Outcomes after STEMI in old multimorbid patients with complex health needs and the effect of invasive management

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Background The aim of this study was to assess one-year outcomes of invasive and non-invasive strategies in ST-elevation myocardial infarction (STEMI) among multimorbid older people with complex health needs.

Methods We included patients, registered between 2006 and 2013 in the SWEDEHEART registry, who were 70 years old or older with STEMI, had multimorbidity and complex health needs and were discharged alive. The one-year outcomes of patients who underwent invasive strategy (examined with coronary angiography ≤14 days) were compared to those who did not. The primary event was a composite of all-cause death, admission due to new acute coronary syndrome, stroke or transient ischemic attack.

Results We identified patients, and 1089 were managed invasively and 570 non-invasively. The mean age was 79 years and 83 years in the 2 groups, respectively. After multivariable adjustment for baseline differences between the groups, including propensity scores, the primary event occurred in 31% of patients in the invasive group and 55% in the non-invasive group, adjusted hazard ratio (95% confidence intervals): 0.67 (0.54-0.83). One-year mortality was 18% in the invasive group and 45% in the non-invasive group, adjusted hazard ratio 0.51 (0.39-0.65).

Conclusions Multimorbid older people with complex health needs and STEMI had high rates of new ischemic events and death. In this cohort of older, high risk STEMI patients, an invasive strategy was associated with lower event rates. Randomized studies are needed to clarify whether these high risk patients who might benefit from invasive care are being managed too conservatively. (Am Heart J 2019;211:11-21.)

The Western population is aging. Among patients with acute coronary syndromes (ACS), around 35% are 75 years old or older.[1] Age is not an isolated condition and at least 64% of patients between 65 and 84 old, and 81% of those who are 85 years old and older, have two or more chronic diseases or medical conditions, also known as multimorbidity.[2,3] Primary percutaneous coronary interventions (PCI) have proven to reduce mortality and recurrent ischemia in older people with ST-elevation myocardial infarction (STEMI)[4] and modern guidelines do not exclude patients from primary PCI due to advanced age.[5]

Most randomized trials exclude older people with extensive multimorbidity.[6] The presence of other conditions alongside STEMI can affect the benefits of the invasive strategy. For example, a comorbid condition can increase the risk of bleeding events in a patient that receives a coronary stent that requires dual antiplatelet therapy for several months. There is concern that strict adherence to guidelines may cause harm in treating those with multimorbidity.[7]

Non-selected registries provide an opportunity to perform observational studies on patients who are not included in most trials. The Swedish National Board of Health and Welfare has defined a group of older people with complex health needs. These patients have

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multimorbidity and large consumption of health care.[8] Almost 90% of them are frail or pre-frail.[9] They can be identified with the Swedish National Patient Registry. The SWEDEHEART Registry (Swedish Web-system for Enhancement and Development of Evidence-based care in Heart Disease Evaluated According to Recommended Therapies) can be combined with the Swedish National Patient Registry. This provides investigators with the opportunity to find a group of older people in SWEDEHEART who are frail and have multimorbidity.

Our objective was to assess one-year outcomes of invasive strategy and non-invasive strategy in STEMI among multimorbid older people with complex health needs.

Methods

Endpoints

The primary event in this study was a composite of 1-year all-cause mortality, readmission due to ischemic stroke or transient ischemic attack (TIA) or readmission due to ACS. ACS included STEMI, non-ST-elevation myocardial infarction and unstable angina. Secondary events were 1-year readmissions due to bleeding events, any single component of the primary event, one-year readmissions due to heart failure, and one-year readmissions due to any cause.

Patients and data sources

This was an observational study of prospectively collected data from the SWEDEHEART registry and the Swedish National Patient Registry. The SWEDEHEART registry contains RIKS-HIA (The Register of Information and Knowledge about Swedish Heart, Intensive Care Admissions) as well as SCAAR (Swedish Coronary Angiography and Angioplasty Registry) together with registries for thoracic surgery and secondary prevention. RIKS-HIA collects data for all patients admitted to Swedish coronary care units and includes over 100 variables for patients' medical history, strategy before admission, clinical conditions, management during hospital stay, treatment at discharge, and diagnosis. SCAAR collects angiographic data, procedural data, demographic data and treatment decisions for all patients who are investigated with coronary angiography and/or revascularized with percutaneous coronary interventions at every Swedish center performing these procedures. Data is registered online and source data verification is performed annually in randomly selected patients from about 20 different hospitals.[10] SWEDEHEART is merged regularly with the Swedish National Cause of Death Registry to obtain date of death and cause of death.

The Swedish National Patient Registry collects information about diagnoses at discharge from all hospital admissions in Sweden, as well as diagnoses from outpatient hospital specialist care.[11] Using information from the Swedish National Patient Registry, the Swedish National Board of Health and Welfares has defined a group of older people with multimorbidity and complex health needs. An individual must meet criteria a-c) and either d), e) or f) at index date; a) be at least 65 years old b) be hospitalized at least three times with main diagnoses from at least two different the *International Classification of Diseases, 10th Revision* (*ICD-10*) chapters, c) at least one hospitalization must be within 12 months prior to index date, d) have more than 19 days of hospitalization or outpatient's visits to specialist clinics during the last 12 months before index date, e) have more than 3 hospitalizations during the last 12 months before index hospitalization or f) have more than 7 visits to specialist in outpatient care during the last 12 months before index date.[8]

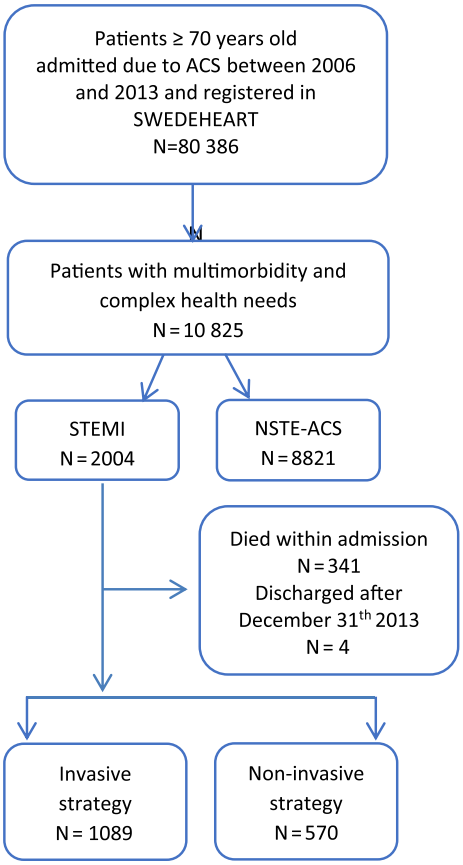
We included patients who were hospitalized due to STEMI from January 1, 2006 to December 31, 2013, registered in SWEDEHEART and who met the criteria for having multimorbidity and complex health needs at admission. Only index admissions were included. Patients who died during admission were excluded to avoid survival bias, i.e., severe disease and death precluded patients from being referred to coronary angiography (CA) (Figure 1).

Date of death was obtained from the Swedish National Cause of Death Registry. Patient characteristics and new episodes of ACS were identified from both by RIKS-HIA and the Swedish National Patient Registry. Other outcomes were identified from the Swedish National Patients Registry. The *ICD-10* codes for both patient characteristics and outcomes can be found in online supplements.

Definitions

Invasive strategy was defined as the performance of coronary angiography ≤14 days of admission. Patients who were referred to CA after 14 days or not at all constituted the non-invasive group.[12] Bleeding events were defined as all hospitalizations with diagnoses of hemorrhage without regard to type or anatomical location implied by the diagnose code, as well as fatal bleeds with the bleeding diagnosis as a first or a second cause of death. *ICD-10* codes for bleeding events can be found in online supplements.[13] The standards of the European Society of Cardiology for definition of myocardial infarctions and ACS are used in Swedish hospitals and RIKS-HIA.[14] The treating physician makes the final diagnosis. STEMI is defined as the presence of ST-elevation on electrocardiogram (ECG) or new left bundle-branch block on electrocardiogram (ECG) in addition to suspicion of ongoing ischemia. Renal function was calculated with Cockcroft Gault formula and presented as estimated glomerular filtration rate (eGFR). Normal renal function was defined as eGFR ≥90 ml/min/1.73 m^3, mild renal disease: 60 ≤ eGFR <90 ml/min/1.73 moderate renal disease: 30 ≤ eGFR <60 ml/min/1.73 m^3,

Figure 1



Patient selection. Multimorbid older patient with complex health needs are defined by the Swedish National Board of Health and Welfares, using The Swedish National Inpatient Registry. An individual must meet criteria a-c) and either d), e) or f) at index date; a) be at least 65 years old b) be hospitalized at least three times with main diagnoses from at least two different *ICD-10* chapters, c) at least one hospitalization must be within 12 months prior to index date, d) have more than 19 days of hospitalization or outpatient's visits to specialist clinics during the last 12 months before index date, e) have more than 3 hospitalizations during the last 12 months before index hospitalization or f) have more than 7 visits to specialist in outpatient care during the last 12 months before index date; ACS: acute coronary syndromes; CCU: coronary care unit; STEMI: ST-elevation myocardial infarction; NSTEMI: non-ST elevation myocardial infarction; UAP unstable angina pectoris; invasive strategy: coronary angiography performed ≤14 days of admission.

and severe renal disease: eGFR ≤30 ml/min/1.73 m^3. Comorbidity burden was measured by CAD specific index, which was described by Sachdev et al. in 2004,[15] a description can be found in online supplements.

Statistical analyses

To compare patient characteristics in the invasive group to the non-invasive, Fisher Exact test was used for dichotomous variables, the Mantel-Haenszel χ^2 test for ordered categorical variables, χ^2 test was used for non-ordered categorical variables and Mann-Whitney *U* test was used for continuous variables.

A propensity score method was used to compare the results of invasive and non-invasive strategy to compensate for the non-randomized study design. It included all the patient characteristics that differed between the invasive and non-invasive group as well as comorbidity burden. Variables tested for difference between the groups were: age, gender, smoking status, year of index date, hypertension, stroke, diabetes, chronic obstructive pulmonary disease (COPD), peripheral vascular disease (PVD), a tumor or lymphoma, tumor with metastases, history of congestive heart failure, anemia, atrial fibrillation, prior myocardial infarction or renal (groups: normal, moderate, severe, eGFR unknown) disease, previous PCI, eGFR, CAD specific index, as well as medications on admission. Medications on admission were: angiotensin-converting enzyme inhibitors (ACE-I), angiotensin receptor blockers (ARB), Acetylsalicylic acid (ASA), P2y12 receptor antagonists, oral anticoagulants, beta blockers,

Table I. Patient characteristics in multimorbid older people with complex health needs and STEMI

	Invasive group # (N = 1089) %	Non-invasive group (N = 570) %	p-value**
Age, years (±SD) *	78.7 (5.7)	83.4 (6.2)	<.0001
70- < 80 years	55.9	26.0	
80- < 90 years	40.7	58.2	<.0001
≥90 years	3.4	15.8	
Women	45.1	55.1	0.0001
Not an active smoker	87.6	90.5	
Active smoker	12.4	9.5	0.14
Missing smoking status†	n = 95	n = 130	
Year of index date			
2006-2008	28.3	43.9	
2009-2011	41.5	40.5	<.0001
2012-2013	30.2	15.6	
Hypertension	58.6	61.9	0.21
Stroke	16.3	23.5	0.0006
Diabetes	25.2	29.1	0.094
COPD‡	12.6	13.9	0.51
PVD§	6.8	12.3	0.0003
Cancer during the last three years	21.9	24.2	0.30
Heart failure	19.9	35.8	<.0001
Anemia	16.6	29.5	<.0001
Atrial fibrillation	21.9	33.2	<.0001
Acute myocardial infarction	25.5	35.2	<.0001
eGFR ml/min/1.73m^2 (±SD)‖	25.1	22.4	0.0004
≥90	9.9	4.7	
60 ≤ eGFR<90	32.3	17.2	
30 ≤ eGFR<60	45.3	54.9	
eGFR<30	12.5	23.2	
Missing eGFR, number	n = 71	n = 122	<.0001
CAD-specific indexes¶			
Low burden	16.7	3.3	
Moderate burden	12.2	5.6	
High burden	71.0	91.0	
Missing CAD index, number	n = 68	n = 90	<.0001

* SD: standard deviation, age and estimated glomerular filtration rate are shown as mean (±SD), missing values are shown as numbers, other results are shown as percentages.
† missing values are not included in the denominator, if no value is given then there are no missing values.
‡ COPD: chronic obstructive pulmonary disease.
§ PVD: peripheral vascular disease.
‖ eGFR: estimated glomerular filtration rate, calculated with Cockcroft Gault formula.
¶ CAD: coronary artery disease, CAD specific index: coronary artery disease specific index, see online supplements.
# invasive group: patients who underwent coronary angiography ≤ 14 days.
** for comparison between groups Fisher's Exact test was used for dichotomous variables, the Mantel-Haenszel Chi square test was used for ordered categorical variables, Chi square was used for non-ordered categorical variables and Mann-Whitney *U* test was used for continuous variables.

lipid-lowering drugs, diuretics, digitalis, long-acting nitroglycerin, and calcium antagonists).

For each outcome, Cox's regression survival analyses were performed to compare the effects of invasive versus non-invasive strategy. Three Cox regression analyses were performed for each outcome: Model 1 included age, sex, eGFR and propensity scores. Model 2 included all covariates in model 1 and additionally adjusted for medications at discharge that differed between the groups (ACE-I or ARB, ASA, P2y12 receptor antagonists, beta-blockers, statins, diuretics, digitalis, long-acting nitroglycerin, and calcium antagonists). Model 3 included all covariates in model 2 and additionally adjusted for variables included in propensity scores for which balance between the groups was not achieved. Unless otherwise stated, the adjusted results are from Model 3. Unknown and missing values were kept as an additional level of the categorical covariates. For one-year mortality the criteria for proportional hazards during 1 year were not fulfilled, data was further analyzed with a flexible parametric survival model (Royston-Parmer model).[16] Thus, the interaction between the treatment group and time in study could be studied and described by continuous hazard ratios (HR). Interactions in the Cox regression analyses were tested between age and treatment strategy, gender and treatment strategy, eGFR group and treatment strategy. Subgroup analyses were performed in those groups.

Table II. Medications at admission and at discharge

	Invasive group* (n = 1089) %	Non-invasive group (n = 570) %	p-value†
Admission			
ACE inhibitors‡	22.5	28.6	0.0084
ARB§	17.0	13.1	0.046
Calcium antagonists	24.1	21.7	0.30
Beta-blockers	45.5	52.4	0.0090
Statins	31.3	30.6	0.81
Acetylsalicylic acid	40.0	49.4	0.0003
$P2Y_{12}$ receptor antagonist	7.5	8.5	0.56
Oral anticoagulants	8.1	11.3	0.042
Digitalis	4.2	9.2	0.0001
Long acting nitroglycerin	13.1	22.2	<.0001
Discharge			
ACE inhibitors	60.9	45.1	<.0001
ARB	17.6	13.4	0.031
Calcium antagonists	16.4	15.5	0.69
Beta-blockers	88.2	79.6	<.0001
Statins	83.8	47.2	<.0001
Acetylsalicylic acid	91.6	78.5	<.0001
$P2Y_{12}$ receptor antagonist	89.8	37.1	<.0001
Oral anticoagulants	10.3	10.4	1.00
Digitalis	6.2	7.4	0.40
Aldosterone blockers	10.0	10.2	1.00
Long acting nitroglycerin	15.3	32.5	<.0001

* Invasive strategy: patients underwent coronary angiography ≤14 days.
† for comparison between groups Fisher's Exact test was used for dichotomous variables, the Mantel-Haenszel Chi square test was used for ordered categorical variables, Chi square was used for non- ordered categorical variables and Mann-Whitney *U* test was used for continuous variables.
‡ ACE: angiotensin-converting enzyme. Missing numbers are not included in the denominator, for other medications than aldosterone blockers at discharge there were less than 20 missing in each group, for aldosterone blockers 482 were missing in non-invasive group and 759 in invasive group.
§ ARB: angiotensin II receptor blockers.

Mortality during admission in the invasive group was compared to mortality in the non-invasive group using new propensity scores built in the same manner for the entire group and the method described for model 3. Mortality during various time periods from admission was compared between the two groups in the same manner. For further sensitivity analyses, the primary event as well as 1-year mortality were analyzed using Cox's regression survival analyses to compare the effects of invasive versus non-invasive strategy in the group who was discharged alive with ASA as well as the group who was discharged alive with ASA, $P2Y_{12}$ receptor antagonist and statins.

Results

We included 1659 patients, 1089 in the invasive group and 570 in the non-invasive group, a flow chart of the patient selection is shown in Figure 1. The mean age was 78.7 (±5.7 [standard deviation]) in the invasive group and 83.4 (±6.2) years in the non-invasive group; women constituted 45% and 55%, respectively. In the invasive group, 926 (85.0%) underwent coronary angiography during the first day, of which 829 (89.5%) underwent primary PCI. The non-invasive group had higher comorbidity burden and more medications at admission (Table I and II). The differences in clinical characteristics and medications at admission were well balanced after adjustment with a propensity score for all variables except ARB at admission (Table III). Medications at discharge were significantly different between the groups and were included in the adjusted models for outcomes.

In the main analyses, patients had to be alive at discharge. The in-hospital mortality was 12.5% in the invasive group and 24.4% in the non-invasive group, adjusted HR 0.74 (0.57-0.94). Mortality during other time periods from admissions is presented in online supplements. In all cases, the mortality rate was lower in the invasive group.

The primary event was reached in 30.9% of the invasive group and 54.6% in the non-invasive, unadjusted HR 0.56 (95% confidence interval: 0.47-0.68). After adjustment with propensity scores, medications at discharge and the one variable that could not be adjusted in the propensity score (ARB at admission), the risk of the primary event was 33% lower in the invasive group, adjusted HR 0.67 (0.54-0.83) (Table IV). Bleeding events occurred in 8.3% of the invasively treated patients and 11.2% in the non-invasive group, adjusted HR 0.66 (0.43-1.02) (Table IV).

Table III. Test between invasive versus non-invasive strategy with respect to variables included in the propensity score model

Variable from the propensity score model	Invasive* versus non-invasive strategy adjusted p-value
Age	0.95
Gender	0.46
Year of index date	0.69
Heart failure	0.79
Anemia	0.34
Atrial fibrillation	0.66
Prior myocardial infarction	0.41
Prior PCI†	0.11
Renal disease‡	0.84
CAD specific index§	0.37
Medications at admission	
ACE inhibitors||	0.41
ARB¶	0.049
Beta-blockers	0.19
ASA#	0.55
Oral anticoagulants	0.74
Digitalis	0.28
Long-acting nitroglycerin	0.49

* Invasive strategy: patients underwent coronary angiography ≤14 days, continuous variables are tested by using t-test and categorical variables by using Chi-square test weighting the individuals by the inverse probability of receiving the treatment that they actually received.
† PCI: percutaneous coronary intervention.
‡ Renal disease was estimated glomerular filtration rate (eGFR), calculated with Cockcroft Gault formula in ml/min/1.73 m^2, groups were eGFR≥90, 30 ≤ eGFR<60, eGFR≤30 and eGFR = unknown.
§ CAD specific index: coronary artery disease specific index.
|| ACE: angiotensin-converting enzyme.
¶ ARB: angiotensin receptor blockers.
# ASA: acetylsalicylic acid.

Among patients who were discharged with ASA, the result for the primary event was consistent with the main findings. Among the 110 patients who were discharged with ASA, $P2Y_{12}$ receptor antagonist and statins and invasively treated, the primary event occurred in 28.7% as compared to 44.5% in those who were not invasively treated. After adjustment, the risk of primary event was 25% lower in the invasive group, although not statistically significant, adjusted HR 0.75 (0.53-1.05). Data from subgroup analyses is in online supplements.

Readmissions due to any cause were 69.8% in the invasive group and 70.8% in the non-invasive group, adjusted HR 0.88 (0.75-1.03).

One-year mortality after discharge was 17.7% in the invasive group and 44.9% in the non-invasive group, adjusted HR 0.51 (0.39-0.65) (Table V). The flexible parametric survival model showed relative risk reduction between 65% and 47% during the first 120 days, adjusted HR 0.35 (0.21-0.58) to 0.53 0.53 (0.36-0.78). At 9 months adjusted HR was 0.69 (0.46-1.03) and at one-year: 0.75 (0.45-1.27) (Figure 2).

Those who were 90 years old and older in the invasive group had adjusted HR 1.57 (0.93-2.64) for the primary event compared to those in the non-invasive group, adjusted HR 1.51 (0.59-3.86) for readmissions due to bleeding events and HR 1.39 (0.78-2.47) for death (Table V). There were 37 nonagenarians in the invasive group and 109 in the non-invasive group (Table II). In the group with severe renal failure (eGFR<30 ml/min/1.73m^2), the invasive group had adjusted HR 0.84 (0.58-1.22) for the primary endpoint compared to those in the non-invasive group, adjusted HR 1.50 (0.66-3.39) for readmissions due to bleeding events and HR 0.88 (0.58-1.32) for death (Table V). No interactions were found between the subgroups and treatment strategy for the following variables: admission due to heart failure, ACS, stroke/TIA or any cause. Data is in online supplements.

Discussion

In this cohort study we have shown that multimorbid older people with complex health needs and STEMI have high risk of new ischemic events and death during one-year after discharge. After extensively matching the two groups with propensity score method which included among other variables the comorbidity burden, invasive strategy was associated with lower risk for the primary endpoint of death and new ischemic events than non-invasive strategy and it was not associated with increased risk of readmissions due to bleeding events. However, the benefits of invasive strategy were neither found in the small group of nonagenarians in this study nor in the group with severe renal failure.

Primary PCI in patients over 70 years old with STEMI reduces the risk of death, stroke and a new myocardial infarction compared to fibrinolysis.[4,17,18] Patients with multimorbidity in the randomized trials were generally excluded and we are not aware of randomized trials in patients with multimorbidity, complex health needs and STEMI. A cohort study of 698 ACS patients, where 25% had STEMI, did not find lower effectiveness of PCI in patients with more multimorbidity, the group with more multimorbidity had relatively more benefits with PCI than those without it.[19] A cohort study in patients over 70 years of age in Switzerland with acute myocardial infarction during the period of 2001-2012, showed increasing age and more multimorbidity during the last four years compared to the first four years. At the same time the use of primary PCI in STEMI increased in all age groups and the in-hospital outcomes improved.[20] Another cohort study in octogenarians with STEMI from 2005 to 2011 also found increased multimorbidity the last years without increase in mortality rates.[21] In concordance with our results, those results suggest that increased multimorbidity and complexity of patients do not attenuate the benefits of PCI in increasing survival and decreasing new ischemic events. Advancing age, frailty and multimorbidity increase the risk for bleeding events and other complications after PCI.[21,22] At the same time those conditions coexist with more CAD burden and higher baseline risk for new ischemic events and death.[23-25] The higher baseline risk for new events and death causes the efficacy of invasive strategy in those with

Table IV. Invasive strategy compared to non-invasive strategy in multimorbid older patients with complex health needs and STEMI

	Invasive group* (n = 1089) %	Non-invasive group (n = 570) %	Invasive vs non-invasive strategy HR (95% CI)† Model 1‡	Model 2‡	Model 3‡
Primary event					
Primary endpoint (death, ACS, Stroke or TIA)§	30.9	54.6	0.56 (0.47-0.68)	0.67 (0.54-0.83)	0.67 (0.54-0.83)
Secondary events:					
Readmission due to a bleeding event	8.3	11.2	0.67 (0.45-0.97)	0.66 (0.43-1.02)	0.66 (0.43-1.02)
Death‖	17.7	44.9	0.42 (0.33-0.52)	0.51 (0.40-0.66)	0.51 (0.39-0.65)
Readmission due to ACS	12.9	16.1	0.76 (0.55-1.03)	0.76 (0.53-1.09)	0.76 (0.54-1.09)
Readmission due to stroke/TIA	4.3	5.1	0.91 (0.53-1.57)	0.74 (0.40-1.37)	0.74 (0.40-1.37)
Readmission due to heart failure	11.8	15.3	0.80 (0.58-1.10)	0.88 (0.61-1.26)	0.88 (0.61-1.26)
Any readmission	69.8	70.8	0.86 (0.75-0.99)	0.88 (0.75-1.03)	0.88 (0.75-1.03)

* Invasive strategy: patients underwent coronary angiography ≤14 days.
† HR: hazards ratio, CI: confidence interval.
‡ model 1: Cox regression, adjusted for age, sex and propensity scores; model 2: model 1, additionally adjusted for medications at discharge that significantly differed between the treatments (angiotensin-converting enzyme inhibitors, angiotensin II receptor antagonists, diuretics, statins, Acetylsalicylic acid, $P2Y_{12}$ antagonist and long acting nitrates), model 3: model 2 additionally adjusted for variables included in propensity score for which balance between the groups was not achieved.
§ ACS: acute coronary syndromes, TIA: transient ischemic attacks.
‖ The criteria for proportional hazards assumption in Cox regression were not met for this endpoint, the endpoint was further analyzed in flexible parametric survival analyses to look at continuous HR, see Figure 2.

multimorbidity to be relatively higher than in those without, and probably offsets the risk associated with the treatment.

There was a large difference in the baseline comorbidity burden between the invasive and the non-invasive groups. Despite excluding those who died during hospital admission and using a propensity scores and cox-regression to adjust for the baseline differences between the groups, the risk for confounding probably remains. Sensitivity analyses were performed among the patients who were discharged with ASA and those who were discharged with ASA, $P2Y_{12}$ receptor antagonist and statins. In patients who were discharged with ASA, the result for the primary event was consistent with the main findings. Among patients discharged with all three medications, only 110 individual did not receive invasive treatment. The risk reduction of invasive treatment was lower than for all patients, and not statistically significant. There might be a subgroup within the non-invasive group who would never have been considered for CA and PCI due to contraindications such as people who live in nursing home and have a very poor performance status, those at extreme risk for bleeding events and patients with very severe renal failure. There are therefore limitations to our study and a risk for residual confounding. Thus, it is likely not possible to refer all of the risk reduction of invasive treatment.

The mortality rate after STEMI is highest during the first months, especially the first thirty days,[26] in accordance with our results where the impact of invasive strategy was relatively highest during the first months. After nine months, the risk difference was not significant between the groups even if the hazard ratios from nine to twelve months remained the same. The widening of the confidence intervals is probably caused by the non-invasive group constituting only 570 patients with 45% one-year mortality. As the months went by, fewer patients remained alive in the non-invasive group for comparison.

Readmissions due to bleeding events were close to 10% in both groups. A randomized trial in octogenarians with NSTE-ACS, showed similar rate of one-year bleeding events as the current study.[27] The risk for bleeding events for older people with ACS varies greatly, in one study the risk during 30 days after ACS varied from 1% to 40%.[28] In a trial of patients with mixed diagnoses of coronary artery disease, duration of dual antiplatelet therapy over one year was not superior to short duration of 3 to 6 months in those at high risk for bleeding events. The risk was measured using age, hemoglobin level, history of prior bleeding events, white cell blood count and eGFR.[29] Another bleeding risk score used the same conditions but added female sex and STEMI/NSTE-ACS as a component.[28] The duration of dual antiplatelet therapy should probably be shortened in older people undergoing PCI who have a high risk of bleeding events. A concomitant use of proton pump inhibitors to reduce gastrointestinal bleeding events might be considered.[30]

There was a trend for increased risk of bleeding events in the nonagenarians in the invasive group compared to the non-invasive group. A study in patients receiving only aspirin as secondary prevention found more than three-fold rate of bleeding events requiring hospital admissions in patients over 85 years old compared to 65 to 74 years old.[30] There was also a trend toward increased risk of death and the composite endpoint in the nonagenarians in the invasive group. All the confidence intervals were

Table V. The effects of invasive versus non-invasive strategy in different subgroups of patients with STEMI

	Subgroup	Invasive vs non-invasive strategy HR (95% CI)‡	p-value for interaction§
Primary event (death, ACS, Stroke, TIA)*	70-79 years	0.61 (0.45-0.97)	.012
	80-89 years	0.62 (0.48-0.80)	
	≥90 years	1.57 (0.93-2.64)	
	Men	0.57 (0.44-0.75)	.07
	Women	0.76 (0.59-0.99)	
	eGFR† ≥ 90 ml/min/1.73m^2	0.62 (0.30-1.29)	.049
	60 ≤ eGFR <90	0.41 (0.28-0.62)	
	30 ≤ eGFR <60	0.73 (0.56-0.96)	
	eGFR <30	0.84 (0.58-1.22)	
	eGFR unknown	0.50 (0.29-0.84)	
Readmission due to a bleeding event	70-79 years	0.42 (0.23-0.77)	.048
	80-89 years	0.73 (0.42-1.25)	
	≥90 years	1.51 (0.59-3.86)	
	Men	0.77 (0.44-1.35)	.39
	Women	0.58 (0.34-0.98)	
	eGFR ≥90 ml/min/1.73m^2	0.40 (0.23-0.77)	.018
	60 ≤ eGFR <90	0.30 (0.14-0.66)	
	30 ≤ eGFR <60	0.75 (0.43-1.32)	
	eGFR <30	1.50 (0.66-3.39	
	eGFR unknown	0.20 (0.04-0.90)	
Death	70-79 years	0.34 (0.23-0.48)	.0022
	80-89 years	0.55 (0.40-0.74)	
	≥90 years	1.39 (0.78-2.47)	
	Men	0.36 (0.26-0.50)	.0016
	Women	0.67 (0.49-0.90)	
	eGFR ≥90 ml/min/1.73m^2	0.21 (0.08-0.51)	<.0001
	60 ≤ eGFR <90	0.23 (0.14-0.38)	
	30 ≤ eGFR <60	0.56 (0.40-0.78)	
	eGFR <30	0.88 (0.58-1.32)	
	eGFR unknown	0.31 (0.15-0.61)	

* ACS: acute coronary syndromes, TIA: transient ischemic attack.
† eGFR: estimated glomerular filtration rate, calculated with Cockcroft Gault formula.
‡ Patients who underwent coronary angiography ≤14 days constituted the invasive strategy, HR: hazard ratio, CI: confidence interval, HR are from Cox regression, adjusted for age, sex, propensity score, medications at discharge (angiotensin-converting enzyme inhibitors at admission, medication angiotensin receptor blockers, diuretics, statins, Acetylsalicylic acid, $P2Y_{12}$ antagonist and long acting nitrates) and for variables included in propensity score for which balance between the groups was not achieved (angiotensin receptor blockers at admission).
§ Interactions between treatment group and subgroup.

wide, and there were only 37 nonagenarians in the invasive group which limits the interpretations of their results. The nonagenarians in this study were not the average nonagenarians. They all had complex health needs already at admission, which further adds to their age-related high risk for bleeding events. In the current study, the patients with severe renal failure showed a trend toward increased risk for readmission due to bleeding events, but at the same time they had a small trend toward lower risk for primary endpoint and death. Worse renal function has in other studies been associated with both increased risk of bleeding events as well as increased risk of ischemic events.[31]

Multimorbidity and prior hospitalizations are both predictors of readmissions in older people[32] which partly explains the high readmission rate in this study. Readmissions during one year in older patients with myocardial infarction have been reported over 40%,[33] and in those with multimorbidity up to 60%.[34,35] In a cohort of NSTE-ACS patients, revascularization did not decrease all cause readmissions, in concordance to our results for STEMI patients.[35] We are not aware of randomized trials looking specifically at reducing readmissions in older patients with STEMI and complex health needs. Some studies in patients with frailty and/or complex health needs and general internal medicine problems suggest that admitting them to acute elderly care units who use interdisciplinary based geriatric care can possibly reduce the frequency of readmissions.[36] Patients with STEMI and complex health needs need to be treated in specialized coronary care units, but a possible way to address their multiple problems is to develop a practice in the coronary care units of screening for frailty, routinely assessing multimorbidity and functional status of the patients, as well as using risk scores to measure the risk of bleeding events with invasive treatment. For high risk patients, an ambulatory geriatric consulting unit might assess the patients during admission and assure follow-up after discharge.[37]

Figure 2

Continuous hazard ratio during one-year in multimorbid patients with ST-elevation myocardial infarctions. The figure shows the continuous hazard ratio (HR) for invasive strategy compared to non-invasive strategy during one-year obtained from flexible parametric survival analyses, Royston-Parmer model. HR (95% confidence interval) are as following: Day 10: 0.35 (0.21-0.58), day 60; 0.45 (0.29-0.71) day 90: 0.49 (0.34-0.71); day 120: 0.53 (0.36-0.78); six months: 0.59 (0.41-0.87); nine months 0.69 (0.46-1.03); and one-year: 0.75 (0.45-1.27).

Strength and limitations

This study provides information about a group that is rarely examined in clinical trials but often encountered in clinical practice. The main limitation is the non-randomized design; as the allocation to invasive or non-invasive strategy was based on clinical decisions and not randomization. The individuals with the highest risk for complications were probably not assigned to invasive strategy. We excluded the patients who died within the admission to partly compensate for this and extensively adjusted for confounding variables with a propensity score method. We performed sensitivity analyses in patients who were discharged with ASA as well as those who were discharged with ASA, $P2Y_{12}$ receptor antagonist and statins. These measures decreases the selection bias but do not erase it. The confidence intervals were wide and the comparison of the two groups was complex, which probably led to residual confounding. There are likely some clinical conditions that are not available in the registries and were therefore not corrected for. Examples of this are functional status prior to hospital admission, the severity of frailty, cognitive status and the severity of heart failure measured by cardiac ultrasound. We did not have data regarding the reasons behind not sending patients to CA during the index admission, this would have given valuable information.

Conclusion

Multimorbid older people with complex health needs and STEMI had high rates of new ischemic events and death after hospital discharge. This observational study using data from Swedish Quality registries found an invasive strategy to be associated with lower event rate than non-invasive. We therefore found no evidence against treating these patients consistently with results from randomized trials in younger and healthier patients. These results need to be confirmed in randomized clinical trials. However, these patients are difficult to enroll in trials. Future studies should focus on how to reduce the risk for bleeding events in this group as well as how to reduce the high readmission rate. The treatment and risk stratification of the nonagenarians with STEMI and complex health needs, as well as older people with STEMI and severe renal failure need to be evaluated in larger studies.

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