ORIGINAL ARTICLE

# Primary percutaneous coronary intervention for ST elevation myocardial infarction in nonagenarians

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## ABSTRACT

**Objective** To assess outcomes following primary percutaneous coronary intervention (PCI) for ST-segment elevation acute myocardial infarction (STEMI) in nonagenarian patients.

**Methods** We conducted a multicentre retrospective study between 2006 and 2013 in five international high-volume centres and included consecutive all-comer nonagenarians treated with primary PCI for STEMI. There were no exclusion criteria. We enrolled 145 patients and collected demographic, clinical and procedural data. Severe clinical events and mortality at 6 months and 1 year were assessed.

**Results** Cardiogenic shock was present at admission in 21%. Median (IQR) delay between symptom onset and balloon was 3.7 (2.4–5.6) hours and 60% of procedures were performed through the transradial approach. Successful revascularisation of the culprit vessel was obtained in 86% of the cases (thrombolysis in myocardial infarction flow of 2 or 3). Major or clinically relevant bleeding was observed in 4% of patients. Median left ventricular ejection fraction post PCI was 41.5% (32.0–50.0). The in-hospital mortality was 24%, with 6 months and 1-year survival rates of 61% and 53%, respectively.

**Conclusions** In our study, primary PCI in nonagenarians with STEMI was achieved and feasible through a transradial approach. It is associated with a high rate of reperfusion of the infarct-related artery and 53% survival at 1 year. These results suggest that primary PCI may be offered in selected nonagenarians with acute myocardial infarction.

## INTRODUCTION

Medical and technical progress has led to increased life expectancy, resulting in a significant proportion of very old patients with specific health problems. In this growing population, cardiovascular disease is frequent and ischaemic heart disease remains one of the leading causes of morbidity and mortality.[1] [2] However, most clinical trials exclude patients aged >75–80 years as prolonged follow-up may be compromised by limited life expectancy. It also appears that side effects of new therapies are mostly observed in patients aged >75 years.[3] Other factors such as atypical symptoms, delayed presentation and associated comorbidities further add to advanced age as being one of the most powerful predictors of adverse outcome in acute coronary syndromes.[4] As a result, elderly patients >75 years old are under-represented in clinical trials.[5–8] Additionally, prior studies have reported an increased rate of vascular complications, bleeding and cardiac mortality associated with percutaneous coronary intervention (PCI) in the elderly.[9–11] As a consequence, it is difficult to assess the risk/benefit balance for care protocols and pharmacological interventions in these patients.[12] To date, no clinical randomised trial is available for the management of ST-segment elevation myocardial infarction (STEMI) in elderly patients. Non-revascularised patients admitted with STEMI are known to carry poor outcomes.[13] [14] Even though primary PCI has been established as the standard of care, a conservative strategy is often adopted when facing this situation in nonagenarians.[15] [16] The first case report of primary PCI in a nonagenarian was published in 2002.[17] Few studies based on cohorts have suggested feasibility for invasive management of STEMI in nonagenarians.[18–21] Our team has recently published the outcome of the largest series of nonagenarians presenting with STEMI, but data are limited to in-hospital follow-up only.[22] Through this paper, we present data of the largest series of consecutive patients aged 90 years or older admitted with STEMI and treated by primary PCI in contemporary practice.

## METHODS

### Study population

We retrospectively enrolled 145 consecutive patients aged ≥90 years hospitalised for STEMI and treated with primary PCI in five international high-volume centres between 2006 and 2013. These centres were Freeman hospital (Newcastle Upon Tine, UK), Pitié-Salpêtrière teaching hospital (Paris, France), Chaim-Sheba Medical Center (Tel-Hashomer, Israel), André Mignot hospital (Versailles, France) and Bichat teaching hospital (Paris, France) and respectively provided 46, 43, 28, 20 and 8 patients. Their respective numbers of primary PCI in 2013 were 250, 350, 290, 112 and 200. All patients had follow-up during in-hospital stay, with completed baseline characteristics, pharmacological management, angiographic findings and procedure results. A 12-month follow-up was obtained during patients' visit to outpatient clinics or by telephone interview. The inclusion criteria for primary PCI were clinical symptoms (such as general weakness, thoracic symptoms, eg, persisting chest pain over 30 min or dyspnoea, digestive

symptoms such as nausea or vomiting, neurological alteration including acute confusional state) combined with electrocardiographic ST-segment elevation over 1 mV in at least two contiguous leads and admission within 12 hours of symptoms onset or 24 hours for patients with evidence of continuing ischaemia. There were no exclusion criteria.

## Cardiac catheterisation

The interventional procedure was performed by senior interventional cardiologists using 6 Fr guiding catheters in all cases once verbal consent for treatment had been obtained from the patient or relatives. The vast majority of patients received a loading dose of two antiplatelet therapies and heparin before PCI. The choice of antithrombotic therapy, the use of thrombus aspiration catheter and the type of stent were left to the discretion of the attending interventionist.

## Outcomes evaluation

All patients were observed in a coronary care unit for at least 24 hours before discharge or transfer. We recorded the incidence of severe clinical events such as death, recurrent myocardial infarction, target vessel revascularisation, stroke, procedure-related complications, acute renal failure and major or clinically relevant bleeding during hospitalisation. Survival data at 6 months and 1 year were collected. A successful procedure was defined as achievement of thrombolysis in myocardial infarction (TIMI) grade 2 or 3 flow, <50% residual stenosis and absence of any major clinical adverse event within 24 hours. A failed procedure was defined as resulting in TIMI grade 0–1 flow regardless of residual stenosis with the absence of any major clinical adverse event within 24 hours. This could result from no reflow phenomenon or coronary dissection. A complicated procedure was defined as resulting in death, recurrent myocardial infarction (ie, at least doubling creatine kinase from the initial value with >10% of creatine kinase-MB fraction (CK-MB)) within 24 hours. Major and minor bleeding events were defined using the criteria of the TIMI trial group and acute renal failure was defined as an absolute increase in serum creatinine of at least 0.3 mg/dL (26.4 µmol/L) or a percentage increase in serum creatinine of at least 50% according to the Risk, Injury, Failure, Loss and End-Stage Kidney Disease criteria.

## Statistical analysis

Continuous variables are expressed as median and IQR, and discrete variables as absolute values and percentages. The log-rank test was used to compute the significance of time-to-event data, and survival rates were estimated using the Kaplan-Meier method. The Kaplan-Meier curve was plotted through day 730 (2 years). An additional Cox proportional hazard regression analysis was performed to describe the effects of gender and age on survival, with and without adjustment on centre. Analyses were performed using SPSS software V.23 (IBM, Armonk, New York, USA).

## RESULTS

### Patient demographics

Median (IQR) age was 92 (91–94) years (extreme 90–102) with the majority female (62%) and associated comorbidities were low. Baseline characteristics of the study population are reported in table 1, and biological parameters are summarised in table 2.

In this cohort, no patient was admitted for asymptomatic acute myocardial infarction. The clinical presentation of these patients was severe with 43% in Killip class II–IV including

**Table 1** Baseline demographics and clinical data

| Baseline characteristics | |
| --- | --- |
| Age (years) | 92.0 (91.0–94.0) |
| Sex ratio (% men) | 38 |
| Body mass index (kg/m$^2$) | 23.4 (21.0–25.5) |
| Hypertension (%) | 53 |
| Hyperlipidaemia (%) | 25 |
| Diabetes mellitus (%) | 14 |
| Active smoker (%) | 8 |
| History of coronary heart disease (%) | |
|    Previous MI | 24 |
|    Previous PCI | 4 |
|    Previous CABG | 5 |
| Clinical presentation (%) | |
|    Chest pain | 86 |
|    Dyspnoea | 21 |
| Killip class at admission (%) | |
|    I | 57 |
|    II | 12 |
|    III | 10 |
|    IV | 21 |
| LVEF at admission (%) | 41.5 (32.0–50.0) |
| Electrocardiographic presentation (%) | |
|    Anterior STEMI location | 39 |
|    LBBB | 4 |
|    STEMI with ST elevation in avR | 3 |

CABG, coronary artery bypass graft; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation MI.

nearly a third presenting with cardiogenic shock or severe pulmonary oedema.

## Antithrombotic management

Antithrombotic management of the patients is recorded in table 3. All patients received an intravenous loading dose of aspirin between 250 and 500 mg before the procedure. P2Y12 inhibitors were administered in 97% of the cases and consisted majorly in clopidogrel loading (300–600 mg). Glycoprotein IIb/IIIa inhibitors, predominantly abciximab, were administered during the cardiac catheterisation in 36% of the patients. Heparin, predominantly unfractionated heparin, was used in

**Table 2** Biological parameters

| Biological data | |
| --- | --- |
| Cardiac troponin (cTnI) peak (ng/mL) | 45.0 (10.9–94.0) |
| Creatine kinase peak (UI/L) | 932.0 (111.5–2468.0) |
| Haemoglobin at admission (g/dL) | 11.9 (11.0–12.8) |
| Nitrogen urea at admission (mmol/L) | 11.9 (6.7–15.2) |
| Serum creatinine at admission (µmol/L) | 111.0 (89.0–139.7) |
| Creatinine clearance (mL/min)—MDRD | 49.0 (36.8–61.0) |
| Cholesterol (g/L) | 1.66 (1.43–1.94) |
| LDL-C (g/L) | 0.92 (0.72–1.09) |
| HDL-C (g/L) | 0.52 (0.42–0.65) |
| Triglyceride (mmol/L) | 0.82 (0.66–1.05) |
| Fibrinogen (g/L) | 4.1 (3.5–5.0) |

HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol. MDRD, Modification of the Diet in Renal Disease.

**Table 3** Antithrombotic therapy pre or per PCI

| Antithrombotic treatment | |
|---|---|
| Aspirin (%) | 99 |
| Clopidogrel (%) | 94 |
| Prasugrel (%) | 3 |
| Ticagrelor (%) | 0 |
| Glycoprotein IIbIIIa inhibitors (%) | 36 |
| Heparin (%) | 90 |
| LMWH (%) | 23 |
| Bivalirudin (%) | 1 |

LMWH, low-molecular weight heparin; PCI, percutaneous coronary intervention.

90% of cases. Unfractionated heparin was administered at 100 UI/kg before the beginning of the procedure with additional doses at the discretion of the physician. When chosen, low-molecular-weight heparin was administered at an intravenous loading dose of 0.5 mg/kg, then additional doses if necessary depending on procedure duration.

### Angiographic and procedural characteristics

The median time from symptom onset to PCI was 3.7 (2.4–5.6) hours. Primary PCI was performed within 6 hours after symptoms onset in 78% of cases. Angiographic findings and interventional procedure are detailed in table 4. The transradial

**Table 4** Angiographic characteristics and procedural information

| Procedural findings | |
|---|---|
| Time from symptoms to PCI (hours) | 3.7 (2.4–5.6) |
| Catheterisation access (%) | |
|   Radial | 60 |
| Single-vessel coronary disease (%) | 53 |
| Single-vessel coronary PCI (%) | 74 |
| Infarct-related coronary artery (%) | |
|   Left main | 4 |
|   Left anterior descending | 41 |
|   Circumflex | 14 |
|   Right | 45 |
|   CABG | 3 |
| Thrombus aspiration (%) | 14 |
| TIMI flow grade after procedure (%) | |
|   0 | 12 |
|   1 | 1 |
|   2 | 6 |
|   3 | 81 |
| Coronary stenting (%) | |
|   BMS | 75 |
|   DES | 9 |
|   POBA | 10 |
| Procedure success (%) | |
|   Successful PCI | 86 |
|   Failed PCI | 11 |
|   Complicated PCI | 3 |
| Use of protection device (%) | 2 |
| IABP (%) | 0 |
| Use of inotropes during procedure (%) | 26 |

BMS, bare metal stent; CABG, coronary artery bypass graft; DES, drug-eluting stent; IABP, intra-aortic balloon pump; PCI, percutaneous coronary intervention; POBA, plain old balloon angioplasty; TIMI, thrombolysis in myocardial infarction.

approach was feasible in the majority (60%) but varied between centres from 40% to 84%. Successful coronary revascularisation was obtained in 94% of the patients with an overall successful procedure rate of 86%. Failed PCI occurred in 11% of the patients, mostly resulting from distal embolisation or coronary dissection or inability to pass the wire through the thrombus. Complicated PCI was observed in 3% of the patients, mostly resulting from cardiac arrest during primary PCI, either due to refractory cardiogenic shock, refractory ventricular fibrillation or asystole. This was due to left main coronary rupture during angioplasty in one case and to no reflow in another one. During procedure, 26% of the patients received inotropic support, mainly with dobutamine, but none had intra-aortic counterpulsation support.

### Clinical outcomes

The median hospital stay was 4.0 (2.0–6.5) days (extreme 1–28 days) with coronary care unit stay not prolonged over 3 days. Longer hospital stay was mostly due to social issues. Very short hospital stays (<2 days) resulted in transfers back to the originating cardiology units from where patients were first referred. In-hospital outcomes are shown in table 5.

Of significance, despite intensive antiplatelet and anticoagulant therapy, major or clinically relevant bleeding events were recorded in only six patients (4%) during in-hospital follow-up. Ventricular arrhythmias occurred in 17% of patients, all within 24 hours of procedure. Acute renal failure complicated the interventional procedure in 10% with favourable resolution in half.

The overall in-hospital mortality was 24%. Patients with Killip class I, II, III and IV at admission experimented in-hospital mortality of 12.2%, 11.8%, 26.7% and 47.8%, respectively.

### Pharmacological management at discharge and follow-up

At discharge, all but one patient were taking aspirin with 94% on dual antiplatelet therapy. No platelet function assessment or genetic tests were performed in these patients. The pharmacological management of patients is presented in table 6.

Complete follow-up was obtained at 6 and 12 months, but 26% of the patients were lost to follow-up at 24 months. In total, 6-month, 1-year and 2-year overall survival rates were 61% (95% CI 53% to 69%), 53% (45% to 61%) and 43% (34% to 52%), respectively (figure 1). Almost all (92%) cardiovascular deaths occurred before day 30 in contrast to non-cardiovascular deaths. Two-year survival was significantly lower in females versus males (p<0.05) and in patients with anterior STEMI (p<0.01) (figure 2). Lower survival in females remained after adjustment on age and centre (Hazard Ratio vs males 1.72, 95% CI 1.08 to 2.77; p<0.03).

**Table 5** In-hospital outcomes

| | |
|---|---|
| Death (%) | 24 |
| Recurrent MI (%) | 1 |
| Target vessel revascularisation (%) | 4 |
| Ventricular arrhythmias (%) | 17 |
| Major or clinically relevant bleeding (%) | 4 |
| Acute renal failure (%) | 10 |
| Stroke (%) | 1 |

MI, myocardial infarction.

**Table 6** Treatment at hospital discharge

| | |
|---|---|
| Aspirin (%) | 99 |
| Clopidogrel (%) | 94 |
| Prasugrel (%) | 3 |
| PPI (%) | 79 |
| Beta-blockers (%) | 66 |
| Statins (%) | 81 |
| CEI or ARA (%) | 62 |
| Aldosterone inhibitors (%) | 0 |
| Vitamin K antagonist (%) | 0 |
| Amiodarone (%) | 21 |

ARA, angiotensin receptors antagonists; CEI, converting enzyme inhibitors; PPI, proton pump inhibitors.

## DISCUSSION

Previous studies have highlighted the increased rate of procedural failure and complications when performing PCI in very old patients,[9] [23] and data consistently report age to be a strong predictor of mortality. This is particularly high in nonagenarians at 30 days and 1 year and increases with the extent of coronary artery disease and associated conditions.[1–4] Nevertheless, the results of this study of contemporary practice show that selected nonagenarians presenting with STEMI can be successfully and safely treated by primary PCI.

This study provides interesting data on the characteristics of highly selected cohort. The clinical presentation of an acute myocardial infarction in this specific population may be very different from that seen in younger patients, ranging from completely asymptomatic to general weakness or various thoracic, digestive or neurological symptoms. In our series, all patients presented with thoracic symptoms (acute chest pain and/or shortness of breath), which may be due to a selection bias. For all that, physicians should be aware of atypical and non-specific symptoms, especially abdominal symptoms such as nausea, vomiting, abdominal pain and diarrhoea, weakness and altered mental status. As expected in this population, the majority in our cohort had multivessel coronary disease and mild-to-severe altered left ventricular dysfunction. The prevalence of presentation in Killip class III and IV was high, >30% in our series. This figure may be higher as a number of this population may have not been identified as Killip class IV at admission due to the absence of hypotension and the paucity of clinical symptoms as hypoperfusion may be difficult to diagnose in the elderly.

The first point to discuss is the unexpectedly low rate of complications in our series. Although PCI was found to be associated with a higher rate of complications and mortality in patients aged >75 years in other studies,[24–26] we noticed acceptable rates of in-hospital major complications, especially regarding stroke or major bleeding complications with low incidence of acute renal failure. Despite intensive antiplatelet

**Figure 1** Kaplan-Meier curves of survival after primary percutaneous coronary intervention for overall mortality (A) and 1-year cardiovascular (B) and non-cardiovascular (C) mortality.
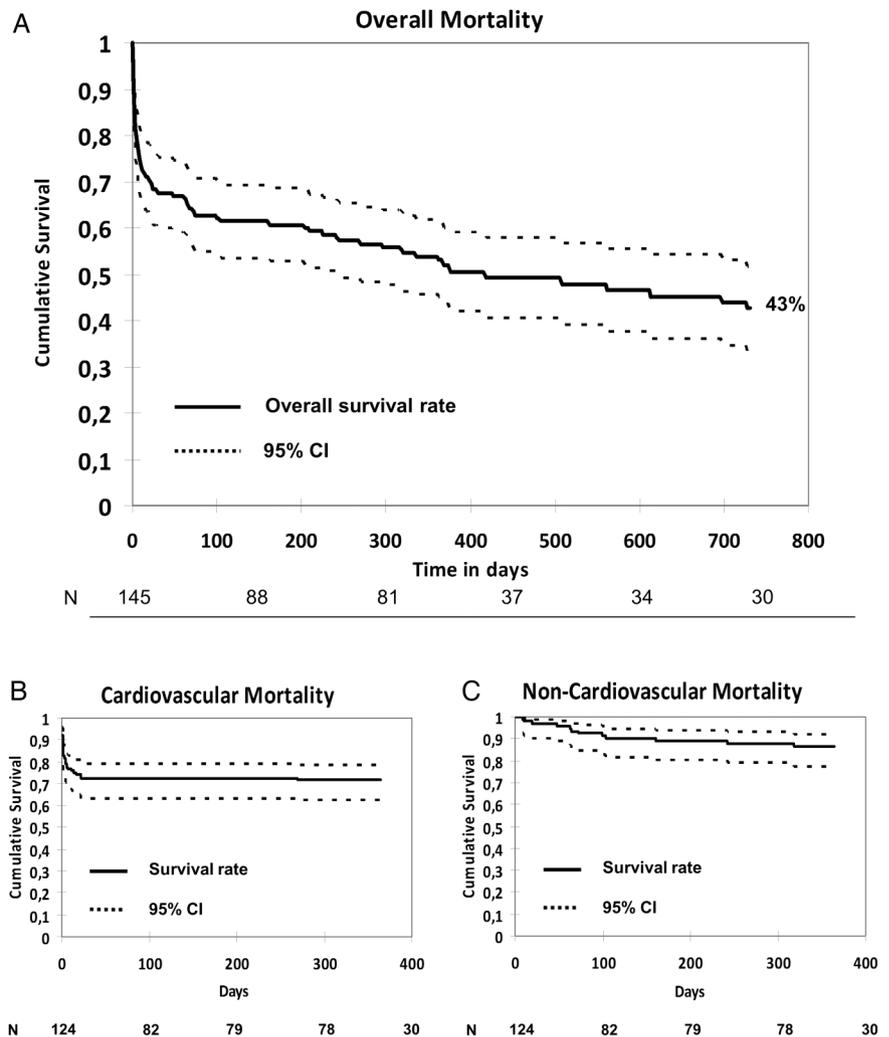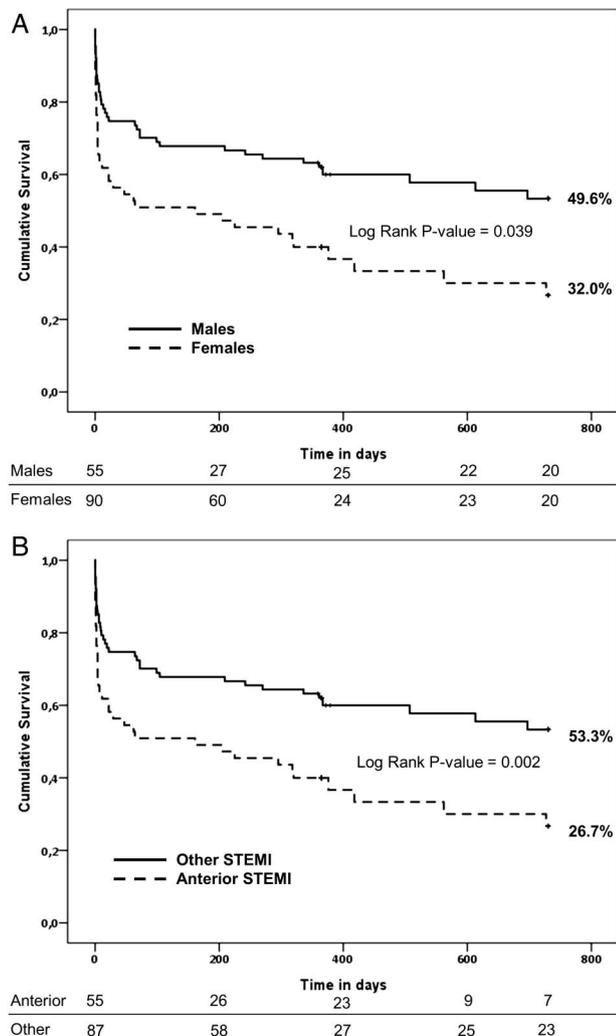
**Figure 2** Kaplan-Meier curves showing survival in males versus females (A) and in patients with anterior versus non-anterior ST-segment elevation myocardial infarction (STEMI) (B).

therapy including use of glycoprotein IIb/IIIa inhibitors and most often 600 mg clopidogrel initial loading dose, no fatal or severely disabling bleeding such as intracranial haemorrhage was reported in-hospital. The high rate of procedures conducted through the transradial approach may explain the low rate of access site bleeding complications. Of the six patients who had clinically relevant bleeding, only one received glycoprotein IIbIIIa inhibitors and two underwent femoral access procedures. The very old patients are also at increased risk of contrast-induced acute renal injury and acute renal failure. Indeed, primary PCI with iodinated contrast agents increases the risk of contrast-induced nephropathy exacerbated by altered renal clearance at admission and the frequent Killip III/IV presentation with associated organ hypoperfusion. However, even though the creatinine clearance may have dropped in some patients during hospital stay, this alteration of renal function was observed to be transient except in those with fatal outcome and it is important to note that no death resulted from a renal-related cause.

The second point of discussion is the antithrombotic strategy. A significant administration of low-molecular-weight heparin was observed in some recruiting centres and is consistent with its benefit over unfractionated heparin previously reported in other studies.[27] However, its role in the oldest old can be questioned as mean creatinine clearance at admission approaches 30 mL/min. Furthermore, the choice of the antiplatelet therapy should be carefully made. Although no early bleeding occurred in our series, to date, data remain consistent for clopidogrel prescription over any other thienopyridine, which could increase the long-term bleeding risk. It must be remembered that in some cases oral administration of clopidogrel could be compromised or delayed as a high proportion of the patients may be unable to swallow anything in the context of pulmonary oedema or cardiogenic shock and altered conscious state. Nevertheless, bleeding complications may have occurred after hospital discharge. Prasugrel was rarely administered due to the time period of inclusion and advanced age population. However, new P2Y12 inhibitors appear as an interesting alternative to clopidogrel in selected patients.[28] Further data may shortly be available in this field (SENIOR study, NCT 02099617).

The third point of discussion is the delay of primary PCI. We found a mean delay from symptoms to primary PCI at 5.8 ±7.6 hours, which is a consequence of multiple factors including difficulties in diagnosis and sometimes refusal from other healthcare organisations to perform interventional procedures in elderly patients based on outdated data and their own perception of the risk-to-benefit ratio. The recognition of the benefits of primary PCI in the oldest old should lead to carers and public health measures, recognising that the earlier the diagnosis is made and the patient referred to the catheterisation laboratory, the better will be the outcome from primary PCI. Considering this last argument, additional data provided by our study may help to change current perceptions and potentially influence guidelines on the management of STEMI.[29]

The fourth point of discussion is the global short-term and long-term outcomes. Survival rate at hospital discharge is consistent with previous studies, thus making the case for primary PCI in selected nonagenarian patients presenting with STEMI. Helft et al recently reported a 24.9% mortality rate in a cohort of 418 nonagenarians with STEMI and in-hospital follow-up only, very close to the 24% mortality rate that we noticed. In our series, as in both registries authored by Danzi et al[18] and Rigattieri et al,[21] 6-month survival rates looked similar (61%, 67% and 68%, respectively). In patients who were discharged alive, 1-year cardiovascular mortality was very low (only one cardiovascular death from day 30 through 1-year of follow-up). Survival rates were higher than those reported in non-reperfused elderly STEMI patients (in-hospital and 1-year mortality rates of 53% and 69%, respectively, in a cohort of 139 octogenarians).[14] Overall survival was in the range of that in general population aged >90 years in France (age-specific annual death rates between ages 90 and 94 years of 15% in females and 21% in males).[30]

However, we recognised some limitations to our study. The main limitation of this study is that there is no comparison group, such as nonagenarians with STEMI who were not managed with primary PCI. This may be problematic because the study cohort appears to be highly selected with remarkably low comorbidity profile. As our study is retrospective and non-randomised, it is not possible to draw definite conclusions over the absolute benefit of primary PCI. The generalisability of the study findings to other very old patients treated at other institutions with perhaps less experienced interventionalists is also uncertain. Another important limitation is that we cannot provide data on functional outcomes following the procedure. The proportion of patients who were able to return to their previous level of functioning remains unknown. The proportion of

patients who previously lived in the community and subsequently required institutionalisation is lacking as well. An unknown proportion of patients may have had new activities of daily living or instrumental activities of daily living dependencies.

In summary, the developed world is ageing and clinical trials typically exclude elderly patients over the age of 75 years. Following myocardial infarction, the outcomes in the oldest old patients are poor and there are limited data in patients >90 years of age. Our data support the use of primary PCI to benefit this specific category of population. Finally, these findings show that in keeping with previous series primary PCI is technically feasible in very old patients, with a lower rate of complications than expected, a lower mortality than expected and successful angiographic and clinical results at short-term and longer follow-up. The transradial approach may be routinely chosen by experienced operators to reduce adverse events, particularly puncture site-related bleeding complications. The data presented from several centres in different countries are the largest series to date with the longest follow-up. Our study provides some evidence that in contemporary practice mechanical reperfusion of STEMI in nonagenarians may improve the in-hospital and long-term outcomes.

## CONCLUSION

This study suggests that primary PCI can be safely and successfully performed in nonagenarians presenting with STEMI through a transradial approach. Similar to younger patients in previous large randomised trials, this invasive strategy is associated with a high rate of achieved reperfusion of the infarct-related artery and low incidence of procedure-related complications in this specific population. Use of contemporary strategies in our series was associated with a lower mortality rate than expected considering the severe clinical presentation, and this may be further improved with earlier patient referral. These results should encourage primary PCI to be offered to selected

nonagenarians with acute myocardial infarction. Further clinical studies involving a larger cohort of elderly patients and newer antithrombotic approaches may help to better define the benefits and risks ratio of primary PCI in nonagenarians with STEMI especially in terms of quality of life.

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## Key messages

### What is already known on this subject?

Nonagenarians presenting with ST elevation myocardial infarction are a growing population but no randomised clinical trial support invasive management. Percutaneous coronary intervention is associated with a higher rate of complications in the elderly patients. Only a few observational studies based on cohorts with limited follow-up suggest that primary percutaneous angioplasty could improve the outcome.

### What might this study add?

In this cohort of 145 nonagenarians treated by primary percutaneous intervention, 1-year survival rate is 53%. Our results are consistent with previous small series of patients, demonstrating feasibility and safety of emergent myocardial revascularisation through transradial access and suggesting improvement of long-term survival compared with medical management.

### How might this impact on clinical practice?

Primary percutaneous coronary intervention may be feasible and safely performed through transradial approach in carefully selected nonagenarians with ST-segment elevation myocardial infarction.

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