Transferring patients for direct coronary angioplasty: a retrospective analysis of 135 unselected patients with acute myocardial infarction

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Background. **Direct coronary angioplasty (PTCA) represents the most effective treatment for acute myocardial infarction. However, only a minority of patients are initially admitted to hospitals with direct PTCA facilities available 24 hours daily. The safety and benefits of transfer direct PTCA are debated, and we have no data about the early return of patients to the admission hospital.**

Methods. **We report our experience with transfer direct PTCA in unselected patients with acute myocardial infarction, and the early post-procedural return to the referring hospitals.**

Results. **One hundred and thirty-five unselected patients with acute myocardial infarction were referred to our center for direct PTCA during 1998. The majority of patients (n = 93, 69%, group T) were initially admitted to a primary hospital whereas the rest (n = 42, 31%, group NT) were directly admitted to our hospital. One hundred and thirty-four patients underwent coronary angiography, and direct PTCA was attempted in 126 patients. The median time interval between admission and direct PTCA was higher in group T (60 vs 40 min, p < 0.001). Only 3 patients (3.2%) had severe complications during transfer to our center: 1 patient with cardiogenic shock died, and 2 patients had ventricular fibrillation. The procedural and in-hospital outcomes of both groups were similar. The early post-procedural transfer to the referring hospital was possible in 88% of patients; no complications occurred during the transfer. The incidences of cardiac mortality at 6 months and at long-term follow-up were 3.4 and 5.1% respectively.**

Conclusions. **In our experience, interhospital transfer for direct PTCA in unselected patients with acute myocardial infarction is feasible and safe. The early return to the admission hospital is safe and does not negatively influence the in-hospital outcome.**

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Randomized trials have shown that direct coronary angioplasty (PTCA) for the treatment of acute myocardial infarction (AMI) – when performed by experienced operators in qualified centers – offers several advantages over thrombolytic therapy[1-5]. The main limitation of direct PTCA as a first line strategy for AMI is its restricted availability: less than 20% of the hospitals in the United States[6] and less than l0% of those in Europe regularly perform PTCA procedures, and only two thirds of these hospitals are able to perform the procedure on a 24 hour basis. In this scenario, most patients with AMI are admitted to hospitals without direct PTCA facilities. In such hospitals, intravenous thrombolysis is still considered the treatment of choice. It should be borne in mind that the time loss and risks associated with the transfer of patients to the catheterization laboratory (CL) of a referral hospital might blunt the benefits of direct PTCA compared to thrombolytic therapy. The few existing data about the feasibility and safety of interhospital transfer are promising but often characterized by selection biases[7-10]. Besides, data regarding patients transferred back to their original hospital immediately following the procedure are scarce[11].

This report retrospectively analyses our experience with transfer direct PTCA in unselected patients with AMI and with the post-procedural return to the referring hospital.

Methods

The Department of Internal Medicine and Cardiology of the University of Florence has a CL able to perform over 2400

procedures, including about 1000 PTCA yearly and it is a reference unit with facilities for direct PTCA available on a 24 hour basis, supported by cardio-surgical standby. Our CL receives patients directly admitted to our hospital as well as patients from outlying hospitals.

Study population. From January to December 1998, 135 consecutive patients with AMI were referred to our CL for direct PTCA within 12 hours of symptom onset or within 12 to 24 hours if there was evidence of cardiogenic shock or continuing ischemia. AMI was defined as typical chest pain lasting > 20 min associated with ST-segment elevation of at least 1 mm in ≥ 2 contiguous leads or with new complete left bundle branch block. The study population was unselected because patients were referred to the CL exclusively on the basis of the diagnosis of AMI and of the latency of symptoms. Any other criterion (age, sex, infarct location, Killip class, ejection fraction, etc.) was not considered. The majority of patients (n = 93, 69%, group T) were admitted at the S.M. Annunziata Hospital which is 15 km away from our CL and transferred to our CL by ambulances and accompanied by medical personnel (Florence Emergency-118). The remaining 42 patients (31%, group NT) were directly admitted to our hospital.

Early after the procedure, as soon as their clinical condition had stabilized, patients formerly admitted at the S.M. Annunziata Hospital were transferred back to their coronary care unit (CCU) by ambulances and accompanied by medical personnel.

Procedural techniques. Coronary angiography and angioplasty procedures were performed using standard techniques, usually via the femoral artery approach. Before PTCA all the patients were treated with a 100 IU/kg i.v. bolus of unfractionated heparin followed by additional weight-adjusted doses to maintain an activated clotting time (ACT) ≥ 300 s during PTCA. All patients were treated with acetylsalicylic acid administered intravenously, usually at a dosage of 500 mg. The use of abciximab, intracoronary stents and intravascular ultrasound was left to the operator's discretion. After coronary angiography, direct PTCA was attempted only at the site of the culprit lesion.

Data analysis. The two groups of patients (T and NT) were compared with respect to their clinical characteristics, the delay between the diagnosis of AMI and direct PTCA, angiographic results and clinical outcome. Major clinical events during transfer to the CL and during the return trip to the referring hospital were evaluated for group T.

Categorical data were analyzed using the χ^2 test. Continuous variables were analyzed using the Student's t-test for unpaired data. A p value < 0.05 was considered statistically significant. Time intervals are expressed as median and range.

Results

Of 135 referred patients, 134 underwent coronary angiography (1 patient of group T died during transfer to the CL). Direct PTCA was attempted in 126 patients. In 8 patients (6%) direct PTCA was not attempted either owing to the absence of critical stenosis or flow reduction (n = 5) or because of the presence of unfavorable angiographic lesions (n = 3) (critical stenosis of the left main stem in one patient, occlusion of a small-sized branch in two patients).

Baseline characteristics and angiographic findings were similar for the two groups. There were no significant differences with regard to demographic data, risk factors, medical history or type or location of the AMI (Table I). Ten patients (7.5%) had cardiogenic shock upon arrival at the CL: 7 (7.6%) in group T and 3 (7%) in group NT. Six patients (4.4%) had ventricular fibrillation before the procedure.

The time delay between the onset of symptoms and hospital admission was similar for the two groups, with about two thirds of patients reaching the hospital within 6 hours (Table II). On the other hand, the median time interval between hospital admission and coronary angiography was higher for group T: 60 min (range 35 to 240 min) vs 40 min (range 20 to 120 min) (p < 0.001).

Direct PTCA was attempted only at the culprit lesion. The treatment of critical lesions in other vessels was postponed unless an additional subocclusive TIMI grade 2 flow stenosis was present. The overall angiographic success rate – defined as a residual stenosis < 50% with TIMI grade 3 flow in the treated vessel – was 95%, with a similar distribution between group T and group NT (95.2 vs 94% respectively, p = NS).

The details of the 134 procedures are listed in table III. No differences were noted between the two groups. The procedure was unsuccessful in 6 cases: in 3 cases owing to the presence of an occluding dissection, in 2 cases owing to the fact that it was impossible to cross the occlusion with the guide-wire, and owing to a no-reflow phenomenon in 1 case. None of the patients underwent urgent surgical revascularization during the acute phase.

An intra-aortic balloon pump (IABP) was used in 34 patients (25%). The reasons for its insertion were cardiogenic shock – defined by the presence of clinical signs and of a systolic arterial pressure < 90 mmHg despite fluid challenge and the use of inotropic agents – upon arrival (n = 10) or developing during the procedure (n = 8) or an AMI with large areas at risk and Killip class 2 or 3 upon arrival for 16 patients. Abciximab, the only anti-IIb/IIIa agent available at that time, was used in 63 cases (47%) together with heparin administered at adjusted doses (70 IU/kg bolus).

Analysis of complications and transfer. Severe complications during transfer to our CL occurred in 3 pa-

Table I. Clinical and angiographic characteristics of 134 patients with acute myocardial infarction.

	Transferred (n=92)	Non-transferred (n=42)
Clinical characteristics		
Age (years)	63.4 ± 9.1 (range 42-85)	65 ± 8.4 (range 41-88)
Males	73 (79%)	26 (61%)
Age > 70 years	28 (30%)	12 (28%)
Previous AMI (%)	10 (11%)	5 (11%)
Hypertension	52 (56%)	22 (52%)
Diabetes	20 (22%)	10 (23%)
Dislipidemia	29 (31.5%)	13 (30%)
Anterior AMI	41 (44%)	18 (42%)
Non-anterior AMI (inf., lat., post.)	47 (51%)	24 (58%)
EF < 50%	31 (33%)	10 (23%)
Cardiogenic shock	7 (7.6%)	3 (7%)
Out of hospital VF	4 (4.3%)	2 (4.7%)
Angiographic characteristics		
LM stenosis > 50%	0	2 (4.7%)
1 vessel disease	39 (42%)	15 (36%)
2 vessel disease	31 (33.6%)	17 (40%)
3 vessel disease	18 (19.5%)	10 (24%)

AMI = acute myocardial infarction; EF = ejection fraction; LM = left main coronary artery; VF = ventricular fibrillation. p = NS for all categories.

Table II. Time between symptom onset and hospital admission.

	Transferred (n=92)	Non-transferred (n=42)
0-6 hours	66 (71.7%)	32 (76.2%)
6-12 hours	20 (21.7%)	9 (21.4%)
12-24 hours	6 (6.5%)	1 (2.3%)

p = NS for all categories.

Table III. Procedural data.

	No.
Urgent coronarography	134
Attempted PTCA	126 (95%)
Unsuccessful PTCA	6 (4.7%)
No. vessels treated for each PTCA	
1 vessel	124 (98.4%)
2 vessels	2 (1.7%)
No. treated vessels	128
Treated vessel	
LAD	54 (42%)
CX	16 (12.5%)
RCA	45 (35.1%)
Diagonal	8 (6.2%)
Marginal	5 (3.9%)
Stenting	
No. stents (tot.)	122
No. stented vessels	108
Multiple stenting of a single vessel	15
PTCA with stent/PTCA tot.	0.79
IABP	34 (25.3%)
Abciximab	63 (47%)

CX = circumflex coronary artery; IABP = intra-aortic balloon pump; LAD = left anterior descending coronary artery; PTCA = coronary angioplasty; RCA = right coronary artery.

tients (3.2%): 1 patient with cardiogenic shock died, and 2 patients developed ventricular fibrillation successfully treated with electrical shock. No death occurred during direct PTCA. Other complications that occurred in the CL are listed in table IV.

Eighty-one of the 92 group T patients (88%) submitted to direct PTCA were transferred to the CCU of the referring hospital within 2 hours of the end of the intervention (70 ± 35 min). In no case did any complication occur during the transfer from our CL to the referring hospital. Only 11 patients (12%) of group T were kept in our CCU due to severe clinical instability (cardiogenic shock or arrhythmias). Eleven patients (12%) were transferred with IABP after a successful PTCA.

The in-hospital post-procedural complications are listed in table V: no significant differences were ob-

Table IV. Complications occurring in the catheterization laboratory (CL).

Complications	No. patients
Any complication	23 (17.1%)
Asystole or heart block requiring a pacemaker	5 (3.7%)
Ventricular fibrillation	9 (6.7%)
Cardiogenic shock developing in the CL	8 (6%)
Stroke or transient ischemic attack	1 (0.7%)
Pericardial tamponade	0
Emergency bypass surgery due to a CL accident	0
Anaphylaxis	0
Limb ischemia (post-IABP) requiring surgery	1 (0.7%)
Death due to CL complications	0
Death in the CL	0

IABP = intra-aortic balloon pump.

Table V. Post-procedural complications.

	Transferred (n=92)	Non-transferred (n=42)	All patients (n=134)
Any complication	22 (24%)	11 (26%)	31 (23%)
Ventricular fibrillation/tachycardia	2	2	4 (2.9%)
Heart block requiring a pacemaker	1	0	1 (0.7%)
Pulmonary edema	1	0	1 (0.7%)
Pulmonary embolism	1	0	1 (0.7%)
Intrastent thrombosis (reinfarction)	2	0	2 (1.7%)
Post-AMI angina	1	1	2 (1.5%)
Stroke	1	1	2 (1.5%)
Transient ischemic attack	1	1	2 (1.5%)
Inferior limb ischemia	2	1	2 (1.5%)
Bleeding requiring transfusion	6	3	9 (6.7%)
Coronary artery bypass graft	0	1	1 (0.7%)
Hypotension requiring IABP	4	1	5 (3.7%)
Death	3	2	5 (3.7%)

AMI = acute myocardial infarction; IABP = intra-aortic balloon pump.

served between the two groups with respect to the major clinical endpoints: hospital mortality, reinfarction, stroke and severe bleeding. Three patients developed post-AMI angina: two of them were submitted to medical treatment alone where one underwent bypass revascularization. The incidence of acute or subacute thrombosis of the treated vessel was low (1.7%) and occurred in 2 group T patients submitted to stent implantation.

Bleeding requiring transfusions (≥ 2 units) was the most frequent complication (9 patients among 134 procedures, 6.7%) and was observed only among patients who underwent PTCA (3 in group NT and 6 in group T, p = NS): 2 patients had gastrointestinal bleeding, and 7 patients had bleeding at the site of vascular puncture. Two patients developed a minor ischemic stroke and recovered completely. None developed intracranial hemorrhage.

The average length of hospitalization was 6.4 days (range 1-33 days). Five out of a total of 134 patients died during hospitalization (3.7%). Three of them had cardiogenic shock before reaching the CL. The in-hospital mortality rate for patients with cardiogenic shock upon arrival was 30% (3/10 patients) while that for patients without cardiogenic shock upon arrival was only 1.6% (2/124 patients). With regard to the T group, the overall in-hospital mortality was 3.2% (3 deaths). One patient died in our CCU after direct PTCA; in patients without pre-procedural cardiogenic shock, the mortality rate was only 1.1% (1/85 patients).

Follow-up (Table VI). A 6-month follow-up was available for 117 of 121 patients who were discharged alive from hospital after direct PTCA (97%). The total mortality rate was 4.3% (5 patients); the cardiac mortality rate was 3.4% (2 patients died of AMI, 1 of ventricular fibrillation, and 1 during elective coronary artery bypass graft). One patient died of non-cardiac causes. A reinfarction was documented in 3 patients (2.6%). Eight patients (6.8%) underwent elective coronary artery bypass graft; in 1 case (0.8%) a new PTCA on the culprit vessel was performed.

Table VI. Outcome at 6 months and at long-term follow-up for patients discharged alive from hospital.

Outcome	6 months*	Long-term follow-up**
Total mortality	5 (4.3%)	8 (6.8%)
Cardiac mortality	4 (3.4%)	6 (5.1%)
Reinfarction	3 (2.6%)	8 (6.8%)
CABG	8 (6.8%)	9 (7.7%)
PTCA (target vessel)	1 (0.8%)	2 (1.7%)

CABG = coronary artery bypass graft; PTCA = coronary angioplasty. * = available for 117 of 121 patients who were discharged alive; ** = median 34 months (range 1-45 months).

At long-term follow-up (median 34 months, range 1-45 months), the total mortality rate was 6.8%, the cardiac mortality rate 5.1%, the reinfarction rate 6.8%, and the revascularization rate 9.4%.

Discussion

Systemic thrombolysis is the reperfusion strategy of choice in patients with AMI initially admitted to hospitals without PTCA facilities, because the risk and delays due to transfer could blunt the advantages of direct PTCA. Some non-randomized series have shown the feasibility and safety of transfer direct PTCA in high risk patients, and recently two randomized trials have compared thrombolytic therapy with the immediate transfer of patients to the nearest CL where direct PTCA is then performed. In the PRAGUE trial[10], it was observed that transfer direct PTCA showed significant

advantages over thrombolysis with streptokinase in non-selected patients with AMI. The preliminary results of the AIR-PAMI trial[12], a multicenter study which randomized high risk patients with AMI to thrombolysis or transfer direct PTCA, were in the same direction. However, the trial was prematurely stopped due to the impossibility to recruit the anticipated sample size. The MISTRAL study[13], a multicenter nationwide prospective registry which evaluated the in-hospital outcome of patients with high risk AMI admitted in centers with or without direct PTCA programs, did not show any significant differences between direct PTCA and thrombolysis. However, a favorable trend was observed in patients submitted to direct PTCA within 1 hour of admission. Patients without reperfusion therapy, significantly more numerous in centers without direct PTCA programs, showed a worse prognosis; only 1.7% of patients were transferred for direct PTCA. These data confirm the need to increase the use of reperfusion therapy, in particular in peripheral centers, and suggest that transferring patients for direct PTCA represents the option of choice when thrombolysis is contraindicated and if the procedure is performed within 1 hour of admission.

To date, the early return of patients from the CL to the initial admission hospital has not been adequately evaluated. Transfer to the CL and return to the admission hospital require an efficient emergency medical service, a limited distance from the admission hospital to the CL and road conditions permitting a short transfer time.

Since 1988, certain United States hospitals have considered the transfer of patients with AMI to the CL a suitable procedure. Helicopter transfer was characterized by a low incidence of complications and, in any case, treatable during transfer. However, the total arrival time to the CL was high and ranged from 105 to 815 min (an average of 300 min)[14]. More recently, other authors used a strategy of mechanical reperfusion during transferal of patients by ambulance. The transfer times varied from 69 to 85 min depending on the distance between the CL and the admission hospital and the incidence of complications was uniformly low[8-11,15]. In our series, the transfer times are similar to the last mentioned. The wide range is attributable to the presence of 4 cases in which the delay was substantial (120-240 min), owing to a dysfunction of the transfer organization or to a prolonged in-hospital decision time. In 1994, an analysis of the in-hospital delay before the beginning of on-site direct PTCA[16] demonstrated that an average of 30 min were necessary for the initial evaluation of the patient and 45 min were necessary to bring the patient to the CL for a total of 75 min of in-hospital delay. This time delay is comparable to the door to catheter times reported in transfer direct PTCA series.

Our study involves patients suffering of AMI and transferred to the CL solely on the basis of clinical and electrocardiographic diagnostic criteria; no selection was made on the basis of risk stratification.

We believe that the main reason for the low in-hospital mortality in our study (3.7 vs 6% in other transfer direct PTCA series) is probably related to the non-selection of the treated population. Patients without cardiogenic shock upon admission showed a particularly low mortality rate (1.1%), while the data regarding patients with pre-procedural shock were in line with those reported in the most recent studies on direct PTCA[17,18]. Analysis of the 6-month follow-up data showed the efficacy of direct PTCA in our series, with low rates of mortality and other cardiac events (Table VI). We also performed a long-term analysis. For 95 patients, a follow-up > 6 months (median 34 months) and confirming a very high survival rate (over 93%) with few events was available.

The relatively high incidence of major bleeding in our population (6.7%) was especially due to bleeding at the femoral artery access site (7/9, 77.8%) and conditioned by the use of IABP (4/7, 57%) or failed full-dose thrombolysis (2 cases). In patients treated with abciximab, the incidence of major bleeding was 6.3% (4 among 63 treated patients). Even in this case, hemorrhages occurred almost entirely at the arterial access of an IABP sheet (3/4, 75%). With the use of abciximab the heparin dosage was reduced according to data published in the literature. Except for patients in whom an IABP was inserted, this could explain the elevated incidence of bleeding in this group. If we exclude those patients in whom the combination of abciximab and IABP was employed, the incidence of major bleeding with abciximab was 1.6%. This is similar to data published in the literature.

On the whole, mortality and major clinical complications were similar between the two groups studied (T and NT). The post-procedural transfer did not seem to influence the incidence of complications. Owing to the fact that no other data have been published on this subject, no direct comparison with previous results about the early return to the admission hospital is possible. The only study with a significant re-transfer rate is the one by Oude Ophuis et al.[11], in which patients with AMI were treated with thrombolysis and sent to the CL for angiography. Only 67% of the patients were re-transferred within 2 hours of the procedure and notably, only 29% after rescue PTCA.

The main limitation of the re-transfer strategy is the risk of post-procedural complications, in particular early reocclusion requiring a new PTCA. In our study, 88% of the patients who underwent direct PTCA were re-transferred within 2 hours of the procedure. Among those transferred, 12% had had an IABP inserted. This demonstrates that even high risk patients were immediately re-transferred. Only 1 patient (l.l%) had a subacute reocclusion requiring a new transfer for re-PTCA. Moreover, no severe complications occurred during re-transfer to the CCU.

In conclusion, our data show that transferring unselected patients for direct PTCA is safe and effective, and confirm what other authors have reported about high risk patients. In addition, the strategy of an early return from the CL to the initial admission hospital was shown to be feasible and safe. These data are encouraging and are useful for the elaboration of future therapeutic strategies in AMI patients admitted to non-PTCA hospitals. To achieve the maximum effectiveness of this intervention strategy, the in-hospital delay and transfer times must be reduced to the minimum. In order to reach these objectives, there must be a strong collaboration between peripheral hospitals and the reference center. The procedures must be standardized; written guidelines available both to the hospital staff as well as to the emergency medical service could be useful in achieving this goal.

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