Clinical Significance of In-Hospital Reocclusion After Mechanical Reperfusion and Percutaneous Transluminal Coronary Angioplasty for Acute Myocardial Infarction

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Objective - *To analyze the effects of in-hospital reocclusion of reperfused AMI culprit coronary arteries in mortality and to identify the predictors.*

Methods - *The present study comprises a sample of 155 patients with AMI who underwent successful mechanical reperfusion by direct coronary angioplasty and angiographic control during hospitalization or before discharge. Patients were classified into group A: reoccluded patients (n=30) and group B: non-reoccluded patients (n=125).*

Results - *We identified in-hospital reocclusion predictors and found a greater significance in mortality among reoccluded patients (23,3% x 1.6%; p=0.00004). Silent reocclusion or typical angina at reocclusion had a good prognosis. The independent predictors of in-hospital mortality were hypertension, multiarterial lesions, totally occluded AMI culprit lesions, failed redilatation, failed redilatation in comparison with no intention to redilate, no redilatation in comparison with no atempt to redilate, and reocclusion within the first 48 to 72 hours. The decision to redilate, independently of the result, led to a 50.0% reduction in hospital mortality (p=0.0366).*

Conclusion - *In-hospital AMI culprit coronary artery reocclusion had an adverse effect-similar to that reported in clinical studies with high mortality rates (23.3% x 1.6%; p=0.00004). The major contribution of this study is to recommend the reopening of reoccluded AMI culprit coronary arteries as a means for the management of coronary artery reocclusion.*

Keywords: acute myocardial infarction, coronary reocclusion, reinfarction

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Reinfarction, or acute myocardial infarction (AMI) extension, has been reported in many clinical studies as a lethal complication in the outcome of AMI [1-,7] with diagnosis criteria based on clinical data, myocardial enzymes [1,5], EKG [8,9], and also by angiographic data. Reinfarction can occur without an angiographic registry of the total occlusion of the culprit AMI artery [10-13]. The incidence was reported between 8.0 and 30.0% in non-reperfused patients, 17.0% at autopsy, and 5.0 to 15.0% in reperfused patients [5,13-17] and between 18.0 to 25.5% for inferior AMI, and 6.0 to 12.8% for anterior AMI [17-21]. It can be silent in 42.0 to 50.0% of cases [6,22].

Because of the severe implications and because no studies involving the clinical significance of the in-hospital reocclusion after direct mechanical reperfusion and PTCA have been published, we studied these phenomena to better understand the effects and clinical significance of reocclusion and to the predictors, and to especially pay attention to mortality related to the reocclusion phenomenon.

Methods

Patients with a diagnosis of AMI admitted to Irmandade da Santa Casa de Misericórdia, Curitiba, Paraná, Brazil and the Instituto Modelo de Cardiologia, Cordoba, República Argentina from January 1983 to March 1993 received treatment with direct mechanical reperfusion and PTCA. Each patient had AMI confirmed by clinical, hemodynamic, and laboratory data. Patients were consecutive and included those with recovered cardiac arrest, shock, multivessel or associated left main lesions, previous CABG, previous AMI, and advanced age.

All patients were classified according to Killip-Kimbal clinical classifications [23,24], but a group of patients were considered to have no-class because of cardiac arrest, complete A-V block, or shock associated with ventricular tachycardia. AMI sites were defined either by EKG, or hemodynamic patterns, or both. Every patient received nitrates, sedatives, analgesics, and 10,000 units IV of heparin, and after consent, they underwent diagnostic cardiac catheterization

and interventional therapeutics as described in a previous study [15,25]. After the procedure, all patients went to the CCU for continuous monitoring of their EKG, blood pressure, and hemodynamics (temporary pacemaker or IABP in specific indications). All patients were autocoagulated with heparin (1000 units IV/hour) for the first 48 hours or during the entire hospital stay and received antiplatelet agents (ASA). Beta-blockers, calcium antagonists, and other drugs were selected by attending cardiologists. Reocclusion was defined as total occlusion of the culprit AMI artery that had previously been reperfused. All patients had to achieve TIMI grade flow III after PTCA, and only those who did were considered to be successful. The total population of successful PTCAs was 391 AMI patients, but only 155 had an angiogram performed prior to discharge. These 155 patients were then classified into the reocclusion group (group A) and the nonreocclusion group (group B). Clinical data on the posterior analysis were recorded with "Hemopac", an institutional software program.

Student *t* test, the chi-square test, Fisher's exact test, the median test, and the Kruskal-Wallis test were performed for two independent samples, and the binomial test was performed for a unique sample. Multiple regression analysis and Fisher's discriminant analysis were performed with SAEG software [26-28]. The significance level adopted was 5.0% ($p<0.05$).

Results

A total sample of 155 AMI patients underwent mechanical reperfusion with PTCA with initial success and a repeated angiogram before discharge. Ages ranged from 29 to 82 years (57.5±11.4). After repeat cardiac catheterization, patients were classified as group A (reoccluded, n=30) and as group B (nonreoccluded, n=125).

Table I and II show the clinical and angiographic baseline characteristics.

Discriminant analysis applied to 155 patients allowed the identification or classification, or both of patients who previously could or could not be identified as having reocclusion (error probability=10.6%), the formula for strong significance being $F_{calc}=60.24$; $F_{tab}=3.64$; $p<0.001$. This model identified the following 18 variables: in-hospital mortality, clinical class, age, sex, diabetes, hypertension, smoking, family history of CAD, hyperlipidemia, obesity, number of damaged vessels, number of dilated vessels, type of vessels (single vessel or multivessel), AMI culprit artery, type of lesion, AMI site, flow grade, and reperfusion time with a total possibility of correct classification of 79.0% (60.0% for group A and 84.0% for group B).

Although the group A mean age was higher than that of group B (60.6±11.2 x 56.8±11.4) and although when correlated with sex, female patients were older (66.0±12.1 x 59.6±10.9 for group A and 65.2±8.7 x 55.2±11.2 for group B), the univariate analysis did not show significances.

Univariate analysis demonstrated significances favorable to reocclusion (group A) for the following: female sex, hypertension, family history of CAD, hyperlipidemia ($p<0.005$), obesity ($p<0.025$), inferior and associationed AMI site, reperfusion time up to 240min ($p<0.005$), also up to 360 min ($p<0.05$), Killip I class ($p<0.005$), no-class ($p<0.025$), and the sum of III plus IV and no-class patients ($p<0.005$), multives-

Table I - Baseline clinical characteristics

Variables	All patients n = 155	%	Reocclusion n = 30	%	No reocclusion n = 125	%
Sex						
• Male	131	84.5	25	83.3	106	84.8
• Female	24	15.5	05	16.7	19	15.2
CAD Risk Factors						
• None	40	25.8	07	23.3	33	26.4
• Diabetes	16	10.3	06	20.0	10	8.0
• Hipertension	55	35.5	11	36.7	44	35.2
• Smoking	73	47.1	14	46.7	59	47.2
• CAD family history	31	20.0	07	23.3	24	19.2
• Dyslipidemia	44	28.4	11	36.7	33	26.4
• Obesity	40	25.8	12	40.0	28	22.4
Previous CABG	06	3.9	01	3.3	05	4.0
Previous AMI	17	11.0	02	6.7	15	12.0
AMI Site						
• Anterior	60	38.7	09	30.0	51	40.8
• Inferior	52	33.6	12	40.0	40	32.0
• Associations	43	27.7	09	30.0	34	27.2
Clinical class						
• Killip I	80	51.6	16	53.4	64	51.2
• Killip II	35	22.6	05	16.7	30	24.0
• Killip III	14	9.0	04	13.3	10	8.0
• Killip IV	07	4. 5	01	3.3	06	4.8
• No-Class	19	12.3	04	13.3	15	12.0
Mortality						
• Global	09	5.8	07	23.3	02	1.6
• Cardiac	08	5.2	07	23.3	01	0.8
• Non cardiac	01	0.6	-	-	01	0.8
Hospital discharge	146	94.2	23	76.7	123	98.4

Table II - Baseline angiographic characteristics

Variables	All patients n = 155	%	Reocclusion n = 30	%	No reocclusion n = 125	%
Reperfusion time (min)						
• Up to 120	36	23.2	07	23.3	29	23.2
• 121 to 240	58	37.4	12	40.0	46	36.8
• 241 to 360	30	19.4	02	6.7	28	22.4
• Up to 360	30	19.4	09	30.0	21	16.8
• Unknown	01	0.6	-	-	01	0.8
Number of diseased vessels						
• Single artery	77	49.7	14	46.7	63	50.4
• Multi vessel	76	49.0	16	53.3	60	48.0
• Left main	02	1.3	-	-	02	1.6
TIMI Flow						
• Total (0)	130	83.9	25	83.3	105	84.0
• Critical (I or II)	25	16.1	05	16.7	20	16.0
AMI culprit artery						
• LAD	69	44.5	12	40.0	57	45.6
• RCA	58	37.4	14	46.7	44	35.2
• Circumflex	14	9.1	04	13.3	10	8.0
• Secondary branches	09	5.8	-	-	09	7.2
• Saphenous vein graft	05	3.2	-	-	05	4.0

sel lesions, right coronary artery as the culprit AMI artery, critical lesions on first angioplasty (p<0.005), and also global mortality (p=0.0001) and cardiac mortality (p=0.00004).

Univariate analysis permitted identification of the following variables favorable to nonreocclusion (group B): male sex; non-CAD risk factors, smoking, anterior MI, reperfusion time from 241 to 360 minutes; Killip II and the sum of Killip I plus Killip II classes; single vessel lesions, LAD culprit MI artery, and total lesion (TIMI flow 0) at first angiogram with a probability of p<0.005 for all variables.

No significant conclusions were reached about diabetes, previous CABG, previous MI (late), damaged vessels/patients ratio, dilated vessel/patient ratio, and circumflex culprit MI artery.

Global in-hospital mortality was 5.8%, being 5.2% from cardiac causes. Group A mortality was 23.3% (all cardiac causes and group B of 1.6%, with 0.8% from cardiac causes), which was considered highly significant (p=0.00004). Also group A mortality was 4 times the global mortality (p=0.0001), 14.6 times the group B mortality (p<0.0001), and 29.1 times the group B cardiac mortality (p=0.00004). Group B had a reduction in mortality 3.6 times that of the global mortality (1.6% x 5.8%) (p<0.05).

Of the 30 reoccluded patients, 20.0% were asymptomatic at reocclusion, and all of them survived (p<0.005). Of symptomatic patients, 60.0% had isolated clinical data, angina and complete A-V blockage being the most frequent. Also those with isolated clinical data had a better prognosis (p<0.025), better when it was angina (p<0.01). Associated clinical data were found in 40.0% of symptomatic patients, and those with angina had a good prognosis (p<0.025) also.

Every patient who reoccluded while in shock died (p=0.0483). All patients whose reocclusions were suspected because of arrythmias in fact were reoccluded, and they had a higher mortality rate (p=0.0002).

Out of the 30 reoccluded patients, 16 reoccluded within 72 hours post-PTCA, and this accounted for 85.7% of the reoccluded in-hospital mortalities. Within 24 hours, 16.7% of patients reoccluded, and 57.1% died (p=0.0052). After 72 hours post-PTCA, 46.7% of patients reoccluded and 14.3% died.

Five patients reoccluded within the first 24 hours post-PTCA and 3 within the first 6 hours. All these 3 patients died (Table III). So we tested the hypothesis that earlier reocclusion means increased mortality (p=0.0262).

The majority of patients were in Killip class I at reocclusion (56.7%), but 40.0% were in Killip class III, IV, or had no data on class, and had greated mortality (p<0.005).

Every patient who were better clinical class at reocclusion than on admission survived, but those maintaining the same class had 15.8% mortality, and those who were in a worse class had 50.0% mortality.

At reocclusion, 25 patients (83.3%) were redilated; 64.0% of these were successfully dilated, and 5 patients were not redilated; 2 patients went on to CABG electively because of associated lesions.

Redilated patients, despite the results, had a better prognosis (87.0% survive) (p<0.005); but nonredilated patients had higher mortality rates (28.6% x 13.0%) (p<0.025), and failed redilation showed higher mortality also (71.4% x 17.4%) (p=0.0024).

When the intention to redilate versus not to redilate were compared, a 50.0% reduction in mortality favorable to redilation was seen (p=0.0366). Also when redilated patients were compared with failure or no redilation, no significance (p=0.3671) was observed.

Patients who died had a higher mean age (70.0±8.1 x 57.8±10.5 years old) (p<0.01). Also, male patients were older (70.0±4.3 x 59.6±10.9 years old) (p<0.01). Although female sex had a higher mortality (42.9% x 8.7%) (p<0.005), female's older age was not significant.

Of deceased patients, significances were reached for hypertension, a family history of CAD, AMI site associations (p<0.005),a major number of damaged vessel (p<0.025), the total occlusion of the culprit AMI artery (TIMI 0), multivessel lesions (p<0.005), and as related previously, reocclusions with shock (p<0.0483), reocclusion within the first 24 hours (p<0.005), failed redilation(p=0.0024), nonredilated (p<0.025), Killip III plus IV, and no-class at reocclusion (p<0.005), and no-class patients with isolated predictors (p<0.005).

The analysis of independent in-hospital mortality predictors showed hypertension (p=0.0366), dilated damaged vessels ratio (p<0.0001), patients with multivessel disease(p<0.0002), total occlusion of the culprit AMI artery (TIMI 0) (p=0.0366), failed redilation (p=0.0366), failed redilation when compared with not trying to redilate (p=0.0366), not trying to redilate compared with trying to redilate (p=0.0366), and reocclusion time up to 48 hours (p=0.0366), and greater significance up to 72 hours post-PTCA (p<0.0001).

At discharge, only 23 reoccluded patients existed, but 87.0% were in NYHA class I; 16 (69.6%) with patent culprit AMI arteries, and 7 with the AMI culprit artery totally occluded by unsuccessful redilation (4 patients), or no redilation in 3 patients.

Discussion

The small number of angiographic restudies (155/391) and the fact that in all patients suspected of reocclusion a restudy was performed will not permit analysis of the reocclusion rate. Discriminant analysis demonstrated a model with a good probability of identifying or classifying the

Table III - Reocclusion time after initial PTCA

Reocclusion time	Dead patients N	%	Survivours n	%	All patients n	%
Up to 24 hours	4	57.1	01	4.4	05	16.7
24 - 48 hours	1	14.3	04	17.4	05	16.6
After 72 hours	1	14.3	05	21.7	06	20.0
Up to 72 hours	1	14.3	13	56.5	14	46.7
All patients	7	100.0	23	100.0	30	100.0

patients in group A or B with 79.0% accuracy, better for group B (84.0%) than for group A (60.0%). Older patients have been reported to have more in-hospital complications, but not more reocclusions specifically, and this study did not differentiate between them.

Inferior MI have been reported in many studies [18,20,29,30] as the reocclusion rates increase, and now we have found associations too probably because a high number of these associations were with the right AMI, and the right coronary artery has the greatest reocclusion rates. Those studies generated controversy about reperfusion in the the RCA or AMI, but our study showed that if the RCA is the reoccluded artery, the prognosis is very favorable.

Shorter reperfusion time (up to 240 minutes) was significant in accordance with Shirotami et al [30], but we found also a later reperfusion time (up to 360 minutes) to be significant. This finding may be influenced by our small sample size.

O'Keefe et al [15,31] found intimal dissecion, intraluminal thrombus, total occlusion of the culprit artery, and hemodynamic-like variables related to reocclusion, and this study showed critical lesions in place of total occlusion. Ohman et al [6] in a metanalysis of reperfused patients found subtotal occlusions more frequently related to reocclusion, but this study had many patients treated with different reperfusion approaches, both isolated or associated. Vogt et al [32] observed that a TIMI flow 2 postreperfusion showed an in-hospital outcome related to mortality similar to that caused by an occluded artery, but no patients in our study was considered successfully reperfused without TIMI 3 flow. Many authors have considered the geometry of lesion, residual stenosis, grade and quality flow, excentrical lesions, and residual thrombus residual to be strongly related to reocclusion phenomena [12,15,33-44], the thrombus residual being the more thrombogenically ground found on laboratory testing, but our study failed in analysis of the geomety of lesions because we analyzed only the flow grade.

Higher risk patients (Killip III, Killip IV, no-class) and multivessel patients reoccluded more often and had higher mortality, probably because their clinical and hemodynamic performance did not provide them with good coronary perfusion pressure, a condition that seemed too critical to maintain artery patency and also AMI survival [13,15,19,45-51]. The best outcome for reperfusion is the less critical patient [52].

Clinical studies [6,8] have found subendocardial AMI as the main reinfarction predictor because the unstable plaque tends to close over and because its physiopathology is very different from that of the transmural AMI [11], which is referred for treatment because of the major amount of viable myocardium related to the AMI culprit artery [53,54].

Other studies [55,56] have found early ischemia to be an MI extension predictor, which was also the main predictor of subendocarial AMI. The MILIS study [5] found recurrent pain, unleveled ST segment, and early CKMB peak to be reinfarction predictors, but compounds of subendocardial reinfarction also are predictors, and when they considered a "major extension", they found also female gender. Also reported as reinfarction predictors by Morrison et al [9] were obesity, female gender, and recurrent ischemia. In the pharmacological reperfusion era, the AMI can be aborted, and perhaps it will develop the physiopathology of the subendocardial infarction.

Nonreoccluded patients showed predictors that put these patients in a group with a more favorable prognosis. They had only one nonreocclusion predictor that is a predictor of mortality. Also only one CAD risk factor seems to not affect prognosis, and surprisingly it is smoking. A previous report [57] has demonstrated that smokers have a more extensive thrombus component that is more susceptible to pharmacological lysis. Perhaps because anticoagulation with infused heparin was maintained in all patients in our study, it may have prevented reocclusion. On the other hand, Rivers et al [58] found cigarette smoking as a reinfarction predictor at the posthospital, long- term follow-up, although patients had quit smoking.

This study did not find diabetic patients, previous CABG, or previous MI to be significant possibly because the native coronary artery in these patients was more frequently responsible for AMI, and also the circumflex artery did not show a significance as in a previous report [15].

No significance existed in the number of dilated vessels in each patient. It seems to be that although multivessel lesions were a reocclusion predictor, more complete revascularization as a first approach AMI treatment did not influence final reocclusion results.

Many previous reports [1,4,5,22,54-56] have shown reinfarction, AMI extension, or reocclusion as in-hospital associated with a worse prognosis, and this study showed that reocclusion is a fatal complication in 23.3% of patients compared with 1.6% of non-reoccluded patients (p=0.00004). Although in our series redilated patients had a better prognosis and also nonreoccluded patients had a reduction in mortality of 3.6 times compared with the global mortality of 5.8%, surprisingly, Shirotami et al [30] did not find any signifi–cant difference in the mortality of reoccluded patients.

Our results suggest that patients with asymptomatic reocclusion had a good prognosis, which is in accordance with previous reports [6,59]. Also isolated or associated angina may perhaps have the same significance as at primary AMI or perhaps it might have a preconditioning mycardial effect [60]. In contrast, patients who experienced shock or arrythmias at the time of reocclusion had a bad prognosis. Again, higher risk patients (clinical class, II, IV and no-class) had a higher mortality. A better class at reocclusion seems to indicate a better prognosis, but a worse class results in a patient mortality of 50.0%. We have to look at this with caution, because many patients were Killip I, but many also were in more severe classes.

Although the success rates at redilation were very inferior to the initial success rates at first mechanical reperfusion and PTCA, this study suggests that redilation was the best approach, despite unsuccessful redilation, because of the intention to redilate leading to a 50.0% in-hospital reduction in mortality (p=0.0366). Unsuccessful redilatation indicated a poor prognosis, but when it was compared with

not trying to redilate, no difference was found. Other studies reported benefits in open occluded arteries also, because it promotes healing of the myocardium, left aneurysm, and survival [58,61,62]. Also our data suggest that the impact of the nonreopened artery could be equal to or worse than the primary unsuccessful treatment [45,47].

We observed also that seven mortality predictors were also reocclusion predictors, and only one was a nonreocclusion predictor. When we look at independent mortality predictors, hypertension and multivessel lesions were both reocclusion predictors, because the other variables were directly related to reocclusion and its management. Although low success rates occurred at redilatation, surviving patients had a very good NYHA class on discharge.

It has not been defined whether reocclusion is the same as reinfarction or MI extension, but this study demonstrated that reocclusion has a behavior very similar to clinical reinfaction and MI extension.

Because reocclusion is not a frequent phenomenon, despite ten years of data collection and the small number of angiographic restudies before discharge, ours is a very small sample. Also because over the years a great vertiginous advance in technological evolution, especially for "optimal stents" and the clinical use of glycoprotein inhibitors, guide wires, balloons, and new devices, reocclusion could be strongly influenced not in frequency, but perhaps in outcome [63-74]. This study did not analyze the CKMB curves reported in previous clinical studies, and many studies give information after 48 to 72 hours, but the majority of our patients reoccluded earlier, then we can't say whether reocclusion seems to be a reinfarction or a myocardial infarction extension based on the criteria reported in the literature.

Also no similar studies exist about the clinical significance of the in-hospital reocclusion after direct mechanical reperfusion, which is a limitation that needs discussion. Future studies could help us to better understand this phenomenon.

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