Very Late Clinical Progression of Patients with Acute Myocardial Infarction Submitted to Primary Angioplasty

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Summary
Background: Information on the clinical progression, in the long term, of patients submitted to mechanical reperfusion is scarce.

Objective: The objective of this study is to describe the long-term clinical progression of patients submitted to primary stenting.

Methods: Between January 1998 and December 2003 we studied a non-concurring cohort with a fixed population of 202 patients (mean age = 61.2 ± 7.7 years; 74.7% males and 25.3% females) submitted to primary stenting. All the patients were followed up clinically and we assessed the occurrence of deaths, acute myocardial infarction (AMI), cerebral vascular accident (CVA) and surgical or percutaneous myocardial revascularization (MR). Kaplan-Meier survival curves were built for the following events: death, deaths/AMI, deaths/AMI/CVA and major cardiovascular events (MCE).

Results: In 91.5% of the patients the procedure was successful. During hospital stay, mortality was 3.4%; reinfarction was 0.9%; CVA was 1.8%; and urgent MR was 1.4%. Clinical follow-up varied from 29 to 100 months (mean = 58.7 ± 19.7 months). Death-free survival was estimated at 93.6%; death/AMI-free survival at 89.6%; death-AMI/CVA-free survival at 87.1%; and MCE-free survival at 71.3%.

Conclusion: Primary stenting presented excellent results during hospital stay. Very late clinical follow-up demonstrated that these good initial results have held up. (Arq Bras Cardiol 2008; 90(4): 221-226)

Key words: Myocardial infarction; clinical evaluation; angioplasty.

Introduction
In the United States 7,200,000 people have acute myocardial infarction (AMI). New heart attacks occur in 700,000 patients and another 500,000 suffer recurring attacks every year. Acute coronary syndrome (ACS) is the primary diagnosis for 879,000 patients who are hospitalized every year, and this number rises to 1,555,000 if we consider secondary diagnosis. Coronary artery disease (CAD) causes one out of every five deaths in the United States and is the primary or contributing cause of 653,000 deaths. CAD is estimated to cause 330,000 deaths per year outside hospitals or in emergency rooms1,2.

The total occlusion of an epicardial coronary artery due to the presence of an occlusive thrombus underlying an atherosclerotic plaque is mostly the physiopathological substrate of ACS with ST-segment elevation (STEMI)3.

The restoration of the normal flow of the obstructed infarct-related artery by means of percutaneous coronary intervention (PCI) or fibrinolytic drugs is a determinant of the early and late progression of patients with STEMI4.

Results of a comparison between PCI with stenting and fibrinolytic drugs in the treatment of AMI demonstrate that patients treated with primary stenting progress with lower rates of mortality, reinfarction and hemorrhagic cerebral vascular accidents (CVA)5.

Because the information on the clinical progression over three or more years of patients submitted to mechanical reperfusion is scarce, this study was conducted to assess the long-term clinical progression of patients with STEMI submitted to primary angioplasty with stenting.

Methods
In the period from January 1998 through December 2003 we studied a consecutive series with 202 nonselected patients (mean age = 61.2 ± 7.7 years; 74.7% male and 25.3% female) submitted to primary angioplasty with stenting.

We evaluated the clinical profile of patients, the location of the previous AMI on electrocardiogram (anterior, inferior, lateral or other), delays in pain-to-hospital, in presentation to hospital-electrocardiography and in door-to-balloon time, first glycemia in hospital and the interval between the onset of
symptoms and reperfusion (defined by the interval between the onset of symptoms and mechanical reperfusion).

PCI was performed according to the standard technique and the procedure was considered successful when the following criteria were met: residual injury ≤ 20%, TIMI 3 flow and absence of dissections or thrombi.

As regards progression during hospital stay we obtained information on the occurrence of the following complications: congestive heart failure (CHF), reinfarction (new ST-segment elevation or new elevation of creatine phosphokinase MB-fraction), acute mitral insufficiency, urgent surgical myocardial revascularization (MR), atrial fibrillation, acute renal failure (defined as a 25% increase in baseline creatinine or any increase greater than 0.5 mg/dl), malignant ventricular arrhythmias (ventricular fibrillation or sustained ventricular tachycardia), major bleeding (reduction of hemoglobin by 5 g/dl or greater or intracranial bleeding), minor bleeding (reduction of hemoglobin between 3 g/dl and 5 g/dl, macroscopic hematuria, hematemesis > 120 ml), Killip III/IV, complete atrioventricular block, post-AMI angina and CVA.

Late clinical follow-up was conducted with the objective of describing the occurrence of major cardiovascular events (death, CVA, AMI, new percutaneous or surgical revascularization) by means of telephone contact, questionnaires or contact with the physicians who assisted the patients. Based on the information about the late progression of patients the Kaplan-Meier estimators were built for the following events: death, death/AMI, death/AMI/CVA and death/AMI/CVA/PCI/MR.

**Results**

The clinical characteristics of patients are shown on table 1.

Electrocardiography on admission revealed inferior AMI in 49% of the patients, anterior in 38%, lateral in 8%, and AMI in other regions in 5% of the patients; 2.9% of the patients were classified as Killip III and 2% were classified as Killip IV. The value of the first glycemia was 168 ± 77 mg/dl.

The average delay between the onset of symptoms and the arrival at hospital was 184 ± 158 minutes; the door-to-balloon time was 105 ± 66 minutes, and the symptom-to-electrocardiography time was 7.5 ± 6.4 minutes; the door-to-arrival at hospital was 184 ± 158 minutes; the door-to-balloon time was 105 ± 66 minutes, and the symptom-to-balloon time was 12 (5.9%), 1 (0.5%), 13 (6.4%), 24 (12%), 5 (7.4%), 86 (43%), 19 (9.4%), 125 (62%), 98 (49%), 6 (2.9%), 28 (14%), 76 (38%), 42 (21%), 28 (14%), 24 (12%), and 15 (7.4%).

**Table 1 - Clinical characteristics of patients**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAH</td>
<td>125 (62%)</td>
</tr>
<tr>
<td>Smoking Habit</td>
<td>98 (49%)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>86 (43%)</td>
</tr>
<tr>
<td>FH of CoHF</td>
<td>76 (38%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>42 (21%)</td>
</tr>
<tr>
<td>Previous MR</td>
<td>28 (14%)</td>
</tr>
<tr>
<td>Previous PCI</td>
<td>24 (12%)</td>
</tr>
<tr>
<td>Previous AMI</td>
<td>24 (12%)</td>
</tr>
</tbody>
</table>

SAH - Systemic Arterial Hypertension; FH of CoHF - Family History of Coronary Heart Failure; MR - Surgical Myocardial Revascularization; PCI - Percutaneous Coronary Intervention; AMI - Acute Myocardial Infarction.

The late clinical progression of all the patients was successfully obtained. The clinical follow-up varied from 29 to 100 months, and the mean follow-up period was 58.7 ± 19.7 months.

In the clinical follow-up, myocardial revascularization was required in 24.2% of the patients; PCI was employed in 14.8% and MR was employed in 9.4%. Cumulative rates of clinical events were the following: death – 6.4% (94 months), death/AMI – 10.4% (90 months), death/AMI/CVA – 12.9% (88 months), and major cardiovascular events (MCE) 28.7% (73 months).

Kaplan-Meier curves for the probabilities of death, death/AMI, death/AMI/CVA and MCE are shown in figures 1, 2, 3 and 4, respectively.

**Discussion**

In this study, we describe the progression during hospital stay and in late follow-up of 202 patients submitted to primary angioplasty with stenting. The Kaplan-Meier curves of death, death/AMI, death/AMI/CVA and MCE, evidence the good clinical progression of these patients in the long term.

In the literature, late results of patients submitted to primary PCI refer mostly to the clinical progression within 12 to 24 months.

In this context, the Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) study revealed that a subgroup of 428 patients with ST-elevation or a new left bundle branch block that were randomized for primary PCI with stenting with no PCI was successful in 91.5% of the patients. During hospital stay, mortality rate was 3.4%; reinfarction rate was 0.9%; CVA rate was 1.8%, and urgent MR rate was 1.4%. As for the number of vessels affected 54% of the patients had uniarterial lesions and 46% had biarterial and triarterial lesions. Table 2 shows the rates of occurrence of other hospital-related complications assessed.

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Kaplan-Meier curves for the probabilities of death, death/AMI, death/AMI/CVA and MCE are shown in figures 1, 2, 3 and 4, respectively.

**Table 2 - Complications during hospital stay after primary stenting**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major Bleeding</td>
<td>15 (2.4%)</td>
</tr>
<tr>
<td>Minor Bleeding</td>
<td>5 (7.4%)</td>
</tr>
<tr>
<td>CHF</td>
<td>19 (9.4%)</td>
</tr>
<tr>
<td>MI</td>
<td>1 (0.5%)</td>
</tr>
<tr>
<td>AF</td>
<td>6 (2.9%)</td>
</tr>
<tr>
<td>VT/VF</td>
<td>12 (5.9%)</td>
</tr>
<tr>
<td>ARF</td>
<td>1 (0.5%)</td>
</tr>
<tr>
<td>CAVB</td>
<td>13 (6.4%)</td>
</tr>
<tr>
<td>Post-AMI angina</td>
<td>15 (7.4%)</td>
</tr>
</tbody>
</table>

CHF: Congestive Heart Failure; MI: Sustained Mitral Valve Insufficiency; VT: Atrial Fibrillation; VF: Ventricular Tachycardia; AF: Atrial Fibrillation; ARF: Acute Renal Failure; CAVB: Complete Atrioventricular Block; AMI: Acute Myocardial Infarction.
administration of abciximab had, at the end of the first year, a mortality rate of 3.6%; CVA rate of 0.7%; reinfarction rate of 2%; new revascularization of the target lesion (RTL) rate of 10.4%; and MCE of 14.1%.

In the analysis of the records of 183 patients treated with primary conventional stenting, Lemos et al demonstrated that the 300-day MCE-free survival rate was 83%.

The maintenance of the late patency of the artery that at the time of AMI coronary angiography was obstructed (TIMI 0 or 1) and was held open with primary stenting determines the good clinical progression at the end of the first year as demonstrated on the study by Halkin et al.

In this study, at 360 days, patients who didn’t present reocclusion of the AMI-related artery had a mortality rate of 0.8%; reinfarction rate of 0.4%; CVA rate of 0%; RTL rate of 9.8%; and MCE rate of 11%.

Comparison between primary PCI with stenting and without stenting in nine studies with a four to twelve-month clinical follow-up revealed that there were no differences in the mortality and reinfarction rates.

By the end of one year, the higher determinant of MCE rates, more specifically in the RTL for patients submitted...
to primary PCI with stenting, was the need for a second myocardial revascularization procedure due to restenosis.4

Late follow-up on angiography of patients submitted to conventional stenting revealed that the peak of neointimal proliferation takes place between six and twelve months and in some cases may regress after this period11.

After 360 days of progression, the occurrence of MCE in patients submitted to conventional stenting is mostly related to progression or destabilization of atherosclerotic disease in coronary arteries or other vascular sites4.

The survival of patients submitted to primary stenting at the end of one year varies from 96.4% to 99.2%9,10. In their turn, Brodie et al12 demonstrated that the survival rate in seven years of patients also submitted to primary PCI is related to the door-to-balloon time and varied from 78.4% to 87.8%. Every et al13 demonstrated that patients submitted to primary PCI with balloon catheter (PTCA) had a survival rate of 86% in three years. Zijlstra et al14 demonstrated that the five-year survival rate for patients treated with primary PTCA was 87%.

In the study by Brodie et al12, the prolonged door-to-balloon time (≥ 2 hours vs < 2 hours) was associated with a higher late mortality in high-risk patients and in those with pain-to-hospital delay ≥ 3 hours; however, this was not the
case for low-risk patients and for those with pain-to-hospital time > 3 hours. High-risk patients were defined as those classified as Killip III/IV, above 70 years of age or with anterio wall infarction.

The analysis of 2,087 patients submitted to primary balloon angioplasty (77%) or stenting (33%) revealed that after five years of progression the use of stenting correlated with lower mortality rates (odds ratio [OR] = 0.6 [0.42-0.85])

It is possible that the overlapping of mortality, reinfarction and urgent MR rates during hospital stay in this study, as compared with other published material about primary PCI results, among other factors, from the similar clinical profile of the patients, from the pain-to-hospital and door-to-balloon times, from the success of the procedure and from the adjunct pharmacotherapy.

In this phase, the progression of patients depends greatly on factors relating to primary PCI such as, for example, the door-to-balloon delay, platelet antiaggregation therapy, stenting, training of the interventionists of the cardiology team, etc.

It is possible that the difference between the late mortality of this study and others in medical literature may be partly explained by occasional variations in the secondary prevention of patients, since there is consistency among studies as regards results for the hospitalizations phase. The highest rate of restenosis with primary PTCA as compared with primary stenting, implies differences in RTL and in the compounded MCE objective, typically by the end of the first year, but cannot be blamed for the long term mortality, CVA and MCE.

In this study, a sharper drop in the Kaplan-Meier curve for MCE, but not in the mortality, death, AMI and CVA curves in the first year can be explained by restenosis in this period.

Factors that influence early and late mortality alike of those patients submitted to primary PCI are the myocardial salvage rate, ventricular remodeling and electrical stabilization which depend on the time and quality of the lumen of the coronary artery and its late patency.

Progression of atherosclerotic disease (coronary and systemic) and potential destabilization of the atheromatous plaque is several vascular sites are major determinants of long-term mortality and MCE. Stenting in the AMI-related lesion does not impact these factors.

In this context, clinical treatment and secondary prevention measures are essential to maintain the good outcomes obtained during hospitalization in the long term and the so-called late outcomes (12-24 months) of primary PCI.

This study has some limitations, of which the following stand out: it was conducted in a single center; the information about progression during hospital stay was obtained from the patients’ records; there was no information about the medication used in secondary prevention. Another limitation is also the size of the sample studied.

Additional studies, preferably multicenter ones with a larger number of patients are required to confirm these results.

Conclusion
Primary stenting presented excellent results during hospital stay. Very late clinical follow-up demonstrated that these good initial results persisted.

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Potential Conflict of Interest
No potential conflict of interest relevant to this article was reported.

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Study Association
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References


