Primary Percutaneous Coronary Intervention in Nonagenarians: Six-Month Outcomes From a Single-Center Registry

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ABSTRACT: Little is known about the efficacy and medium-term outcomes of primary percutaneous coronary intervention (PCI) in very old patients. We evaluated in-hospital and 6-month outcomes in a retrospective cohort of nonagenarian patients presenting at our hospital with ST-segment elevation myocardial infarction (STEMI) and treated by primary PCI from January 2003 to May 2012. During this period, primary PCI was performed in 1598 consecutive patients; twenty-seven patients (age, 92.5 ± 2.5 years) were enrolled in the study. Four patients (15%) were in advanced Killip class at presentation. STEMI location was anterior in 44%. Patients received aspirin, 300 mg clopidogrel loading dose, and heparin. Abciximab was given to 41% of patients. Coronary angiography showed multivessel disease in 52% of patients. Pain-to-balloon and door-to-balloon times were 375.0 ± 410.2 minutes and 107.3 ± 47.6 minutes, respectively. Intra-aortic balloon pump was implanted in 1 patient. An average of 1.3 ± 0.7 stents (95% bare-metal stents) were implanted per patient. Procedural success rate, defined as Thrombolysis in Myocardial Infarction (TIMI) flow grade ≥2 and residual stenosis <20%, was 89%. Hospital mortality was 18.5%. TIMI major bleeding and acute renal failure, defined as an absolute increase of 0.5 mg/dL serum creatinine, occurred in 7% and 22% of patients, respectively. Overall 6-month survival rate was 67%. Our data suggest that primary PCI can be performed in nonagenarian patients with high success rate and with an acceptable bleeding risk, even when aggressive antithrombotic drugs, such as glycoprotein IIb/IIIa inhibitors, are given.

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The proportion of elderly people in Western countries is growing and cardiovascular mortality remains the leading cause of death in this subset of the population.[1] Age is one of the most powerful predictors of adverse outcome in acute coronary syndromes[2] for many reasons, including delay in presentation,[3] presence of comorbidities, lower success rate of revascularization procedures as compared to younger patients,[4] and increased risk of bleeding.[5] Although elderly patients, being at higher risk, could derive higher benefit from evidence-based treatment,[6] they are generally excluded from randomized controlled trials.[7] Very old patients, such as nonagenarians, represent a subset in which the outcomes of contemporary reperfusion strategies are poorly defined.

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Methods

We designed a retrospective registry in order to evaluate in-hospital and 6-month outcomes in patients ≥90 years old presenting at our hospital with ST-segment elevation myocardial infarction (STEMI), who were treated by primary percutaneous coronary intervention (PCI) within 12 hours from symptom onset. Patients were included if the electrocardiogram (ECG) at admission showed ST-segment elevation of at least 0.1 mV in at least 2 contiguous leads, true posterior myocardial infarction, or new (or presumably new) left bundle branch block. During the study period, all STEMI patients fulfilling the aforementioned criteria were referred to primary PCI unless absolute contraindications to the procedure, such as severe anemia from active, uncontrolled bleeding, or very severe comorbidities, such as concomitant terminal illness or advanced dementia, were present.

All patients provided written informed consent to the procedure. Clinical and procedural characteristics were collected through careful review of clinical records.

Procedural success was defined as Thrombolysis in Myocardial Infarction (TIMI) flow grade ≥2 with residual stenosis <20%. The left ventricular ejection fraction was measured at discharge by echocardiography with the Simpson's method. The following endpoints were assessed during hospitalization: death from any cause, recurrent myocardial infarction, target vessel revascularization, stroke, bleeding, and acute renal failure. *Recurrent myocardial infarction* was defined as recurrent chest pain, lasting at least 30 minutes, or new ST-segment elevation associated with increase in CK-MB >2 times the initial value. *Major and minor bleedings* were defined according to the TIMI criteria. *Acute renal failure* was defined as an increase of 0.5 mg/dL in plasmatic creatinine. The survival status at 6 months from admission was evaluated by review of outpatient ambulatory records

Table 1. Clinical characteristics.

Variable	
Age (years)	92.5 ± 2.5
Women	18 (67%)
Smoking	2 (7%)
Hypertension	12 (44%)
Diabetes mellitus	5 (19%)
Hypercholesterolemia	3 (11%)
Atrial fibrillation	6 (22%)
History of myocardial infarction	3 (11%)
Previous coronary bypass	0 (0%)
Previous percutaneous coronary intervention	1 (4%)
ST-elevation myocardial infarction location	
Anterior	12 (44%)
Non-anterior	15 (66%)
Killip class	
1-2	23 (85%)
3-4	4 (15%)
Symptom-to-balloon time (minutes)	375 ± 410
Creatinine at admission (mg/dL)	1.21 ± 0.44
Hemoglobin at admission (g/dL)	13.43 ± 1.86

Data are given as number (percentage) or mean ± standard deviation.

Table 2. Procedural characteristics.

Variable	
Door-to-balloon time (minutes)	107.3 ± 47.6
Vascular access	
Femoral	24 (88.9%)
Radial	2 (7.4%)
Brachial	1 (3.3%)
Number of diseased vessels	
Single-vessel disease	13 (48%)
Double-vessel disease	10 (37%)
Triple-vessel disease	4 (15%)
Left main disease	2 (7.4%)
Culprit vessel	
Left anterior descending	12 (44.4%)
Circumflex	3 (11.1%)
Right coronary artery	12 (44.4%)
Infarct-related artery stenting	25 (92.6%)
Thrombus aspiration	9 (33%)
Number of stents per patient	1.3 ± 0.7
Drug-eluting stents	2 (5%)
Intra-aortic balloon pump	1 (4%)
Temporary pacing	3 (11%)
TIMI flow after procedure	
0	3 (11.1%)
1	0 (0%)
2	4 (14.8%)
3	20 (74.1%)
Abciximab use	11 (41%)
Troponin I peak (ng/mL)	81.0 ± 45.9

Data are given as number (percentage) or mean ± standard deviation.

or, in case of missing scheduled visits, by telephone contact. Continuous variables are presented as mean ± standard deviation; categorical variables are presented as number and percentage. Six-month survival curve was obtained using the Kaplan-Meier method. Statistical analysis were performed by SPSS version 20 software (SPSS, Inc).

Results

We retrospectively selected a cohort of 27 patients (age, 92.5 ± 2.5 years; age range, 90-98 years) out of a global population of 1598 patients treated by primary PCI at our hospital from January 2003 to May 2012. Clinical characteristics of patients are reported in Table 1. Female gender was predominant (67%); cardiovascular risk factors, except active or recent smoking and hypercholesterolemia, were quite prevalent. Six patients (22%) had atrial fibrillation at presentation or in the following days. Cardiac history was negative in most patients, since only 3 had previous myocardial infarction and only 1 had previous coronary revascularization. Most patients (85%) were in Killip class 1 or 2 at presentation; the mean time from symptom onset to reperfusion was quite long (about 6 hours, 375 ± 410 minutes).

Before PCI, all patients received intravenous aspirin 250 mg, intravenous heparin 70 UI/kg, and clopidogrel 300 mg loading dose. Procedural data are reported in Table 2. Average door-to-balloon time was 107.3 ± 47.6 minutes, but a time less than 90 minutes was only achieved in 55% of patients. Most procedures were performed by femoral approach. The majority of patients had multivessel coronary disease, whereas left main disease was present in 2 patients. Manual thrombus aspiration with the Export catheter (Medtronic) was performed in one-third of patients; intra-aortic balloon pump and temporary pacemaker were inserted in 1 and 3 patients, respectively. Abciximab was given in 41% of patients, whereas bivalirudin was given in 1 patient. All patients except 2 (in whom the procedure failed) received at least 1 coronary stent. The overall number of stents implanted was 35 (1.3 ± 0.7 per patient), of which only 2 were drug-eluting stents (both in the same patient). Procedural success rate was 89%.

Five patients (18.5%) died during hospitalization; one patient died during the procedure, whereas the others died in the following days from cardiac death, except 1 patient with pneumonia. Recurrent myocardial infarction, target vessel revascularization, and stroke were not observed in any patient. Two patients presented with TIMI major

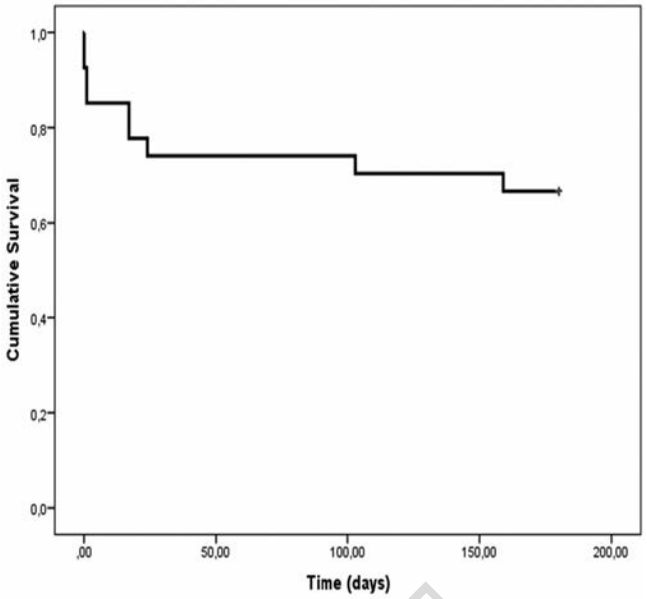

Figure 1. *Kaplan-Meier survival curve at 180 days from admission.*

bleeding, requiring transfusions in 1 case, whereas 2 patients presented with TIMI minor bleeding. Six patients (22%) had reversible acute renal failure that was treated by aggressive hydration. Two patients underwent a staged PCI on a non-culprit vessel. Average length of hospitalization was 9 ± 5 days. Mean left ventricular ejection fraction at discharge was 42.6 ± 8.5%.

Six-month follow-up after admission was available in all surviving patients. Four patients died after discharge; two died at home (apparently from cardiac death) at 3 and 5 months, respectively, whereas the other 2 died within 2 weeks of discharge (1 from cardiac death and 1 following a major stroke). Eighteen (67%) out of the initial cohort were alive at 180 days (Figure 1).

Discussion

The management of acute coronary syndromes in the elderly represents a challenge because these patients, although numerically growing, are underrepresented in randomized clinical trials.[7]

Very old patients, such as nonagenarians, represent an even more elusive subgroup; indeed, there is a paucity of outcome data after PCI in this population, limited to small series.[8,9]

Data from the CRUSADE registry in non-ST segment elevation acute coronary syndromes (NSTEACS) show that nonagenarians have different clinical characteristics as compared to elderly patients ages 75-89 years; in nonagenarians, indeed, there is a higher prevalence of female gender, consistent with the longer life expectancy of women, whereas coronary risk factors and previous cardiovascular disease are less frequent. Nonagenarians are also less likely to receive guideline-recommended therapies such as statins, glycoprotein (GP) IIb/IIIa inhibitors, and cardiac catheterization.[10] In the setting of STEMI, there is evidence supporting reperfusion therapy in eligible patients up to the age of 85 years.[11] A meta-analysis of three randomized trials comparing primary PCI with fibrinolysis in elderly patients showed the superiority of percutaneous revascularization, with a statistically significant lower rate of death, reinfarction, and stroke; however, mean age of patients enrolled in these trials was 80 years.[12]

Data from the EUROTRANSFER registry showed that patients >85 years old are less likely to achieve TIMI flow grade 3 after PCI and are more likely to have PCI complications, with a 30-day mortality of 20.4%.[13] There are several observational registries reporting the outcome of primary PCI in nonagenarians. In a series of 22 patients, Koutouzis et al reported an 82% procedural success rate with a 27% hospital mortality rate.[14] In a multicenter Italian retrospective registry of 100 patients, Danzi et al reported a 85% procedural success rate with a 19% hospital mortality rate.[15] In a multicenter Spanish retrospective registry (38 patients) Salinas et al reported a 90% procedural success rate and a 34.2% hospital mortality rate.[16] In all these registries, procedural success was defined as TIMI flow grade ≥2 after PCI and no significant residual stenosis, as we did in our study. However, such a definition is questionable, since in randomized controlled trials, procedural success is commonly defined as the achievement of TIMI flow grade 3 and <30% residual stenosis. Moreover, postprocedural TIMI flow grade 3 is associated to a significantly lower 1-year mortality rate as compared to TIMI flow grade 2.[17]

In our series, we observed an 89% procedural success rate and a 18.5% hospital mortality rate. The rate of postprocedural TIMI flow grade 3 was 74%, similar to the rate reported by Salinas et al (76%), but lower than reported by Danzi et al (82%).

Consistently with most of the aforementioned studies, we observed a higher prevalence of female gender and a low prevalence both of some coronary risk factors, such as smoking and hypertension, and of previous history of ischemic heart disease. This is likely secondary to a selection bias, since all these factors play a major role in allowing the population to achieve advanced age.

Nonagenarian patients are less likely to receive aggressive antiplatelet therapies, such as GP IIb/IIIa inhibitors; indeed, in NSTEACS, the use of these drugs was found to be associated to increased mortality in this population, possibly mediated by an increase in major bleeding rates.[10] In the setting of STEMI, the risk/benefit ratio of GP IIb/IIIa inhibitors might be more favorable, since in our series, as well as in the series by Koutouzis et al and Danzi et al, abciximab and eptifibatide were used in about 40% of patients and were not associated with increased bleeding, despite a large prevalence of femoral vascular approach for primary PCI. In one study, the administration of abciximab was actually found to be associated with a decrease in 6-month mortality.[15]

The incidence of acute renal failure in our study was relevant (22%) and is attributable to contrast-induced nephropathy, since serum creatinine peaked 48 to 72 hours after the procedure. Contrast-induced nephropathy is

known to be associated both with urgent procedures and with advanced age;[18] in animal models, age *per se* was shown to increase the susceptibility to nephrotoxicity induced by iodinated contrast media.[19] However, acute renal failure was responsive to aggressive hydration and no patient needed hemodialysis.

Another important issue is the fate of nonagenarian patients who survive an acute coronary syndrome and are discharged alive from the hospital. Indeed, medium-term follow-up data are lacking, since most studies reported only in-hospital or 30-day outcomes. In our series, as in the registry authored by Danzi et al, 6-month survival status was assessed in all patients and looked very similar in the 2 studies (67% vs 68%, respectively).

Study limitations. Our study has several limitations, such as the low number of patients and the retrospective, single-center design. Indeed, we cannot exclude a selection bias in enrollment, since some patients could not have been referred to primary PCI because of severe comorbidities, terminal illness, or dementia. Nevertheless, the prevalence of nonagenarians in our primary PCI population was similar to that reported in other studies (0.7%-2.0%).[14,15]

Moreover, due to the long period of enrollment (9 years), the impact of more recent strategies associated with mortality benefit in primary PCI, such as bivalirudin[20] and radial approach,[21] could not be evaluated. All these limitations are common to the other studies investigating such a complex and infrequent population.

Conclusion

Our data suggest that primary PCI is feasible and effective in nonagenarian patients with STEMI. Most adverse events are confined to the early phase (within 30 days from admission), whereas medium-term follow-up is satisfactory, especially considering the limited life expectancy of these patients. Major bleeding seems not to be an issue and should not discourage the administration of guideline-recommended antithrombotic therapies.

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