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CLINICAL STUDIES

Surgical Versus Interventional Procedures in Patients With Multivessel Coronary Artery Disease

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Objective. This study examined the clinical characteristics, risk factors, indications and post-intervention complications of patients with multivessel coronary artery disease (CAD) submitted to either percutaneous transluminal coronary angioplasty (PTCA) and/or stent placement versus isolated coronary artery bypass grafting (CABG).

Background. Several studies have examined the relative safety and outcome of patients submitted to those interventional procedures compared to CABG. Limited information is available regarding that subject in Puerto Rico.

Methods. We performed a retrospective analysis of the clinical, angiographic, operative, interventional, post-operative and post-interventional data of patients submitted to those procedures in our institution from January 1998 to August 1998. There were 53 patients in the interventional group and 206 patients in the CAGB group. Comparison of quantitative variables by procedure was based on Student t test or Mann-Whitney-Wilcoxon test; categorical variables were compared using Pearson's chi-square or Fisher's exact test.

Results. There were no significant differences in age, body surface area, or cardiac risk factors. The most common pre-existing cardiovascular diagnosis was unstable angina. Three-vessel disease was the most common angiographic finding among CABG patients (61.7%). Two-vessel disease without left anterior descending coronary artery obstruction was significantly more common in the PTCA/Stent patients (58.5%). The vast majority (97.6%) of patients in the PTCA/Stent group and 52.4 % of the CABG group had two-vessel intervention. A significantly higher frequency of complications occurred in the CABG group. However, the incidence of major complications, in both groups was not statistically different. Atrial arrhythmias were significantly more frequent in the CABG group.

Conclusion. A larger prospective study should be conducted in order to corroborate these preliminary findings and seek effective solution to any identifiable problem.

Key words: Coronary artery bypass grafting (CABG), Percutaneous transluminal coronary angioplasty (PTCA), Stent, Multivessel coronary artery disease, Puerto Rico

C oronary artery disease (CAD) is the leading cause of mortality and morbidity in the industrialized world. Numerous advances in medical therapy and technology have led to a decline in the mortality rate of this condition during the past decades (1). Despite this observed reduction, this disorder continues to be a serious and potentially catastrophic illness and one which entails a great burden to the health resources of our community.

Medical management was the only available option for patients with this condition prior to the introduction of coronary artery bypass grafting (CABG) in 1968 (2). The Veterans Administration Cooperative Study was the first randomized trial to compare standard medical therapy versus surgical treatment for patients with stable angina and angiographically documented CAD (3,4). Subsequently, the Coronary Artery Surgery Study (CASS) showed that CABG resulted in better survival and quality of life in patients with left main CAD and those with

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multivessel disease with left ventricular dysfunction, as compared to others who received only medical therapy (5).

Since the introduction of percutaneous transluminal coronary angioplasty (PTCA) by Gruentzig in 1977, several research trials have compared this less-invasive therapeutic technique with CABG, particularly in patients with multivessel disease (6-11). Some of those studies showed no significant difference in the composite endpoint of overall mortality between the PTCA and CABG modalities. However, the largest of these trials, the Bypass Angioplasty and Revascularization Investigation (BARI), demonstrated that PTCA was similar to CABG regarding mortality; it also revealed that the outcome of diabetic patients was better when submitted to CABG as compared to PTCA (12).

Despite the remarkable advances in catheter technology and operator technique, PTCA remains limited by an 83% primary success rate, a 7% incidence of abrupt vessel closure and 38 to 50% late restenosis (13). Those limitations and the failure of new devices and drugs to impact on restenosis led to the development of intracoronary stent technology. Initially this technique was only indicated in the management of discrete stenosis (<15 mm of length) of native coronary arteries. However, an abundance of clinical experience has expanded its indications which now include saphenous vein bypass grafts, total occlusion, complex morphologies, restenotic lesions, abrupt vessel closure or dissection. Two of the most important studies related to stent placement, the Stent Restenosis Study (STRESS) in the United States and the Benestent (Belgium/Netherlands STENT) trials I and II in Europe, demonstrated better immediate angiographic results, fewer ischemic complications and a significant decrease in restenosis rate as compared to those submitted only to PTCA (14-16).

A previous study conducted at our institution in patients submitted to isolated CABG demonstrated that the rate of major complications such as death, perioperative myocardial infarction, reoperation to control bleeding, pulmonary embolism, and stroke was low (<3%) and similar to the rate of such complications reported elsewhere (17). Although many reports and research have been directed to compare the safety and outcome of patients undergoing those interventional procedures versus CABG in patients with multivessel CAD, limited information is available regarding that subject in Puerto Rico. Thus, the objectives of this study were to: 1) compare the clinical characteristics and cardiac risk factors of patients with multivessel CAD submitted for PTCA and/or stent implantation versus isolated CABG in our institution from January 1998 to August 1998, 2) describe the indications for those procedures, and 3) compare the post-procedural complications in both groups.

Methods

Patient group. The study was based on a retrospective analysis of clinical charts and procedure reports of consecutive patients with significant multivessel CAD ($\geq$ 50% diameter) who required isolated CABG, PTCA and/or stent implantation for two or three vessel CAD at the Cardiovascular Center of Puerto Rico and the Caribbean during the period from January 1998 to August 1998. Patients with single vessel CAD, single vessel intervention, significant left main coronary artery stenosis, previous CABG, PTCA or stent placement or valvular or congenital heart disease were excluded.

Study variables. Data on patient characteristics such as age, gender, cardiac risk factors, medical history, physical or angiographic findings, medical therapy prior to procedures, interventional and surgical priority, intra-procedural data (perfusion and clamp time, number of vessels intervened) and procedural-related complications were obtained from medical records.

Significant coronary artery occlusion was considered to be present if the luminal diameter was less than 50%. Surgical and interventional priority were defined as follows: a) emergency procedures: those performed the same day of cardiac catheterization and angiography, b) urgent procedures: those performed within 2-6 days of cardiac catheterization and angiography and c) elective: all the remaining procedures. Procedural complications were defined as any adverse reaction occurring prior to hospital discharge. A written permission for medical record review was requested and obtained from the Ethical and Research Committee of the Cardiovascular Center of Puerto Rico and the Caribbean.

Statistical analysis. Comparison of quantitative variables by procedure was performed using Student t test or Mann-Whitney-Wilcoxon test, when appropriate. Pearson's chi-square test or Fisher's exact test, when pertinent, were used to determine the presence of statistical associations among type of procedure, clinical characteristics and post-procedural complications. All characteristics that were statistically significant ($p<0.05$) in the bivariate analysis were included in a logistic regression model. This analysis was performed to determine if the development of in-hospital complications was associated with the type of procedure after adjusting for potential cofounders. Epi-Info version 6.04c was used for data entry and validation and the Statistical Analysis System (SAS) version 6.12 to perform the statistical analysis (18,19).

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Results

The distribution of clinical characteristics for the 206 patients submitted to CABG and the 53 patients who received PTCA/Stent placement are summarized in Table 1. No significant differences in age, body surface area or cardiac risk factors were observed for each group (p>0.05). The most frequent risk factor present for CAD was arterial hypertension (82.5% for CABG and 86.8% for PTCA/Stent, respectively). The most common pre-existing cardiovascular diagnosis was unstable angina in

Table 1. Characteristics of Patients Undergoing CABG (n=206) or PTCA/Stent Placement (n=53) *

Characteristic	CABG	PTCA/Stent	P value
Age (years)	63.0±8.9	64.6±11.6	0.362
Body surface area (m²)	1.81±0.20	1.82±0.21	0.078
Triglycerides (mg/dl)	227.7±139.8	187.5±85.9	0.678
Total cholesterol (mg/dl)	213.9 ± 45.5	192.8±37.6	0.295
Creatinine (mg/dl)	1.1 ± 1.2	1.0 ± 0.3	0.860
Cardiac risk factors			
Hypertension	170 (82.5)	46 (86.8)	0.456
Hypercholesterolemia	130 (63.1)	32 (60.4)	0.714
Male gender	120 (58.3)	34 (64.2)	0.435
Diabetes mellitus	108 (52.4)	27 (50.9)	0.847
Smoking history	97 (47.1)	19 (35.8)	0.142
Pre-existing cardiovascular diagnosis			
Unstable angina	141 (68.4)	34 (64.1)	0.551
Myocardial infarction	128 (62.1)	29 (54.7)	0.324
Peripherovascular disease	41 (19.9)	5 (9.4)	0.075
Stable angina	26 (12.6)	11 (20.7)	0.131
Congestive heart failure	26 (12.6)	3 (5.7)	0.221
Cerebrovascular disease	11 (5.3)	5 (9.4)	0.269
Comorbid conditions			
COPD	21 (10.2)	1 (1.9)	0.037
Asthma	19 (9.2)	1 (1.9)	0.087
Thyroid disease	10 (4.9)	4 (7.5)	0.494
Renal insufficiency	10 (4.9)	1 (1.9)	0.470
Medications			
Nitrates	178 (86.4)	39 (73.6)	0.024
Antiplatelets	151 (73.3)	51 (96.2)	<0.001
ACE † inhibitors	100 (48.5)	25 (47.2)	0.858
Beta blockers	96 (46.6)	29 (54.7)	0.292
Calcium channel blockers	72 (35.0)	16 (30.2)	0.514
Lipid lowering drugs	53 (25.7)	17 (32.1)	0.353
Diuretics	49 (23.8)	4 (7.5)	0.009

Cont.

Table 1. Characteristics of Patients Undergoing CABG (n=206) or PTCA/Stent Placement (n=53)*

Characteristic	CABG	PTCA/Stent	P value
Heparin	40 (19.4)	13 (24.5)	0.411
Digitalis	20 (9.7)	6 (11.3)	0.728
Alpha blockers	15 (7.3)	2 (3.8)	0.537
Angiotensin II receptor blockers	11 (5.3)	5 (9.4)	0.270
Streptokinase	10 (4.9)	1 (1.9)	0.339
Interventional Priority			
Elective	118 (57.3)	35 (66.0)	0.350
Urgent	70 (34.0)	16 (30.2)	
Emergent	18 (8.7)	2 (3.8)	
Indication for cardiac catheterization			
Stable angina	3 (1.5)	5 (9.4)	0.010
Unstable angina	61 (29.6)	18 (34.0)	0.655
Angina post myocardial infarction	55 (26.7)	14 (26.4)	0.967
Post-myocardial infarction	38 (18.4)	6 (11.3)	0.218
Positive exercise treadmill test	27 (13.1)	4 (7.5)	0.266
Positive exercise radionuclide scintigraphy	14 (6.8)	3 (5.7)	1.000
Positive pharmacologic radionuclide scintigraphy	4 (1.9)	3 (5.7)	0.153
Coronary angiographic findings			
Two vessel disease with proximal LAD	53 (25.7)	11 (20.8)	0.454
Two vessel disease without proximal LAD	27 (13.1)	31 (58.5)	0.009
Three vessel disease with proximal LAD	77 (37.4)	7 (13.2)	<0.001
Three vessel disease without proximal LAD	50 (24.3)	4 (7.5)	0.007
Left ventricular ejection fraction (%)	50.5 ± 12.6	54.1 ± 10.9	0.068

*Where applicable, data are shown as mean ± standard deviation. Numbers in parentheses are percentages.
† Angiotensin converting enzyme.
LAD = left anterior descending coronary artery.

both the CABG (68.4%) and PTCA/Stent (64.1%) groups. There was a higher proportion of chronic obstructive pulmonary disease (COPD) among CABG patients (10.2%) compared with 1.9% in PTCA/Stent and this difference was statistically significant (p=0.037). In patients submitted to CABG, the most common medications were nitrates (86.4%) and antiplatelet agents (73.3%), however, antiplatelets (96.2%) followed by nitrates (73.6%) were most commonly utilized in the PTCA/Stent group. These differences were also statistically significant (p<0.05). In addition, a higher proportion of diuretic use was observed in CABG patients

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(23.8%) compared with only 7.5% in the PTCA/Stent group (p=0.009). CABG was elective in 118 patients (57.3 %) whereas PTCA/Stent was elective in 35 patients (66%). The most frequent indications for cardiac catheterization were unstable angina (CABG, 29.6% versus PTCA/Stent, 34.0%), angina post myocardial infarction (CABG, 26.7% versus PTCA/Stent, 26.4%) and myocardial infarction (CABG, 18.4% versus PTCA/Stent, 11.3%), but these differences were not statistically significant (p>.05). A higher proportion of patients with stable angina was present in the PTCA/Stent group (9.4%) as compared with 1.5% in the CABG group (p=0.01).

Three-vessel disease with or without proximal left anterior descending (LAD) coronary artery occlusion was the most common angiographic finding among CABG patients, whereas two-vessel disease without proximal obstruction was more common among the PTCA/Stent group (p<0.05). There was a trend for a higher mean left ventricular ejection fraction in patients submitted to PTCA/Stent as compared to the CABG group (p=.068).

Table 2 summarizes the intraoperative and post-operative characteristics of patients who underwent CABG. More than half (52.4%) of those patients underwent two vessel intervention. The median cardiopulmonary bypass time was 72 minutes, whereas the median ischemic time was 46 minutes. The most common vessel used for CABG was the LAD artery (97.6%), followed by the circumflex artery (62.6%) and the right coronary artery (52.9%).

Of the 53 patients who underwent PTCA/Stent, the vast majority (96.2%) had two vessel intervention (Table 3). The LAD artery was the dominant target vessel (43.4%), followed by the right coronary artery (42.1%) and the circumflex artery (42.1%).

Approximately 63.1% (130/206) of patients in the CABG group and 15.1% (8/53) in the PTCA/Stent group

Table 2. Intraoperative and Postoperative Characteristics of Patients who Underwent CABG (n=206)*

Characteristic	Number of patients
Number of vessels intervened	
Two vessels	108 (52.4)
Three vessels	98 (47.6)
Median cardiopulmonary bypass time (minutes)	72 (30-197)
Median ischemic time (minutes)	46 (22-121)
Median CKMB levels (IU/L)	22.8 (5.6-655)
Type of vessels	
LAD artery + circumflex artery	60 (29.1)
LAD artery + circumflex artery + right coronary artery	52 (25.2)
LAD artery + right coronary artery	36 (17.5)
LAD artery + diagonal branch	23 (11.2)
LAD artery + diagonal branch + right coronary artery	17 (8.2)
LAD artery + diagonal branch + circumflex artery	13 (6.3)
Right coronary artery + circumflex artery	3 (1.5)
Right coronary artery + circumflex artery + diagonal branch	1(0.5)
Diagonal branch	1 (0.5)
Need for transfusions	132 (64.1)
Packed red blood cells	129 (62.6)

*Where applicable, data are shown as median (Minimum-maximun). Numbers in parentheses are percentages. CKMB = Creatine kinase MB isoenzyme; LAD = left anterior descending coronary artery. Circumflex artery includes the obtuse marginal and the ramus branches; right coronary artery includes the posterior descending and the posterolateral branches.

Table 3. Intraprocedural and Postprocedural Characteristics of Patients who Underwent PTCA/Stent placement (n=53)*.

Characteristics	Number of patients
Number of vessels intervened	
Two vessels	51 (96.2)
Three vessels	2 (3.8)
Type of vessels	
Circumflex artery	14 (18.4)
LAD artery	14 (18.4)
Right coronary artery	12 (15.8)
Right coronary artery and circumflex artery	11 (14.5)
LAD artery + right coronary artery	9 (11.8)
LAD artery + circumflex artery	6 (7.9)
Diagonal branch	5 (6.6)
LAD artery + diagonal branch	4 (5.3)
Circumflex artery + diagonal branch	1 (1.3)

*Numbers in parentheses are percentages. LAD = left anterior descending coronary artery. Circumflex artery includes obtuse marginal and the ramus branches; right coronary artery includes the posterior descending and the posterolateral branches. These categories are not mutually exclusive and therefore the frequencies exceed the number of patients who underwent these procedures.

developed at least one complication (p<0.0001). The higher frequency of complications observed in the CABG group persisted after adjusting for potential confounders in the logistic regression model (p<0.0001) (data not shown). Table 4 shows the procedural-related major complications by study group. Differences in major complications including death, cardiac arrest, cerebrovascular accident, myocardial infarction, cardiogenic shock and pulmonary embolism were not statistically significant (p>0.05). Among the minor

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Table 4. Procedural-related Major Complications of Patients Undergoing CABG (n=206) or PTCA/Stent Placement (n=53)*.

Complication	CABG	PTCA/Stent	P value
Death	10 (4.9)	2 (3.8)	1.000
Excessive bleeding	10 (4.9)	0 (0.0)	0.222
Intubation > 48 hours	7 (3.4)	1 (1.9)	1.000
Ventricular arrhythmias	5 (2.4)	0 (0.0)	0.587
Renal dysfunction	5 (2.4)	0 (0.0)	0.587
Cardiac arrest	4 (1.9)	2 (3.8)	0.605
Cerebrovascular accident	4 (1.9)	0 (0.0)	0.585
Myocardial infarction	3 (1.5)	3 (5.7)	0.102
Cardiogenic shock	1 (0.5)	1 (1.9)	0.368
Pulmonary embolism	1 (0.5)	0 (0.0)	1.000
Need for intra-aortic balloon pump	1 (0.5)	0 (0.0)	1.000

*Numbers in parentheses are percentages.

procedural-related complications, a significant difference was observed: atrial arrhythmias were more frequent in the CABG group (p=.006) (Table 5). Other identified CABG related complications were: low cardiac output (11.2%), respiratory failure (7.3%), pleural effusion (5.8%), pneumothorax (2.4%), sepsis (1%) and pericarditis (0.5%). Complications particularly related to PTCA/Stent were coronary artery dissection (5.7%) and restenosis (3.8%) (data not shown).

Table 5. Procedural-related Minor Complications of Patients Undergoing CABG (n=206) or PTCA/Stent Placement (n=53)*.

Complication	CABG	PTCA/Stent	P value
Atrial arrhythmias	23 (11.2)	0 (0.0)	0.006
AV block requiring pacemaker	6 (2.9)	2 (3.8)	0.668
Pneumonia	5 (2.4)	0 (0.0)	0.587
New right bundle branch block	4 (1.9)	0 (0.0)	0.585
Bronchospasm	3 (1.5)	0 (0.0)	1.000
Need for reprocedure	3 (1.5)	0 (0.0)	1.000
Pulmonary congestion	2 (1.0)	0 (0.0)	1.000
Arterial thrombosis	2 (1.0)	0 (0.0)	1.000
Delirium	1 (0.5)	0 (0.0)	1.000

*Numbers in parentheses are percentages.

Discussion

We retrospectively studied a sample of patients with multivessel CAD submitted to either isolated CABG or PTCA/Stent placement at our institution from January 1998 to August 1998. The comparative analysis disclosed that similarly to a previous review of 200 consecutive patients submitted to CABG from March 1997 through June 1997 at this center, arterial hypertension was the most frequently related risk factor for CAD (17). The study also disclosed that hypercholesterolemia was more prevalent in the group of patients submitted to CABG. A finding of concern was that the utilization of lipid lowering agents was relatively low in both groups of patients. This suggests that in spite of the ample dissemination of the guidelines of the National Cholesterol Education Program Adult Treatment Panel (NCEP-ATPII) and the published beneficial effects of cholesterol lowering in primary and secondary prevention trials, many patients remain suboptimally treated (20). Similar findings and concerns have appeared in several recent reports in the medical literature (21). The analysis also disclosed a less than optimal utilization of beta blockers in both groups of patients and of antiplatelet agents in the CABG group. Both findings evidently show that a significant number of CAD patients are still receiving less than adequate medical therapy (22). Both situations illustrate the need to strengthen the education of physicians and of further disseminating the results of key clinical trials, to reduce the variations in treatment practices and assure that patients receive the most appropriate and effective medications in accordance with valid clinical evidence. In addition, there seems to be a need for patient counseling sessions to emphasize the importance of adequate compliance of the prescribed therapy. The observed increased ratio of utilization of antiplatelet agents in the group of patients that underwent PTCA/Stent, probably reflects the routine use of such agents in the protocol of patients submitted for those procedures.

Another finding of this study was that a significant higher proportion of CABG patients were on treatment with diuretics as compared to those in the PTCA/Stent group. A possible explanation for that finding is that, although not statistically significant, the number of patients with heart failure and lower ejection fraction were in the group that underwent CABG as compared to the ones in the PTCA/Stent group. The presence of lower ejection fraction values among CABG patients was consistent with the observations previously made in the studies by King (10) and Weintraub (23). A significantly higher frequency of COPD was found among the CABG patients compared with the PTCA/Stent group; a finding that placed these patients at higher risk of cardiorespiratory

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complications both during the operative and the post-operative periods.

Unstable angina was found to be the most common indication for cardiac catheterization in both the surgical and non-surgical groups; this was followed in frequency by post-myocardial infarction angina. The study disclosed a lower frequency of stable angina as indication for both procedures. One possible explanation for this finding was probably related to limited documentation on various medical records.

The PTCA/Stent group had a higher proportion of patients who underwent two-vessel without proximal LAD intervention. Three-vessel disease intervention was more common among CABG patients, with a higher frequency of those undergoing three vessel with proximal LAD surgery. These interventions were consistent with the findings of Bernstein and colleagues and the recommendations of the American Heart Association/American College of Cardiology Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures (24-26).

Several studies have demonstrated similar in-hospital complications and outcomes between patients with multivessel CAD submitted to CABG and percutaneous coronary interventions (27). The present study evaluated the in-hospital complications in patients who underwent either CABG or PTCA/Stent in two or three vessels. It showed that CABG patients were four times more likely to experience at least one complication when compared to the PTCA/Stent group. However, no statistically significant differences were observed in the frequency of major complications between both groups. Although the majority of these complications were minor and reversible, like atrial arrhythmias, the slightly higher than expected percentage of deaths in both groups and of myocardial infarction and cardiac arrest in the PTCA/Stent group during the evaluation period, merits further attention. A larger prospective study with emphasis on examining these parameters should be conducted in order to corroborate these preliminary findings and seek effective solution to any identifiable problem.

Resumen

Este estudio analizó las características clínicas, los factores de riesgo, las indicaciones, y las complicaciones durante y luego de cirugía de puente aorto-coronario o procedimientos de intervención por cateteres (angioplastía o implante de 'Stent') en pacientes con enfermedad de las arterias coronarias. Se analizaron los expedientes médicos de 206 pacientes quirúrgicos y 53 pacientes sometidos a angioplastía o implante de 'Stent' en el Centro Cardiovascular de Puerto Rico y del Caribe de enero de 1998 a agosto de 1998. No hubo diferencias en la edad, la superficie de área corporal o los factores de riesgo. La angina inestable fue la condición cardiovascular pre-existente más frecuente. Los hallazgos angiográficos principales fueron: enfermedad de tres vasos en los pacientes quirúrgicos (61.7%) y enfermedad de dos vasos sin obstrucción de la rama anterior descendente de la coronaria izquierda (58.5%) en el grupo de intervención por cateteres. La intervención más frecuente fue en dos vasos, tanto en el grupo de intervención por cateteres (97.6%) como en el grupo quirúrgico (52.4%). La incidencia de complicaciones fue significativamente mayor en el grupo quirúrgico. Sin embargo, aunque la frecuencia de complicaciones mayores en ambos grupos fue levemente superior a la informada en otros estudios, no hubo diferencia estadísticamente significativa entre los dos grupos. La frecuencia de arritmias atriales fue significativamente mayor en el grupo quirúrgico. Se recomienda la conducción de un estudio prospectivo dirigido a corroborar estos hallazgos preliminares para facilitar la búsqueda de soluciones efectivas a los problemas que se identifiquen.

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