

A Comparison of Rescue and Primary Percutaneous Coronary Interventions for Acute Myocardial Infarction. A Multicenter Registry Report of 9,371 Patients

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Objective

To perform a comparative analysis of in-hospital results obtained from AMI patients who underwent rescue or primary PTCA.

Methods

From the Brazilian Interventional National Registry (CENIC), we selected all consecutive patients who underwent a percutaneous coronary intervention for myocardial infarction (≤ 24 hours), between 1997 and 2000, analyzing those undergoing a rescue ($n=840$) or a primary ($n=8,531$) procedure, and comparing their in-hospital results.

Results

Rescue patients were significantly younger males with anterior wall infarctions, associated with left ventricular dysfunction, but had less multivessel disease, compared with those treated with primary intervention. Coronary stents were implanted in at similar rates (56.9% vs. 54.9%; $P=0.283$). Procedural success were lower for rescue cases (88.1% vs. 91.2%; $P<0.001$), with higher mortality (7.4% vs. 5.6%; $P=0.034$), compared with the primary intervention group; target vessel revascularization ($\leq 0.5\%$), emergency bypass surgery ($\leq 0.3\%$) and reinfarction ($\leq 2.6\%$) rates were similar for both strategies. Multivariate analysis identified the rescue procedure as a predictor of in-hospital death [OR(CI=95%) = 1.60 (1.17-2.19); $P=0.003$].

Conclusion

Patients who underwent a rescue coronary intervention had higher in-hospital death rates compared with those who underwent a primary coronary intervention.

Key words

angioplasty, myocardial infarction, reperfusion, thrombolysis, stent, platelet inhibitors

Fibrinolytic therapy and primary percutaneous transluminal coronary angioplasty are effective methods used to promote myocardial reperfusion in acute myocardial infarction (AMI) ¹. However, the re-establishment of normal epicardial flow (TIMI grade 3) is not achieved in a significant number of patients who undergo fibrinolytic treatment ^{2,3}. The strategy of a rescue percutaneous coronary intervention (PCI) early after failure of fibrinolytic treatment has a logical indication; however, the clinical impact and the selection of the precise strategy is still controversial and still has inferior results when compared with the results of a primary procedure ^{4,8}. Therefore, primary PCI, when available, is considered the gold standard for coronary reperfusion ⁹.

The objective of this study was to perform a comparative analysis of in-hospital results obtained from AMI patients who underwent rescue or primary PTCA, consecutively included in a national registry of interventional cardiology (CENIC - Central Nacional de Intervenções Cardiovasculares).

Methods

The CENIC registry was created in 1991 and sponsored by the Brazilian Society of Interventional Cardiology (SBHCI). The procedures were established in a spontaneous fashion. The consistency of the results have been analyzed in former publications¹⁰⁻¹³. The PCI procedures started being gathered in a central nationwide database in 1992; the new coronary percutaneous device technology was incorporated in 1996. From January 1997 until December 2000, the CENIC databank received consecutive information on 68,236 patients who underwent PCI, either with balloon or coronary stent implantation, performed by 215 invasive cardiologist members of SBHCI, in 185 different hospitals, encompassing all 5 different geographic regions in Brazil. The PCI procedure report was sent to the CENIC coordinating center in Sao Paulo, by conventional or electronic mail, on a prespecified and equal database sheet. This file contains the clinical and angiographic baseline plus the procedural results, as well as the occurrence of major in-hospital adverse cardiac events. Additional information may be obtained at the SBHCI Web site (www.sbhci.org.br).

We analyzed files that indicated that a primary or a rescue PCI had been performed in the first 24 hours after AMI onset. Only complete files were analyzed. All the information obtained



from the files was displayed. Data with consistent and frequent flaws were discarded. The diagnosis of AMI was performed in each center. During this period, 9,371 (13.7% of the total) patients fulfilled these criteria, and their data were then analyzed in a comparative fashion: 840 (1.2%) underwent a rescue and 8,531 (12.5%) a primary PCI.

In the rescue group, patients were previously treated with streptokinase, alteplase, or with a combination. Patients underwent rescue PCI according to the discretion of the clinician, during the first 24 hours of the acute event. We analyzed only patients with a culprit AMI vessel clearly identified and with a visual estimation of a lesion $\leq 90\%$. All primary PCI patients were analyzed (patients who did not receive previous fibrinolytics).

In more than 90% of the patients, aspirin were administered plus ticlopidine or clopidogrel, in the event of a coronary stent implantation. Abciximab was administered at the operator's discretion, and was the only IIb/IIIa blocker recorded in the registry. We classified the AMI location as being anterior or nonanterior related to the culprit AMI vessel presentation, either the left anterior descending or a surgical graft. The left ventricular ejection fraction and the diameter of stenosis of the vessels were analyzed with a qualitative method (visual), performed in each center without interference from the CENIC center.

The PCI success was defined as a final stenosis diameter less than 50% with TIMI flow grade 2 or 3¹⁴, and major adverse events were considered until hospital discharge: reinfarction as recurrent chest pain associated with any secondary increase in the creatinine kinase, new target vessel-revascularization (TVR) as the performance of a new PCI of the culprit vessel or coronary bypass surgery in patients with recurrent ischemic symptoms, emergency surgical revascularization as the need for the patient to undergo a coronary bypass revascularization within the first 24 hours after the index procedure, and all-cause deaths were considered.

The statistical analysis was done with SPSS 10.0 statistical software. All continuous variables were expressed as mean \pm SD. Univariate analysis included the chi-square test for evaluating dichotomous variables and the Student *t* test for continuous variables. Cox progressive regression analysis was performed to

identify the independent influence of each baseline variable in the in-hospital death rate. *P* values ≤ 0.05 were considered significant.

Results

Streptokinase was the fibrinolytic agent more frequently administered before rescue PCI was performed [$n=733$ (87.3%)], followed by alteplase [$n=61$ (7.3%)]. In 46 (5.4%) patients, the fibrinolytic strategy was combination of these. Rescue PCI procedures were performed in younger patients, more frequently men, with significantly more infarctions located in the anterior wall, when compared with those who underwent a primary procedure, without previous fibrinolytic therapy (tab. I). The angiographic variables demonstrated that by the time of the rescue procedure, significantly more patients had a severe reduction in ejection fraction, but with fewer diagnoses of multivessel coronary heart disease (tab. I). A higher incidence of visible thrombi ($\geq 70\%$) was noted for both PCI strategies, with the treatment of a native coronary artery in the vast majority of the cases ($>90\%$), represented by complete occlusion (TIMI 0-1) of the culprit vessel ($\geq 90\%$), in either forms of PCI in AMI. Overall, abciximab usage was below 15%, but even lower in the rescue PCI group compared with its use in primary procedures (4.6% vs. 15.2%, $P<0.001$). At least half of the patients received a coronary stent implant, in similar rates either for rescue or primary intervention (56.9% vs. 54.9%, $P=0.283$) (tab. II).

The achievement of procedural success was significantly higher in patients who had not received previous fibrinolytic therapy (91.2% vs. 88.1%, $P=0.003$). The final diameter of stenosis was significantly lower in patients who underwent primary versus rescue PCI (13.2 \pm 12% vs. 15.9 \pm 14%, $P<0.001$) (tab. II).

The need for emergency bypass surgery or a new and urgent TVR were uncommon events, for both PCI strategies ($\leq 0.5\%$). Reinfarctions were observed in less than 3% of the patients, similarly for rescue or primary PCI (2.3% vs. 2.6%, $P=0.552$). In-hospital death rates were significantly higher for patients who underwent rescue PCI, after the failure of previous fibrinolytic therapy (7.4% vs. 5.6%, $P=0.034$). The association of PCI failure and in-hospital mortality indicated similar casualties for both groups

Table I - Baseline variables according to PCI procedure

Variables	Rescue PCI (n = 840)	Primary PCI (n = 8,531)	p Value
Age (years) (mean SD)	57.4 \pm 12.2	60.1 \pm 11.5	<0.001
Age ≥ 70 years	118 (14.0%)	2,070 (24.2%)	<0.001
Females	217 (25.8%)	2,539 (29.8%)	0.019
Diabetics	141 (16.8%)	1,331 (15.6%)	0.369
Prior coronary events			
percutaneous coronary intervention	47 (5.6%)	681 (8.0%)	0.017
bypass surgery	35 (4.2%)	410 (4.8%)	0.456
Anterior wall infarction	448 (53.3%)	4,057 (47.5%)	0.002
Multivessel coronary disease	377 (44.9%)	5,226 (61.2%)	<0.001
Moderate to severe global LVEF dysfunction	130* (19.7%)	1,081** (15.6%)	0.006
Thrombus present	587 (69.9%)	6,105 (71.6%)	0.304
Culprit vessel			
native coronary artery	836 (99.5%)	8,465 (99.2%)	0.456
bypass graft	4 (0.5%)	66 (0.8%)	
TIMI flow (0-1) pre	762 (90.7%)	7,839 (91.9%)	0.238

LVEF- left ventricular ejection fraction; Ventriculography performed: * n = 658 (78.3%) and ** n = 6,925 (81.2%)

[23 (23.0%) vs. 173 (23.1%); $P=0.977$]. Hospital discharge was effective at the end of the first week either for rescue or primary PCI (7.36 ± 3.0 vs. 7.26 ± 3.2 days, $p=0.360$) (tab. III).

Multivariate analysis identified independent predictors for in-hospital mortality. Patients who underwent a rescue procedure had a higher chance of suffering a fatal event until hospital discharge [OR (95%CI) = 1.60 (1.17-2.19); $P=0.003$]. Other demographic variables were also identified, most of them already known as independent predictors of a worse procedural and clinical outcome (tab. IV).

Discussion

Rescue PCI remains an uncommon procedure in this recent national registry analysis, when compared with primary coronary intervention in myocardial infarction^{15,16}.

Patients who underwent a PCI after fibrinolytic failure were identified as more likely to be young, with an anterior myocardial infarction, and with more extensive left ventricular dysfunction, when compared with patients admitted for primary PCI. Otherwise, primary patients were older and with a more frequent diagnosis of multivessel coronary heart disease. More than 90% of the AMI patients had a totally occluded vessel. We observed a balance between the adversity of the baseline variable distribution between both groups, regarding the ones considered more prone to the occurrence of death. Probably they reflected the bias of the indication of each procedure, for example, the anterior MI location for rescue patients and older age for those undergoing a primary procedure.

Abciximab was not used very often and even less in rescue procedures compared with its use in primary PCI. The predominance of streptokinase as the fibrinolytic of first choice might have warranted its use related to the fear of the occurrence of major bleeding events. Despite coronary stent implantation in more than half of the patients, like primary procedures, the success was significantly lower for rescue patients.

In-hospital major adverse events occurred at similar rates but with the exception of mortality. In-hospital death was nearly 25% higher in rescue patients. The relationship between procedural failure and death was not demonstrated because both mechanical

Variables	OR (95% CI)	p Value
Moderate to severe global LVEF dysfunction	8.01 (6.34-10.01)	<0.001
Procedural failure	7.14 (5.55-8.33)	<0.001
Multivessel coronary heart disease	2.37 (1.93-2.91)	<0.001
Rescue percutaneous coronary intervention	1.60 (1.7 - 2.19)	0.003
Females	1.57 (1.30-1.91)	<0.001
Previous bypass surgery	1.51 (1.02-2.27)	0.040
Diabetics	1.45 (1.17-1.81)	<0.001
Balloon coronary angioplasty	1.26 (1.03-1.56)	0.030
Age ≥ 70 years	1.04 (1.03-1.05)	<0.001

LVEF- left ventricular ejection fraction

strategies had similar rates, up to 20%. After multivariate analysis, rescue PCI was identified as an independent predictor for higher hospital mortality.

The analysis of primary PCI results resembles other results already published, either regarding procedural success (>90%) or in-hospital deaths (<6%)¹⁷⁻¹⁹. However, these results were not transferred for patients who underwent rescue PCI. Randomized trials that studied the performance of PCI after fibrinolytic treatment (PRAGUE 1 and 2^{8,20}) corroborate these findings, with a significant trend toward higher death rates in these patients. These trials may be a good comparison with the Brazilian registry because the fibrinolytic regimen was the same (streptokinase). A word of caution should be mentioned, regarding the inclusion criteria of the PRAGUE 1 and 2 trials in which the analysis was focused on transferring patients to PCI centers and not only on those with failure of lytic treatment²¹.

Former consecutive series and randomized trials reported the results obtained after rescue PCI, using in the vast majority of patients, only the balloon. These series also showed higher death rates when rescue was compared with primary PCI^{4,6,22-26}. In the RESCUE III study, the death rates were greater than 5% and close to 10%⁷. The higher reocclusion rates (20-30%) might be responsible for that, a reflection of the balloon PCI era. Coronary stent implantation had strongly reduced the in-hospital rates of recurrent ischemia and as a consequence, vessel reocclusion²⁷.

One Dutch registry is the exception. This study²⁴ also compared rescue and primary PCI with similar in-hospital mortality rates (4.7% vs. 6.6%, $P=0.37$) in a scenario of a lower rate of stent usage (<40%). The authors speculated that lower time to treatment delay might have helped them (<3 hours). Our results were different, and one of the multiple explanations might be the interaction of the baseline variables, some not reported in the CENIC registry.

How can we explain the higher death rate after a rescue PCI? These patients had a worse prognosis related to a more extensive and thicker atherosclerotic plaque, associated with extensive myocardial damage, especially to microvascular circulation^{28,29}. Former analysis of randomized data emphasizes the importance of the protection of the distal coronary circulation, measured by the tissue myocardial perfusion grade (TMPG). In the TIMI 10B trial³⁰, patients who achieved a higher TMPG score (grade 2 or 3) had a lower mortality rate in the 2-year follow-up after a rescue PCI, compared with those with lower (0 or 1) TMPG scores (9.1% vs. 4.8%, $P=0.038$)^{31,32}.

Table II - Procedural results according to PCI procedure

Variable	Rescue PCI (n = 840)	Primary PCI (n = 8,531)	p Value
Abciximab usage	39 (4.6%)	1,296 (15.2%)	<0.001
Coronary stent implantation	478 (56.9%)	4,684 (54.9%)	0.283
Procedural success	740 (88.1%)	7,783 (91.2%)	0.003
Final diameter stenosis (mean SD)	15.9 \pm 14%	13.2 \pm 12%	<0.001

Table III - In-hospital major adverse events according to PCI procedure

Variable	Rescue PCI (n = 840)	Primary PCI (n = 8,531)	p Value
Emergency bypass surgery	3 (0.3%)	21 (0.2%)	0.803
New target vessel revascularization	4 (0.5%)	31 (0.4%)	0.786
Reinfarction	19 (2.3%)	222 (2.6%)	0.552
Death	62 (7.4%)	477 (5.6%)	0.034



Is it possible to optimize rescue PCI results? There is a strong trend toward the more liberal use of potent antiplatelet agents (IIb/IIIa inhibitors) in these high-risk AMI patients, justified by their capacity to protect the microvascular coronary circulation. Their use is still not frequent, but most often is related to the administration of the nonfibrin-specific agents, like streptokinase. A recent metaanalysis of 12 trials that included AMI patients who underwent treatment with the last generation of fibrin-specific agents, demonstrated a more liberal and concomitant use of IIb/IIIa inhibitors³. In 3,418 rescue procedures, 1,032 patients had a trend toward a reduced 30-day death rate [4.6% vs. 6.6%; OR (CI=95%)=0.71 (0.49-1.01)], without significantly increasing the cerebral vascular bleeding rate [0.4% vs. 0.9%; OR (CI=95%) 1.64 (0.19-1.90)], compared with those who did not receive IIb/IIIa agents. However, the total sum of moderate or severe bleeding rates was higher in these patients [10.2% vs. 8.1%; OR=(CI=95%)= 1.64(1.24-2.16)]. The prescription of these agents (IIb/IIIa inhibitors) to patients who are undergoing rescue PCI is expanding, as is the association of new percutaneous devices that enhance distal microcirculation protection like thrombi extractors or distal vessel filters^{27,33-35}. Ongoing trials will clarify and stratify the use of these new pharmacological and mechanical strategies for those patients undergoing rescue PCI.

The CENIC registry promoted the possibility of analyzing a large cohort of patients in a short period, reflecting the real and daily practice of PCI in Brazil. Former analyses were performed and the results published, already proving the consistency of these data¹⁰⁻¹³. However, the registry has its own pitfalls. Many other clinical, angiographic, and procedural variables were not collected, such as the Killip class, AMI vessel TIMI flow, and the occurrence of other major adverse events like bleeding with their consequences. Other important variables were registered but frequently had flaws, like time to treatment delay and the size and number of percutaneous devices used. Also, it has already been mentioned that this is a spontaneous registry that might not reflect all the nationwide PCI procedures, and finally, the judgment of the PCI results was performed at each center and not by an independent center. We hope to optimize and correct these limitations in the near future.

We concluded from this comparative analysis between 2 different strategies of PCI performance in AMI patients that rescue PCI had less procedural success with higher in-hospital death rates. Rescue PCI was identified as an independent predictor of a higher death rate. Future research should be focused on improving the results in this subgroup of patients who still exhibit worse results when compared with those treated with the gold standard, primary PCI.

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