-year follow-up. Three (2.85%) reinterventions were required in the surgical group patients, and 26 (24.76%) additional reinterventions were required in the TCA group ( $P < 0.001$ ) (fig. 4).

In the 5-year follow-up, a significant difference was found in the presence of angina in the groups studied. Therefore, of the 75 patients in the CABG group who reported anginal symptoms at the beginning of the study, 65 were angina-free at the end of the study ( $P = 0.001$ ).

In regard to the TCA group, the same tendency was observed as follows: of the 83 patients with anginal symptoms at the beginning of the study, 63 were angina-free at the end of the study ( $P = 0.001$ ).

Regarding the presence of exercise-induced ischemia, statistical significance was also found among patients in both groups, who had an exercise test with an ischemic response. In the CABG group, the statistical significance was similar: of the 45 patients who developed exercise-induced ischemia at the beginning of the study, 23 did not reproduce the same test at the end of the study ( $P = 0.001$ ) (fig. 5).

In the TCA group, of the 35 patients who developed exercise-induced ischemia at the beginning of the study, 17 did not reproduce the same test at the end of the study ( $P = 0.002$ ) (fig. 6).

## Discussion

The present study aimed at comparing the efficacy of myocardial revascularization between 2 different methods (CABG and TCA), involving 210 patients who survived for 5 years after their procedures and were discharged from the hospital. The 2 interventions led to significant relief of the anginal symptoms during the follow-up period. However, the 5-year results showed that the proportion of asymptomatic patients with ischemic tests was similar in the 2 types of intervention. Those results were obtained with a significant increase in the need for a new revascularization in the TCA group.

The CASS study showed that, in patients with multivessel coronary disease with normal left ventricular function, stable angina, predominance of 2-vessel (40%) and 3-vessel impairment in a

**Table I - Demographic, clinical and angiographic characteristics of patients undergoing TCA and CABG**

Variable Level	Groups		P
	TCA n=105	CABG n=105	
<b>Clinical findings</b>			
Age (years)	62.12±9.63	60.93±8.91	0.354
Sex Male	69 (65.7%)	73 (69.5%)	0.555
Female	36 (34.3%)	32 (30.5%)	
Diabetes	30 (28.6%)	45 (42.9%)	0.153
Smoking	42 (40.0%)	29 (27.6%)	0.067
Hypertension	69 (65.7%)	68 (64.8%)	0.885
AMI	63 (60.0%)	42 (40.0%)	0.004
Stable Angina	97 (92.4%)	91 (86.7%)	0.176
<b>Laboratory</b>			
<b>(values in mg/dL)</b>			
<b>Means and standard deviations</b>			
Cholesterol	229.70±51.26	220.83 ± 48.70	0.204
Triglycerides	195.98 ± 109.12	199.31 ± 119.12	0.834
LDL-Cholesterol	151.40 ± 42.94	147.51 ± 42.23	0.529
HDL-Cholesterol	37.74 ± 9.83	36.53 ± 10.34	0.397
Glucose	123.36 ± 54.58	124.70 ± 44.12	0.846
<b>Exercise electrocardiographic test</b>			
Ischemic	51 (48.57%)	62 (59.04%)	NS
Nonischemic	13 (12.38%)	13 (12.38%)	NS
Inconclusive	26 (24.76%)	17 (16.19%)	NS
<b>Angiographic data</b>			
Impaired arteries (n)			
2-vessel	45 (42.85%)	34 (32.38%)	0.117
3-vessel	60 (57.15%)	71 (67.62%)	0.117
Ejection fraction	67 ± 7.3	68 ± 7.5	0.329

n - number; AMI - acute myocardial infarction; LDL - low-density lipoprotein; HDL - high-density lipoprotein; TCA - transluminal coronary angioplasty; CABG - coronary artery bypass grafting.

**Table II - Medication used in patients undergoing TCA and CABG**

Medication	Group				P
	TCA		CABG		
	n	%	n	%	
Beta-blocker	77	73,30	89	84,8	0,042
Calcium channel blockers	48	45,70	63	60,0	0,038
Aspirin	105	100,00	100	95,2	0,060
ACE inhibitors	37	35,20	32	30,5	0,463
Statins	19	18,10	15	14,3	0,454
Oral antidiabetic agents	21	20,00	15	14,28	0,147
Insulin	9	8,60	30	28,60	0,193

n - number of patients; TCA - transluminal coronary angioplasty; CABG - coronary artery bypass grafting.



smaller percentage (31.5%), the mean annual mortality rate for patients undergoing CABG was 1.1% (0.7%, 1.0%, and 1.4%, respectively, for 1, 2, and 3 vessels), indices similar to the indices for clinical treatment at that time <sup>7</sup>.

The CASS study showed no difference between the clinical treatment and CABG in regard to mortality, Q-wave myocardial infarction, or the event-free survival rate in the 5-year follow-up. The benefit of CABG was restricted to the 3-vessel subgroup with ventricular dysfunction, and EF < 50%, whose annual mortality rate with clinical treatment reached 12.5% <sup>30</sup>.

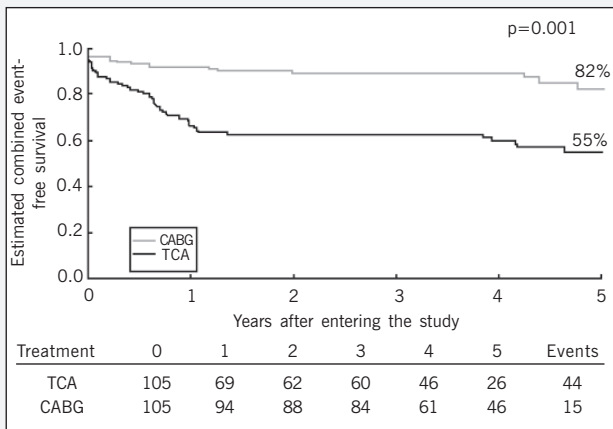


Fig. 1 - Probability of combined event-free survival in patients in the TCA and CABG groups.

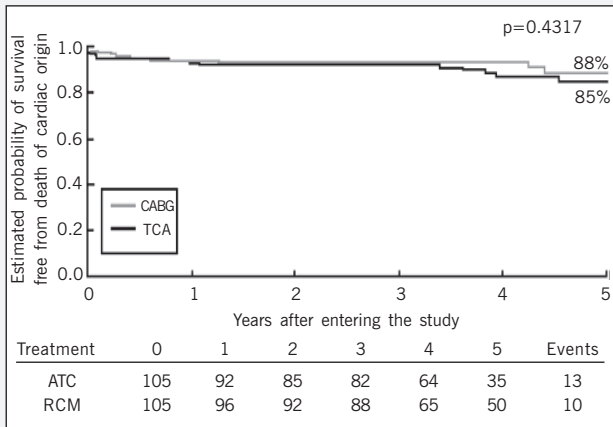


Fig. 2 - Probability of survival free from death of cardiac origin in patients in the TCA and CABG groups.

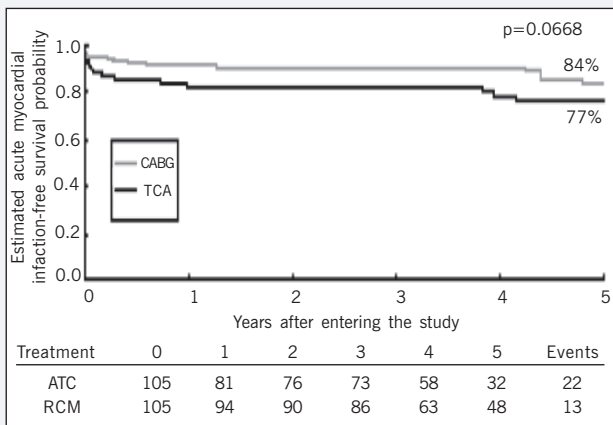


Fig. 3 - Probability of acute myocardial infarction-free survival in patients in the TCA and CABG groups.

At the end of the 1980s and throughout the 1990s, several studies were carried out aiming at comparing the 2 forms of myocardial revascularization, allowing the use of multiple arterial grafts in CABG, and stents and atheroablation devices in TCA.

The profile of the population involved in the present study reflects a sample similar to that of multicenter studies around the world. The groups comprised patients predominantly white and of the male sex, with a mean age of 60 years, with a high prevalence

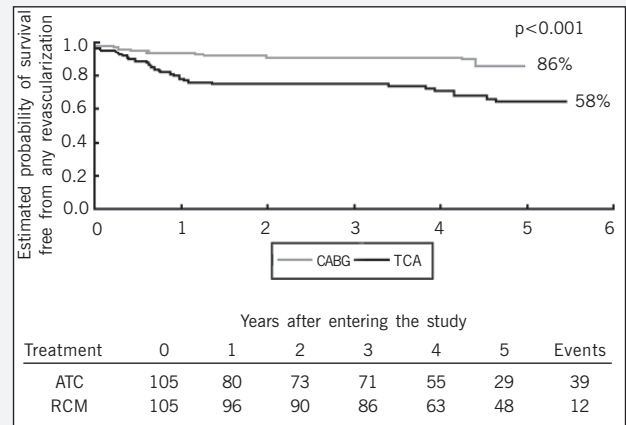


Fig. 4 - Probability of survival free from any revascularization in patients in the TCA and CABG groups.

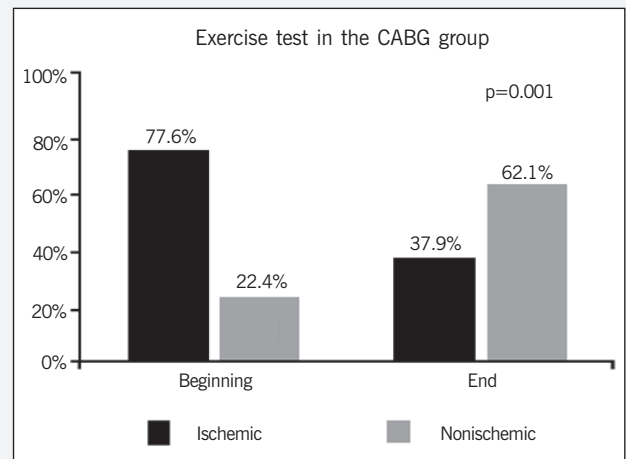


Fig. 5 - Exercise-induced ischemia at the beginning and end of the study in the CABG group. CABG = coronary artery bypass grafting.

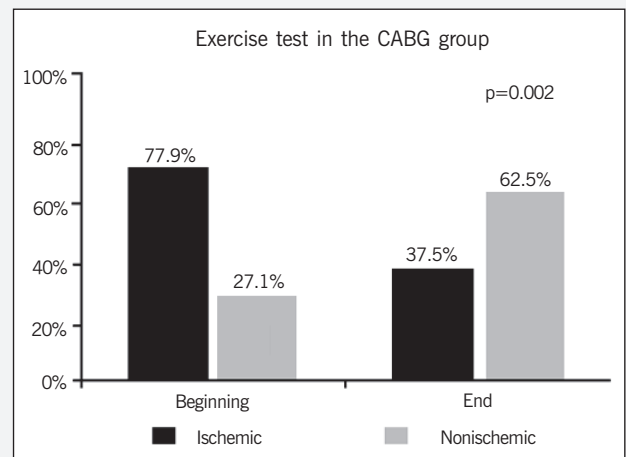


Fig. 6 - Exercise-induced ischemia at the beginning and end of the study in the TCA group. TCA = transluminal coronary angioplasty.

of previous acute myocardial infarction, systemic arterial hypertension, dyslipidemia, diabetes mellitus, and smoking. Stable angina and CCS FC II and III prevailed in the clinical studies, ranging from 14% to 65% (RITA<sup>9</sup>, GABI<sup>10</sup>, ERACI<sup>11</sup>, CABRI<sup>12</sup>, EAST<sup>17</sup>, BARI<sup>14</sup>). Therefore, comparisons between the results of the present study and those reported in the literature could be established.

Analyzing the characteristics of myocardial revascularization in the present study, in which 3-vessel patients predominated, complete revascularization was achieved in 72.38% of the CABG group and in 50.48% of TCA group. This difference was explained by the greater freedom of choice and encouragement allowed to the cardiovascular surgeon to perform a greater number of anastomoses in vessels with lesions = 50% or occluded vessels.

More recent studies involving incomplete myocardial revascularization through TCA have concluded that early coronary re-intervention was required more (a 2.5-fold greater risk) due to recurring angina. However, no change was observed in the rate of major cardiac events such as death and nonfatal infarction<sup>18,30-36</sup>.

The BARI trial, which compared patients undergoing incomplete revascularization referred for TCA and CABG and who were followed up for 5 years, showed a longer survival without angina and revascularization in the CABG group patients as compared with those in the TCA group<sup>36</sup>. In that same study, when complete revascularization was compared with the incomplete one in the TCA group, survival free from surgical revascularization was significantly longer in the group with complete revascularization. However, no difference was observed in the following events during a 5-year follow-up: death of cardiac origin, acute myocardial infarction, and unstable angina.

In the present study, the surgical result was better than that of angioplasty in regard to cardiac event-free survival due to the significantly smaller need for re-intervention induced by recurring angina (13.7% vs 41.6%) ( $P < 0.0001$ ). However, no difference in the incidence of death of cardiac origin or acute myocardial infarction was observed between the 2 groups in a follow-up of 5 years at most. This superiority may be explained by the use of multiple arterial grafts, complete revascularization in the CABG group, and elevated indices of symptomatic restenosis, requiring revascularization within the first 12 months in the TCA group.

The studies with an objective similar to that of the present study and a follow-up period ranging from 1 to 5 years, involving 4,130 patients with a predominance of stable coronary artery disease, showed no difference in mortality between the TCA and CABG groups<sup>14,17</sup>. A meta-analysis including the CABRI, EAST, ERACI, GABI, and RITA studies with a total of 2,943 patients assessed, showed no significant differences in regard to the incidence of death or acute myocardial infarction in a follow-up period ranging from 1 to 3 years, but showed a longer angina-free survival in the CABG group as compared with that in the TCA group (odds ratio = 1.57, CI = 1.32 to 1.87,  $P < 0.00001$ )<sup>36</sup>.

More recent studies with clinical follow-up of up to 8 years (EAST and BARI) have shown similar indices of death and acute myocardial infarction between the groups randomized for TCA and CABG. On the other hand, a significant difference was observed in the need for re-intervention for angina control (BARI: 72.8% vs 13.8%;  $P < 0.001$ ; EAST: 65.3% vs 26.5%)<sup>37,38</sup>.

More recently with implementation of the use of new devices

for percutaneous coronary intervention, some randomized studies stand out, such as the ARTS study, which analyzed 1,205 patients randomized into 2 groups: TCA-stents or CABG. The primary objective included the occurrence of cardiac event-free survival and stroke in a 1-year follow-up. No significant difference between the 2 groups was evident when the primary objective was achieved, but a difference was observed in the need for more revascularizations in the TCA-stent and CABG groups (16.8% vs 3.5%). Cardiac event-free survival was smaller in the TCA-stent group (73.8%) than in the CABG group (87.8%) ( $P < 0.001$ )<sup>39</sup>.

The present study allowed the comparative analysis of symptomatic myocardial ischemia and anginal state, as well as of exercise-induced myocardial ischemia at different times between the 2 groups (TCA and CABG).

The analysis of angina in comparative studies between CABG and TCA using a balloon catheter showed a greater prevalence in the TCA group by the end of the first year of follow-up<sup>40</sup>. The RITA study already showed a progressive decrease in the prevalence of angina in the third year of follow-up<sup>41</sup>.

At the end of the fifth year of follow-up, 38% of the CABG group and 40% of the TCA group had angina, with a significant improvement in the initial moment, but without any difference between the 2 types of treatment. These results are similar to those of the BARI trial and a meta-analysis of 7,964 patients in 13 randomized studies comparing TCA and CABG up to the year 2001, which allowed the inclusion of studies using stents in the comparative analysis. Those results may be justified by the elevated number of reinterventions in the TCA group and the progression of atherosclerotic disease in the native bed and in the grafts in the medium run in patients with 3-vessel coronary artery disease<sup>41,42</sup>.

The results of the exercise test have shown a similar and significant reduction in the exercise-induced ischemic response in the CABG and TCA groups (37.9% and 37.5%, respectively) in 5 years. The BARI trial, in the same follow-up period, reported similar results in the TCA and CABG groups (28% and 31%, respectively); however, in the sample studied here, patients with 3-vessel coronary artery disease predominated, while in the BARI trial, 2-vessel coronary artery disease predominated<sup>43</sup>.

Despite the advances in the techniques and in the types of endoprostheses, the rate of restenosis after angioplasty remains elevated, between 20% and 40% in 6 months. At the end of the 1990s, drug-eluting stents appeared, such as the stent coated with rapamycin, a drug capable of inhibiting the neointimal proliferation of smooth muscle cells<sup>44</sup>. A randomized multicenter study with 238 patients, 50% of whom had unstable angina and whose mean age was 60.7 years, assessed regular stents and the rapamycin-coated stent. The need for revascularization was 22.9% in the regular stent group as compared with 0% in the rapamycin-coated stent group ( $P = 0.001$ ) in a 1-year follow-up<sup>45</sup>. However, the rate of noncritical restenosis was not revealed.

In regard to survival without a new revascularization, the surgical therapy in the present study was better than the percutaneous coronary intervention. That superiority may be reflected by a small rate of perioperative complications, improvement in symptoms, and a more complete myocardial revascularization. The broad use of arterial grafts may have played a relevant role during the 5-year follow-up.



An advantage of the percutaneous intervention option is the possibility that cardiologists may review their initial decisions based on the clinical and angiographic results of each lesion considered. The advantage of surgeons is that they may use grafts for the arteries with small degrees of stenosis (<50%), as well as for those with a high degree of stenosis and also chronically occluded. Based on the number of vessels treated, the degree of revascularization achieved with surgery certainly seems more anatomically complete than that achieved with angioplasty ( $P < 0.0001$ ).

In addition, the technological advances achieved with angioplasty have greatly improved in recent years. The resources of atherectomy, laser, regular stents, and, more recently, the drug-eluting stents may be commonly used for treating coronary stenosis. However, no evidence exists that those resources provide better results regarding death and nonfatal infarction in patients with multivessel coronary artery disease. However, we believe that in the near future, the solution to the problem of restenosis may favorably influence the results.

Finally, the satisfactory results obtained with CABG may be due to the use of arterial grafts as anastomosis, as well as to the normal ventricular function, which, per se, provides a good prognosis in most patients. These results lead to reflection and create expectations and questions about the so-called underuse of the number of grafts<sup>46</sup>.

The limitations of this study need to be considered, and there is a consensus that, in the absence of contraindications, all patients should receive complete medicamentous therapy during the outpa-

tient clinic follow-up, independently of the randomized strategy. This study, initiated in 1995, did not contemplate the current diffuse and beneficial use of statins and angiotensin-converting enzyme inhibitors (ACE) in the primary, secondary, and tertiary prevention of coronary artery disease. However, no significant difference existed between the groups studied regarding the proportion of patients receiving statins and ACE inhibitors, although they were used in a small percentage. In addition, the use of anti-ischemic and lipid-lowering drugs is similar to that of the BARI trial.

Another potential limitation was the constant development of the revascularization techniques, both surgical and percutaneous. The appearance of synthetic polymer-eluting stents, which store and slowly release drugs that inhibit neointimal hyperplasia, has contributed to a reduction in restenosis of the treated lesion, and, consequently, to a significant decrease in the need for reintervention in the TCA group. Another inevitable limitation of this study is its long period of follow-up, during which new drugs appeared in clinical practice, such as clopidogrel and IIb/IIIa inhibitor, which were not previously available. Finally, the size of the sample studied did not have the power to test intergroup differences; however, these differences are relevant to the results of the research.

In conclusion, surgical and percutaneous myocardial revascularization provided a significant and similar reduction in anginal symptoms and exercise-induced myocardial ischemia. In addition, the incidence of death of cardiac origin was similar in the 2 groups studied. When the need for new interventions during long-term follow-up was considered, surgery provided significantly better results.

## References

- Varnauskas E, and the European Coronary Surgery Study Group. Twelve-year follow-up of survival in the randomized European Coronary Surgery Study. *N Engl J Med* 1988; 319:332-37.
- Bell MR, Gersh BJ, Schaff HV et al and The Investigators of the Coronary Artery Surgery Study. Effect of completeness of revascularization on long-term outcome of patients with three-vessel disease undergoing coronary artery bypass surgery. A report from the Coronary Artery Surgery Study (CASS) Registry. *Circulation* 1992; 86: 446-57.
- Bourassa MG, Campeau L, Lespérance J, Grondin CM. Changes in grafts and coronary arteries after saphenous vein aortocoronary bypass surgery: results at repeat angiography. *Circulation* 1982; 65 (suppl II):90-7.
- Fitzgibbon GM, Leach AJ, Kafka HP, Keon WJ. Coronary bypass graft fate: long-term angiographic study. *J Am Coll Cardiol* 1991; 17: 1075-80.
- Goldman S, Copeland J, Moritz T et al. Long-term patency (3 years) after coronary artery surgery. Effects of aspirin: results of a VA Cooperative Study. *Circulation* 1994; 89:1138-43, 1994.
- Grondin CM, Campeau L, Thornton JC et al. Coronary bypass grafting with saphenous vein. *Circulation* 1989; 79 (suppl): 24-9.
- CASS Principal Investigators and Their Associates. Coronary Artery Study (CASS): a randomized trial of coronary artery bypass surgery. Survival data. *Circulation* 1983, 68: 939-50.
- Green GE, Stertzer SH, Gordon RB, Tice DA. Anastomosis of the internal mammary artery to distal left anterior descending coronary artery. *Circulation* 1970; 41:II-79-II-84.
- RITA Trial Participants. Coronary angioplasty versus coronary artery bypass surgery: the Randomized Intervention Treatment of Angina (RITA) trial. *Lancet* 1993; 341: 573-80.
- Hamm CW, Reimers J, Ischinger T et al for the German Angioplasty Bypass Surgery Investigation (GABI). A randomized study of coronary angioplasty compared with bypass surgery in patients with symptomatic multivessel coronary disease. *N Engl J Med* 1994; 331: 1037-43, 1994.
- Rodríguez A, Bouillon F, Perez-Baliño N et al on behalf of the Eraci Group. Argentine randomized trial of percutaneous transluminal coronary angioplasty versus coronary artery bypass surgery in multivessel disease (ERACI): in-hospital results and 1-year follow-up. *J Am Coll Cardiol* 1993; 22: 1060-67.
- CABRI Trial Participants. First-year results of CABRI (Coronary Angioplasty versus Bypass Revascularization Investigation). *Lancet* 1995; 346: 1179-84.
- King III SB, Lembo NJ, Weintraub WS et al for the East Investigators. Emory Angioplasty versus Surgery Trial (EAST): design, recruitment, and baseline description of patients. *Am J Cardiol* 1994; 75: 42C-59C.
- BARI Investigators. Comparison of coronary bypass surgery with angioplasty in patients with multivessel disease. *Engl J Med* 1996; 335: 217-25.
- Cameron A, Kemp HGJ, Green GE. Bypass surgery with the internal mammary artery graft: 15 year follow up. *Circulation* 1986; 74(suppl II): 30-6.
- Fiore AC, Naunheim KS, Dean P et al. Results of internal thoracic artery grafting over 15 years: single versus double grafts. *Ann Thorac Surg* 1990; 49: 202-8.
- King III SB, Lembo NJ, Weintraub WS et al for the Emory Angioplasty Versus Surgery Trial (EAST). A randomized trial comparing angioplasty with coronary bypass surgery. *Emory Angioplasty versus Surgery Trial. N Engl J Med* 1994; 331: 1044-50.
- Bourassa MG, Yeh W, Holubkov R, Sopko G, Detre KM, for the Investigators of the NHLBI Ptca Registry. Long-term outcome of patients with incomplete vs complete revascularization after multivessel PTCA. A report from the NHLBI PTCA Registry. *Eur Heart J* 1998; 19: 103-11.
- Thomas ES, Most AS, Williams DO. Coronary angioplasty for patients with multivessel coronary artery disease: follow-up clinical status. *Am Heart J* 1988; 115: 8-13.
- Reeder GS, Holmes Jr DR, Detre K, Costigan T, Kelsey SF. Degree of revascularization in patients with multivessel coronary disease: a report from the National Heart, Lung and Blood Institute Percutaneous Transluminal coronary Angioplasty Registry. *Circulation* 1988; 77: 638-44.
- Campeau L. Grading of angina pectoris. *Circulation* 1976; 54: 522-23.
- BARI Protocol. Protocol for the Bypass Angioplasty Revascularization Investigation (BARI). *Circulation* 1991; 84(suppl V):V-1-V-27.
- Chaitman BR, Rosen AD, Williams DO et al. Myocardial infarction and cardiac mortality in the Bypass Angioplasty Revascularization Investigation (BARI) randomized trial. *Circulation* 1997; 96: 2162-70.
- Seldinger SY. Catheter replacement of the needle in percutaneous arteriography. A new technique. *Acta Radiol* 1953; 39: 368-76.
- Dodge HT, Sandler HS, Baxley WA, Hawley RR. Usefulness and limitations of radiographic methods for determining left ventricular volume. *Am J Cardiol* 1966; 18: 10-24.
- Ryan TJ, Bauman WB, Kennedy JW et al. Guidelines for percutaneous transluminal coronary angioplasty. A report for the American College of Cardiology / American Heart Association Task Force on Assessment of Diagnostic and Therapeutic

- Cardiovascular Procedures (Committee on Percutaneous Transluminal Coronary Angioplasty). *J Am Coll Cardiol* 1993; 22: 2033-54.
27. Kirklin JW, Akins CW, Blackstone EH et al. Guidelines and indications for coronary artery bypass graft surgery. A report of the American College of Cardiology / American Heart Association Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures (Subcommittee on Coronary Artery Bypass Graft Surgery). *J Am Coll Cardiol* 1991; 17: 543-89.
  28. Leon MB, Baim DS, Popma JJ et al for the Stent Anticoagulation Restenosis Study Investigators. A clinical trial comparing three antithrombotic-drug regimens after coronary-artery stenting. *N Engl J Med* 1998; 339: 1665-71.
  29. Rosner B. *Fundamentals of Biostatistics* 2<sup>nd</sup> ed. Boston, PWS Publishers 1986; 584.
  30. Cowley MJ, Vandermael M, Topol EJ et al for the Multivessel Angioplasty Prognosis Study (MAPS) Group. Is traditionally defined complete revascularization needed for patients with multivessel disease treated by elective coronary angioplasty? *J Am Coll Cardiol* 1993; 22: 1289-97.
  31. Deligonul U, Vandormael MG, Kern MJ et al. Coronary angioplasty: a therapeutic option for symptomatic patients with two and three vessel coronary artery disease. *J Am Coll Cardiol* 1988; 11: 1173-9.
  32. Faxon DP, Ghalillli MD, Jacobs AK et al. The degree of revascularization and outcome after multivessel coronary angioplasty. *Am Heart J* 1992; 123: 854-9.
  33. Samson M, Meester HJ, De Feyter PJ, Strauss B, Serruys PW. Successful multiple segment coronary angioplasty: effect of completeness revascularization in single-vessel multilesions and multivessels. *Am Heart J* 1990; 120:1-12.
  34. Vandormael MG, Chaitman BR, Ischinger T et al. Immediate and short-term benefit of multilesion coronary angioplasty: influence of degree of revascularization. *J Am Coll Cardiol* 1985; 6: 983-91.
  35. Rita Trial Participants. Coronary angioplasty versus medicine therapy for angina: the second Randomized Intervention Treatment of Angina (RITA-2) trial. *Lancet* 1997; 350: 461-8.
  36. Sim I, Gupta M, McDonald K, Bourassa MG, Hlatky MA. A meta-analysis of randomized trials comparing coronary artery bypass grafting with percutaneous transluminal coronary angioplasty in multivessel coronary artery disease. *Am J Cardiol* 1995; 76:1025-9.
  37. King III SB, Kosinsky AS, Guyton RA, Lembo NJ, Weintraub WS, for the Emory Angioplasty Versus Surgery Trial (EAST) Investigators. Eight-year mortality in the Emory Angioplasty versus Surgery Trial (EAST). *J Am Coll Cardiol* 2000; 35: 1116-21.
  38. BARI Investigators. Seven-year outcome in the Bypass Angioplasty Revascularization Investigation (BARI) by treatment and diabetic status. *J Am Coll Cardiol* 2000; 35: 1122-9.
  39. Serruys PW, Unger F, Souza JE et al for the Arterial Revascularization Therapies Study Group (ARTS). Comparison of coronary-artery bypass surgery and stenting for the treatment of multivessel disease. *N Engl J Med* 2001; 344: 1117-24.
  40. Pocock SJ, Henderson RA, Rickards AF et al. Meta-analysis of randomized trials comparing coronary angioplasty with bypass surgery. *Lancet* 1994; 346:1184-9.
  41. Pocock SJ, Henderson RA, Seed P, Treasure T, Hampton JR, for the Rita Trial Participants. Quality of life, employment status, and anginal symptoms after coronary angioplasty or bypass surgery. *Circulation* 1996; 94: 135-42.
  42. Hoffmann SN, Tenbrook Jr. JA et al. A meta-analysis of randomized controlled trials comparing coronary artery bypass graft with percutaneous transluminal coronary angioplasty: One to eight-year outcomes. *J Am Coll Cardiol* 2003; 41:1293-304.
  43. Bari Investigators. Five-year clinical and functional outcome comparing bypass surgery with angioplasty in patients with multivessel coronary disease. *JAMA* 1997; 277: 715-21.
  44. Babapulle MN, Eisenberg MD. Coated stents for the prevention of restenosis: Part I. *Circulation* 2002, 106: 2734-40.
  45. Morice MC, Serruys PW, Sousa JE et al. For the Ravel Study Group. *N Engl J Med* 2002; 346: 1773-80.
  46. Hemingway H, Crook AM, Feder G et al. Underuse of coronary revascularization procedures in patients considered appropriate candidates for revascularization. *N Engl J Med* 2001; 344: 645-54.