Safety and Efficacy of Angioplasty with Intracoronary Stenting in Patients with Unstable Coronary Syndromes. Comparison with Stable Coronary Syndromes

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Objective – *To assess safety and efficacy of coronary angioplasty with stent implantation in unstable coronary syndromes.*

Methods – *Retrospective analysis of in-hospital and late evolution of 74 patients with unstable coronary syndromes (unstable angina or infarction without elevation of the ST segment) undergoing coronary angioplasty with stent placement. These 74 patients were compared with 31 patients with stable coronary syndromes (stable angina or stable silent ischemia) undergoing the same procedure.*

Results – *No death and no need for revascularization of the culprit artery occurred in the in-hospital phase. The incidences of acute non-Q-wave myocardial infarction were 1.4% and 3.2% (p=0.6) in the unstable and stable coronary syndrome groups, respectively. In the late follow-up (11.2±7.5 months), the incidences of these events combined were 5.7% in the unstable coronary syndrome group and 6.9% (p=0.8) in the stable coronary syndrome group. In the multivariate analysis, the only variable with a tendency to significance as an event predictor was diabetes mellitus (p=0.07; OR=5.2; 95% CI=0.9-29.9).*

Conclusion – *The in-hospital and late evolutions of patients with unstable coronary syndrome undergoing angioplasty with intracoronary stent implantation are similar to those of the stable coronary syndrome group, suggesting that this procedure is safe and efficacious when performed in unstable coronary syndrome patients.*

Keywords: coronary angioplasty, stent, unstable corona-

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Coronary angioplasty with stent implantation in patients with unstable coronary syndromes, theoretically, has an increased risk of thrombogenic complications, considering the instability of the atherosclerotic plaque associated with the thrombogenic potential of metallic prostheses [1]. Therefore, initially, this approach was contraindicated in patients with unstable angina or acute non-Q-wave myocardial infarction. With developments in the technique of stent implantation, this therapy has proved safe in those patients and is often indicated in those conditions [2-4].

Intracoronary stent implantation is advantageous as compared with conventional angioplasty in the following regards: reduction in the need for urgent revascularization with decrease in the rate of acute occlusion during the procedure; increase in the immediate gain after angioplasty (smaller residual stenosis and negative residual stenosis in some cases); reduction in the restenosis rate due to the greater amplification of the lumen and decrease in late luminal remodeling. Considering the higher risk of thrombotic complications of balloon catheter coronary angioplasty in patients with unstable angina [3-8], and due to its thrombogenic potential, the use of the stent was limited for approximately 3 years to stable patients or those in complicated situations of balloon angioplasty [1].

The recent technique of optimal stent deployment (high pressure balloon inflation) [5,6] associated with the additional benefits of antiplatelet agents, such as ticlopidine [7], clopidogrel [8], and intra venous infusion of glycoprotein IIb/IIIa [9,10] antagonists has provided a greater safety to angioplasty with stent placement in unstable atherosclerotic plaques, turning this into an ordinary procedure and creating the need for careful investigation of the evolution of the patients.

Aiming to assess the safety and efficacy of angioplasty with intracoronary stent implantation in patients with unstable angina or non-Q-wave myocardial infarction, we retrospectively compared the in-hospital and late evolution of those patients with a population of patients with stable coronary syndromes.

Methods

From February '95 to August '98, 370 consecutive patients underwent percutaneous coronary angiography in our hospital, 209 of whom had intracoronary stent implantation. Out of these 209 patients, 105 were screened for this retrospective cohort study and divided into 2 groups according to the following clinical characteristics: 1) stable group: patients with clinical findings of stable angina (precordial pain on physical efforts for more than 60 days) or silent myocardial ischemia detected on a functional assessment, such as exercise testing, stress or pharmacological stress myocardial scintigraphy, or stress echocardiography; 2) unstable group: patients with clinical findings of unstable angina according to the Braunwald classification (class I, II, III) [11], or myocardial infarction without ST segment elevation after stabilization of the clinical findings, and who underwent angioplasty in the first 60 days after infarction.

The following patients were excluded: 1) postacute Q-wave myocardial infarction patients who underwent angioplasty with stent implantation, either for late opening of the occluded artery or whose procedure resulted from postinfarction risk stratification; 2) patients whose stent implantation was decided upon during the procedure as a result of complicated balloon angioplasty; 3) patients who underwent balloon catheter angioplasty (without stent) in another artery on the same day of stent implantation or during the follow-up; 4) patients who underwent angioplasty with stent in venous or arterial grafts.

Balloon catheters for stent implantation were chosen to obtain an artery/balloon diameter relation close to 1:1. The inflation pressure was at least 12 atm. Unfractioned heparin (10,000 to 15,000 IU) was administered intravenously only during the procedure, and no indication for routine heparinization occurred after the procedure. The arterial catheter was withdrawn after the activated partial thromboplastin time reached a level lower than 60 s. Manual compression was performed for as long as needed to obtain hemostasis after withdrawal of the introducer, and then a compression dressing was applied. Electrocardiogram was routinely performed right after angioplasty, before discharge from the coronary unit, and in case of chest pain. Cardiac enzymes (CPK and CK-MB) were measured every 6 hours after angioplasty, totaling at least 3 measurements during the stay in the coronary unit. Acetylsalicylic acid orally at a dosage of 100 mg once a day and ticlopidine at a dosage of 500 mg orally twice a day were started at least 3 days before the procedure, and acetylsalicylic acid at a dosage of 100 mg/day were used chronicelly, while ticlopidue at a dosage of 200 mg tweel e drug were maintened for at least 15 days and ticlopidine at a dosage of 250 mg twice a day were maintained for at least 15 days.

Primary success was defined as TIMI-3 flow and visual residual stenosis smaller than 20% after stent implantation. Primary events consisted in death, acute myocardial infarction (appearance of a new Q wave on the electrocardiogram or elevation of the CK-MB enzyme more than twice its normal value, or both), and new revascularization (angioplasty or surgery) of the artery that had previously undergone stent implantation (culprit artery). The following events were considered secondary: hemoglobin variation resulting from the procedure and the need for a new coronary angiographic study. The events were separately analyzed in the in-hospital phase and late follow-up (11.2±7.5 months), which occurred through phone contact with the patient or the assistant physician, or both.

Continuous variables were expressed as mean ± standard deviation. The chi-square test for categorical data or the unpaired Student *t* test for continuous variables were used for analyzing population characteristics and comparing the variables representing the clinical evolution in the 2 groups. Results regarding the clinical events were expressed in confidence intervals of the relative risk of the unstable group as compared with the stable group. Multivariate analysis was performed through logistic regression, aiming to correct for eventual differences in the characteristics of the 2 groups that could confound the statistical results, in addition to analyzing the interaction between several variables. Despite this being a cohort study, the results from the multivariate analysis were expressed through a confidence interval of odds ratio, according to the method of logistic regression. The Kaplan-Meier method and the log-rank test were used in the analysis of event-free survival. A two-tail significance level lower than 5% were considered statistically significant. The 5.0 version of the Stata Statistical Software [12] was used for data analysis.

Results

We analyzed 105 patients, 31 of whom belonged to the stable coronary syndrome group and 74 patients to the unstable coronary syndrome group. Two patients in each group underwent stent implantation in 2 vessels; therefore, 109 angioplasties with stent implantation were analyzed. The mean age of the population studied was 61±10 years, and 60% of the patients of the unstable coronary syndrome group were males, as were 68% of the patients of the stable coronary syndrome group. Prevalences of hypertension, diabetes, dyslipidemia, tobacco smoking, multiarterial impairment, and left ventricular dysfunction through echocardiographic analysis or ventriculography with contrast medium were similar for both groups. In the unstable group, the mean time between the diagnosis and the procedure (time of stabilization) was 10.7±11.9 days, and the median was 7 days. Out of these patients, 90% were within the first 30 days after acute angina or myocardial infarction. Most of the patients with unstable angina were Braunwald class II (73% of the unstable group, n=55), and the remaining were equally distributed between classes I and III. Patients in Braunwald class B corresponded to 75% of the unstable group (n=56), and patients in Braunwald class C (postin–farction angina) corresponded to 15% (n=11). In the unstable group, 8 patients had a diagnosis of infarction without elevation of the ST segment (table I).

Most angioplasties (52%) were performed in the anterior descending coronary artery, 24% in the right coronary

Table II - Angiographic characteristics of the treated lesions

	Stable group	Unstable group	p value
Treated arteries	33	76	
LAD	16(49%)	41(54%)	0.73
CxA	3(9%)	17(22%)	0.14
RCA	11(33%)	14(19%)	0.15
Diagonallis artery	3(9%)	3(4%)	0.33
LMCA	0	1(1.3%)	0.70
Types of lesion			
A	2(6%)	14(19%)	0.12
B1	10(30%)	23(30%)	0.98
B2	14(43%)	32(42%)	0.97
C	7(21%)	7(9%)	0.13
Previous restenosis	3(9%)	8(11%)	0.8

LAD– left anterior descending coronary artery; CxA– circumflex coronary artery; RCA- right coronary artery; LMCA– left main coronary artery.

artery, and 18% in the circumflex coronary artery. Six angioplasties were performed in the diagonal artery and one in the left main coronary artery. No significant difference existed between the groups in regard to distribution of the type of the manipulated artery. In regard to the morphology of the lesion, the majority of the cases were type B lesions (73%), and the distribution of these type B lesions was similar in the 2 groups. The number of type A lesions in the unstable group (19%) was higher than that in the stable group (6%, p=0.12), and type C lesions were more prevalent in the stable group (21% vs 9%, p=0.13) (Table II). All patients used heparin and acetylsalicylic acid, but 2 patients of the stable group did not use ticlopidine. This, however, did not influence the results because none of these patients had in-hospital or late events. Only one patient used abciximab.

Primary angiographic success was obtained in all patients. No death occurred nor did a need arise for revascularization of the culprit artery during the in-hospital phase. The incidences of acute myocardial infarction during hospitalization and after the procedure were similar in both groups (3.2% in the stable group and 1.4% in the unstable group, p=0.6), and no patient had Q wave infarction. In the multivariate analysis of logistic regression, no significant difference in the incidence of events occurred between the groups after controlling for confounding variables: p=0.31; odds ratio = 0.31; 95% CI = 0.03-2.7. No variable proved to be a predictor of complication in this analysis. The mean of reduction in the hemoglobin measured after the procedure was 0.91±1.47 g% in the stable group and 0.97±1.42 g% in the unstable group (p=0.8) (table III).

Table I – Clinical characteristics of the population

	Stable group	Unstable group	p value
Number	31	74	
Age (mean ± SD)	61.4±10	60.8±9.8	0.8
Male sex	21(68%)	45(60%)	0.4
Hypertension	20(65%)	48(65%)	0.97
Diabetes mellitus	7(23%)	25(33%)	0.3
Dyslipidemia	19(61%)	53(71%)	0.5
Tobacco smoking	5(16%)	17(23%)	0.5
Systolic LVD	2(7%)	13(17%)	0.3
Multiarterial (>1 artery)	16(52%)	34(45%)	0.3
Previous CABG	2(7%)	6(8%)	0.7
Previous angioplasty	5(16%)	16(21%)	0.5
Braunwald classification			
I		6(8%)	
II		55(73%)	
III		6(8%)	
A		0	
B		56(75%)	
C		11(15%)	
Infarction with no ST segment elevation		8(11%)	

CABG- Coronary artery bypass graft; LVD– left ventricular dysfunction; MR– myocardial revascularization.

Data on the posthospital evolution of 29 and 70 patients of the stable and unstable groups, respectively, were obtained. Table IV shows the results. The time between patient discharge and data collection was 11.4±1.5 months (median of 9 months) in the stable group and 9.5±0.7 months (median of 8 months) in the unstable group, which was not a significant difference (p=0.2). The incidence of combined events (death, acute myocardial infarction, and revascularization of the culprit artery) was similar for both groups: 6.9% in the stable group and 5.7% in the unstable group, p=0.8. Analysis of the event-free survival showed no difference in the curves of the two groups (p=0.8) (fig. 1). One death occurred in each group, corresponding to an incidence of 3.5% and 1.4% in the stable and unstable groups, respectively (p=0.6). Acute myocardial infarction occurred in only one patient of the unstable group (1.4%, p=0.7), with no Q wave and no elevation of the ST segment. The need for revascularization of the culprit artery had a similar distribution in both groups (6.5% in the stable group and 5.4% in the unstable group, p=0.8). The only infarcted patient of the unstable group underwent revascularization surgery, which resulted in death.

Analysis of the incidence of infarction considering the in-hospital and the posthospital phases showed no significant difference between the groups: 6.1% for the stable group and 3.9% for the unstable group, p=0.6. During the follow-up period, a greater number of patients in the unstable group underwent a new coronary angiography due to clinical indication. This difference, however, did not reach statistical significance: 10.3% in the stable group and 18.6% in the unstable group, p=0.4. In the analysis of logistic regression, diabetes mellitus was the only predictor of events (OR=5.2; 95% CI=0.9-29.9; p=0.7).

Discussion

Our results show that intracoronary stent implantation in patients with unstable coronary syndromes is a safe and efficacious procedure, because of the similarity in the in-hospital and late complication rates as compared with the evolution of patients with stable coronary disease undergoing the same procedure. The relative risk of combined events in the unstable group as compared with the stable group was 0.4 in the in-hospital phase and 0.8 in the late follow-up,

Table III – In-hospital results

	Stable group	Unstable group	RR (95% CI)	p value
Number	31	74		
Primary success	31 (100%)	74 (100%)		
Infarction*	1(3.2%)	1(1.4%)	0.4 (0.01-32.9)	0.6
Death	0	0		
Revascularization	0	0		
Hb drop	0.9±1.5 g%	1.0±1.4 g%		0.8

Hb – hemoglobin; * All non-Q-wave infarctions.

Table IV - Results of the late follow-up

	Stable group	Unstable group	RR (95% CI)	p value
Number	29	70		
Follow-up (months)	11.4±1.5	9,5±0,7		0.2
Combined events	2(6.9%)	4(5.7%)	0.8 (0.1-9.2)	0.8
Infarction*	0	1(1.4%)		0.7
Revascularization	2(6.9%)	4(5.7%)	0.8 (0.1-9.2)	0.8
Death	1(3.5%)	1(1.4%)	0.4 (0.01-32.5)	0.6
Coronary angiography	3(10.3%)	13(18.6%)	1.8(0.5-9.8)	0.4

* All non-Q-wave infarctions.

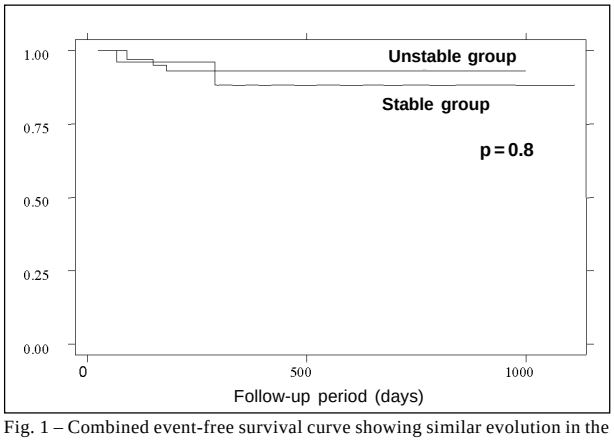

Fig. 1 – Combined event-free survival curve showing similar evolution in the unstable and stable patient groups.

which are differences without statistical significance.

Balloon catheter coronary angioplasty in patients with unstable angina has a higher incidence of thrombosis or acute occlusion within the first 24 hours after the procedure [13]. Angioplasty followed by stent implantation provides a greater mechanical support, and recent developments in the implantation technique [5,6] and antiplatelet regimens [7-10] have provided greater safety in the use of stents in conditions of instability according to Alfonso et al [14]. These authors performed angioplasty with stent implantation in a series of patients with thrombosis adjacent to the atherosclerotic plaque and had a low incidence of thrombotic complications. Marzocchi et al [15] compared patients with unstable and stable angina undergoing stent implantation without reaching statistical significance, but a higher incidence of complications occurred in the unstable group. On the other hand, our group did not find any difference favoring the stable group, and the relative risk of the unstable group was always lower than 1.0. Considering that the result of angioplasty is influenced by the time of stabilization [16,17], this difference may result from the mean time of 7 days that our patients had between the diagnosis and the procedure, while that study analyzed a more heterogeneous population, which also included patients in semi-elective and emergency situations with a higher risk.

Inflating balloon pressures of at least 12 atm in addition to the use of ticlopidine and acetylsalicylic acid may reduce the thrombogenic potential of the stent, providing the unstable population a therapy with a lower risk of restenosis in the medium- and long-therm. This hypothesis would be ideally tested if a population with unstable angina could be randomized for the use of stent or conventional angioplasty. Considering the benefit of stenting in the restenosis rate, however, this type of study is not likely to become a reality. We believe that our study confirms this hypothesis.

In the analysis of our data, the repetition rate of coronary angiography was higher in the unstable group (not statistically significant), suggesting a worse evolution in that group. These data, however, are limited to this analysis, because this test could have been performed due to ischemia resulting from a lesion in another artery. In addition, assessment of a new procedure in the culprit lesion, a more reliable criterion, did not show a significant difference between the groups.

In the multivariate analysis, diabetes mellitus was the only predictive variable of postangioplasty events. Controversy in regard to this result exists because recent studies with great samples of patients with diabetes undergoing

stent implantation have shown that only insulin-dependent diabetic patients have a worse late prognosis [18-20].

Our conclusion is limited by the small number of patients in the sample examined, resulting in a higher chance of type II statistical errors. Unlike the study by Marzocchi et al [15], the incidences of complications in the 2 groups were very similar, even tending to be greater in the stable group, resulting in a smaller probability of this statistical error favoring the determination of a false safety in the unstable group. Even though not statistically significant, a higher prevalence of type A lesions occurred in the unstable group and of type C lesions in the stable group, and some confusion may have occurred in the results. Adjustment of these variables through multivariate analysis, however, did not cause changes in the results obtained. In the same way, the follow-up period was smaller in the unstable group (with no statistical difference), but the multivariate analysis did not reveal any significant influence of this factor in the final results.

As confirmed by the EPISTENT study [17,21], the use of abciximab significantly reduces the incidence of large non-Q-wave infarctions (elevation of CPK higher than 5 times its normal value), and an evident synergism of that drug with stent implantation occurs. In addition, the incidence of revascularization of the target lesion after 6 months is smaller in diabetic patients using abciximab. Despite the importance of this therapy, our patients underwent the procedure when abciximab was not part of the routine adjuvant therapy to stent implantation. In spite of this, our data suggest that stenting is safe in unstable situations.

Ideally, patients with unstable angina or non-Q-wave myocardial infarction should undergo a period of stabilization of at least 48 hours before any angioplasty. In this study. The unstable group had a median of 7 days for stabilization, and the great majority of the patients with unstable angina were Braunwald class II. Therefore, these results apply to those patients with at least some days of stabilization before angioplasty, leading to the conclusion that this procedure should not be performed in the hyperacute phase of clinical presentation.

In conclusion, our study suggests that coronary angioplasty with stenting is a safe (in-hospital evolution) and efficacious (late evolution) procedure in patients with unstable coronary syndromes.

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