Primary Percutaneous Coronary Interventions in Nonagenarians

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ABSTRACT

Background: The optimal treatment of very elderly patients with ST elevation myocardial infarction (STEMI) is not yet defined. The aim of this study is to present the feasibility and safety of primary percutaneous coronary interventions (PCI) in nonagenarians.

Methods: A retrospective analysis of all patients who underwent primary PCI due to STEMI between 2004 and 2008 was performed. Patients age 90 years or older at the time of the procedure were identified and studied.

Results: Twenty-two patients fulfilled the study criteria (median age 92 years; range, 90–97 years; 50% women). The procedural success rate was 82%. Bare metal stent implantation was performed in 82% of the procedures, whereas only balloon angioplasty was performed on the rest of them. One patient experienced a minor bleeding complication. Procedural mortality was 9% (2 out of 22 patients), and it was due to “no flow” phenomenon in both patients. In-hospital mortality was 27% (6/22 patients) and 30-day mortality was 32% (7/22 patients). All 3 patients with Killip class III–IV on admission died within 30 days compared with 4 of the 19 patients with Killip class I–II ($P = 0.023$). Furthermore, of 11 patients with anterior infarction, 7 died within 30 days compared with none of the 11 patients with infarction of other location ($P = 0.004$).

Conclusions: Although primary PCI is feasible in patients 90 years or older suffering from STEMI, the short-term mortality rate is high especially in patients with anterior infarct location and/or severely depressed myocardial function.

Introduction

Elderly patients with myocardial infarction represent a continuously growing population. They are also a population with increased risk for complications and death.¹ On the other hand, they are the ones who have better absolute benefit from reperfusion treatments, when compared with younger patients.² The fact that very elderly patients were excluded from randomized trials has resulted in a lack of evidence regarding the best treatment for this specific population. The aim of this study is to evaluate the feasibility and safety of primary percutaneous coronary intervention (PCI) in patients age ≥ 90 years old.

Methods

A retrospective evaluation of all procedures performed in our institution between January 2004 and December 2008 was performed. Patients with ST elevation ≥ 1 mm in more than 1 contiguous lead, with new left bundle branch block or true posterior myocardial infarction, who were eligible for primary PCI and were 90 years or older at the day of the procedure, were evaluated.

Procedures were performed through the radial or the femoral approach, using 6 French guiding catheters. The choice of approach was at the operator's discretion.

All patients received a bolus dose of aspirin (320 mg) and clopidogrel (300 or 600 mg) if not already on these medications, followed by 75 mg aspirin daily for the rest of their lives, and 75 mg clopidogrel daily for a period of

1 to 6 months. Patients on warfarin treatment received only a 300-mg clopidogrel loading dose, plus 75 mg clopidogrel daily for 1 month, followed by 75 mg aspirin daily for the rest of their lives.

The 3 following anticoagulation treatment strategies were followed under PCI procedures in our hospital during the study period: heparin only, heparin plus eptifibatide, and only bivalirudin. The heparin-only patients received a 100-U/kg intravenous bolus, followed by additional doses during PCI in order to maintain an activated clotting time of more than 250 seconds. The heparin plus eptifibatide group received 60 U/kg heparin and a 180- μ g/kg bolus of eptifibatide, followed by a second intravenous bolus dose after 10 minutes, and a 2- μ g/kg/min intravenous infusion for 18 hours. Additional doses of heparin were administered in order to maintain an activated clotting time of over 200 seconds. The bivalirudin patients received a 0.75-mg/kg bolus, followed by a 1.75-mg/kg/h intravenous infusion, which was terminated immediately after the end of the procedure. Adjustments of the doses of eptifibatide and bivalirudin were performed in patients with renal failure. The anticoagulation regimen that was applied for each procedure was at the operator's discretion.

Procedures were performed according to the widely accepted medical standards and the routine use of bare metal stents. The use of drug-eluting stents in patients with ST elevation myocardial infarction was not a clinical routine in our institution during the study period.

The use of thrombus aspiration devices, intravascular ultrasound, or closure devices was also at the operator's discretion.

Procedural success was defined by establishment of Thrombolysis in Myocardial Infarction (TIMI) flow grade II or III and <50% residual stenosis when only balloon angioplasty was performed, or <20% residual stenosis when a stent was implanted. Myocardial blush grade was assessed for successful procedures.³ The left ventricular function was measured the day after the procedure with Simpson's method from a 4- and 2-chambers' view.

Continuous parameters are reported as mean $\pm$ standard deviation or as median (interquartile range), and categorical variables as percentages. Student *t* test or the *U* test was used for continuous variables between 2 groups, as appropriate. Categorical variables were compared using the χ^2 test or Fisher exact test. A *P* value <0.05 was considered significant.

Results

Patients' Characteristics

During the study period 3139 primary PCIs were performed at our institution. Twenty-two of them (0.7%) were performed in patients ≥ 90 years old (range, 90–97 years; 50% women); 761 (24%) procedures were performed in patients aged 89 to 75 years, and 2356 (75%) procedures were performed in patients younger than 75 years. The clinical baseline characteristics of these 3 groups are presented in Table 1. The nonagenarians group consisted of more females compared to the younger than 75 years group, and less smokers compared to the 89- to 75-year-old patients' group.

Other clinical, laboratory, and echocardiographic findings of the main study group are presented in Table 2.

Procedural characteristics and anticoagulant regimens applied are presented in Table 3. Coronary angiography showed extended coronary artery disease in the majority of the patients (50% of patients had left main or 3 vessels disease).

Two patients had cardiogenic shock on presentation, but only 1 of them received an intra-aortic balloon pump. The second patient could not receive it due to extreme atherosclerosis and calcifications of the iliac arteries.

Transfemoral temporary pacemaker implantation was performed in 1 patient due to third-degree atrioventricular block and symptomatic severe bradycardia.

Thrombus aspiration with the Export XT catheter (Medtronic, Minneapolis, MN) was attempted in 3 patients, but it was successful only in 1 of them due to the inability to advance the catheter distally to the culprit lesion.

Procedures were performed only in infarct-related arteries and were successful in 18 patients (82%). Myocardial blush grade ≤ 2 was observed in 10 patients, whereas the other 8 patients with successful angiographic reperfusion had efficient myocardial perfusion (myocardial blush

Table 1. Baseline Patients' Characteristics

Age groups, y	≥ 90 (n = 22)	89–75 (n = 761)	< 75 (n = 2356)
Median age, y (range)	92 (90–92)	80 (77–83)	62 (54–68)
Female	11 (50%) ^a	327 (43%)	520 (22%)
Predisposing factors			
Hypertension	12 (55%)	327 (47%) {58}	734 (33%) {106}
Hyperlipidemia	3 (14%)	172 (25%) {72}	478 (21%) {137}
Ever smoker	2 (9%) ^b	243 (30%) {195}	561 (29%) {442}
Diabetes mellitus	1 (5%)	102 (14%) {39}	271 (12%) {66}
Prior myocardial infarction	2 (9%)	172 (29%) {64}	320 (14%) {78}
Prior coronary artery bypass grafting	0 (0%)	40 (5%)	91 (4%)
Prior percutaneous coronary intervention	0 (0%)	40 (5%)	251 (11%)
Missing values are expressed as numbers within brackets {}.			
^a <i>P</i> < 0.05 when compared with < 75-year-old patients' group.			
^b <i>P</i> < 0.05 when compared with 89–75-year-old patients' group.			

grade > 2). Eighteen patients received bare metal stents, whereas in 4 patients only balloon angioplasty was performed. The fact that 4 patients received no stents was due to difficulties in advancing the stents at the culprit lesion (due to extreme tortuosity or calcifications) or due to the inability of having full balloon expansion during plain balloon angioplasty.

The mean contrast volume used was 138 ± 10 mL and the mean radiation time was 703 ± 81 seconds.

Outcomes

One patient suffered minor access-site bleeding in the right femoral artery area without any significant drop in the hemoglobin levels or prolonged hospital stay.

Two patients died during the procedure (procedural mortality, 9%). Both of them had a Thrombolysis in Myocardial Infarction Grade 3 (TIMI III) flow after balloon angioplasty and experienced a “no flow” phenomenon after stenting in

Table 2. Clinical, Laboratory, and Echocardiographic Findings of the Main Study Group

Laboratory findings	
Hemoglobin (g/dL)	13.1 ± 0.4
Leukocyte count (× 10 ⁹ /L)	11.3 ± 1.1
Platelet count (× 10 ⁹ /L)	301 ± 24
Serum creatinine (μmol/L)	117 ± 11
Serum creatine kinase MB (μg/L)	139 ± 48
Serum troponin T (μg/L)	3.6 ± 1.1
STEMI localization	
Anterior	11 (50%)
Inferior	10 (45%)
Lateral	1 (5%)
Killip class on presentation	
I–II	19 (86%)
III	1 (5%)
IV	2 (9%)
Others	
Atrial fibrillation	2 (9%)
Prior warfarin treatment	3 (14%)
Ejection fraction, %	41 ± 4
Abbreviations: STEMI, ST elevation myocardial infarction.	

the left anterior descending artery and died almost immediately thereafter in a state of pulseless electrical activity despite cardiopulmonary resuscitation attempts.

Another 4 patients died during hospitalization after 2, 2, 4, and 5 days, respectively. Three of them died due to acute heart failure and the fourth due to sudden cardiac death with pulseless electric activity. None of these patients had clinical or electrocardiographic signs of a new infarction. One more patient died 25 days after the procedure due to sudden cardiac death. Thus, the in-hospital mortality rate was 27%, and the 30-day mortality rate was 32%. These mortality rates are considerably higher than those observed in the other age groups. The 89- to 75-year old group had a 7% in-hospital mortality rate (53 out of 761 patients, $P = 0.002$) and a 13.5% 30-day mortality rate (103 out of 761 patients, $P = 0.041$), whereas the group of patients younger than 75 years had a 1.5% in-hospital mortality rate (37 out of 2356 patients, $P < 0.001$) and a 4% 30-day mortality rate (96 out of 2356 patients, $P < 0.001$).

All 3 nonagenarians with Killip class III–IV on presentation were dead 30 days after the procedure,

Table 3. Procedural Characteristics

Variable	
Approach	
Transradial	4 (18%)
Transfemoral	18 (82%)
Coronary angiography findings	
Left main disease	2 (9%)
Three vessels disease	9 (41%)
Two vessels disease	5 (23%)
One vessel disease	6 (28%)
Anticoagulation treatment	
Bivalirudin	13 (59%)
Unfractionated heparin plus eptifibatide	8 (36%)
Unfractionated heparin only	1 (5%)
Infarct related artery	
Left anterior descending artery	11 (50%)
Left circumflex artery	3 (14%)
Right coronary artery	8 (36%)
TIMI flow before PCI	
0–I	21 (95%)
II–III	1 (5%)
TIMI flow after PCI	
0–I	3 (14%)
II–III	19 (86%)
Treatment times	
Pain to balloon time, min (range)	194 (120–373)
Door to balloon time, min (range)	31 (25–46)
Needle to balloon time, min (range)	18 (14–25)
Procedural success	
Procedures with stents	18 (82%)
Number of stents used	1.6 ± 0.15
Total stent length, mm	30 ± 17
Abbreviations: TIMI, Thrombolysis in Myocardial Infarction; PCI, percutaneous coronary interventions.	

whereas only 4 of 19 patients with Killip class I–II on presentation had such an unfavorable outcome ($P = 0.023$).

Also, 7 of the 11 patients with anterior infarct location died during the 30 days after the intervention, compared with none of the 11 patients with another infarct location ($P = 0.004$). No other adverse events, such as new myocardial infarction or stroke, were recorded 30 days after the procedure.

Discussion

This is the first attempt to describe the population of patients 90 years or older who were treated with primary PCI due to ST elevation myocardial infarction. The main findings of this study are that with the current medical practices, this population has a high periprocedural, in-hospital, and 30-day mortality rate, but very low bleeding rates.

The elderly patients with myocardial infarction have characteristics that may differentiate them from the younger ones. The aged are characterized by altered cardiac physiology, decreased peripheral compliance, and ventricular hypertrophy.^{4,5} All of these may contribute to the high rate of complications in elderly patients with myocardial infarction.⁶ Papillary muscle rupture, myocardial edema, and intramyocardial hemorrhage are common autopsy findings in elderly patients with myocardial infarction treated with thrombolysis.⁷

The treatment of choice in elderly patients with acute coronary syndromes, and especially with ST elevation myocardial infarction, is not well defined. The current treatment of very elderly patients with STEMI is extrapolated from data coming from younger patients. There is evidence supporting reperfusion therapy in patients who are eligible for this treatment up to the age of 85.⁸ Only a small number of patients enrolled in randomized trials for patients with STEMI were elderly, and there is a difference in the presentation of elderly patients in randomized trials and in registries.^{9,10} Elderly patients with STEMI often have comorbidities that influence their treatment, such as dementia, prior disabling stroke, anemia, or renal failure. They also often have atypical symptoms, atypical electrocardiographic findings, and delayed presentation.¹¹ Communication between patients and medical staff may be jeopardized by hearing or visual deficits. These factors can explain the low reperfusion rate in elderly patients with STEMI. Registry data show a clear benefit of elderly patients receiving reperfusion therapy compared to those not receiving this kind of treatment.^{12,13} Among the available reperfusion therapies, PCI seems to be beneficial compared to thrombolysis. These data come from the subgroup of elderly patients participating in PAMI-1,¹⁴ GUSTO-IIb,¹⁵ and DANAMI-2¹⁶ studies. The small randomized trials addressing the same question in elderly patients were also in favor of PCI.^{17,18}

There are a few studies evaluating the outcomes of primary PCI in very elderly patients with STEMI. Antoniucci et al¹⁹ reported 16%, 30-day mortality rates in patients over

80 years old (mean age, 84 years) treated with primary PCI. Valente et al²⁰ reported a 17% in-hospital mortality rate in STEMI patients over 85 years old (mean age, 88 years) treated with PCI. They also found that age over 90 years as well as Killip class $\geq$ III on admission and PCI failure were independently correlated with in-hospital mortality. Hovanesyan et al²¹ previously reported similar 30-day mortality rates in nonagenarians with STEMI (34% compared with 32% in our cohort), even if only 46% of them were treated invasively.

There are no randomized data about differences of only balloon angioplasty vs PCI with stent in very elderly patients with STEMI. A subgroup analysis from the CADILLAC study²² showed that patients over 65 years old randomized to stent implantation had reduced the composite endpoint of death, recurrent myocardial infarction, disabling stroke, and target vessel revascularization compared with only balloon angioplasty patients. The fact that the 2 periprocedural deaths were both due to no-flow phenomenon immediately after stent implantation (although these patients had TIMI III flow with only balloon angioplasty) may again raise the question of stent implantation in this patients' population in the future.

The low rate of bleeding complications observed (only 1 minor bleeding in 22 treated patients) may be due to different causes. We assume that the use of bivalirudin as an anticoagulant during PCI in 59% of these patients was beneficial. In the HORIZONS study,²³ bivalirudin was associated with 50% less major bleeding complications compared with the combination of heparin plus IIb/IIIa platelet receptor blocker in patients with STEMI undergoing primary PCI. The use of a transradial approach in 18% of our patients and the routine use of femoral puncture site closure devices may also contributed to this favorable result.

The relatively low incidence of risk factors can be explained as due to selection bias (patients with minimal risk factors manage to live until their 90s and are still suitable and willing to undergo a primary PCI procedure).

All patients that underwent primary PCI had ST elevation in their electrocardiogram, despite the fact that 33% of patients over 85 years old have a left bundle branch block. This finding raises the question of treatment delays in patients with this electrocardiogram pattern. A more aggressive evaluation in elderly patients with left bundle branch block may minimize treatment delays and improve outcomes.

The fact that 45% of these procedures were performed in 2008 shows a trend towards more aggressive treatment of the very elderly patients with STEMI by the PCI operators of our institution.

Study Limitations

The small number of the patients and the retrospective nature of study are the major limitations of this study.

Conclusion

Primary PCI may be feasible in patients ≥ 90 years old, but it is accompanied by high mortality rates, especially in patients with anterior infarct location and/or severely depressed ventricular function on presentation.

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