ORIGINAL ARTICLE

Acute myocardial infarction in the elderly: treatment strategies and 28-day-case fatality from the MONICA/KORA Myocardial Infarction Registry

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Objectives: Aim of this observational study was to analyze today's real-life treatment strategies in elderly patients with an acute myocardial infarction (AMI) and to assess the association between 28-day-case fatality and invasive strategy (percutaneous coronary intervention/coronary artery bypass grafting).

Background: Elderly patients increasingly constitute a large proportion of the AMI population.

Methods: The present study is an analysis of all patients aged 75–84 years, who were enrolled in the German population-based MONICA/KORA MI registry between 2009 and 2012 and who were defined as nonfatal at least 24 hours surviving AMI cases according to MONICA definition. Multivariable logistic regression analyses were conducted for the total study population and stratified by type of AMI (ST-segment elevation MI [STEMI], Non-ST-segment elevation MI [NSTEMI], and bundle branch block [BBB]).

Results: Out of the 1,191 elderlies, 61.9% were treated invasively. In the multivariable analysis, the odds ratio (OR) for 28-day-case fatality in patients treated with invasive versus conservative strategy was 0.43 (95% CI 0.27–0.69). Stratified analyses revealed an OR of 0.27 (95% CI 0.13–0.56) for patients with NSTEMI. In patients with STEMI or BBB also a positive trend for invasive strategy was observed (OR 0.40; 95% CI 0.13-1.27 and OR 0.76; 95% CI 0.16-3.66, respectively).

Conclusions: Invasive revascularization therapy was independently associated with short-term survival in elderly patients, particularly in those with NSTEMI.

INTRODUCTION

Elderly patients account for an increasing proportion of all patients admitted to hospital with acute coronary syndromes (ACS) [1,2]. In Germany for example, around one quarter of all ACS patients was between 75 and 84 years and 4.3% were ≥ 84 years of age in 2008 [3]. So far patients ≥ 75 years were mainly excluded or underrepresented in randomized controlled trials (RCTs) which assessed the treatment benefit after acute myocardial infarction (AMI) [1,4-6]. However, from 2000 onwards, the ACS guidelines explicitly support early medical and interventional therapies for elderly patients [7]. Along with an increase in invasive strategies such as percutaneous coronary intervention (PCI), improvements in use of adjunctive medications are assumed to contribute to the reduction in short-term mortality post-AMI in the elderly [2,8]. Lack of clinical data, higher prevalence of comorbidities, and age-associated conditions such as frailty, cognitive and functional impairment, as well as higher risk of bleeding and other complications assumed from guideline-recommended therapies might explain that several clinicians use a conservative or selective invasive approach in elderly patients in real-world practice [9]. In addition, the role of a routine invasive strategy in patients with Non-ST-segment elevation (NSTE)-ACS, which constitute a very heterogeneous population in terms of risk and prognosis and is more common in elderly patients, is still under discussion [10,11].

Aim of this study was firstly to analyze real-life patient care including medication therapy among patients aged 75–84 years consecutively hospitalized with an AMI between 2009 and 2012 using data from a population-based myocardial infarction (MI) registry. Secondly, to determine the association between invasive treatment strategy and 28-day-case fatality compared with a conservative treatment strategy stratified by type of AMI.

METHODS

Study design and data source

The present study is based on data from the population-based MI registry in Augsburg, Germany, which was established in 1984 as part of the World Health Organization MONICA Project (MONItoring Trends and Determinants in CArdiovascular disease). After the termination of MONICA in 1995, the MI registry became part of the framework of KORA (Cooperative Health Research in the Region of Augsburg). Since 1984, coronary deaths and nonfatal (at least 24 hours surviving) AMI cases of the 25- to 74-year old inhabitants of the city of Augsburg and 2 adjacent counties (about 600,000 inhabitants) have been continuously registered. From 2009 onwards, the registry was extended for the elderly up to 84 years. The methods of case identification, diagnostic classification of events, and data quality control have been described in detail elsewhere [12,13]. Since 2001, diagnostic criteria according to the European Society of Cardiology and American College of Cardiology criteria were used for case identification, including assessment of troponin levels especially for identification of Non-ST-segment elevation MI (NSTEMI) [14].

Data collection

Patients were interviewed during hospital stay by trained nurses using a standardized questionnaire to collect sociodemographic characteristics, cardiovascular risk factors, medical history of previous MI, stroke and comorbidities, drug treatment prior AMI, and information on the acute event. Further information on laboratory data, type of AMI, treatment procedures and complications during hospital stay, vital signs, medical history, and medication use were collected by review of medical chart and discharge report. Information provided by the patient concerning the risk factors and comorbidities had to be confirmed by chart review. Information on renal dysfunction was collected by review of medical chart. All medications were recorded and classified in the registry according to the active pharmaceutical ingredients. Data collection of the MONICA/KORA MI registry has been approved by the ethics committee of the Bavarian Medical Association (Bayerische Landesärztekammer) and all study participants gave written informed consent.

Study population

Out of 2,977 patients aged 75–84 years who were consecutively enrolled in the MONICA/KORA MI registry with either coronary death or a nonfatal AMI between January 1, 2009, and December, 31, 2012, we selected all patients who were hospitalized and who were defined as nonfatal (at least 24 hours surviving) AMI cases according to MONICA definition (n=1,223). As 32 patients had incomplete data on any of the relevant covariables we had to exclude them for the analyses. Thus, the study population of the present study covered 1,191 elderly patients (Figure 1). Of the 32 patients excluded due to missing values, 15 were of the invasive strategy group, 17 of the conservative strategy group; of those one person of the conservative but none of the invasive strategy group died within the 28-day follow-up period.

Definition of treatment strategy and patient groups analyzed

The following two groups of treatment strategies were compared in the analysis: 1. Patients receiving invasive strategy, defined as PCI with stent implantation and/or balloon dilatation and/or coronary artery bypass grafting (CABG), and 2. Patients receiving conservative strategy, defined as thrombolysis or without any invasive revascularization. Patients with cardiac catheterization but without a treatment procedure (PCI) were also included in this group. Both strategy groups were further stratified by type of AMI. The type of AMI was defined as STEMI, NSTEMI, bundle branch block (BBB), or non-classifiable/missing. The BBB group contains newly developed left BBB, right BBB, and chronic BBB; because we do not exactly know whether all patients with a BBB had a newly developed left BBB, which is considered as STEMI equivalent, we displayed the BBB group as separate category.

Outcome

The outcome of this study was 28-day-case fatality after AMI. Mortality was assessed by checking the vital status of all registered persons of the MONICA/KORA MI registry on a regular basis. Death certificates were obtained from local health departments.

Data analysis

Categorical variables were expressed as absolute numbers and percentages, continuous variables as median with interquartile range (25^{th} and 75^{th} percentiles). For descriptive purpose, the two groups of treatment strategy and similarly the subgroups by type of AMI were compared using Chi^2-test or Fisher's exact test for categorical variables and the Wilcoxon-Mann-Whitney Test for continuous variables. The outcome variable '28-day-case fatality' (yes/no) was cross-tabulated with the potential confounding factors. Only variables that were statistically significantly associated at the 10% level with the outcome were included in the logistic regression analyses. Variables analyzed as potential confounding factors were sex (male/female), age (continuous), smoking (at time of the acute event) (yes/no/missing), employed (yes/no/missing), married (yes/no/missing), body mass index (BMI) ≥ 30 kg/m^2 (yes/no), medical history of stroke, diabetes, hyperlipidemia, hypertension, and angina pectoris (yes/no/missing), renal dysfunction reported in medical chart (yes/no/missing), pre-hospital delay time (continuous), type of AMI (STEMI, NSTEMI, BBB, or non-classifiable/missing), in-hospital cardiac arrest (yes/no), any other in-hospital complication (cardiogenic shock or ventricular fibrillation or ventricular tachycardia or recurrent infarction or pulmonary edema or bradycardia [heart rate <50/min] or stroke or any bleeding complication [intracranial or retroperitoneal or any other major spontaneous bleeding]) (yes/no), peak serum creatine phosphokinase (CPK) level (U/l) during hospital stay (continuous), serum level of creatinine (mg/dl) at admission (continuous), and the following in-hospital medications: beta-blockers, renin-angiotensin system inhibitors (angiotensin-converting-enzyme inhibitors or angiotensin receptor blockers [ACEIs/ARBs], statins, calcium channel blockers (CCB), nitrates and dual antiplatelet therapy (DAPT). As almost all patients received at least one antiplatelet agent such as acetylsalicylic acid, clopidogrel or prasugrel (thienopyridines) we omitted this variable.

To investigate the associations between invasive strategy and 28-day-case fatality, odds ratios (ORs) were calculated using multivariable logistic regression models. We considered full models and also parsimonious models by using forward and backward selection techniques. All models were adjusted for age and sex (forced-in variables). Additional

adjustment was performed for all bivariately significant variables except for ‘in-hospital cardiac arrest’ and ‘CPK level’ due to high correlation with the variables ‘any other in-hospital complication’ and ‘type of AMI’, respectively. However, in the analyses stratified by type of AMI the CPK levels were included as cardiac biomarker. Variables with missing data were ‘dummy’-coded. The variables ‘hypertension’ and ‘hyperlipidemia’ were omitted to avoid multicollinearity with medication variables. In the logistic regression analyses, a significance level of 5% was applied. All analyses were performed using SAS version 9.2 (SAS Institute Inc., Cary, North Carolina).

RESULTS

From the 1,191 elderly patients (54.0% men) who were included in our study population, 646 (54%) men and women presented with a NSTEMI, 309 (26%) with a STEMI, 179 (15%) with a BBB and 57 (5%) with a non-classifiable MI or missing data regarding type of AMI. The proportion of patients receiving an invasive treatment strategy was 81.9%, 55.7%, and 51.4% in STEMI, NSTEMI and BBB patients, respectively (Figure 1). In the invasive strategy group (n=737; 61.9%) there were 601 (81.5%) patients who were treated with PCI, 117 (15.9%) received a CABG and 19 patients (2.6%) were treated with both PCI and CABG. The conservative strategy group included 454 (38.1%) patients without any invasive revascularization therapy and only one person who received thrombolysis. Of those, 166 patients received a cardiac catheterization without a treatment procedure that is without a PCI. Table 1 displays characteristics of the study population according to treatment strategy. Patients in the invasive strategy group were younger, more likely to be of male gender, had more frequently a STEMI, higher serum CPK levels, and showed more frequently a medical history of hypertension and hyperlipidemia. On the contrary, the conservative strategy group contains more octogenarians, presented more frequently with NSTEMI and BBB, and showed more often a medical history of a previous MI, stroke, diabetes mellitus, and renal dysfunction. Further stratification by type of AMI revealed that patients with a BBB had more frequently a previous MI and angina pectoris regardless of treatment strategy. In addition

serum glucose levels were significantly higher in STEMI patients within the invasive strategy group; however, diabetes mellitus was more frequent in NSTEMI patients within the conservative strategy group (Table 1).

During hospitalization the invasive strategy group received more frequently adjunctive drug treatment with beta-blockers, ACEIs/ARBs, statins, antithrombotic agents, DAPT, nitrates, CCBs, catecholamines, and antiarrhythmics (Table 2). Cardiac arrest occurred more frequently in the conservative strategy group, whereas patients in the invasive strategy group were more likely to have cardiogenic shock, bradycardia, ventricular fibrillation and tachycardia. During the follow-up period of 28 days, 165 (13.9%) patients died, of those 68 (9.2%) deaths occurred in the invasive strategy group and 97 (21.4%) in the conservative strategy group (Table 2). Further stratification by type of AMI revealed a higher proportion of cardiac arrest and any in-hospital complications (without cardiac arrest) in STEMI patients regardless of treatment strategy (Table 2).

In the multivariable logistic regression analysis invasive strategy showed a strongly inverse relation with 28-day-case fatality compared with the conservative strategy (Table 3). In the parsimonious model the OR was 0.43 (95% CI 0.27-0.69) and from the in-hospital medications only ACEIs/ARBs and beta-blockers remained significant confounders in this model. Table 3 also displays the results of the multivariable models stratified by type of AMI. In the parsimonious model the OR for patients with NSTEMI was 0.27 (95 % CI 0.13–0.56). In patients with STEMI or BBB, the variable “treatment strategy” did not meet the 0.05 significance level for entry into the parsimonious models. However, in the full model a positive trend for invasive strategy was observed for STEMI and BBB (OR 0.40; 95% CI 0.13-1.27 and OR 0.76; 95% CI 0.16-3.66, respectively).

DISCUSSION

In the present observational study including all consecutive patients aged 75–84 years with AMI occurring between 2009 and 2012, we observed a high proportion of invasively treated

patients; we found that invasive treatment strategy was independently associated with improved short-term survival, particularly in patients with NSTEMI.

From the 1,191 24-hour survivors included in our analysis, about 62% (82% presenting with STEMI, 56% with NSTEMI), were treated invasively. Previous studies in elderlies reported lower proportions of patients with an invasive treatment approach, for example 24% in Sweden [15], 31% in France [10] (only NSTEMI patients), and 52% in Germany [16] (only NSTEMI patients) were selected for invasive strategy. The lower proportion in these studies might be partially explained by an earlier time period and by an inclusion of patients older than 84 years. In a recently published study of the national registry for ACS in England and Wales [17] including 155,818 patients, 70.5% of STEMI patients and 44.1% of NSTEMI patients aged 75-84 years received reperfusion or angiography between 2006 and 2010.

Only one patient in our conservative strategy group was treated with thrombolysis. The low number of thrombolysis was not surprising due to the reported superiority of PCI compared with thrombolytic strategies in elderly patients [5,6], and the usefulness of PCI reported in elderly patients [4,6,18] and in very old (≥85 years) STEMI patients [19,20]. In concordance with an earlier study in STEMI patients, the conservative treated group was older, more likely to be of female sex and showed extremely high short-term mortality rates in subgroups with severe cardiac comorbidities or complications [4]. Moreover, as also reported in earlier studies [16,21], we observed lower use of guideline-recommended drug treatment with antiplatelet agents, beta-blockers, ACEIs/ARBs and statins in patients with conservative strategy. This potential under-use could be explained by the often reported “high-risk paradox” that patients above 65 years less often receive effective treatment despite of higher risk of death [2,22,23]. Less intensive treatment might also occur due to the presence of contraindications, higher rate of comorbidities such as diabetes mellitus, asthma and renal dysfunction, or the higher risk of drug interactions [5]. However, other more compelling reasons for the less frequent use of medications in our study might be the higher rates of cardiac arrest observed in the conservative strategy group, or the complex clinical interplay

of comorbidities, functional and cognitive status, altered pharmacokinetics, individual biologic variability and patients' preferences [5,24].

In the multivariable analyses we found that the invasive strategy was independently associated with improved short-term survival. In accordance with earlier studies in elderly ACS patients [1,22,24-26], we observed a clear short-term survival benefit associated with invasive revascularization therapies in patients up to 84 years. Moreover, the risk reduction was more pronounced in the subgroup diagnosed with NSTEMI. Our results might be interpreted in concordance with earlier RCTs which found that risk reduction with routine invasive strategy were highest in high-risk patients [9, 10], as diabetes mellitus, previous MI, angina pectoris and hyperlipidemia was more common in our NSTEMI subgroup compared to the STEMI subgroup. Therefore, the international guidelines for the management of patients with unstable angina and NSTEMI recommend a routine invasive approach in high-risk patients and highlight the role of patient's individual risk score in the decision process [9,27]. Puymirat et al. [10] investigated the role of a routine invasive strategy in all adult patients with NSTEMI and reported fewer in-hospital death (OR 0.13; 95% CI 0.08-0.22) and fewer blood transfusion (OR 0.48; 95% CI 0.31-0.76) in all patients receiving invasive strategy and a higher 3-survival (HR 0.48; 95% CI 0.35-0.66) in invasive treated patients aged 74 years and older compared with the noninvasive strategy. In accordance with this earlier study, we used a similar NSTEMI definition that excluded patients with unstable angina, a condition in which an invasive strategy is less useful [11].

Strength and Limitations

Major strength of our study is the setting in a population-based registry with patients consecutively hospitalized with all types of AMI and data collection performed soon after the AMI during the hospital stay. Furthermore, our research covers recent data up to 2012, and included a number of medications which were not incorporated in analyses of earlier studies. Some limitations for interpretation of our study results should be kept in mind. Despite adjustment for a number of confounding variables, residual confounding cannot be entirely

excluded due to further unknown comorbidities or complications such as frailty, and psychosocial risk factors which could have influenced short-term mortality. Also, we cannot exclude that patients in the conservative strategy group had a higher risk to start with (e.g. severe multimorbidity or on the verge of death) and were not suitable to receive recommended medical and hospital care (e.g. cardiac catheterization). Therefore, the observed effect of invasive strategy could also be partly influenced by non-analyzed factors. As we did not know the character of coronary artery lesions, the specific PCI/CABG strategies used and the success rate of invasive strategies, we were not able to consider this valuable information in our analysis. Our data set contained only one person treated with thrombolysis between 2009 and 2012; therefore we were not able to contribute to the discussion about possible benefits of primary fibrinolysis followed by routine invasive approach (also known as a pharmacoinvasive strategy) in STEMI patients where timely PCI is not possible as reported in the STREAM study [28]. In addition, our results are limited to elderly patients aged 75 to 84 years.

CONCLUSION

In today's real-life patient care we observed that an invasive treatment strategy compared with conservative treatment showed a strongly inverse relationship with 28-day-case fatality in elderly AMI patients aged 74-84 years. Moreover, the positive impact of an invasive intervention was more pronounced in patients with NSTEMI.

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Conflict of interest statement

The authors have no conflicts of interest to declare.

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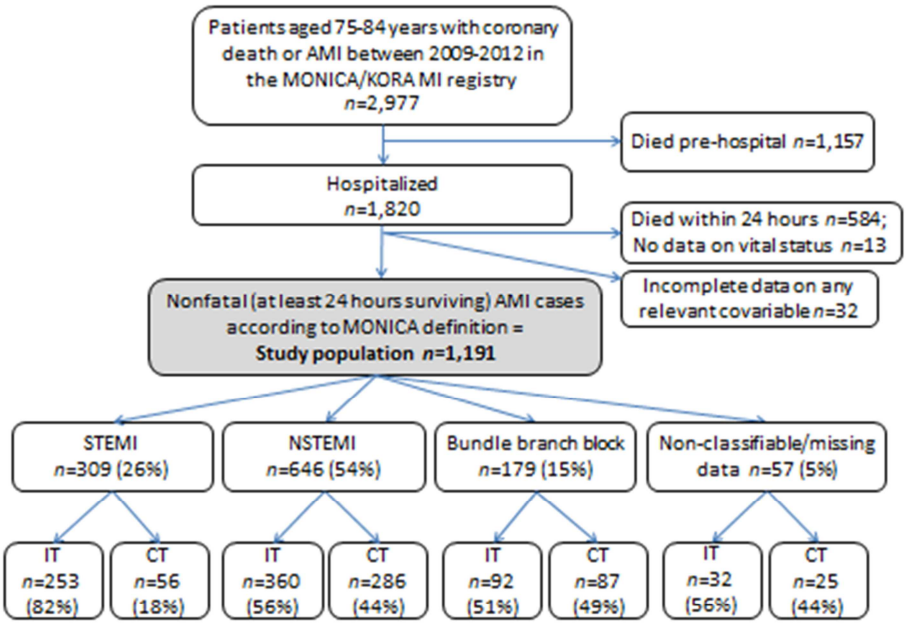
None.

Figure

Figure1:

Title: Definition of the study population



Legend: AMI: acute myocardial infarction; STEMI: ST-segment elevation MI, NSTEMI: Non-ST-segment elevation MI; IT: invasive treatment strategy; CT: conservative treatment strategy.

Tables

Tab 1. Characteristics of the study population stratified by treatment strategy and type of acute MI (n=1,191)

	Invasive strategy (n=737; 61.9%)					Conservative strategy (n=454; 38.1%)					p-value
	All# (n=737)	STEMI (n=253)	NSTEMI (n=360)	BBB (n=92)	p-value	All# (n=454)	STEMI (n=56)	NSTEMI (n=286)	BBB (n=87)	p-value	
Baseline characteristics											
Age*	79 (76; 81)	79 (76; 81)	78 (76; 81)	79 (77; 82)	0.15	80 (77; 82)	80 (77; 83)	80 (77; 82)	80 (78; 82)	0.95	<.0001
Age - 80-84y (%)	293 (39.8)	99 (39.1)	137 (38.1)	42 (45.7)	0.41	252 (55.5)	28 (50.0)	160 (55.9)	47 (54.0)	0.71	<.0001
Male gender (%)	419 (56.9)	133 (52.6)	201 (55.8)	61 (66.3)	0.08	224 (49.3)	25 (44.6)	133 (46.5)	47 (54.0)	0.41	0.01
BMI ≥ 30 kg/m²	131 (17.8)	44 (17.4)	60 (16.7)	19 (20.7)	0.67	73 (16.1)	10 (17.9)	41 (14.3)	18 (20.7)	0.34	0.45
Smoking status					0.21					0.04	<.0001
Smoker (%)	56 (7.6)	25 (9.9)	26 (7.2)	5 (5.4)		26 (5.7)	1 (1.8)	19 (6.6)	6 (6.9)		
Non-Smoker (%)	579 (78.6)	187 (73.9)	291 (80.8)	77 (83.7)		257 (56.6)	28 (50.0)	155 (54.2)	59 (67.8)		
Insufficient/missing data (%)	102 (13.8)	41 (16.2)	43 (11.9)	10 (10.9)		171 (37.7)	27 (48.2)	112 (39.2)	22 (25.3)		
Medical history of**											
Previous MI (%)**	148 (20.1)	34 (13.4)	78 (21.7)	27 (29.4)	0.002	128 (28.2)	11 (19.6)	72 (25.2)	37 (42.5)	0.002	0.001
Stroke (%)**	88 (11.9)	33 (13.0)	45 (12.5)	9 (9.8)	0.20	96 (21.2)	11 (19.6)	58 (20.3)	17 (19.5)	0.72	<.0001
Diabetes mellitus (%)**	290 (39.4)	87 (34.4)	144 (40.0)	43 (46.7)	0.09	212 (46.7)	17 (30.4)	143 (50.0)	42 (48.3)	0.03	0.01
Hypertension (%)**	660 (89.6)	220 (87.0)	326 (90.6)	84 (91.3)	0.29	388 (85.5)	44 (78.6)	243 (85.0)	78 (89.7)	0.19	0.04
Hyperlipidaemia (%)**	326 (44.2)	99 (39.1)	172 (47.8)	38 (41.3)	0.09	171 (37.7)	21 (37.5)	96 (33.6)	42 (48.3)	0.05	0.03
Angina pectoris (%)**	142 (19.4)	30 (11.9)	80 (22.2)	22 (23.9)	0.002	91 (20.6)	10 (17.9)	48 (16.8)	29 (33.3)	0.003	0.63
Renal dysfunction (%)***	181 (24.6)	55 (21.7)	89 (24.7)	29 (31.5)	0.25	175 (38.6)	16 (28.6)	104 (36.4)	41 (47.1)	0.17	<.0001

Laboratory data: peak serum level during hospitalization											
Serum creatine phosphokinase (U/l)*	549 (242; 1321)	1257 (556; 2266)	368 (189; 773)	361 (164; 724)	<.0001	226 (113; 554)	481 (174; 1051)	217 (114; 486)	192 (95; 418)	0.0002	<.0001
Serum glucose level (mg/dl)*	153 (125; 203)	164 (135; 221)	147 (116; 194)	153 (125; 220)	<.0001	161 (128; 214)	152 (124; 214)	167 (129; 221)	162 (131; 203)	0.95	0.05
Laboratory data: serum level at admission											
Serum glucose level (mg/dl)*	138 (113; 177)	150 (121; 198)	128 (107; 163)	143 (120; 200)	<.0001	146 (115; 193)	146 (115; 205)	150 (115; 193)	149 (117; 202)	0.92	0.11
Serum creatinine level (mg/dl)*	1.2 (0.9; 1.5)	1.2 (1.0; 1.5)	1.1 (0.9; 1.4)	1.2 (1.0; 1.5)	0.16	1.3 (1.1; 1.7)	1.2 (0.9; 1.5)	1.3 (1.0; 1.7)	1.4 (1.1; 2.0)	0.10	<.0001

MI: myocardial infarction; STEMI: ST-segment elevation MI, NSTEMI: Non-ST-segment elevation MI; BBB: bundle branch block; BMI: body mass index

[#] The total study population includes 57 patients (32 in the invasive and 25 in the conservative strategy group) with non-classifiable or missing data regarding the type of acute MI.

* Median (25th and 75th percentiles)

** Patient-reported medical history of known comorbidities before the acute event, which was collected with a standardized interview during hospital stay and further data were gathered in a concluding chart review. If the information on comorbidities from patient-report and medical chart differed, the chart information was used.

*** Information on renal dysfunction was collected by review of medical chart.

Tab 2. Medications during hospitalization, clinical complications and short-term outcome of the study population stratified by treatment strategy and type of acute MI (n=1,191)

	Invasive strategy (n=737; 61.9%)					Conservative strategy (n=454; 38.1%)					p-value
	All[#] (n=737)	STEMI (n=253)	NSTEMI (n=360)	BBB (n=92)	p-value	All[#] (n=454)	STEMI (n=56)	NSTEMI (n=286)	BBB (n=87)	p-value	
Medications during hospitalization											
Beta-blockers (%)	701 (95.1)	235 (92.9)	344 (95.6)	90 (97.8)	0.13	408 (89.9)	50 (89.3)	257 (89.9)	78 (89.7)	0.99	0.001
ACEIs/ARBs (%)	665 (90.2)	226 (89.3)	328 (91.1)	82 (89.1)	0.71	342 (75.3)	37 (66.1)	216 (75.5)	69 (79.3)	0.19	<.0001
Statins (%)	694 (94.2)	239 (94.5)	338 (93.9)	89 (96.7)	0.57	342 (75.3)	40 (71.4)	214 (74.8)	68 (78.2)	0.65	<.0001
Antiplatelet agents (%)	736 (99.9)	252 (99.6)	360 (100)	92 (100)	0.36	433 (95.4)	54 (96.4)	272 (95.1)	85 (97.7)	0.62	<.0001
Acetylsalicylic acid (%)	724 (98.2)	250 (98.8)	354 (98.3)	89 (96.7)	0.36	414 (91.2)	51 (91.1)	262 (91.6)	81 (93.1)	0.88	<.0001
Thienopyridines (%)	649 (88.1)	234 (92.5)	305 (84.7)	82 (89.1)	0.01	233 (51.3)	32 (57.1)	135 (47.2)	53 (60.9)	0.05	<.0001
DAPT (%)	638 (86.6)	232 (91.7)	300 (83.3)	79 (85.9)	0.01	217 (47.8)	30 (53.6)	127 (44.4)	49 (56.3)	0.10	<.0001
GP IIb/IIIa antagonists (%)	198 (26.9)	84 (33.2)	89 (24.7)	22 (23.9)	0.05	28 (6.2)	8 (14.3)	14 (4.9)	5 (5.8)	0.03	<.0001
Anticoagulants (%)	734 (99.6)	252 (99.6)	358 (99.4)	92 (100)	0.99	447 (98.5)	56 (100)	283 (99.0)	85 (97.7)	0.38	0.05
Diuretics (%)	620 (84.1)	212 (83.8)	291 (80.8)	86 (93.5)	0.01	385 (84.8)	40 (71.4)	244 (85.3)	78 (89.7)	0.01	0.75
Nitrates (%)	610 (82.8)	192 (75.9)	310 (86.1)	81 (88.0)	0.002	200 (44.1)	22 (39.3)	126 (44.1)	42 (48.3)	0.57	<.0001
Calcium channel blockers (%)	308 (41.8)	88 (34.8)	166 (46.1)	41 (44.6)	0.02	148 (32.6)	15 (26.8)	99 (34.6)	27 (31.0)	0.48	0.002
Catecholamines (%)	269 (36.5)	98 (38.7)	125 (34.7)	33 (35.9)	0.59	98 (21.6)	20 (35.7)	55 (19.2)	17 (19.5)	0.02	<.0001

Antiarrhythmics (without beta-blockers) (%)	216 (29.3)	90 (35.6)	90 (25.0)	29 (31.5)	0.02	67 (14.8)	11 (19.6)	35 (12.2)	16 (18.4)	0.18	<.0001
Insulins (%)	281 (38.1)	104 (41.1)	125 (34.7)	41 (44.6)	0.12	177 (39.0)	19 (33.9)	115 (40.2)	34 (39.1)	0.41	0.42
Other antidiabetic agents (%)	142 (19.3)	40 (15.8)	73 (20.3)	21 (22.8)	0.23	71 (15.6)	5 (8.9)	48 (16.8)	14 (16.1)	0.33	0.21
In-hospital complications											
Cardiac arrest (%)	108 (14.7)	48 (19.0)	41 (11.4)	16 (17.4)	0.05	94 (20.7)	19 (33.9)	55 (19.2)	15 (17.2)	0.03	0.01
Cardiogenic shock (%)	84 (11.4)	37 (14.6)	35 (9.7)	8 (8.7)	0.12	33 (7.3)	11 (19.6)	19 (6.6)	2 (2.3)	0.001	0.02
Pulmonary edema (%)	45 (6.1)	20 (7.9)	18 (5.0)	7 (7.6)	0.31	22 (4.9)	4 (7.1)	9 (3.2)	8 (9.2)	0.04	0.36
Bradycardia (%)	54 (7.3)	21 (8.3)	24 (6.7)	8 (8.7)	0.58	15 (3.3)	4 (7.1)	10 (3.5)	0 (0)	0.04	0.01
Recurrent infarction (%)	21 (2.9)	4 (1.6)	15 (4.2)	1 (1.1)	0.09	9 (2.0)	0 (0)	5 (1.8)	4 (4.6)	0.18	0.35
Ventricular tachycardia (%)	44 (6.0)	20 (7.9)	17 (4.7)	5 (5.4)	0.25	14 (3.1)	2 (3.6)	5 (1.8)	6 (6.9)	0.04	0.02
Ventricular fibrillation (%)	29 (3.9)	16 (6.3)	8 (2.2)	3 (3.3)	0.03	8 (1.8)	2 (3.6)	4 (1.4)	0 (0)	0.21	0.04
Stroke (%)	6 (0.8)	3 (1.2)	2 (0.56)	1 (1.1)	0.51	3 (0.7)	1 (1.8)	2 (0.7)	0 (0)	0.43	0.77
Bleeding complication (intracranial or retroperitoneal or any other major spontaneous bleeding) (%)	17 (2.3)	7 (2.8)	5 (1.4)	4 (4.4)	0.19	7 (1.5)	1 (1.8)	4 (1.4)	1 (1.2)	0.84	0.36
Any in-hospital complication (without cardiac arrest) (%)	202 (27.4)	87 (34.4)	83 (23.1)	25 (27.2)	0.008	85 (18.7)	18 (32.1)	44 (15.4)	17 (19.5)	0.01	0.001
Outcome											
28-day-case fatality (%)	68 (9.2)	32 (12.7)	26 (7.2)	8 (8.7)	0.07	97 (21.4)	19 (33.9)	58 (20.3)	14 (16.1)	0.03	<.0001

MI: myocardial infarction; STEMI: ST-segment elevation MI, NSTEMI: Non-ST-segment elevation MI; BBB: bundle branch block; ACEIs/ARBs: angiotensin-converting-enzyme inhibitors or angiotensin receptor blockers; DAPT: dual antiplatelet therapy; GP IIb/IIIa antagonists: glycoprotein IIb/IIIa antagonists.

[#] The total study population includes 57 patients (32 in the invasive and 25 in the conservative strategy group) with non-classifiable or missing data regarding the type of acute MI.

Tab 3. Association between invasive versus conservative strategy and 28-day-case fatality for the total study population and stratified by type of acute MI

	OR [95% CI]	p-value
Total (n=1,191)[#]		
Full model*	0.43 [0.25-0.74]	0.002
Parsimonious model**[1]	0.43 [0.27-0.69]	<.001
STEMI (n=308)[##]		
Full model*	0.40 [0.13-1.27]	0.12
Parsimonious model**[2]	n.a.	
NSTEMI (n=634)[##]		
Full model*	0.29 [0.13-0.66]	0.003
Parsimonious model**[3]	0.27 [0.13-0.56]	<.001
BBB (n=178)[##]		
Full model*	0.76 [0.16-3.66]	0.74
Parsimonious model**[2]	n.a.	

MI: myocardial infarction; STEMI: ST-segment elevation MI, NSTEMI: Non-ST-segment elevation MI; BBB: bundle branch block

The total study population includes 57 patients (32 in the invasive and 25 in the conservative strategy group) with non-classifiable or missing data regarding the type of acute MI; "dummy"-coding was used for the variable "type of acute MI" in the models of the total study population.

As 14 patients had missing information on serum creatine phosphokinase (1 in the STEMI, 12 in the NSTEMI and 1 in the BBB group, respectively), we excluded them for the stratified analyses.

* Multivariable logistic regression model adjusted for age, sex, smoking, body mass index ≥ 30 kg/m², history of diabetes, any in-hospital complication (without cardiac arrest), serum creatinine level (mg/dl) at admission, in-hospital medication: beta-blockers, statins, ACEIs/ARBs, nitrates, calcium channel blockers, dual antiplatelet therapy and type of acute MI (for the total study population) / serum creatine phosphokinase (for analyses stratified by type of acute MI).

** Parsimonious multivariable logistic regression model using forward selection.

[**1] adjusted for smoking, any in-hospital complication (without cardiac arrest), in-hospital medication: beta-blockers and ACEIs/ARBs.

[**2] n.a. = the variable "treatment strategy" did not meet the 0.05 significance level for entry into the model.

[**3] adjusted for smoking, any in-hospital complication (without cardiac arrest), in-hospital medication: beta-blockers and ACEIs/ARBs, history of diabetes, and serum creatine phosphokinase.