# Comparison of Immediate Results and Follow-up of Patients with Single-Vessel and Multivessel Coronary Artery Disease Younger than 50 Years of Age Undergoing Coronary Stent Implantation

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***Objective -*** *To assess the in-hospital results and clinical follow-up of young patients (< 50 years) with multivessel coronary artery disease undergoing stent implantation in native coronary arteries and to compare their results with those of patients with single-vessel coronary artery disease.*

***Methods -*** *We retrospectively studied 462 patients undergoing coronary stent implantation. Patients were divided into 2 groups: group I (G-I) - 388 (84%) patients with single-vessel coronary artery disease; and group II (G-II) - 74 (16%) patients with multivessel coronary artery disease.*

***Results -*** *The mean age of the patients was 45±4.9 years, and the clinical findings at presentation and demographic data were similar in both groups. The rate of clinical success was 95% in G-I and 95.8% in G-II (P=0.96), with no difference in regard to in-hospital evolution between the groups. Death, acute myocardial infarction, and the need for myocardial revascularization during clinical follow-up occurred in 10.1% and 11.2% (P=0.92) in G-I and G-II, respectively. By the end of 24 months, the actuarial analysis showed an event-free survival of 84.6 % in G-I and 81.1% in G-II (P=0.57).*

***Conclusion -*** *Percutaneous treatment with coronary stent implantation in young patients with multivessel disease may be safe with a high rate of clinical success, a low incidence of in-hospital complications, and a favorable evolution in clinical follow-up.*

**Keywords:** multivessel, stent percutaneous, coronary angioplasty

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The prevalence of coronary artery disease, especially in its multivessel form, in the population aged less than 50 years has increased. This fact may be partially explained by the current lifestyle favoring sedentary habits, stress, obesity, smoking, and the greater incidence of type II diabetes mellitus, well-known factors of coronary risk [1-3].

Before the appearance of stents, the use of coronary angioplasty in the treatment of patients with multivessel disease was limited by the impossibility of approaching more complex lesions and the elevated rate of restenosis [4-6]. With the increased use of devices in the treatment of coronary artery disease, several studies have assessed their use in select or unselect groups of patients with multivessel disease[7,8]; however, the reports on the benefits of these devices in younger patients are scarce.

The objective of this study was to assess the in-hospital results and the clinical follow-up of patients with multivessel disease aged less than 50 years undergoing coronary stent implantation in native coronary arteries and to compare them with those of patients with single-vessel disease.

## Methods

This study comprised a consecutive series of 462 patients aged less than 50 years, undergoing percutaneous coronary intervention with coronary stent implantation from July 1997 to June 2002 at the Hospital da Beneficência Portuguesa of São Paulo.

The study sample comprised patients with "de novo" lesions in the native coronary artery with clinical findings of stable or unstable angina or documented myocardial ischemia. Patients undergoing angioplasty in the acute phase of myocardial infarction, adjunct procedures of atheroablation, and those with contraindications for antithrombotic or platelet antiaggregating therapy were excluded.

The patients were divided into the following 2 groups

according to the number of vessels treated: group I (G-I) - 388 (84%) patients with single-vessel coronary artery disease; and group II (G-II) - 74 (16%) patients with multivessel coronary artery disease.

All patients underwent 12-lead electrocardiography, before and after the procedure, for detecting ischemic changes or the appearance of new Q waves, or both. Blood samples were collected before the procedure and every 8 hours after the procedure for measuring the CKMB isoenzyme. Acute myocardial infarction was defined as an increase in CKMB isoenzyme greater than 3 times its normal value or the appearance of new Q waves in 2 or more contiguous leads in the electrocardiogram, or both [9].

Contrast-induced nephropathy was characterized by an elevation in creatinine greater than 50% of the value on admission or the need for dialysis.

Effort angina was classified according to the criterion of the Canadian Society of Cardiology [10], and unstable angina was classified according to the TIMI risk score [11].

The vascular complications were classified as follows: a) major – bleeding with a reduction > 5g/dL in the hemoglobin levels (puncture site, gastrointestinal, or genitourinary systems), hemorrhagic cerebral stroke, or the need for surgical repair of the artery used as an access route; b) minor - bleeding with a reduction > 3g/dL and < 5g/dL in the hemoglobin levels.

Clinical follow-up was performed through medical visits or telephone contact.

Significant coronary artery lesion was defined as a stenosis ≥ 70% assessed on quantitative digital angiography. The patients with multivessel disease selected had this degree of obstruction in at least 2 major epicardial vessels or in branches with a diameter > 2.5 mm.

The complexity of the lesions was classified into types A, B1, B2, or C, according to the criteria of the American Heart Association and American College of Cardiology [12] modified by Ellis et al [13].

Angiographic success was defined as a residual lesion < 20% with TIMI III flow, and clinical success [14] was defined as angiographic success in the absence of death, acute myocardial infarction, and need for emergency myocardial revascularization in the in-hospital phase.

The patients were medicated with oral acetylsalicylic acid (200 mg/day for an indefinite time) and ticlopidine (500 mg/day) or clopidogrel (attack dose of 300 mg followed by 75 mg/day) initiated, whenever possible, 3 days before the intervention and maintained for 30 days.

The femoral access route was preferred for the intervention. At the beginning of the procedure, intravenous heparin was administered at a dosage of 100 UI/kg of weight. After passing a 0.014 extrasupport guidewire, predilation with a balloon catheter was performed or a stent was directly implanted in selected cases.

All stents implanted during the study period were included in this analysis, and their implantation aimed at reaching a balloon/artery diameter ratio of 1.1-1.2. The mean final pressure of inflation was 15 atmospheres.

When the procedure was over, the arterial introducers were removed when the activated clotting time was < 180 seconds.

The use of glycoprotein (GP) IIb/IIIa inhibitors was up to the surgeon.

The primary outcome of the study was to assess the association of major cardiac events as follows: death from a cardiovascular cause, nonfatal acute myocardial infarction, and need for a new revascularization during clinical follow-up.

The following were considered secondary outcomes: clinical success index, in-hospital evolution, and recurrence of angina during clinical follow-up.

The continuous variables were expressed as mean and standard deviation and were compared using the Student *t* test. The categorical variables were presented as percentages, and the groups were compared using the chi-square test or Fisher exact test. The statistical significance level of $P \leq 0.05$ was adopted.

Event-free survival was analyzed using the Kaplan-Meier curve.

## Results

The mean age of the patients studied was 45±4.9 years. The mean ages of G-I and G-II patients were, respectively, 45±5 years and 46±7.9 years (P=0.11). In regard to sex, females represented 23.5% and 18.9% of G-I and G-II patients, respectively (P=0.59).

The clinical findings at the patient's presentation and the incidence of diabetes mellitus, systemic arterial hypertension, smoking, previous acute myocardial infarction, previous surgical or percutaneous revascularization, and ejection fraction < 30% were similar between the groups (tab. I).

The mean number of lesions treated in G-I and G-II was, respectively, 1.09 ± 0.42 and 2.42±0.35 (P<0.001), and the stent/patient ratio in G-I and G-II was, respectively, 1.03±0.55 and 1.47±0.54 (P<0.001). Stents were implanted in 62% of the lesions treated in the patients with multivessel coronary artery disease (G-II).

In G-II, 95.9% of the patients had lesions in 2 coronary arteries and 4.1% had lesions in 3 arteries.

No difference was observed in regard to the type of lesions treated in G-I and G-II, respectively: A + $B_1$ 33.4% vs 27.4% (P=0.33), $B_2$ 39.1% vs 40.8% (P=0.86), and C 27.5% vs 31.8% (P=0.48). Comparing the coronary arteries approached, the major artery treated in G-I was the anterior descending artery (50% vs 31.4% in G-II) (P=0.009), while in G-II, the major artery treated was the circumflex artery (34.6% vs 18% in G-I) (P<0.001). The right coronary artery and the left main coronary artery were treated in the same proportion in both groups.

The inhibitors of GP IIb/IIIa were used in 8% and 9.5% of the procedures in GI and GII, respectively (P=0.87) (tab. II).

Clinical follow-up data were obtained in 443 patients, 372 (98.9%) in G-I and 71 (97.3%) in G-II (P=0.93), with a mean follow-up of 206 ± 204 days for G-I and 196±160 days for G-II (P=0.69).

**Table I - Clinical characteristics**

| | Total | Group I | Group II | *p* |
|---|---|---|---|---|
| Total | 462 (100%) | 388 (84%) | 74 (16%) | - |
| Age (years)† | 45 ± 4.95 | 45 ± 4.96 | 46 ± 4.79 | 0.11 |
| Female sex | 105 (22.7%) | 91 (23.5%) | 14 (18.9%) | 0.59 |
| Clinical findings | | | | |
| Asymptomatic | 98 (21.2%) | 83 (21.4%) | 15 (20.3%) | 0.98 |
| Stable angina | 200 (43.3%) | 166 (42.8%) | 34 (45.9%) | 0.84 |
| Unstable angina | 164 (35.5%) | 139 (35.8%) | 25 (33.8%) | 0.91 |
| Diabetes mellitus | 85 (18.4%) | 71 (18.3%) | 14 (18.9%) | 0.95 |
| Smoking | 209 (45.2%) | 174 (44.8%) | 35 (47.3%) | 0.90 |
| Dyslipidemia | 198 (42.9%) | 168 (43.3%) | 30 (40.5%) | 0.87 |
| Arterial hypertension | 282 (61%) | 236 (60.8%) | 46 (62.2%) | 1.00 |
| LVEF < 30% | 15 (3.2%) | 13 (3.4%) | 2 (2.7%) | 0.94 |
| Previous AMI | 207 (44.8%) | 179 (46.1%) | 28 (37.8%) | 0.48 |
| Previous MR | 21 (4.5%) | 15 (3.9%) | 6 (8.1%) | 0.22 |
| Previous PCI | 32 (6.9%) | 27 (7%) | 5 (6.8%) | 0.85 |

LVEF- left ventricular ejection fraction; AMI- acute myocardial infarction; MR- myocardial revascularization surgery; PCI- percutaneous coronary intervention; † mean± standard deviation.

**Table II - Angiographic characteristics**

| | Total | Group I | Group II | *p* |
|---|---|---|---|---|
| Total of patients | 462 (100%) | 388 (84%) | 74 (16%) | - |
| Lesions treated | 601 (100%) | 422 (70.2%) | 179 (29.8%) | - |
| Implanted stents | 510 (100%) | 400 (78.4%) | 110 (21.6%) | - |
| Lesions/patient† | 1.30 ± 0.37 | 1.09 ± 0.42 | 2.42 ± 0.35 | <0.001 |
| Stents/patient† | 1.10 ± 0.55 | 1.03 ± 0.55 | 1.47 ± 0.54 | <0.001 |
| Double-vessel | 71 (15.4%) | - | 71 (95.9%) | - |
| Triple-vessel | 3 (0.6%) | - | 3 (4.1%) | - |
| Types of lesions | | | | |
| $A + B_1$ | 190 (31.6%) | 141 (33.4%) | 49 (27.4%) | 0.33 |
| $B_2$ | 238 (39.6%) | 165 (39.1%) | 73 (40.8%) | 0.86 |
| C | 173 (28.8%) | 116 (27.5%) | 57 (31.8%) | 0.48 |
| Right coronary | 194 (32%) | 134 (31.6%) | 60 (33.5%) | 0.83 |
| LCA # | 3 (0.5%) | 2 (0.4%) | 1 (0.5%) | 0.62 |
| Anterior descending artery | 267 (44.5%) | 211 (50%) | 56 (31.4%) | 0.009 |
| Circumflex artery | 37 (23%) | 75 (18%) | 62 (34.6%) | <0.001 |
| Use of inhibitor of GP IIb/IIIa | 38 (8.2%) | 31 (8%) | 7 (9.5%) | 0.87 |

† mean ± standard deviation; # LCA – main left coronary artery.

Primary outcome, such as death from a cardiovascular cause, acute myocardial infarction, and need for new revascularization, occurred in 10.1% and 11.2% of the G-I and G-II patients, respectively (P=0.92).

The incidence of death during that period in G-II was 0% and in G-II 0.8% (P=0.97). The rates of acute myocardial infarction and need for new revascularization were 0.8% and 1.4% (P=0.84), respectively, in G-I, and 8.5% and 9.8% (P=0.88), respectively, in G-II (tab. IV).

The actuarial analysis by the end of 24 months showed an event-free survival of 84.6% and 81.1% (P=0.57) in G-I and G-II, respectively (fig. 1).

Clinical success was high and similar in G-I and G-II: 95% and 95.8% (P=0.96), respectively.

The in-hospital evolution showed rates of major adverse cardiac events of 1.9% and 2.8% in G-I and G-II, respectively (P=0.96). No deaths occurred during the in-hospital phase. The incidences of stroke were 1.8% and 1.4% in G-I and G-II, respectively (P=0.82), and the incidences of renal failure after the intervention were 0.8% and 2.7% in G-I and G-II, respectively (P=0.4) (tab. III).

Recurrence of angina pectoris during clinical follow-up was observed in 12.6% of the patients in G-I and in 7% of the patients in G-II (P=0.31).

## Discussion

When choosing the invasive strategy for the treatment of multivessel coronary artery disease, it is important to consider the degree of revascularization that may be obtained, because this, when total revascularization is achieved, enables better angina control and longer survival during clinical follow-up [15].

The technique of percutaneous treatment using coronary angioplasty with a balloon catheter has limitations, mainly due to the impossibility of approaching more com-

**Table III - Results of in-hospital phase**

| | Total | Group I | Group II | *p* |
|---|---|---|---|---|
| Successful procedure | 449 (97.2%) | 376 (96.9%) | 73 (98.6%) | 0.99 |
| Clinical success | 440 (95.4%) | 369 (95%) | 71 (95.8%) | 0.97 |
| Failure | 13 (2.8) | 12 (3.1) | 1 (1.4) | 0.67 |
| MACE | 9 (1.8%) | 7 (1.9%) | 2 (2.8%) | 0.96 |
| Death | - | - | - | - |
| AMI | 5 (1%) | 4 (1.1%) | 1 (1.4%) | 0.71 |
| Emergency MR | 4 (0.8%) | 3 (0.8%) | 1 (1.4%) | 0.84 |
| Surgical | 2 (0.4%) | 2 (0.5%) | 0 (0%) | 0.73 |
| Percutaneous | 2 (0.4%) | 1 (0.3%) | 1 (1.4%) | 0.73 |
| Vascular complications | 9 (1.9%) | 8 (2.1%) | 1 (1.4%) | 0.95 |
| Minor | 6 (1.3%) | 5 (1.3%) | 1 (1.4%) | 0.60 |
| Major | 3 (0.6%) | 3 (0.8%) | 0 (0%) | 0.97 |
| ARF | 5 (1.1%) | 3 (0.8%) | 2 (2.7%) | 0.40 |
| Stroke | 8 (1.7%) | 7 (1.8%) | 1 (1.4%) | 0.83 |

MACE- major adverse cardiac event; AMI- acute myocardial infarction; ARF- acute renal failure.

**Table IV - Results of clinical outcome**

| | Total | Group I | Group II | *p* |
|---|---|---|---|---|
| Total of patients followed up | 443 (98.7%) | 372 (98.9%) | 71 (97.3%) | 0.93 |
| Mean time (days)† | 204 ± 197.4 | 206 ± 204.2 | 196 ± 160.2 | 0.70 |
| Clinical findings | | | | |
| Asymptomatic | 383 (86.5%) | 316 (84.9%) | 66 (93%) | 0.64 |
| Recurring angina | 50 (11.3%) | 47 (12.6%) | 5 (7%) | 0.31 |
| Stable angina | 32 (7.2%) | 29 (7.8%) | 4 (5.6%) | 0.73 |
| Unstable angina | 18 (4.1%) | 18 (4.8%) | 1 (1.4%) | 0.34 |
| MACE | 45 (9.9%) | 37 (10.1%) | 8 (11.2%) | 0.93 |
| Death | 3 (0.7%) | 3 (0.8%) | 0 (0%) | 0.97 |
| AMI | 4 (0.6%) | 3 (0.8%) | 1 (1.4%) | 0.84 |
| Revascularization | 38 (8.6%) | 31 (8.5%) | 7 (9.8%) | 0.88 |
| Death | | | | |
| Cardiac | 2 (0.5%) | 2 (0.6%) | 0 (0%) | 0.73 |
| Noncardiac | 1 (0.2%) | 1 (0.3%) | 0 (0%) | 0.35 |
| Revascularization | | | | |
| Percutaneous | 34 (7.7%) | 27 (7.3%) | 7 (9.8%) | 0.65 |
| Surgical | 4 (0.9%) | 4 (1.2%) | 0 (0%) | 0.85 |

† mean ± standard deviation.

plex lesions and to the high rate of coronary restenosis. With the appearance of coronary stents, the indications for percutaneous treatment increased, and a simultaneous significant reduction in the rates of restenosis and in the immediate complications of the procedure occurred, providing a better clinical evolution according to the STRESS and BENESTENT randomized studies [16-18]. After these studies, the comparison of the percutaneous treatment with stents and the surgical treatment in patients with multivessel coronary artery disease became necessary.

The ARTS trial [7] compared the use of stents and surgery in patients with multivessel coronary artery disease and showed a significant evolution in the group undergoing percutaneous treatment. The capacity of revascularization of the 2 methods was the same: 2.7 lesions treated with stents and 2.7 anastomoses. In addition, a similar clinical evolution, assessed by the occurrence of death, nonfatal acute myocardial infarction, and stroke, was observed. The need for new revascularization, although smaller, as compared with the studies using only the balloon catheter, was greater in the percutaneous group (21% vs 3.8%) by the end of 1 year (P<0.01).

The SoS trial [19], which also compared the use of stents and surgery in patients with multivessel coronary artery disease, with 2.7 lesions treated with stents and 2.8 with anastomoses, showed a similar incidence of death or nonfatal Q infarction in the groups in a 2-year follow-up. The overall mortality was 5% in the group treated with stent and 2% in the group treated with surgery (P=0.01); however, 60% of the deaths in the intervention group were of noncardiac cause. Need for new revascularization was greater in the percutaneous revascularization group (21%) than in the surgery group (6%) (P<0.001).

The ERACI-II [20], a randomized multicenter study comparing percutaneous revascularization using stents and surgical revascularization in patients with multivessel coronary artery disease, reported a lower rate of cardiac events in the percutaneous group in 30 days. In the follow-up of

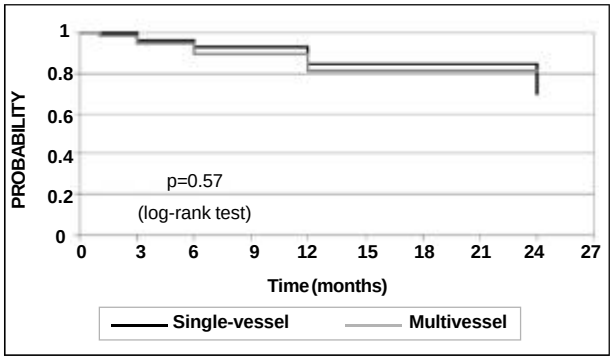


Fig. 1 - Event-free survival

18.5±6.4 months, a greater mortality was observed in the surgical group (7.5% vs 3.1%) (P<0.01), as was a greater incidence of Q infarction (6.3% vs 2.3%) (P<0.01); however, the need for revascularization was more frequent in the group undergoing percutaneous treatment (16.8% vs 4.8%) (P<0.01).

Our results showed event rates (death, infarction, and need for revascularization) lower than those found in the above-cited studies [7,19,20], which may be explained by the nonrandomization with selection of more appropriate patients for coronary intervention, a low prevalence of patients with triple-vessel disease, and shorter clinical follow-up.

Considering that coronary atherosclerosis is an evolutionary chronic disease, the percutaneous therapy, being less invasive as compared with the surgical treatment, is an attractive treatment option, mainly for young patients with coronary artery disease.

Hernandez-Antolin et al [21], in a case series with 136 patients with multivessel coronary artery disease undergoing percutaneous treatment with stents, reported a 3-year event-free survival of 75%.

The study by Kornowski et al [8] compared 398 patients with multivessel coronary artery disease with 1941 patients with single-vessel coronary artery disease treated with stents, both groups with a mean age of 62±11 years, and also found favorable results similar to ours. In the group of patients with multivessel coronary artery disease, the procedure was successful in 96% of the patients, and the need for new revascularization by the end of 1 year was 21%.

Mathew et al [22], in a study with 175 patients with multivessel coronary artery disease, reported a successful procedure in 98% of the patients, and, in the 12-month clinical follow-up, the need for new revascularization was 18.3% and the event-free survival was 80%.

The rates of need for new revascularization in the above-cited studies [8,21,22], greater than those observed in our patients, may be explained, as already cited, by the fact that our population sample was mainly formed by patients with double-vessel disease (95.9%), in addition to the shorter clinical follow-up in our study.

Our findings in patients with multivessel coronary artery disease younger than 50 years undergoing coronary stent implantation in a native artery showed favorable in-hospital results and rates of major adverse events in the clinical follow-up similar to that found in patients with single-vessel coronary artery disease. The multivessel group showed no increase in the risk of developing renal failure or stroke after coronary intervention. The high rate of clinical success (95.8%) is worth noting. On late follow-up, 93% of the patients with multivessel coronary artery disease were asymptomatic, and the rate of new coronary revascularization was 9.8%. The actuarial analysis at the end of 24 months showed an event-free survival of 81.1%.

The use of stents coated with drugs, sirolimus and Taxol, which, in recent randomized studies showed a significant reduction in the rates of restenosis, even in the group of diabetic patients, may provide greater efficacy in the percutaneous treatment of coronary artery disease [23-25].

Our study had some limitations, because it was a retrospective study with a relatively small number of patients and a large variety of stent designs. Most patients treated had double-vessel coronary artery disease with favorable angiographic characteristics and good ejection fraction. The results cannot necessarily be reproduced in a population with predominantly triple-vessel coronary artery disease, diffuse coronary artery disease, and significant ventricular dysfunction.

In conclusion, our results suggest that percutaneous treatment with coronary artery stents in young (<50 years) patients with multivessel coronary artery disease may be safely performed with a high rate of success, low rate of in-hospital complications, and favorable clinical outcome.

The percutaneous treatment of patients with multivessel coronary artery disease did not increase the rate of in-hospital complications or the need for new revascularization as compared with that of patients with single-vessel coronary artery disease.

Stent implantation was an effective strategy in the treatment of patients with multivessel coronary artery disease, mainly the population with predominantly double-vessel coronary artery disease and with good ventricular function.

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