

Age-Related Differences in the Use of Guideline-Recommended Medical and Interventional Therapies for Acute Coronary Syndromes: A Cohort Study

Andreas W. Schoenenberger, MD,^{*†} Dragana Radovanovic, MD,[‡] Jean-Christophe Stauffer, MD,[§] Stephan Windecker, MD,^{||} Philip Urban, MD,[#] Franz R. Eberli, MD,^{**} Andreas E. Stuck, MD,^{*†} Felix Gutzwiller, MD, DrPH,[‡] and Paul Erne, MD,^{††} for the Acute Myocardial Infarction in Switzerland Plus Investigators

OBJECTIVES: To compare the use of guideline-recommended medical and interventional therapies in older and younger patients with acute coronary syndromes (ACSs).

DESIGN: Prospective cohort study.

SETTING: Fifty-five hospitals in Switzerland.

PARTICIPANTS: Eleven thousand nine hundred thirty-two patients with ACS enrolled between March 1, 2001, and June 30, 2006. ACS definition included ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI), and unstable angina pectoris (UA).

MEASUREMENTS: Use of medical and interventional therapies was determined after exclusion of patients with contraindications and after adjustment for comorbidities. Multivariate logistic regression models were used to calculate odds ratios (ORs) per year increase in age.

RESULTS: Elderly patients were less likely to receive acetylsalicylic acid (OR = 0.976, 95% confidence interval (CI) = 0.969–0.980) or beta-blockers (OR = 0.985, 95% CI = 0.981–0.989). No age-dependent difference was found for heparin use. Elderly patients with STEMI were less likely to receive percutaneous coronary intervention (PCI) or thrombolysis (OR = 0.955, 95% CI = 0.949–0.961). Elderly patients with NSTEMI or UA less often underwent PCI (OR = 0.943, 95% CI = 0.937–0.949).

CONCLUSION: Elderly patients across the whole spectrum of ACS were less likely to receive guideline-recommended therapies, even after adequate adjustment for comorbidities. Prognosis of elderly patients with ACS may be improved by increasing adherence to guideline-recommended medical and interventional therapies. *J Am Geriatr Soc* 56:510–516, 2008.

Key words: cohort studies; myocardial ischemia; elderly; aged 80 and over; coronary angiography

The American College of Cardiology (ACC) and the American Heart Association (AHA) periodically release guidelines for the management of patients across the spectrum of acute coronary syndromes (ACS). Early guidelines from the 1990s did not detail recommendations for older persons because of a lack of data on the elderly from clinical trials. During the late 1990s, evidence increased that older persons benefited from medical and interventional therapies for ACS. For the first time, the 1999 ACC/AHA guideline for the management of ST-segment elevation myocardial infarction (STEMI)¹ and the 2000 ACC/AHA guideline for the management of unstable angina pectoris (UA) and non-ST-segment elevation myocardial infarction (NSTEMI)² explicitly recommended early medical and interventional therapies for older persons to improve their worse prognosis than that of younger patients.^{3–6}

Previous studies showed that elderly patients with ACS are less likely to receive guideline-recommended therapies.^{7–13} Most of the previous studies documenting inappropriate therapy use in elderly patients enrolled patients before the release of the 1999 and 2000 ACC/AHA guidelines.^{7–12} Only two of these studies from the 1990s adequately considered comorbidities beyond the cardiovascular risk profile, although noncardiovascular comorbidities may substantially

From the ^{*}Department of Geriatrics, Inselspital University of Bern Hospital, Bern, Switzerland; [†]Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland; [‡]Institute of Social and Preventive Medicine, Zurich University, Zurich, Switzerland; [§]Division of Cardiology, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland; ^{||}Department of Cardiology, University Hospital Bern, Bern, Switzerland; [#]Cardiovascular Department, La Tour Hospital, Geneva, Switzerland; ^{**}Department of Cardiology, University Hospital, Zurich, Switzerland; ^{††}Department of Cardiology, Kantonsspital Luzern, Lucerne, Switzerland.

Address correspondence to Prof. Paul Erne, Department of Cardiology, Kantonsspital Luzern, CH-6000 Luzern 16, Switzerland.
E-mail: Paul.Erne@ksl.ch

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and justly influence treatment decisions of physicians.^{10,12} This study sought to determine whether older patients with ACS receive the same guideline-recommended medical and interventional therapies as younger patients in a population adjusted for comorbidities.

METHODS

Study Population

The Acute Myocardial Infarction in Switzerland (AMIS) Plus project is a prospective cohort study of patients admitted with ACS to 55 participating hospitals in Switzerland.^{14–16} All participating hospitals were required to have a facility to perform percutaneous coronary intervention (PCI) (12 hospitals) or a contract with a nearby hospital guaranteeing access to PCI within a maximum of 1.5 hours for all patients (43 hospitals). In 2003, 106 Swiss hospitals conformed to these requirements. Participating and nonparticipating hospitals were not statistically different with regard to size, available skills, or quality grading.¹⁷

For inclusion in the cohort, patients had to conform to one of the following final diagnoses: STEMI, NSTEMI, or UA. Definition of STEMI required ST-segment elevation or new left bundle branch block on initial electrocardiogram (ECG) and elevated cardiac enzymes (total creatinine kinase (CK) or CK, muscle and brain, at least twice the upper limit of normal range). NSTEMI was diagnosed according to the presence of symptoms, ECG changes compatible with ACS, or both and elevated cardiac enzymes, but without criteria for STEMI being fulfilled. Diagnosis of UA required symptoms, ECG changes compatible with ACS, or both and normal cardiac enzymes. The study population comprised all patients enrolled in the AMIS Plus registry between March 1, 2001, and June 30, 2006. The Above-Regional Ethics Committee for Clinical Studies and the Swiss Board for Data Security approved the study.

Data Collection

Participating centers provided anonymized data for each patient through a standardized Internet or paper-based questionnaire. The standardized questionnaire comprised 140 items for each patient and was filled in by the coordinator of each institution. It sought information regarding previous medical history, clinical presentation at hospital admission, in-hospital management, and in-hospital prognosis. In-hospital management included the use of medical and interventional therapies. The questionnaire allowed determining the degree of comorbidity using the Charlson Comorbidity Index (CCI).¹⁸ The CCI was shown to predict mortality in patients with coronary artery disease.¹⁹

All data were centralized at the Institute of Social and Preventive Medicine at the University of Zurich, where data were checked for plausibility and consistency. Incomplete questionnaires were returned to the enrollment centers for completion. In 2003, 19% of questionnaires were returned to the enrollment center, in most cases due to one implausible or incomplete variable. This procedure ensured a low percentage of missing data, markedly below 1% for all therapies and age groups. In December 2004, an indepen-

dent physician reviewed hospital case records on a random sample of 20 patients for internal validation; the sample demonstrated good agreement with data obtained from questionnaires (κ scores >0.8 for baseline data and therapeutic interventions). The error rate was 0% for therapeutic interventions, 0% to 0.9% for baseline characteristics, and 1.2% for time variables (e.g., time of symptom onset, time of PCI).

Measurements

The use of early in-hospital medical therapy, defined as the medical therapy provided within 48 hours after symptom onset or within 24 hours after hospital admission, was measured. The following drugs were selected: acetylsalicylic acid, clopidogrel, heparin (including unfractionated heparin and low molecular weight heparin), beta-blockers, and nitrates (including oral, transdermal, and intravenous nitrates). According to the 1999 and 2000 ACC/AHA guidelines, acetylsalicylic acid, heparin, and nitrates should be given to patients with STEMI and NSTEMI or UA who have no contraindications to these medications.^{1,2} Clopidogrel is recommended if there is an allergy to acetylsalicylic acid or if a PCI with stent implantation is planned. Beta-blockers should be administered in the absence of contraindications if there is ongoing chest pain. Contraindications for acetylsalicylic acid, clopidogrel, and heparin were active bleeding, recent surgery, uncontrolled hypertension, a recent cerebral event, or current use of anticoagulants. Contraindications for beta-blockers included heart rate less than 50 per minute, systolic blood pressure less than 90 mmHg, or history of congestive heart failure. The analysis was performed after exclusion of patients with these contraindications.

Interventional therapies constituted a further measurement. For the analysis of interventional therapies, patients in the cohort were divided in two subgroups according to the differentiation in the 1999 and 2000 ACC/AHA guidelines.^{1,2} The first subgroup included patients with STEMI, the second patients with NSTEMI or UA. For the subgroup of patients with STEMI amenable to primary reperfusion therapy, primary PCI (defined as PCI within the first 24 hours of the index hospitalization), any PCI during the index hospitalization (defined as primary, elective, or rescue PCI), and thrombolysis were analyzed. For patients with NSTEMI or UA, the assessment of interventional therapy included the use of primary PCI and the use of any PCI during the index hospitalization. According to the 1999 and 2000 ACC/AHA guidelines, primary PCI or thrombolysis should be performed in patients with STEMI who have no contraindications to these therapies. Primary PCI should also be performed in patients with NSTEMI or UA who are at high risk. Advanced age as a marker of high risk should favor PCI in older patients. Contraindications to PCI use included moderate to severe renal failure (serum creatinine $>160 \mu\text{mol/L}$). Contraindications for thrombolysis included active bleeding, noncompressible puncture site, recent surgery, uncontrolled hypertension, recent cerebral event, and current use of anticoagulants. The analysis was performed after exclusion of patients with these contraindications.

Statistical Analyses

SPSS software (version 14.0, SPSS Inc., Chicago, IL) was used for all statistical analyses. A P -value $< .05$ was considered significant. For baseline characteristics, data are presented as percentages for discrete variables and as means \pm standard deviations or medians for continuous variables after stratification into five age groups (≤ 50 , 51–60, 61–70, 71–80, and ≥ 81 years). Age groups comprised the 1-year interval before the corresponding birthday. Differences in baseline characteristics between age groups were compared using the unpaired t test and chi-square test. For descriptive statistical analysis of medical and interventional therapies, data are given as percentages after stratification into the five age groups. For the analysis of guideline-recommended therapy use, odds ratios (ORs) with 95% confidence intervals (CIs) per year increase in age were calculated using multivariate logistic regression models. All models were done with and without adjustment for other variables that may have influenced treatment decisions. Models for the analysis of medical therapies were adjusted for sex, CCI, and Killip class (Class I = no clinical signs of heart failure, Class II = rales in the lungs, Class III = frank pulmonary edema, Class IV = cardiogenic shock).²⁰ Models for interventional therapies were adjusted for sex, CCI, Killip class, catheter laboratory availability in hospital, and severity of ACS (CK). Because guidelines require time to be implemented in clinical practice, an additional analysis was performed of the subgroup of patients included between January 1, 2004, and June 30, 2006.

RESULTS

Baseline Characteristics

Between March 1, 2001, and June 30, 2006, the participating centers enrolled 11,932 patients in the AMIS plus registry. Clinical characteristics of enrolled patients are presented in Table 1 according to age group.

The proportion of women was 11.3% in the youngest patients (≤ 50) and 49.7% in the oldest patients (≥ 81 years). Pain was the most frequent symptom at hospital admission in all age groups. Dyspnea was present in 14.9% of the youngest age group and increased markedly to 41.6% in the oldest age group ($P < .001$). Accordingly, the proportion of patients with Killip Class I decreased with age, whereas the proportion of patients with clinical signs of heart failure (Killip Classes II and III) increased with age ($P < .001$). Heart failure has to be recognized as an important primary symptom of ACS in elderly people in order not to delay hospital admission and adequate treatment.

The proportion of patients with a prior myocardial infarction increased with age (Table 1). The most prevalent cardiovascular risk factors in the youngest age group were smoking (70.8%) and dyslipidemia (64.9%); hypertension was present in 31.3% of patients. In the oldest age group, hypertension (70.7%) and dyslipidemia (46.6%) were most prevalent. The prevalence of diabetes mellitus increased to 25.2% in the oldest patients ($P < .001$). The CCI increased from 0.42 in the youngest age group to 1.84 in patients aged 81 and older ($P < .001$).

Use of Guideline-Recommended Medical Therapy

The proportion of patients receiving medical therapy in a specific age group is shown in Table 2 (unadjusted analysis). The proportion of patients receiving acetylsalicylic acid, clopidogrel, heparin, or beta-blockers decreased significantly with age ($P < .001$ for all). An increase of nitrate use was observed in older patients ($P < .001$).

ORs of the multivariate logistic regression are shown in Table 3. The use of acetylsalicylic acid, clopidogrel, and beta-blockers significantly decreased with increasing age ($P < .001$ for both), even after exclusion of patients with potential contraindications for these therapies and after adjustment for the number of comorbidities using the CCI.

Use of Guideline-Recommended Interventional Therapies

There were 6,713 patients with STEMI and 5,185 patients with NSTEMI or UA. Thirty-four patients with missing initial ECG were excluded from the subsequent analysis. The proportion of patients receiving a PCI during the course of the index hospitalization decreased significantly with age ($P < .001$ for all) (Table 2). In patients with STEMI, primary PCI was performed in 74.8% of the youngest age group and 24.6% of the oldest age group. In patients with NSTEMI or UA, the proportion of patients receiving primary PCI decreased from 59.6% in the youngest age group to 11.9% in the oldest. A similar decrease regarding the use of any PCI during the index hospitalization was seen in patients with STEMI or NSTEMI or UA (Table 2). The proportion of patients treated using thrombolysis also decreased with increasing age, although it was less commonly used overall. The use of coronary artery bypass graft surgery did not explain why patients were not treated using PCI (Table 2).

ORs of the multivariate logistic regression are shown in Table 4. Elderly patients were less likely to undergo PCI (primary or any PCI) even after exclusion of patients with potential contraindications for these therapies and adjustment for factors that may have influenced treatment decisions, including the number of comorbidities. The use of thrombolysis significantly decreased with increasing age ($P < .001$) (Table 4).

Additional Analysis

In the subgroup of 6,879 patients enrolled between January 1, 2004, and June 30, 2006, elderly patients still received less medical and interventional therapies. In multivariate logistic regression, the use of acetylsalicylic acid, beta-blockers, and primary PCI decreased with increasing age ($P < .001$ for all).

DISCUSSION

This analysis of a contemporary cohort study in 11,932 patients with ACS primarily shows that elderly patients received fewer guideline-recommended medical and interventional therapies. An increasing underuse of acetylsalicylic acid, clopidogrel, beta-blockers, and PCI was found with increasing age even after allowing for contraindications and controlling for comorbidities.

Previous studies reported similar age-dependent results,^{7–13} although many previous studies on this topic were published before the release of the 1999 and 2000 ACC/AHA guidelines.¹⁰ Some of the recent publications

Table 1. Baseline Characteristics of 11,932 Patients with Acute Coronary Syndromes According to Age Group

Characteristic	Age					P (for Trend)
	≤50 (n = 1,727)	51–60 (n = 2,515)	61–70 (n = 2,875)	71–80 (n = 3,134)	≥81 (n = 1,681)	
Age, mean ± standard deviation	44.7 ± 4.9	55.8 ± 2.9	65.6 ± 2.9	75.5 ± 2.9	85.6 ± 3.7	<.001
Men, %	88.7	83.3	77.0	62.6	50.3	<.001
Admission symptoms and electrocardiogram						
Time between onset of symptoms and hospital admission, minutes, median	194	218	250	270	260	.64
Pain, %	80.8	78.8	77.0	73.0	71.7	<.001
Dyspnea, %	14.9	16.1	19.4	29.6	41.6	<.001
Killip class, %*						<.001
I	92.1	88.3	82.6	70.8	52.7	
II	5.1	7.7	12.3	20.5	34.7	
III	0.6	1.2	2.4	5.7	9.6	
IV	1.8	2.3	2.3	2.3	2.3	
ST-segment elevation myocardial infarction, %	64.4	60.8	54.4	52.1	52.0	<.001
Past medical history, %						
Prior myocardial infarction	11.1	14.0	17.9	23.6	27.5	<.001
Prior heart failure	0.9	1.3	2.9	7.0	12.1	<.001
Prior cerebrovascular disease	1.2	2.9	5.2	10.3	11.9	<.001
Hypertension	31.3	47.8	59.1	67.9	70.7	<.001
Dyslipidemia	64.9	67.4	65.3	61.4	46.6	<.001
Diabetes mellitus	9.6	16.7	22.3	25.4	25.2	<.001
Diabetes mellitus with target organ damage	1.6	1.7	4.8	6.0	6.1	<.001
Current smoking	70.8	54.5	35.1	19.8	9.0	<.001
Chronic lung disease	2.7	3.9	6.4	9.5	9.7	<.001
Obesity (body mass index ≥30 kg/m ²)	18.8	20.2	18.2	14.7	8.6	<.001
Moderate to severe renal disease (serum creatinine > 160 μmol/L)	1.7	1.7	4.3	8.8	16.9	<.001
Dementia	0.1	0.1	0.4	2.8	6.8	<.001
Malignant neoplasm	0.8	2.2	4.3	6.3	9.0	<.001
Charlson Comorbidity Index, mean (95% confidence interval for mean) [†]	0.42 (0.37–0.47)	0.60 (0.56–0.65)	0.94 (0.88–0.99)	1.46 (1.39–1.52)	1.84 (1.74–1.93)	<.001
Outcome						
In-hospital mortality on first day after admission	0.8	0.8	1.0	2.5	5.4	<.001

* Killip classes: Class I, no clinical signs of heart failure; Class II, rales in the lungs; Class III, frank pulmonary edema; Class IV, cardiogenic shock.²⁰

[†] Higher values indicate greater number of comorbidities.¹⁸

enrolled patients when these guidelines were not yet available.^{7–9,11,12} Furthermore, many investigations focused on patients with STEMI or patients with NSTEMI or UA.^{9–13} It is therefore likely that these data add to the literature in showing that contemporary elderly patients across the whole spectrum of ACS still receive less guideline-recommended treatment.

The question arises as to why older adults continue to receive less guideline-recommended treatment. First, this finding might be attributable to the increasing number of comorbidities with age.^{1,2} In the current study, increasing age was independently and significantly associated with less treatment use even after adjustment for CCI. Therefore, this study clearly demonstrates an age-related effect. Only two previous studies adequately considered comorbidities.^{10,12} Therefore, because most previous studies did not allow for a measure of comorbidity, they probably failed to truly separate age- and comorbidity-related effects. Second, the

question may arise as to whether older patients died faster and did not have a chance to get treated, but the mortality rates on the first day after hospital admission (Table 1) do not explain the increasing underuse of guideline-recommended therapies. Third, patient refusal might have led to this underuse. However, most elderly patients are willing to consider interventional therapy if recommended by their physician.²¹ It is therefore likely that the underuse of guideline-recommended treatment in older adults points to physicians' attitudes toward withholding treatment in older adults because of their age. The increasing use of nitrates in older patients might reinforce this hypothesis, because this was most probably due to a primarily symptomatic initial therapeutic strategy in older patients.

This study exhibits several potential limitations. First, it is conceivable that unmeasured factors may have influenced the study findings, despite the prospective and multicentric character of the study. In particular, this could

Table 2. Proportion of Patients Receiving Therapy

Therapy	Age										P-Value (for Trend)
	≤50	51–60	61–70	71–80	≥81	n/N*(%)					
Medical therapy											
Acetylsalicylic acid	1,664/1,721	96.7	2,418/2,509	96.4	2,709/2,871	94.4	2,868/3,122	91.9	1,459/1,674	87.2	<.001
Clopidogrel	1,235/1,719	71.8	1,754/2,503	70.1	1,848/2,858	64.7	1,741/3,115	55.9	612/1,655	37.0	<.001
Acetylsalicylic acid, clopidogrel, or both	1,689/1,722	98.1	2,453/2,509	97.8	2,765/2,872	96.3	2,939/3,126	94.0	1,504/1,677	89.7	<.001
Heparin	1,490/1,718	86.7	2,207/2,506	88.1	2,500/2,868	87.2	2,667/3,123	85.4	1,376/1,668	82.5	<.001
Beta-blocker	1,345/1,714	78.5	1,971/2,496	79.0	2,155/2,864	75.2	2,186/3,116	70.2	1,001/1,667	60.0	<.001
Nitrates	908/1,710	53.1	1,382/2,493	55.4	1,588/2,849	55.7	1,836/3,106	59.1	1,074/1,664	64.5	<.001
Interventional therapy											
Primary PCI[†]											
Patients with STEMI	827/1,105	74.8	1,072/1,521	70.5	1,015/1,557	65.2	861/1,629	52.9	214/870	24.6	<.001
Patients with NSTEMI or UA	358/601	59.6	511/974	62.5	590/1,292	45.7	469/1,483	31.6	95/799	11.9	<.001
Any PCI[†]											
Patients with STEMI	1,005/1,112	90.4	1,353/1,529	88.5	1,309/1,564	83.7	1,111/1,633	68.0	270/874	30.9	<.001
Patients with NSTEMI or UA	501/608	82.4	773/981	78.8	953/1,302	73.2	818/1,493	54.8	164/800	20.5	<.001
Thrombolysis											
Patients with STEMI	154/1,112	13.8	241/1,528	15.8	231/1,564	14.8	205/1,633	12.6	62/874	7.1	<.001
Coronary artery bypass graft surgery performed [‡]	31/1,675	1.9	67/2,433	2.8	96/2,787	3.4	109/3,035	3.6	16/1,633	1.0	<.001

* Number of treated patients/number of patients without missing data.

[†] Primary percutaneous coronary intervention (PCI) was defined as PCI within the first 24 hours after hospital admission; any PCI was defined as any PCI during the course of the index hospitalization.

[‡] Coronary artery bypass graft surgery performed during the course of the index hospitalization.

STEMI = ST-segment elevation myocardial infarction; NSTEMI = non-ST-segment elevation myocardial infarction; UA = unstable angina pectoris.

apply to patients' will, which was not assessed. Other potential factors play only a minor part in Switzerland; access to medical and interventional therapies is guaranteed for everyone regardless of age, insurance, income, or residency.²² Second, this study may exhibit selection bias, although 55 hospitals participated in this study, representing more than half of the 106 hospitals treating ST-segment elevation ACS in Switzerland.¹⁷ There was no statistically significant

difference between participating and nonparticipating hospitals with regard to size, available skills, and quality grading.¹⁷ Approximately 11,000 patients have an ACS treated in a Swiss hospital each year.¹⁷ It is estimated that the cohort included 40% of all patients being treated for an ACS in the participating institutions and 20% of all patients being treated for an ACS in Switzerland during the investigated time period. It is therefore likely that the study

Table 3. Odds Ratio for Guideline-Recommended Medical Therapies in Older Patients Compared with Younger Patients

Medical Therapy	Patients, n*	OR [†] (95% Confidence Interval) P-Value			
		Unadjusted		Adjusted [‡]	
Acetylsalicylic acid [§]	11,805	0.960 (0.956–0.968)	<.001	0.976 (0.969–0.980)	<.001
Clopidogrel [§]	11,759	0.965 (0.962–0.968)	<.001	0.975 (0.973–0.979)	<.001
Acetylsalicylic acid, clopidogrel, or both [§]	11,906	0.954 (0.947–0.961)	<.001	0.969 (0.961–0.976)	<.001
Heparin [§]	11,791	0.996 (0.996–0.997)	<.001	0.999 (0.994–1.003)	.63
Beta-blocker [§]	10,359	0.979 (0.976–0.983)	<.001	0.985 (0.981–0.989)	<.001

* Number of patients suitable for analysis after exclusion of patients with contraindications or patients with missing values.

[†] Odds ratio (OR) for using a medical therapy per year increase in age.

[‡] Adjusted for sex, Charlson Comorbidity Index,¹⁸ and Killip class.²⁰

[§] Contraindications for acetylsalicylic acid, clopidogrel, and heparin included active bleeding, recent surgery, uncontrolled hypertension, recent cerebral event, or current use of anticoagulants; contraindications for beta-blockers included heart rate <50 per minute, systolic blood pressure <90 mmHg, or history of congestive heart failure.

Table 4. Odds Ratio for Guideline-Recommended Interventional Therapies in Older Patients Compared with Younger Patients

Interventional Therapy	Patients, n*	OR† (95% Confidence Interval) P-Value			
		Unadjusted	Adjusted‡		
Primary PCI§					
Patients with STEMI	6,302	0.955 (0.951–0.959)	< .001	0.968 (0.964–0.973)	< .001
Patients with NSTEMI or UA	4,778	0.951 (0.946–0.956)	< .001	0.964 (0.959–0.969)	< .001
Any PCI§					
Patients with STEMI	6,332	0.924 (0.919–0.930)	< .001	0.938 (0.932–0.944)	< .001
Patients with NSTEMI or UA	4,812	0.930 (0.925–0.935)	< .001	0.943 (0.937–0.949)	< .001
Thrombolysis, patients with STEMI§	6,654	0.989 (0.983–0.994)	< .001	0.992 (0.986–0.999)	.02
Primary PCI and thrombolysis combined, patients with STEMI§	6,288	0.935 (0.872–0.939)	< .001	0.955 (0.949–0.961)	< .001

* Number of patients suitable for analysis after exclusion of patients with contraindications or patients with missing values.

† Odds ratio (OR) for using an interventional therapy per year increase in age.

‡ After adjustment for sex, Charlson Comorbidity Index,¹⁸ Killip class,²⁰ catheter laboratory availability within hospital, and creatinine kinase.

§ Primary percutaneous coronary intervention (PCI) was defined as PCI within the first 24 hours after hospital admission; any PCI was defined as any PCI during the course of the index hospitalization. Contraindications for PCI included moderate to severe renal failure (serum creatinine > 160 μmol/L); contraindications for thrombolysis included active bleeding, noncompressible puncture site, recent surgery, uncontrolled hypertension, recent cerebral event, or current use of anticoagulants.

STEMI = ST-segment elevation myocardial infarction; NSTEMI = non-ST-segment elevation myocardial infarction; UA = unstable angina pectoris.

population was representative of the Swiss population. As a third limitation, this Swiss study may not accurately reflect the situation in other countries, thus limiting its generalizability, although overall, the results are concordant with those from other countries.^{7–13} The results may probably be generalized to other similar countries.

This study has clinical implications. The medical and interventional therapies investigated in the study have been shown to improve prognosis in elderly patients with ACS.^{23,24} Consequently, the underuse of these therapies results in a worse prognosis for elderly patients. Elderly patients are of particular interest regarding the increasing prevalence of ACS with age and the shifting population pyramid in developed countries. The findings suggest that better implementation of and adherence to guideline-recommended treatment could dramatically influence quality of care in the elderly.²⁴ Guidelines affect clinical practice and have improved care of patients with ACS in recent years.²⁵ Guideline implementation programs may help to improve implementation in the future.²⁶ Furthermore, monitoring the implementation of guidelines by the use of registries, allowing for the potential influence of comorbidities, contraindications, and patients' will, is recommended.

In summary, the Swiss AMIS Plus cohort study provided important information on the use of guideline-recommended therapies in adults with ACS. It showed that older adults are less likely to receive guideline-recommended therapies than younger adults even after exclusion of potential confounding by comorbidities. There may be important opportunities to improve outcomes of ACS care for older adults; further research is needed to better understand this important domain of care.

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Steering Committee

P. Erne, President, Lucerne; O. Bertel, Zurich; F. Eberli, Zurich; M. Essig, Zweisimmen; F. Gutzwiller, Zurich;

P. Hunziker, Basel; P.-F. Keller, Geneva; M. Maggiorini, Zurich; G. Pedrazzini, Lugano; H. Rickli, St. Gallen; J.-C. Stauffer, Lausanne; P. Urban, Geneva; S. Windecker, Bern.

Participating Centers

The following hospitals participated from 2001 to 2006 in the AMIS project on which this report is based (in alphabetical order): Affoltern am Albis, Bezirksspital (F. Hess); Altdorf, Kantonsspital (R. Simon); Altstätten, Kantonales Spital (P.-J. Hangartner/M. Rhyner); Baden, Kantonsspital (M. Neuhaus); Basel, Kantonsspital (P. Hunziker); Basel, St. Claraspital (C. Grädel); Bern, Inselspital (B. Meier/S. Windecker); Biel, Spitalzentrum (H. Schläpfer); Brig-Glis, Oberwalliser Kreisspital (D. Evéquoz); Bülach, Spital (R. Pampaluchi/A. Ciurea-Löchel/M. Kruhl); Davos Platz, Spital (G. Niedermaier); Dornach, Spital (A. Koelz); Flawil, Kantonales Spital (T. Langenegger); Frauenfeld, Kantonsspital (H.-P. Schmid); Fribourg, Hôpital cantonal (B. Quartenoud); Frutigen, Spital (S. Moser/Kuengolt Bietenhard); Genève, Hôpitaux universitaires de Genève (J.-M. Gaspoz); Glarus, Kantonsspital (W. Wojtyna); Grenchen, Spital (P. Schlup/A. Oestmann); Herisau, Kantonales Spital (P. Staub/M. Schmidli); Interlaken, Spital (P. Sula/E.-M. Weiss); Lachen, Regionalspital (I. Poepping/C. Steffen); Langnau im Emmental, Regionalspital Emmental (J. Sollberger); Lugano, Cardiocentro Ticino (G. Pedrazzini); Laufenburg, Gesundheitszentrum Fricktal (E. Koltai); Luzern, Kantonsspital (P. Erne); Mendrisio, Opitale regionale (A. Pagnamenta); Männedorf, Kreisspital (J. von Meyenburg/T. Luterbacher); Meyrin, Hôpital de la Tour (P. Urban); Münsingen, Regionales Spital Zentrum (F. Repond); Münsterlingen, Kantonsspital (F. Widmer); Muri, Kreisspital für das Freiamt (A. Spillmann/F. Scheibe/K. Rudaz-Schwaller); Rheinfelden, Gesundheitszentrum Fricktal Regionalspital (H.-U. Iselin); Rorschach, Kantonales Spital (M. Pfister); Samedan, Spital Oberengadin (P. Egger); Sarnen, Kantonsspital Obwalden (T. Kaeslin); Schaffhausen, Kantonsspital (R. Frey); Schlieren, Spital Limmattal (B. Risti/V. Stojanovic/T. Herren); Schwyz,

Spital (P. Eichhorn); Scuol, Ospital d'Engiadina Bassa (G. Flury/C. Neumeier); Solothurn, Bürgerspital (P. Hilti); St. Gallen, Kantonsspital (W. Angehrn/H. Rickli); Thun, Spital (U. Stoller); Uster, Spital (D. Maurer/J. Muntwyler); Uznach, Kantonales Spital (A. Weber); Wädenswil, Schwerpunktspital Zimmerberg-Horgen (G. Garzoli/B. Kälin); Walenstadt, Kantonales Spital (H. Matter/D. Schiesser); Wetzikon, GZO (M. Graber); Winterthur, Kantonsspital (A. Haller); Wolhusen, Kantonales Spital (M. Peter); Zofingen, Spital (H. J. Vonesch/H. J. Meier/S. Gasser); Zollikerberg, Spital (P. Siegrist/R. Fatio); Zürich, Universitätsspital (F. Eberli/M. Maggiorini); Zürich, Stadtspital Triemli (O. Bertel); Zürich, Stadtspital Waid (M. Brabetz/S. Christen).

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REFERENCES

- Ryan TJ, Antman EM, Brooks NH et al. ACC/AHA guidelines for the management of patients with acute myocardial infarction: Executive summary and recommendations: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Acute Myocardial Infarction). *Circulation* 1999;100:1016–1030.
- Braunwald E, Antman EM, Beasley JW et al. ACC/AHA guidelines for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction: Executive summary and recommendations. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients with Unstable Angina). *Circulation* 2000;102:1193–1209.
- Soiza RL, Leslie SJ, Harrild K et al. Age-dependent differences in presentation, risk factor profile, and outcome of suspected acute coronary syndrome. *J Am Geriatr Soc* 2005;53:1961–1965.
- Granger CB, Goldberg RJ, Dabbous O et al. Global registry of acute coronary events investigators. Predictors of hospital mortality in the global registry of acute coronary events. *Arch Intern Med* 2003;163:2345–2353.
- Avezum A, Makkisse M, Spencer F et al. GRACE investigators. Impact of age on management and outcome of acute coronary syndrome: Observations from the Global Registry of Acute Coronary Events (GRACE). *Am Heart J* 2005;149:67–73.
- Halon DA, Adawi S, Dobrecky-Mery I et al. Importance of increasing age on the presentation and outcome of acute coronary syndromes in elderly patients. *J Am Coll Cardiol* 2004;43:346–352.
- Yan RT, Yan AT, Tan M et al. Canadian Acute Coronary Syndromes (ACS) Registry investigators. Age-related differences in the management and outcome of patients with acute coronary syndromes. *Am Heart J* 2006;151:352–359.
- Rosengren A, Wallentin L, Simoons M et al. Age, clinical presentation, and outcome of acute coronary syndromes in the Euroheart acute coronary syndrome survey. *Eur Heart J* 2006;27:789–795.
- Barchielli A, Buiatti E, Balzi D et al. AMI-florence working group. Age-related changes in treatment strategies for acute myocardial infarction: A population-based study. *J Am Geriatr Soc* 2004;52:1355–1360.
- Giugliano RP, Camargo CA Jr, Lloyd-Jones DM et al. Elderly patients receive less aggressive medical and invasive management of unstable angina: Potential impact of practice guidelines. *Arch Intern Med* 1998;158:1113–1120.
- Rathore SS, Mehta RH, Wang Y et al. Effects of age on the quality of care provided to older patients with acute myocardial infarction. *Am J Med* 2003;114:307–315.
- Mehta RH, Rathore SS, Radford MJ et al. Acute myocardial infarction in the elderly: Differences by age. *J Am Coll Cardiol* 2001;38:736–741.
- Alexander KP, Roe MT, Chen AY et al. CRUSADE investigators. Evolution in cardiovascular care for elderly patients with non-ST-segment elevation acute coronary syndromes: Results from the CRUSADE national quality improvement initiative. *J Am Coll Cardiol* 2005;46:1479–1487.
- Fassa AA, Urban P, Radovanovic D et al. AMIS plus investigators. Trends in reperfusion therapy of ST segment elevation myocardial infarction in Switzerland: Six year results from a nationwide registry. *Heart* 2005;91:882–888.
- Erne P, Radovanovic D, Urban P et al. Early drug therapy and in-hospital mortality following acute myocardial infarction. *Heart Drug* 2003;3:134–140.
- Fassa AA, Urban P, Radovanovic D et al. Temporal trends in treatment of ST segment elevation myocardial infarction in Switzerland from 1997 to 2005. *Rev Med Suisse* 2006;2:1393–1396, 1398.
- Medizinische Statistik 2004. Neuchâtel: Swiss Federal Statistical Office, 2006.
- Charlson ME, Pompei P, Ales KL et al. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. *J Chronic Dis* 1987;40:373–383.
- Chirinos JA, Veerani A, Zambrano JP et al. Evaluation of comorbidity scores to predict all-cause mortality in patients with established coronary artery disease. *Int J Cardiol* 2007;117:97–102.
- Killip T, Kimball JT. Treatment of myocardial infarction in a coronary care unit: A two year experience of 250 patients. *Am J Cardiol* 1967;20:457–464.
- Alexander KP, Harding TM, Coombs LP et al. Effect of age on goals from cardiac care. *Am J Geriatr Cardiol* 2002;11:134A.
- Schoenenberger AW, Stuck AE. Health care for older persons in Switzerland: A country profile. *J Am Geriatr Soc* 2006;54:986–990.
- Bach RG, Cannon CP, Weintraub WS et al. The effect of routine, early invasive management on outcome for elderly patients with non-ST-segment elevation acute coronary syndromes. *Ann Intern Med* 2004;141:186–195.
- Alter DA, Manuel DG, Gunraj N et al. Age, risk-benefit trade-offs, and the projected effects of evidence-based therapies. *Am J Med* 2004;116:540–545.
- Mehta RH, Roe MT, Chen AY et al. Recent trends in the care of patients with non-ST-segment elevation acute coronary syndromes: Insights from the CRUSADE initiative. *Arch Intern Med* 2006;166:2027–2034.
- Liem SS, van der Hoeven BL, Oemrawsingh PV et al. MISSION!: Optimization of acute and chronic care for patients with acute myocardial infarction. *Am Heart J* 2007;153:14.e1–e11.