Age-Related Changes in Treatment Strategies for Acute Myocardial Infarction: A Population-Based Study

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OBJECTIVES: To compare across four age groups (<65, 65–74, 75–84, ≥85) the determinants of coronary reperfusion therapy (CRT) use in ST-segment elevation acute myocardial infarction (STE-AMI).

DESIGN: Population-based, observational study.

SETTING: Performed in the health district of Florence, Italy, where percutaneous coronary intervention (PCI) is the preferred CRT.

PARTICIPANTS: Nine hundred thirty patients with STE-AMI prospectively enrolled in the Florence AMI registry.

MEASUREMENTS: Use of CRT, clinical factors associated with CRT use.

RESULTS: CRT use was reduced from 71% at younger than 65 to 31% at aged 85 and older ($P<.001$). After adjusting for chronic comorbidity, Killip class, admission hospital category, hospitalization delay, and AMI location, CRT use was 29% ($P=.17$) lower at age 75 to 84 and 63% ($P<.001$) lower at age 85 and older than at younger than 65. Within each age group, the probability of receiving CRT was three to five times greater in patients directly admitted to the hospital with PCI facilities. Acute cardiac failure and chronic comorbidity were associated with lower CRT use only in patients aged 65 and older. Patients aged less than 85 years who received reperfusive therapy had a significantly lower risk of death (-44%, $P=.045$) at 1 year, whereas it was less evident and nonsignificant (-27%, $P=.27$) in patients aged 85 and older.

CONCLUSION: Results confirm that, although they might substantially benefit from CRT during STE-AMI, older patients are excluded from CRT even when eligible. This further indicates that clinicians are not yet completely prepared to manage most efficiently frail elderly with AMI, a task requiring a specific interdisciplinary training program in geriatric cardiology. **J Am Geriatr Soc 52: 1355–1360, 2004.**

Key words: acute myocardial infarction; treatment; reperfusion; older; PCI

European and U.S. guidelines indicate that coronary reperfusion therapy (CRT) is the first-choice treatment of ST-segment elevation acute myocardial infarction (STE-AMI).[1,2] Of CRT strategies, primary percutaneous coronary intervention (PCI) has been shown to reduce the mortality and the complication rates of STE-AMI[3] more markedly than thrombolysis; such clinical benefits have been shown in older patients.[4,5] Despite this, and in the absence of specific limitations posed by guidelines to the use of PCI in older patients,[6] observational studies have demonstrated that CRT during AMI is still underused in advanced age.[7–9] Moreover, although greater comorbidity,[10,11] delayed hospital admission,[12] and increased risk of procedural complications[10,13] have all been advocated to justify the limited use of CRT in the elderly, it has been shown that even eligible older patients quite often do not receive CRT.[7]

The Florence Acute Myocardial Infarction (AMI-Florence) registry is a population-based study performed in the Florence (Italy) health district, where primary PCI is the most widely used CRT.[14] Using this data set, the present analysis was aimed at comparing across age groups the frequency and the determinants of use of CRT in patients with STE-AMI admitted to hospital within 24 hours of symptom onset.

METHODS

The structure and setting of the AMI-Florence registry have been detailed elsewhere.[14] Briefly, the Florence health

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district (about 800,000 inhabitants) comprises five community hospitals and one teaching hospital, the latter implementing high-volume programs for primary PCI. All patients arriving alive with a diagnosis of STE-AMI of 0.1 mV or greater in two or more adjacent leads or new onset left bundle-branch block on first electrocardiogram at one of the six hospitals between March 2000 and February 2001 were prospectively screened for eligibility and enrolled in the study if AMI was confirmed by a rise in serum total creatine phosphokinase activity at least twice above the upper normal limit within 72 hours of symptom onset. Although the eligibility criteria for CRT were substantially uniform across the six hospitals, the indication of primary PCI or thrombolysis was left to the emergency department or coronary care unit physicians.

Data Collection and Check

As detailed elsewhere,[14] information on demographics, medical history, clinical and electrocardiogram features of AMI, time between onset of symptoms and hospital admission, and treatment and outcome during hospitalization was collected using standard case-report forms. These were sent periodically from each participating center to the study coordinating center for database entry. The completeness of enrollment was periodically checked through a hospital discharge system that records all admissions to regional hospitals. The discharge diagnosis of AMI for patients residing in the Florence district and admitted alive to study hospitals was matched with the database of patients enrolled in the study, and for nonmatching cases, the original clinical record was checked. When enrollment criteria were met, the case was included in the study. Therefore, the series of AMI cases in the study is population-based and fully representative of the incident cases in the area over the study period.

A follow-up study was performed by consulting the registry office of the municipality of residence, to assess all participants' life status at 1 year.

Statistical Analysis

Analyses were performed using the Stata statistical package (version 6.0, Stata Corp., College Station, TX). Categorical and continuous variables were compared across subgroups using two-tailed chi-square and Student *t* tests, respectively. Because, in the study area, thrombolysis was used in only a minority of cases,[14] for the purpose of the present analysis, PCI and thrombolysis were grouped into a single CRT variable. Univariate and multivariate stepwise logistic regression models (forward method with $P < .10$ for entrance into and $P > .15$ for removal from the model) were fitted to identify factors significantly associated with use of CRT. Odds ratios (ORs) and 95% confidence intervals (CIs) were also calculated, with an OR of more than 1.0 indicating an association with a higher probability and an OR of less than 1.0 a lower probability of receiving CRT than for the reference stratum. The goodness of fit of the model was checked using the Hosmer-Lemeshow test. In addition, multivariate Cox regression models were used to assess the prognostic effect of treatments on 1-year survival, adjusting for clinical and demographic variables. To this purpose, hazard ratios (HRs) and 95% CIs were calculated. Patients with multiple episodes of AMI during the study period were included only once in survival analysis, with follow-up observation starting from the first episode.

RESULTS

Patients' Characteristics by Age Group

Of 930 cases of STE-AMI admitted to hospital within 24 hours of symptom's onset,[14] 290 (31.1%) were younger than 65, 246 (26.5%) were 65 to 74, 246 (26.5%) were 75 to 84, and 148 (15.9%) were 85 and older (Table 1). There were significant age trends for sex distribution, with a progressive reduction in the prevalence of men, and for the frequency of chronic comorbidity. The prevalence and the mean number of associated chronic cardiovascular (previous myocardial infarction, angina pectoris for >1 month, cardiac arrhythmias, congestive heart failure) and noncardiovascular diseases (cerebrovascular disease, peripheral artery disease, chronic renal failure, chronic obstructive pulmonary disease, active cancer, anemia, diabetes mellitus) progressively increased with increasing age (Table 1). Several other characteristics were different across age groups. In particular, the proportion of patients admitted directly to the hospital with PCI facilities and that of patients transferred to the hospital from other hospitals without such facilities was progressively lower with advancing age. The interval between symptom onset and hospital arrival (data not shown) was shorter in patients younger than 65 than in the other age groups, although this difference did not attain statistical significance (median: 120 and 150 minutes, respectively, $P = .12$). Moreover, the proportion of patients who were in Killip Class 1 on hospital admission was progressively lower, whereas that of patients in Killip Class 2 to 3 was markedly higher, with increasing age. Finally, although cases with anterior Q-waves AMI were similarly frequent across age groups, cases with nonanterior Q-waves and non-Q waves AMI were less and more frequent, respectively, in older patients (Table 1).

Use of CRT by Age Group

The proportion of patients who received any form of CRT progressively and significantly ($P < .001$) decreased with increasing age (Table 2). As reported in a previous analysis of the AMI-Florence registry,[14] primary PCI was the most common reperfusion strategy at any age, with PCI representing about 90% of all reperfusion treatments (range across age groups: 89–93%), but use of PCI decreased with increasing age, from 66% at younger than 65, to 54% at age 65 to 74, 39% at age 75 to 84, and 28% at age 85 and older, with the highest proportion of thrombolysis as an alternative treatment being, respectively, 5%, 6%, 4% and 3%. The median door-to-balloon time for primary PCI was lowest (30 minutes) in patients younger than 65, and although this difference was not significant ($P = .07$), it doubled in those aged 75 to 84 and 85 and older. In patients who underwent primary PCI, the proportions of those who were treated with at least one coronary stent, and of those in whom a thrombolysis in myocardial infarction grade 3 flow was restored, were similar across age groups (range: 95–98%, $P = .50$, and 94–95%, $P = .80$, respectively).

Table 1. Demographic and Clinical Characteristics, by Age Group

Characteristic	Age				*P*-value
	<65 (n = 290)	65–74 (n = 246)	75–84 (n = 246)	≥85 (n = 148)	
Male, %	85.9	71.5	58.1	43.9	<.001
Medical history, %					
Previous myocardial infarction	11.7	17.5	20.3	23.0	.01
Angina pectoris onset					
>1 month	16.2	19.5	26.4	21.0	
≤1 month	19.0	24.0	13.4	8.8	<.001
Cardiac arrhythmias	6.2	16.3	24.4	29.7	<.001
Congestive heart failure	2.8	4.5	17.1	18.9	<.001
Cerebrovascular disease	1.7	10.6	13.0	12.8	<.001
Peripheral artery disease	6.9	18.7	17.9	10.8	<.001
Chronic renal failure*	2.8	7.3	13.0	15.5	<.001
Chronic obstructive pulmonary disease	5.5	7.7	17.1	13.5	<.001
Cancer					
Onset≤5 years	0.7	2.9	5.7	4.1	
Onset>5 years	2.8	3.3	6.9	6.1	.004
Anemia	1.4	4.9	8.5	10.1	<.001
Diabetes mellitus	18.6	27.2	27.2	20.3	.036
Number of chronic CVD, mean	0.37	0.58	0.88	0.93	<.001
Number of chronic non-CVD, mean	0.6	1.04	1.35	1.33	<.001
Hospital admission, %					
Direct admission to hospital with PCI	52.8	43.1	34.6	31.1	<.001
Transfer to hospital with PCI	56.2	47.9	33.5	17.7	<.001
AMI characteristics, %					
Killip class					
1	90.0	74.4	54.1	43.9	
2	4.5	14.2	18.7	30.4	
3	2.8	8.5	16.3	16.9	.036
4	2.8	2.9	11.0	8.9	
AMI					
Anterior location, Q-waves	30.7	35.8	34.6	34.5	
Other location, Q-waves	54.5	44.3	40.2	25.2	.008
Any location, non-Q-waves	14.8	19.9	25.2	25.0	

Note: Only variables significantly ($P<.05$) differing across age groups are reported in the table.
* Creatinine >1.5 mg/dL.
CVD = cardiovascular diseases; AMI = acute myocardial infarction; PCI = percutaneous coronary intervention.

The univariate probability of being treated with CRT was markedly lower in each age stratum above 65 years (reference), with patients aged 85 and older showing the lowest probability (Table 2), an age-associated trend that was reduced at multivariate analysis. However, after adjusting for comorbid conditions and other potential confounders (Killip class, admission hospital category, time between onset of symptoms and hospital arrival, and AMI location), use of CRT was still 29% less likely, although not significantly so, in patients aged 75 to 84 but remained markedly (−63%) and significantly less likely at age 85 and older (Table 2).

In all age groups, use of CRT was significantly ($P<.001$) more frequent in patients admitted directly to the hospital with onsite PCI facilities (from 88% of cases aged <65 to 59% of those aged 85 and older) than in those admitted to hospitals without such facilities (from 53% of cases aged <65 to 19% of those aged 85 and older). Using multivariate analysis, direct admission to the hospital with onsite PCI facilities was the single most important positive predictor of use of CRT at any age, whereas Killip Class 3 (vs 1), number of previous chronic cardiovascular or noncardiovascular diseases, and nonanterior Q-wave or non-Q-wave AMI were all negative predictors, which had variable weight across age groups (Table 3). Killip Class 3 at admission and previous noncardiovascular comorbidity were significant, independent negative predictors of use of CRT only in patients older than 65.

Effect of CRT on Long-Term Prognosis by Age Group

At any age, the probability of 1-year death was lower in patients who received CRT than in those treated with conservative therapy, but such clinical benefit was slightly lower with advancing age (Table 4). In particular, after adjusting for clinical variables, CRT was associated with a

Table 2. Univariate and Multivariate Probability of Use of Coronary Reperfusion Therapy (CRT*), by Age Group

			Univariate		Multivariate†	
Age	n	CRT (%)	Odds Ratio (95% Confidence Interval)	*P*-value	Odds Ratio (95% Confidence Interval)	*P*-value
<65‡	290	71	1.00	—	1.00	—
65–74	246	60	0.60 (0.41–0.83)	.005	0.97 (0.59–1.58)§	.90
75–84	246	43	0.30 (0.21–0.43)	<.001	0.71 (0.43–1.17)§	.17
≥85	148	31	0.18 (0.12–0.28)	<.001	0.37 (0.22–0.62)	<.001

* Percutaneous coronary intervention or thrombolysis.
† Adjusted for other variables with an independent effect on use of coronary reperfusion: presence of comorbidity (number of chronic cardiovascular diseases, angina pectoris of recent onset, number of noncardiovascular chronic diseases), Killip class, admission hospital category, time between symptom onset and hospital arrival, and acute myocardial infarction location.
‡ Reference.
§ Forced into the model.

39% but nonsignificant reduction in 1-year mortality in patients younger than 65, a 53% and significant risk reduction in those aged 65 to 74, and a 38% and marginally significant risk reduction in those aged 75 to 84. Overall, the reduction in 1-year risk of death was significant when patients younger than 85 were pooled (HR = 0.56, 95% CI = 0.38–0.99; $P = .045$). Patients aged 85 and older showed a less-evident (−27%) and nonsignificant reduction in the 1-year risk of death.

DISCUSSION

Studies have demonstrated that the superiority of CRT with thrombolysis or PCI over conservative treatment of AMI is preserved in advanced age,[4,5] and guidelines do not pose limitations to the use of primary PCI in older patients.[6] Nevertheless, in accordance with previous findings,[7–9] the present analysis of data from a large, population-based registry[14] confirmed that the proportion of patients treated with any type of CRT was markedly lower with increasing age. Indeed, patients aged 65 to 74, 75 to 84, and 85 and older had, respectively, about a 40%, 70%, and 80% lower univariate probability of being treated with any form of CRT than those younger than 65. Moreover, this study suggested that patients receiving CRT had an apparently lower risk of death at 1 year, at least when they were aged 85 and older. Although these results should be cautiously interpreted, because they were not obtained in a trial, it is important to stress that the observed benefit was maintained after adjusting for other relevant prognostic variables.

The higher prevalence of previous cardiovascular and noncardiovascular chronic conditions, and a more frequently compromised clinical profile, accounted only in part for the progressively lower use of CRT with advancing age. After adjusting for these potential confounders, the probability of receiving CRT was similar up to age 75, was 29%, although not significantly, lower at age 75 to 84, and remained remarkably and significantly lower in those aged 85 and older. However, although there was an age-associated increase in the prevalence of several chronic comorbidities, the frequency of specific contraindications to

Table 3. Multivariate Predictors of Use of Coronary Reperfusion Therapy, by Age Group

	Age							
	<65		65–74		75–84		85	
Variable	Odds Ratio (95% Confidence Interval)	*P*-value	Odds Ratio (95% Confidence Interval)	*P*-value	Odds Ratio (95% Confidence Interval)	*P*-value	Odds Ratio (95% Confidence Interval)	*P*-value
Onsite percutaneous coronary PCI (yes vs no)	5.10 (2.59–10.03)	<.001	5.14 (2.37–11.16)	<.001	3.18 (1.63–6.18)	.001	3.23 (1.31–8.40)	.009
Killip class 3 (vs Killip 1)	0.19 (0.03–1.39)*	.10	0.03 (0.01–0.17)	<.001	0.30 (0.11–0.82)	.02	0.28 (0.06–1.30)*	.10
CV disease†	0.50 (0.30–0.84)	.008	0.65 (0.39–1.10)*	.10	0.80 (0.53–1.22)*	.31	0.61 (0.31–1.17)*	.14
Non-CV disease†	0.76 (0.50–1.17)*	.21	0.67 (0.48–0.94)	.02	0.63 (0.46–0.86)	.004	0.46 (0.29–0.73)	<.001
Non-anterior AMI (vs anterior)	0.59 (0.28–1.26)*	.17	0.30 (0.13–0.69)	.004	0.84 (0.44–1.63)*	.61	1.15 (0.44–3.01)*	.78
Non-Q-wave AMI (vs anterior)	0.06 (0.02–0.17)	<.001	0.03 (0.01–0.08)	<.001	0.08 (0.03–0.24)	<.001	0.05 (0.01–0.47)	.008

* Forced into the model.
† Number of conditions as a continuous variable.
CV = cardiovascular; AMI = acute myocardial infarction.
PCI = percutaneous coronary intervention.

Table 4. One-Year Mortality and Multivariate Risk of Death, by Treatment and Age Group

	1-Year Mortality (%)			Multivariate Risk of 1-Year Death†	
Age	CRT*	Conservative Therapy	*P*-value	Hazard Ratio (95% Confidence Interval)	*P*-value
<65	2.9	8.5	.039	0.61 (0.15–2.43)	.48
65–74	10.2	22.5	.009	0.47 (0.22–0.98)	.045
75–84	22.6	33.1	.073	0.62 (0.37–1.03)	.065
≥85	39.1	52.6	.13	0.73 (0.42–1.28)	.27

* Percutaneous coronary intervention or thrombolysis.
† Risk of death of patients treated with coronary reperfusion therapy (CRT) compared with conservative therapy (reference stratum), adjusted for other variables with an independent effect on 1-year prognosis (number of chronic cardiovascular diseases, angina pectoris of recent onset, number of noncardiovascular chronic diseases, Killip class, and acute myocardial infarction location).

thrombolysis (e.g., recent stroke or gastrointestinal bleeding) or PCI (e.g., severe chronic renal failure) was low at any age and, in any case, did not fully account for the reduced utilization rate of CRT in older patients. Furthermore, the Global Use of Strategies to Open Occluded Coronary Arteries in Acute Coronary Syndromes (GUSTO) IIb trial demonstrated that PCI is associated with a remarkably lower cumulative incidence of stroke in older patients with AMI than thrombolysis.[15,16] Therefore, because PCI was the most commonly adopted reperfusion strategy in the current study, harm of more frequent cerebral complications in older patients treated with CRT can hardly justify the lower usage of reperfusion in this segment of population. Thus, these findings cannot be entirely interpreted as the result of reduced eligibility of older patients, but rather suggest that attending physicians favored the adoption of the most aggressive, but potentially most life-saving, treatment in younger and, to some extent, in less severely ill patients. Some of the results from the age-stratified multivariate analysis (Table 3) further support the view of an attitude toward a systematic exclusion of older patients from the potential benefits of CRT; Killip Class 3 versus 1 and the number of chronic noncardiovascular diseases were negative predictors of CRT use in patients older but not in those younger than 65. This suggests that critically ill older patients were more likely to be excluded from CRT than their younger counterparts with comparable clinical profiles.

The results further suggest that the probability of receiving any type of CRT, the most widely accepted treatment for AMI, was more the result of the inclination and opinion of attending physicians than of an evidence-based[8,17–19] process of clinical decision-making. Indeed, in accordance with previous findings,[20] in the current study, the multivariate probability of being treated with CRT was, at any age, from three to five times higher in patients admitted directly to the teaching hospital with PCI facilities than in those admitted to the other hospitals in the area, but still markedly lower in older individuals.

PCI is associated with greater immediate and long-term coronary patency rate[21,22] greater clinical improvement[3,23] than thrombolysis and also with fewer complications.[15,16,24] Therefore, particularly in a health district where PCI is the prevalent modality of coronary revascularization during AMI, the finding of systematic underuse of CRT in older patients further stresses the need for enriching the training of medical specialists (emergency medicine physicians and cardiologists) to target frail older patients and those with multiple concomitant medical problems who, being at highest risk, might benefit the most from an aggressive therapeutical strategy.[25] From a more general point of view, elderly persons remain underrepresented in the published randomized trial of acute coronary syndromes, undermining efforts to provide evidence-based care to all cardiac patients.[26]

As a consequence of the aging of the general population, the average age of the clinical population also has been increasing over the last decades.[25] Previous findings[7–9] and the results of the present analysis suggest that clinicians are not yet completely prepared to manage most efficiently the multifaceted clinical problems of frail elderly with acute coronary syndromes, a task requiring a specific interdisciplinary training program toward geriatric cardiology.[25]

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