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Invasive Management and 1-Year Outcomes in Patients Aged ≥75 Years with Acute Coronary Syndrome: Age and Clinical Vulnerability

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Abstract

Background/Objectives: Older adults with acute coronary syndrome (ACS) are clinically heterogeneous, and treatment decisions should not rely on chronological age alone. We examined associations of age and clinical vulnerability with coronary angiography, subsequent percutaneous coronary intervention (PCI), and mortality in patients aged ≥75 years. **Methods**: We retrospectively studied 1043 consecutive patients hospitalized with ACS between January 2021 and April 2026. Clinical vulnerability was assessed using the exploratory, study-specific Senior ACS Clinical Vulnerability Score (SAF-75). **Results**: Mean age was 81.0 years; 47.6% were women. Coronary angiography was performed in 571 patients (54.7%) and PCI in 208 (19.9%). Angiography declined from 68.6% at age 75–79 years to 30.1% at ≥85 years. Age was independently associated with lower odds of angiography (OR 0.86 per year, 95% CI 0.82–0.89; $p < 0.001$), but not with subsequent PCI among patients undergoing angiography (OR 1.01, 95% CI 0.95–1.06; $p = 0.852$). In-hospital and Kaplan–Meier estimated 1-year mortality were 18.1% and 35.7%. Greater vulnerability was associated with lower angiography use and higher mortality; no independent association with PCI after angiography was detected. **Conclusions**: Age-related and vulnerability-related differences were most evident at angiography selection. SAF-75 was strongly associated with prognosis but requires external validation.

Keywords: acute coronary syndrome; older adults; coronary angiography; percutaneous coronary intervention; clinical vulnerability; mortality

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1. Introduction

Adults aged ≥75 years account for a substantial proportion of patients hospitalized with acute coronary syndrome (ACS), representing approximately 38% of ACS hospitalizations in a large contemporary nationwide European registry [1]. This population is highly

heterogeneous, ranging from functionally independent individuals to patients with substantial renal, hematologic, nutritional, functional, and cognitive vulnerability, all of which may influence procedural risk, recovery, and the potential benefit of invasive management.

Older adults remain underrepresented in randomized clinical trials [2,3]. Contemporary recommendations emphasize individualized assessment of ischemic and bleeding risk, frailty, comorbidity burden, functional and cognitive status, life expectancy, procedural risk, and patient preferences when considering invasive management [3–6]. Observational studies consistently show declining use of coronary angiography and revascularization with advancing age and increasing vulnerability [1,7–9]. Frailty and broader clinical vulnerability are also associated with adverse outcomes, while functional status, physical performance, and cognitive or mental-status impairment provide additional prognostic information in older patients with ACS [1,3,7–13].

Previous studies have often examined the overall use of coronary angiography or revascularization without clearly separating two sequential clinical decisions: whether to perform coronary angiography and, among patients who undergo angiography, whether to proceed with percutaneous coronary intervention (PCI). This distinction may be particularly relevant in older patients, in whom chronological age and multidimensional clinical vulnerability may influence different stages of the invasive-management pathway.

The primary aim of this study was therefore to examine how chronological age, acute clinical severity, and multidimensional clinical vulnerability were associated with coronary angiography and subsequent PCI in adults aged ≥75 years with ACS. Because formal frailty assessment was not routinely available across the cohort, we developed the study-specific Senior ACS Clinical Vulnerability Score (SAF-75) as an exploratory framework integrating functional, hematologic, renal, inflammatory, nutritional, and mental-status vulnerability. These domains were represented by mobility status, hemoglobin, estimated glomerular filtration rate, neutrophil-to-lymphocyte ratio, serum albumin, and mental-status vulnerability, respectively. We additionally evaluated in-hospital and 1-year all-cause mortality and explored the prognostic performance of SAF-75.

2. Materials and Methods

2.1. Study Population and Data Collection

This retrospective, single-center observational study included 1043 consecutive patients aged ≥75 years who were hospitalized with acute coronary syndrome (ACS) at the Cardiology Clinic, University Clinical Center Niš, a major tertiary referral center for southern and southeastern Serbia, between 1 January 2021 and 15 April 2026.

ACS comprised ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI), and unstable angina, defined according to contemporary clinical criteria [4]. Myocardial infarction was classified according to the Fourth Universal Definition of Myocardial Infarction [14]. Patients with acute myocardial injury without myocardial infarction and those with type 2 myocardial infarction primarily attributable to an acute non-coronary condition causing oxygen supply–demand imbalance were excluded. Only the index hospitalization was analyzed.

Baseline clinical characteristics, laboratory findings, echocardiographic parameters, invasive procedures, in-hospital complications, and outcomes were obtained from medical records. One-year vital status was determined from institutional and electronic records and, when necessary, by telephone contact. Formal linkage to the national death registry was not available.

Follow-up was calculated from the date of index admission to death or the last confirmed vital-status contact and was truncated at 365 days. Patients who remained alive without completing 365 days of observation were right-censored at their last available

contact, with administrative censoring on 7 June 2026. Median potential follow-up was estimated using the reverse Kaplan–Meier method.

2.2. Clinical Characteristics, Invasive Management, and Outcomes

Clinical variables included age, sex, ACS presentation, cardiovascular risk factors, comorbidities, Killip class, mobility status, laboratory variables, and left ventricular ejection fraction (LVEF), when available. Estimated glomerular filtration rate (eGFR) was calculated using the 2021 CKD-EPI equation [15].

Invasive management was examined as a sequential clinical pathway. The first stage was the decision to perform coronary angiography. For the primary analyses, coronary angiography was considered performed when explicitly recorded in the procedural data; records without an explicit angiography code were classified as having no documented angiography. Among patients undergoing angiography, the subsequent treatment decision included percutaneous coronary intervention (PCI), consideration for surgical revascularization, or medical therapy, as appropriate. Angiography timing was recorded when available, and treatment decisions were made by attending physicians as part of routine clinical care. In patients with STEMI, PCI performed during the index hospitalization was classified as primary PCI according to the local catheterization-laboratory database. Because information on fibrinolysis administered before referral was not systematically available, we could not independently verify whether all procedures classified as primary PCI represented true primary PCI rather than possible rescue PCI.

The primary outcomes were in-hospital and 1-year all-cause mortality. Secondary outcomes included major and minor in-hospital complications and cardiovascular rehospitalization. Major complications comprised cardiogenic shock, resuscitated cardiac arrest, mechanical complications of myocardial infarction, stroke, and major bleeding requiring blood transfusion and/or invasive intervention. Minor complications comprised non-sustained ventricular tachycardia, supraventricular tachyarrhythmias, transient conduction disturbances not requiring pacing, hypotension without cardiogenic shock, and minor bleeding.

Cardiovascular rehospitalization was defined as rehospitalization for ACS, heart failure, arrhythmia, or another cardiovascular cause.

2.3. Assessment of Clinical Vulnerability

Multidimensional clinical vulnerability was assessed using the study-specific Senior ACS Clinical Vulnerability Score (SAF-75), comprising mobility status, hemoglobin, estimated glomerular filtration rate (eGFR), neutrophil-to-lymphocyte ratio (NLR), serum albumin, and mental-status vulnerability. These domains were selected on the basis of the previous literature supporting their clinical and prognostic relevance in older patients with ACS [10–13,16–19]. Sex-specific anemia thresholds were based on conventional criteria and previous ACS data [17,20], while renal-function categories followed KDIGO thresholds [21].

All six SAF-75 components were obtained from the initial admission assessment. Mobility and mental status were obtained from the first clinical examination, while laboratory measures were based on the admission samples. The scoring algorithm is presented in Table 1.

Accordingly, SAF-75 was considered an exploratory measure of multidimensional clinical vulnerability and acute illness status, rather than a validated frailty instrument. Primary SAF-75 analyses were restricted to patients with complete data for all six components. A multiple-imputation sensitivity analysis was additionally performed for the association between SAF-75 and 1-year all-cause mortality.

Table 1. Components, scoring, and interpretation of the Senior ACS Clinical Vulnerability Score (SAF-75).

SAF-75 Domain	0 Points	1 Point	2 Points
Mobility	Independent	Requires assistance	Non-ambulatory
NLR	<3.5	≥3.5	—
Hemoglobin (g/L)	Women ≥120 Men ≥130	Women 100–119 Men 100–129	<100 (both sexes)
eGFR	≥60	30–59	<30
Serum albumin (g/L)	≥40	35.0–39.9	<35
Mental status	Communicative and oriented; no acute mental-status change	Impaired communication and/or disorientation; no documented acute deterioration	Documented acute mental-status deterioration or clinically evident new change already present on admission
Scoring and interpretation			
Total SAF-75 score	Sum of all six domain scores: 0–11 points		
Vulnerability category	**Low** 0–2 points	**Intermediate** 3–4 points	**High** ≥5 points

All components reflect the initial admission assessment, before subsequent in-hospital complications; laboratory values were obtained from the first admission samples. SAF-75 was calculated retrospectively for research and did not guide angiography or PCI decisions. The domains were selected based on clinical rationale and the previous literature; thresholds, scoring rules, and vulnerability categories were investigator-defined, not derived from regression coefficients or optimized against observed study outcomes. SAF-75 is an exploratory combined measure of admission clinical vulnerability and acute illness status, not a validated instrument of premorbid frailty. Abbreviations. eGFR, estimated glomerular filtration rate (mL/min/1.73 m^2); NLR, neutrophil-to-lymphocyte ratio.

2.4. Statistical Analysis

Continuous variables were summarized as mean (standard deviation) or median (interquartile range), as appropriate, and categorical variables as counts and percentages. Between-group comparisons were performed using Student's *t*-test or the Mann–Whitney U test for continuous variables and the chi-square or Fisher's exact test for categorical variables. Comparisons across more than two groups were performed using analysis of variance, the Kruskal–Wallis test, or the chi-square test, as appropriate.

Factors associated with coronary angiography were examined using multivariable logistic regression. Among patients who underwent coronary angiography, factors associated with subsequent PCI were evaluated in a separate multivariable logistic regression model. In-hospital all-cause mortality was analyzed using logistic regression, whereas 1-year all-cause mortality was analyzed using Cox proportional hazards regression.

Multivariable models included age, sex, ACS presentation, Killip class, mobility status, eGFR, hemoglobin, presentation within 12 h, and cardiac arrest at admission. Covariates were entered without stepwise selection or univariable pre-screening. Model diagnostics showed no relevant multicollinearity or material deviation from linearity for continuous predictors, and the number of outcome events was considered adequate relative to the number of model parameters. Adjusted odds ratios (ORs) or hazard ratios (HRs) with 95% confidence intervals (CIs) are reported. eGFR and hemoglobin were modeled per 10-unit increase.

Complementary logistic regression models examined age and SAF-75 simultaneously in relation to coronary angiography and, among patients undergoing angiography, subsequent PCI. These analyses were restricted to patients with complete SAF-75 data and were adjusted for sex, ACS presentation, cardiac arrest at admission, and calendar year of hospitalization. Individual SAF-75 components were not additionally entered as covariates.

Several sensitivity analyses were performed to assess the robustness of the main invasive-management findings. The association between age and coronary angiography was re-examined in the full cohort using covariates with complete data: age, sex, ACS presentation, and cardiac arrest at admission. Calendar year of hospitalization was then added to the primary coronary angiography and post-angiography PCI models. Among all patients undergoing angiography, an additional parsimonious model examined the association between age and subsequent PCI after adjustment for sex, ACS presentation, cardiac arrest at admission, and calendar year.

Post hoc complete-case analyses examined coronary angiography and subsequent PCI separately in patients with STEMI and NSTE-ACS (NSTEMI or unstable angina). The same covariates as in the primary models were used, with an unstable-angina indicator retained in the NSTE-ACS models. Standard logistic regression was used for the angiography analyses. Because separation occurred in the NSTE-ACS PCI model, Firth logistic regression was used for both subgroup PCI analyses. Age-by-STEMI interactions were assessed in pooled logistic regression models. These analyses were exploratory, and no adjustment for multiple testing was applied.

The proportional hazards assumption was assessed using scaled Schoenfeld residuals. Where evidence of non-proportionality was observed, sensitivity analyses allowing time-varying effects were performed. Kaplan–Meier methods were used to estimate 1-year survival, and survival curves were compared using the log-rank test.

The discriminative performance of SAF-75 for in-hospital mortality was assessed using receiver-operating-characteristic analysis with 2000 bootstrap resamples. One-year prognostic performance was evaluated using the Cox model, Harrell's C-index, the inverse probability of censoring weighted (IPCW) Brier score at 365 days, and calibration intercept and slope with bootstrap correction. Calibration at 365 days was assessed by comparing model-predicted mortality with observed Kaplan–Meier estimates across deciles of predicted risk.

As a sensitivity analysis addressing missing SAF-75 components and Killip class, multiple imputation was performed using 20 completed datasets. A Cox model including SAF-75, age, sex, ACS presentation, and Killip class was fitted in each dataset, and pooled estimates were obtained using Rubin's rules.

For additional sensitivity analyses of invasive management, missing baseline covariates were imputed in 30 completed datasets. The same baseline covariates as in the main angiography and post-angiography PCI models were used, and estimates were pooled using Rubin's rules. Coronary angiography and PCI outcomes were not imputed.

The original GRACE point-based score for in-hospital mortality was calculated from its eight standard components [22]. Comparison with SAF-75 was restricted to patients with complete data for both scores. Discrimination was compared using the paired DeLong test. Incremental prognostic performance after adding SAF-75 to GRACE was explored using change in area under the curve (AUC), likelihood-ratio testing, and Akaike information criterion (AIC). Internal validation of the combined model used 1000 bootstrap resamples, with a separate 3000-resample bootstrap procedure used to estimate the 95% CI for the change in AUC.

As an additional post hoc analysis, we compared SAF-75 with GRACE 2.0 for 1-year mortality. Predicted 1-year mortality was calculated using the published GRACE 2.0 model [23].

Comparisons were restricted to patients with complete data for both scores. Discrimination was assessed using Harrell's C-index and the inverse probability of censoring weighted (IPCW) time-dependent AUC at 365 days. Paired bootstrap 95% confidence intervals were calculated for between-score differences.

Unless otherwise specified, analyses used available-case denominators, and primary multivariable analyses were based on complete cases. All tests were two-sided, with $p < 0.05$ considered statistically significant. Analyses were performed using IBM SPSS Statistics version 26.0 and R version 4.5.3.

During manuscript preparation and revision, ChatGPT (GPT-5.6 Sol) and ChatGPT Images 2.5 (OpenAI, San Francisco, CA, USA) were used to assist with English-language refinement and with the wording and visual design of the graphical abstract. All AI-assisted content was reviewed and approved by the authors.

3. Results

3.1. Study Population and Outcomes

A total of 1043 patients aged ≥75 years hospitalized with ACS were included. Mean age was 80.98 (4.47) years, and 496 (47.6%) were women. Overall, 544 patients (52.2%) presented with NSTEMI, 426 (40.8%) with STEMI, and 73 (7.0%) with unstable angina. Baseline characteristics are summarized in Table 2, and data completeness is shown in Supplementary Table S1. The study cohort and analytic populations are summarized in Figure 1.

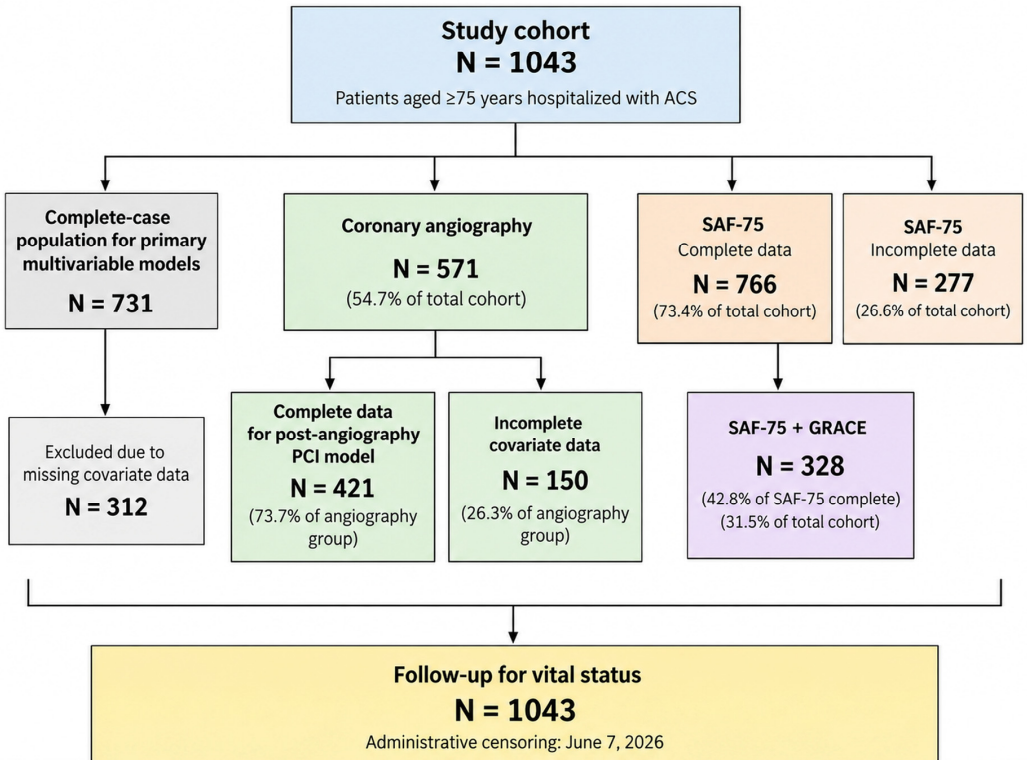


Figure 1. Study cohort and analytical populations. Flow diagram showing the overall cohort (N = 1043), the complete-case populations used for multivariable analyses, patients undergoing coronary angiography and the post-angiography PCI analytic population, patients with complete and incomplete SAF-75 data, the subgroup with complete SAF-75 and GRACE data, and follow-up for vital status with administrative censoring on 7 June 2026.

Table 2. Baseline clinical characteristics, invasive evaluation, management, and outcomes of the study population.

Variable	Overall Cohort, N = 1043
Demographic and clinical characteristics	
Age, years	80.98 (4.47)
Female sex	496 (47.6%)
ACS presentation	
STEMI	426 (40.8%)
NSTEMI	544 (52.2%)
Unstable angina	73 (7.0%)
Mobility status	
Independent	874/1016 (86.0%)
Requires assistance	74/1016 (7.3%)
Non-ambulatory	68/1016 (6.7%)
Killip class	
I	604/835 (72.3%)
II	129/835 (15.4%)
III	50/835 (6.0%)
IV	52/835 (6.2%)
Cardiac arrest at admission	21 (2.0%)
Presentation within 12 h	521/994 (52.4%)
Cardiovascular risk factors and comorbidities	
Hypertension	827/1018 (81.2%)
Diabetes mellitus	369/986 (37.4%)
Dyslipidemia	473/970 (48.8%)
Chronic kidney disease	260/967 (26.9%)
Peripheral vascular disease	92/967 (9.5%)
COPD	62/743 (8.3%)
Previous myocardial infarction	281/978 (28.7%)
Previous PCI	158/970 (16.3%)
Previous CABG	46/971 (4.7%)
Previous stroke	78/955 (8.2%)
Selected laboratory and echocardiographic characteristics	
Hemoglobin, g/L	125.57 (22.13)
NLR	6.49 (5.81)
eGFR, mL/min/1.73 m^2	50.47 (21.64)
Albumin, g/L	38.26 (4.62)
CRP, mg/L	8.70 (2.90–43.85)
LVEF, %	46.44 (13.58)
Diagnostic/invasive evaluation	
Performed coronary angiography	571 (54.7%)
Management	
PCI	208 (19.9%)
Primary PCI among patients with STEMI	131/426 (30.8%)
SAF-75 vulnerability category †	
Low vulnerability	311/766 (40.6%)
Intermediate vulnerability	238/766 (31.1%)
High vulnerability	217/766 (28.3%)
Clinical outcomes	
In-hospital mortality	189 (18.1%)
1-year all-cause mortality, % ‡	35.7
Major in-hospital complications	86/1035 (8.3%)
Minor in-hospital complications	152/1035 (14.7%)
Major bleeding	33 (3.2%)
Cardiovascular rehospitalization	170/1042 (16.3%)

Data are mean (SD), median (IQR), n (%), or n/available N (%), as appropriate. For categorical variables with missing data, the available denominator is shown explicitly; continuous variables are summarized using available-case data. † SAF-75 categories were available in 766 patients with complete data for all six components. ‡ Kaplan–Meier estimate.

In-hospital all-cause mortality was 18.1%, and Kaplan–Meier estimated 1-year all-cause mortality was 35.7%. During follow-up, 371 patients died within 365 days, 629 were alive

with complete 365-day observation, and 43 (4.1%) were right-censored before day 365. The median potential follow-up, estimated using the reverse Kaplan–Meier method, was 365 days, corresponding to the maximum observation period. In a sensitivity analysis restricted to 981 patients who had the opportunity to complete 365 days of follow-up, estimated 1-year mortality was 35.9% (95% CI 33.0–39.0%), compared with 35.7% (95% CI 32.8–38.6%) in the overall cohort (Supplementary Table S3, Part D).

At 0, 30, 180, and 365 days, 1043, 802, 715, and 629 patients, respectively, remained at risk. Major and minor in-hospital complications occurred in 8.3% and 14.7% of patients, respectively, and cardiovascular rehospitalization occurred in 16.3%.

Across age groups of 75–79, 80–84, and ≥85 years, coronary angiography declined from 68.6% to 53.5% and 30.1%, respectively, while overall PCI declined from 24.7% to 19.1% and 12.1% (both $p < 0.001$). In contrast, PCI among patients who underwent angiography was similar across age groups (36.0%, 35.7%, and 40.3%; $p = 0.766$). High SAF-75 vulnerability increased from 20.4% to 32.1% and 37.4% across the same age groups ($p < 0.001$). In-hospital mortality increased from 14.2% to 18.2% and 25.5% ($p = 0.001$), while Kaplan–Meier estimated 1-year mortality increased from 26.3% to 37.1% and 51.5% (log-rank $p < 0.001$) (Table 3).

Table 3. Invasive management, clinical vulnerability, and outcomes according to age group.

Variable	75–79 Years, N = 458	80–84 Years, N = 346	≥85 Years, N = 239	*p* Value
Coronary angiography	314 (68.6%)	185 (53.5%)	72 (30.1%)	<0.001
PCI, overall	113 (24.7%)	66 (19.1%)	29 (12.1%)	<0.001
PCI among patients undergoing angiography	113/314 (36.0%)	66/185 (35.7%)	29/72 (40.3%)	0.766
Primary PCI among STEMI *	66/181 (36.5%)	40/140 (28.6%)	25/105 (23.8%)	0.065
High SAF-75 vulnerability †	68/333 (20.4%)	79/246 (32.1%)	70/187 (37.4%)	<0.001
In-hospital all-cause mortality	65 (14.2%)	63 (18.2%)	61 (25.5%)	0.001
1-year all-cause mortality, % ‡	26.3	37.1	51.5	<0.001

Data are presented as n (%) or n/available N (%), as appropriate. Coronary angiography and overall PCI percentages are calculated within the full age stratum. PCI among patients undergoing angiography is calculated using the number of patients undergoing coronary angiography within each age group as the denominator. * Primary PCI percentages are calculated among patients with STEMI. † High SAF-75 vulnerability was defined as a SAF-75 score ≥5 and was assessed only in patients with complete data for all six score components. ‡ Kaplan–Meier estimated 1-year all-cause mortality; *p* value from the log-rank test.

3.2. Invasive Management and Treatment Patterns

Coronary angiography was performed in 571 patients (54.7%), and PCI in 208 (19.9%). Patients selected for coronary angiography were younger and had a more favorable clinical profile, including better mobility and renal function, higher hemoglobin and albumin levels, and lower inflammatory burden. Patients undergoing PCI also had a more favorable clinical profile, with better mobility and renal function and lower inflammatory burden (Supplementary Table S2).

The multivariable analysis of coronary angiography included 731 complete cases. Advancing age was independently associated with lower odds of coronary angiography (OR per year 0.86, 95% CI 0.82–0.89; $p < 0.001$). STEMI presentation was associated with

greater use of angiography (OR 2.67, 95% CI 1.85–3.86; $p < 0.001$), whereas higher Killip class and non-ambulatory status were associated with lower use. Sex was not independently associated with coronary angiography (Table 4).

Table 4. Multivariable associations with coronary angiography and subsequent PCI.

Variable	Coronary Angiography, Adjusted OR (95% CI)	*p* Value	Subsequent PCI Among Patients Undergoing Angiography, Adjusted OR (95% CI)	*p* Value
Age, per year	0.86 (0.82–0.89)	<0.001	1.01 (0.95–1.06)	0.852
Female sex	0.87 (0.62–1.22)	0.420	1.03 (0.67–1.57)	0.910
ACS presentation				
NSTEMI	Ref.	—	Ref.	—
STEMI	2.67 (1.85–3.86)	<0.001	2.48 (1.57–3.90)	<0.001
Unstable angina	0.54 (0.27–1.05)	0.069	2.22 (0.83–5.95)	0.114
Killip class				
I	Ref.	—	Ref.	—
II	0.46 (0.29–0.71)	<0.001	0.49 (0.25–0.96)	0.037
III	0.35 (0.16–0.75)	0.007	0.80 (0.22–2.92)	0.739
IV	0.44 (0.20–0.95)	0.037	7.14 (1.79–28.44)	0.005
Mobility status				
Independent	Ref.	—	Ref.	—
Requires assistance	0.51 (0.26–1.00)	0.051	0.98 (0.35–2.72)	0.961
Non-ambulatory	0.43 (0.20–0.93)	0.033	0.63 (0.15–2.61)	0.522
eGFR, per 10 mL/min/1.73 m^2 increase	1.09 (1.00–1.19)	0.061	1.04 (0.95–1.15)	0.388
Hemoglobin, per 10 g/L increase	1.08 (1.00–1.17)	0.053	1.01 (0.91–1.13)	0.833
Presentation within 12 h	1.17 (0.83–1.66)	0.373	0.73 (0.47–1.13)	0.154
Cardiac arrest at admission	0.78 (0.23–2.66)	0.692	0.20 (0.02–2.03)	0.174

Data are adjusted odds ratios (ORs) with 95% confidence intervals (CIs) from multivariable logistic regression models. The coronary angiography model included 731 complete cases, of whom 421 underwent angiography. The subsequent PCI model was restricted to 421 complete-case patients who underwent coronary angiography, of whom 178 underwent PCI. Both models included age, sex, ACS presentation, Killip class, mobility status, eGFR, hemoglobin, presentation within 12 h, and cardiac arrest at admission. NSTEMI, Killip class I, and independent mobility were reference categories. eGFR and hemoglobin effects are shown per 10-unit increase. No stepwise selection or univariable pre-screening was used. No imputation was performed. Because of sparse observations in the individual Killip III and IV categories, estimates for these categories should be interpreted cautiously. In a sensitivity analysis combining Killip III–IV, the association with subsequent PCI was attenuated (adjusted OR 2.44, 95% CI 1.03–5.80; $p = 0.043$).

In a sensitivity analysis including the full cohort, age remained independently associated with lower odds of angiography after adjustment for sex, ACS presentation, and cardiac arrest at admission (OR 0.85, 95% CI 0.82–0.88; $p < 0.001$). Addition of calendar year to the primary model did not alter the association between age and angiography (OR 0.86, 95% CI 0.82–0.89; $p < 0.001$), and calendar year was not independently associated with angiography (OR 0.98, 95% CI 0.84–1.13; $p = 0.752$) (Supplementary Table S3).

In a further sensitivity analysis restricted to patients with explicitly recorded angiography status, increasing age remained associated with lower odds of coronary angiography (n = 666; adjusted OR per year 0.851, 95% CI 0.813–0.890; $p < 0.001$) (Supplementary Table S3, Part A).

As a post hoc sensitivity analysis, we excluded 107 patients who died on the calendar date of admission (n = 52) or the following calendar date (n = 55), of whom 27 had documented coronary angiography. The association between increasing age and lower odds of angiography remained similar after exclusion (adjusted OR per year 0.853, 95% CI 0.817–0.891; n = 672) compared with the original complete-case model (OR 0.856, 95% CI 0.821–0.892; n = 731).

Among the 571 patients who underwent coronary angiography, 421 had complete data for all model covariates and were included in the multivariable model of subsequent PCI (Supplementary Table S1). Within this selected post-angiography population, no statistically significant independent association was detected between chronological age and subsequent PCI (OR per year 1.01, 95% CI 0.95–1.06; $p = 0.852$). This finding remained consistent in sensitivity analyses including all patients undergoing angiography and after additional adjustment for calendar year (Supplementary Table S3, Part A).

Multiple-imputation sensitivity analyses produced similar age associations: coronary angiography (N = 1043), OR 0.860 per year (95% CI 0.831–0.890; $p < 0.001$), and subsequent PCI among patients undergoing angiography (N = 571), OR 1.010 per year (95% CI 0.963–1.061; $p = 0.674$) (Supplementary Table S3, Part C).

Among patients undergoing coronary angiography, PCI was performed in 45.8% of those with STEMI and 24.9% of those with NSTEMI. Similarly, PCI after angiography occurred in 36.0%, 35.7%, and 40.3% of patients aged 75–79, 80–84, and ≥85 years, respectively ($p = 0.766$) (Table 3).

In Killip class IV, 15 of 18 patients who underwent coronary angiography received PCI. Because of the small number of patients in this category, the corresponding estimate was considered unstable and was not interpreted as an independent association.

Among 426 patients with STEMI, coronary angiography was performed in 286 (67.1%) and primary PCI in 131 (30.8%). Presentation timing was available in 410 patients; 263 (64.1%) presented within 12 h of symptom onset and 147 (35.9%) after 12 h. Symptom presentation was available in 419 patients, of whom 73 (17.4%) presented without typical chest pain. Among STEMI patients who underwent coronary angiography but did not undergo primary PCI, multivessel disease was present in 60.8%, left main disease in 14.9%, and surgical revascularization was considered indicated in 19.0% of patients with available data (Supplementary Table S4).

Patients undergoing primary PCI had a more favorable vulnerability profile. Among those with complete SAF-75 data, the mean SAF-75 score was lower in patients undergoing primary PCI than in those who did not (2.82 ± 1.80 vs. 3.70 ± 2.25; $p = 0.001$), and high vulnerability was less frequent (12.7% vs. 34.0%; $p < 0.001$) (Supplementary Table S4). Primary PCI declined numerically across age groups, from 36.5% to 28.6% and 23.8%, although this trend did not reach statistical significance ($p = 0.065$) (Table 3).

3.3. Baseline Factors Associated with Mortality

The multivariable mortality analyses included 731 patients with complete data for all covariates (Table 5; Supplementary Table S1).

Table 5. Baseline multivariable associations with in-hospital and 1-year all-cause mortality.

Variable	In-Hospital Mortality OR (95% CI)	*p* Value	1-Year Mortality HR (95% CI)	*p* Value
Age, per year	1.02 (0.97–1.09)	0.402	1.05 (1.02–1.08)	0.001
Female sex	0.63 (0.38–1.06)	0.081	0.93 (0.72–1.20)	0.554
ACS presentation				
NSTEMI	Ref.	—	Ref.	—
STEMI	0.96 (0.57–1.64)	0.891	1.00 (0.76–1.30)	0.972
Unstable angina	0.39 (0.09–1.62)	0.195	0.57 (0.27–1.17)	0.122
Killip class				
I	Ref.	—	Ref.	—
II	1.42 (0.73–2.78)	0.304	1.97 (1.42–2.73)	<0.001
III	5.65 (2.62–12.19)	<0.001	2.26 (1.46–3.50)	<0.001
IV	41.79 (15.51–112.61)	<0.001	7.88 (5.24–11.87)	<0.001
Mobility status				
Independent	Ref.	—	Ref.	—
Requires assistance	1.50 (0.65–3.47)	0.341	1.24 (0.81–1.91)	0.327
Non-ambulatory	4.25 (1.81–9.99)	<0.001	2.48 (1.66–3.69)	<0.001
eGFR, per 10 mL/min/1.73 m^2 increase	0.66 (0.57–0.77)	<0.001	0.82 (0.77–0.89)	<0.001
Hemoglobin, per 10 g/L increase	0.95 (0.85–1.07)	0.429	0.93 (0.88–0.98)	0.012
Presentation within 12 h	2.06 (1.19–3.57)	0.010	1.28 (0.98–1.67)	0.071
Cardiac arrest at admission	2.00 (0.52–7.70)	0.315	2.52 (1.33–4.77)	0.004

Data are adjusted ORs for in-hospital all-cause mortality and adjusted HRs for 1-year all-cause mortality, with 95% CIs. Both models included the same baseline covariates and were restricted to complete cases (N = 731). NSTEMI, Killip class I, and independent mobility were reference categories. eGFR and hemoglobin effects are shown per 10-unit increase. No imputation was performed.

For in-hospital all-cause mortality, Killip classes III and IV, non-ambulatory status, lower eGFR, and presentation within 12 h were independently associated with mortality. Killip class IV showed the strongest association, whereas chronological age was not independently associated with in-hospital mortality.

For 1-year all-cause mortality, increasing age, Killip classes II–IV, non-ambulatory status, lower eGFR, lower hemoglobin, and cardiac arrest at admission were independently associated with mortality. Killip class IV again showed the strongest association. ACS presentation was not independently associated with either in-hospital or 1-year mortality.

Evidence of non-proportional hazards was observed for some covariates in the 1-year Cox model, primarily Killip class, eGFR, and presentation within 12 h. The overall interpretation was unchanged in sensitivity analyses allowing time-varying effects.

3.4. Clinical Vulnerability and Exploratory Prognostic Assessment

SAF-75 could be calculated in 766 patients (73.4%). Of these, 311 patients (40.6%) were classified as having low vulnerability, 238 (31.1%) as intermediate vulnerability, and 217 (28.3%) as high vulnerability.

Across low-, intermediate-, and high-vulnerability categories, PCI use declined from 26.0% to 22.3% and 10.6%, respectively ($p < 0.001$). In-hospital all-cause mortality increased from 4.2% to 16.8% and 39.6%, while Kaplan–Meier estimated 1-year mortality increased from 17.2% to 36.6% and 64.6% (both $p < 0.001$). Major in-hospital complications were also more frequent in the high-vulnerability group (16.9%) than in the low- and intermediate-vulnerability groups (5.2% and 4.6%, respectively; $p < 0.001$). Cardiovascular rehospitalization occurred in 15.8%, 16.4%, and 13.8% of patients across the three SAF-75 categories and was presented descriptively because death was not analyzed as a competing event (Table 6; Supplementary Figure S1).

Table 6. PCI use and clinical outcomes according to SAF-75 vulnerability category.

Variable	Low Vulnerability, n = 311	Intermediate Vulnerability, n = 238	High Vulnerability, n = 217	*p* Value
PCI	81 (26.0%)	53 (22.3%)	23 (10.6%)	<0.001
Major in-hospital complications	16/309 (5.2%)	11/238 (4.6%)	36/213 (16.9%)	<0.001
In-hospital all-cause mortality	13 (4.2%)	40 (16.8%)	86 (39.6%)	<0.001
1-year all-cause mortality, % *	17.2	36.6	64.6	<0.001
Cardiovascular rehospitalization	49 (15.8%)	39 (16.4%)	30 (13.8%)	—

Data are presented as n (%), n/available N (%), or Kaplan–Meier estimates, as appropriate. SAF-75 categories were defined as low vulnerability (0–2 points), intermediate vulnerability (3–4 points), and high vulnerability (≥5 points). SAF-75 analyses were restricted to 766 patients with complete data for all six score components. * Kaplan–Meier estimated 1-year all-cause mortality; *p* value from the log-rank test. Cardiovascular rehospitalization is presented descriptively because death was not analyzed as a competing event.

In complementary multivariable models including both chronological age and SAF-75, increasing age (OR 0.847 per year, 95% CI 0.815–0.882; $p < 0.001$) and higher SAF-75 score (OR 0.748 per point, 95% CI 0.690–0.811; $p < 0.001$) were independently associated with lower odds of coronary angiography (n = 766). Among patients who had undergone angiography (n = 422), neither age (OR 1.009, 95% CI 0.956–1.065; $p = 0.745$) nor SAF-75 (OR 0.919, 95% CI 0.817–1.033; $p = 0.157$) showed a statistically significant independent association with subsequent PCI (Supplementary Table S5).

The continuous SAF-75 score showed an AUC of 0.792 for in-hospital mortality and a Harrell's C-index of 0.722 for 1-year mortality. In the univariable complete-case Cox analysis (n = 766), each 1-point increase in SAF-75 was associated with higher 1-year mortality (unadjusted HR 1.41, 95% CI 1.34–1.48). In the multiple-imputation sensitivity analysis including the full cohort (N = 1043), SAF-75 remained associated with 1-year mortality after adjustment for age, sex, ACS presentation, and Killip class (pooled adjusted HR 1.32,

95% CI 1.26–1.38; $p < 0.001$) (Supplementary Table S3, Part B). Calibration is shown in Supplementary Figure S2.

Among 328 patients with complete data for both SAF-75 and GRACE, the AUCs for in-hospital mortality were 0.852 and 0.815, respectively, with no significant difference on paired DeLong testing ($p = 0.394$). Adding SAF-75 to GRACE increased the AUC to 0.877 (ΔAUC 0.062; $p = 0.011$), with consistent improvement on likelihood-ratio testing and bootstrap internal validation (Supplementary Table S6).

In an additional post hoc analysis of 1-year mortality, GRACE 2.0 and SAF-75 showed similar discrimination among the same 328 patients. Harrell's C-indices were 0.756 and 0.755, respectively, while the corresponding IPCW time-dependent AUCs at 365 days were 0.776 and 0.782 (difference −0.006; 95% paired bootstrap CI −0.063 to 0.050).

In adjusted subgroup analyses, increasing age was associated with lower odds of coronary angiography in both STEMI (OR per year 0.902, 95% CI 0.851–0.956) and NSTE-ACS (OR 0.813, 95% CI 0.764–0.864; both $p < 0.001$), with a stronger inverse association in NSTE-ACS (interaction $p = 0.011$). No statistically significant independent association between age and subsequent PCI was detected in either STEMI (OR 1.036, 95% CI 0.970–1.108; $p = 0.294$) or NSTE-ACS (OR 0.962, 95% CI 0.868–1.062; $p = 0.451$). The pooled interaction for subsequent PCI was not statistically significant ($p = 0.159$) (Supplementary Table S7).

4. Discussion

In this consecutive cohort of 1043 patients aged ≥75 years with ACS, advancing age and higher admission clinical vulnerability were independently associated with lower odds of coronary angiography. Among patients already selected for angiography, neither chronological age nor SAF-75 showed a statistically significant independent association with subsequent PCI in the complementary models. Greater vulnerability was strongly associated with in-hospital and 1-year mortality. These findings emphasize the need to distinguish selection for angiography from decisions regarding PCI after coronary anatomy is known.

Large contemporary registries consistently show that older and frail patients with ACS undergo coronary angiography and revascularization less frequently and have worse outcomes [1,7,8]. Randomized trials in older patients with NSTE-ACS have not shown a consistent benefit of a routine invasive strategy across all clinical outcomes. AFTER EIGHTY showed a reduction in its primary composite endpoint with an invasive strategy [24], whereas SENIOR-RITA did not significantly reduce cardiovascular death or nonfatal myocardial infarction, although nonfatal myocardial infarction was less frequent [25]. In frail patients, MOSCA-FRAIL did not demonstrate an improvement in days alive and out of hospital during the first year [26]. A subsequent meta-analysis similarly found fewer myocardial infarctions and repeat revascularizations, but no significant reduction in all-cause mortality and a higher risk of major bleeding [27]. These studies show how heterogeneous older patients with ACS are and why the expected benefit and risk of invasive treatment need to be considered for each patient.

Our findings add an important point to this discussion. The strongest age-related difference was observed at the decision to perform coronary angiography. Angiography declined markedly with advancing age, whereas no statistically significant independent association between age and subsequent PCI was detected among patients already selected for angiography. This finding should be interpreted in the context of potential selection bias. Ravindran et al. reported a similar pattern, with lower use of angiography at more advanced age without a corresponding age-related decline in PCI among patients undergoing angiography [28]. In the ISACS-TC registry, patients aged ≥75 years with STEMI underwent coronary angiography less frequently than younger patients, while anemia and later

presentation were also associated with lower angiography use [29]. In the SENIOR-RITA angiographic substudy, patients undergoing PCI and those managed without PCI were also of similar age, whereas frailty, poorer cognitive performance, and more complex coronary disease were more frequent among patients who did not undergo PCI [30]. Together, these findings suggest that an important part of age-related selection occurs before coronary anatomy is known, at the stage when the decision about angiography is made. Lower angiography use with advancing age may reflect individualized clinical selection, but our observational data cannot exclude potential undertreatment of functionally preserved older patients. The inverse association between age and coronary angiography was present in both STEMI and NSTE-ACS and was stronger in NSTE-ACS. These findings should be considered in the context of different management pathways: STEMI generally requires urgent reperfusion, whereas the timing and selection of invasive management in NSTE-ACS depend on acute instability, ischaemic risk, and the anticipated balance of benefit and harm [4,6]. In older adults, treatment decisions are also influenced by comorbidity burden and functional status [3]. Differences in this decision-making context may contribute to the stronger age association observed in NSTE-ACS. After angiography, no statistically significant independent association between age and subsequent PCI was detected in either selected subgroup.

This distinction between coronary angiography and PCI is clinically important. Angiography defines coronary anatomy, while the subsequent decision regarding revascularization depends on the coronary findings, technical feasibility, clinical condition, and available treatment alternatives. In our STEMI patients who underwent angiography without primary PCI, multivessel and left main disease were frequent, and some patients had an indication for surgical revascularization. Therefore, absence of PCI after angiography does not necessarily indicate conservative management, because coronary anatomy may lead to surgical revascularization or medical treatment.

Clinical vulnerability was independently associated with angiography selection, although its association with PCI after angiography was less certain. In complementary models including both age and SAF-75, neither variable was independently associated with subsequent PCI among the selected patients who had undergone angiography (Supplementary Table S5). Patients undergoing angiography also had better mobility and renal function, higher hemoglobin and albumin concentrations, and a lower inflammatory burden. Previous studies have similarly shown that frailty, impaired mobility, and cognitive impairment are associated with lower use of invasive treatment and with adverse outcomes in older patients with ACS [7–13]. In the LONGEVO-SCA registry, frailty was less frequent among patients aged ≥80 years with NSTE-ACS undergoing invasive management than among those managed conservatively [31]. These findings illustrate the clinical heterogeneity of this population: patients of the same chronological age may differ substantially in functional status, renal function, hematologic reserve, nutritional status, cognition, and overall physiological reserve. Beyond its relevance at ACS presentation, physical function remains clinically important during recovery, as individualized exercise-based cardiac rehabilitation after PCI may improve functional capacity [32].

Recent frailty analyses provide further context. In the SENIOR-RITA frailty analysis, an invasive strategy did not significantly reduce the primary outcome among frail patients, and treatment effects appeared to vary across the spectrum of frailty [33]. In contrast, the FIRE frailty analysis showed that the benefit of physiology-guided complete revascularization compared with culprit-only PCI was maintained across frailty categories in older patients with myocardial infarction and multivessel disease [34]. These studies address different clinical decisions. SENIOR-RITA concerns whether an older patient should undergo an invasive strategy, whereas FIRE concerns the extent of revascularization in patients already

undergoing invasive treatment. This distinction is relevant to our findings because the decision to perform angiography and the decision to proceed with revascularization are not the same clinical question.

SAF-75 was developed to describe multidimensional clinical vulnerability using information routinely available during the initial assessment of an older patient with ACS, rather than to replace a formal frailty instrument. Its components include mobility and mental status together with markers of anemia, renal dysfunction, inflammation, and nutritional status. However, NLR, albumin, and acute mental-status abnormalities present at admission may also reflect the severity of the presenting illness, making SAF-75 a combined measure of clinical vulnerability and acute illness status. Higher SAF-75 scores were associated with lower odds of angiography and higher mortality; the adjusted association with PCI following angiography was not statistically significant. The continuous score showed moderate discrimination for both in-hospital and 1-year mortality, and its association with 1-year mortality remained strong in the multiple-imputation sensitivity analysis. In the subgroup with complete data for both SAF-75 and GRACE, discrimination for in-hospital mortality did not differ significantly between the two scores. An exploratory analysis suggested improved discrimination when SAF-75 was added to GRACE, although this finding requires external validation. For 1-year mortality, SAF-75 and GRACE 2.0 showed similar discrimination in the same complete-case subgroup. However, the limited sample size and wide confidence intervals for between-score differences do not establish equivalence or superiority of either score. Previous studies have also suggested that frailty assessment may provide prognostic information beyond conventional ACS risk assessment [35]. The potential value of SAF-75 is therefore in describing vulnerability that is not captured by chronological age alone. However, it remains a study-specific exploratory score and requires external validation before clinical use.

The STEMI subgroup deserves separate consideration. Primary PCI was recorded in 30.8% of patients with STEMI, substantially lower than the rate reported among patients aged ≥75 years in the Spanish ATHOS registry [36]. These figures cannot be directly compared because of differences in study populations, referral pathways, study periods, and healthcare systems. In our cohort, more than one third of patients with documented symptom timing presented after 12 h, a relevant proportion did not report typical chest pain, and patients undergoing primary PCI had a more favorable vulnerability profile. Coronary anatomy was also complex in many STEMI patients who underwent angiography without primary PCI. The observed primary PCI rate is therefore likely to reflect several factors rather than a single explanation.

Mortality in our cohort was high, with in-hospital mortality of 18.1% and estimated 1-year mortality of 35.7%. High mortality is well recognized in very old and frail patients with ACS, although direct numerical comparison between registries is difficult because of differences in age distribution, case mix, frailty burden, and treatment pathways [1,28]. In-hospital mortality was associated with acute clinical severity, particularly advanced Killip class, together with non-ambulatory status and renal dysfunction, whereas chronological age was not independently associated with in-hospital death. At 1 year, age was associated with mortality together with Killip class, mobility, renal function, hemoglobin, and cardiac arrest at admission. Killip class IV showed the strongest association with both outcomes. These findings emphasize the importance of acute hemodynamic severity and functional and physiological reserve in determining prognosis in older patients with ACS. Similar observations from SILVER-AMI have shown that mobility provides prognostic information beyond chronological age [9].

The association between presentation within 12 h and higher in-hospital mortality was unexpected. Patients with more severe acute presentations may have presented or been

referred earlier, but this cannot be established from our data and the finding should therefore be interpreted cautiously. ACS presentation itself was not independently associated with mortality after adjustment, suggesting that in this older population acute severity and the overall clinical condition of the patient provided substantial prognostic information beyond the STEMI or NSTEMI diagnosis.

Cardiovascular rehospitalization did not increase across SAF-75 categories despite the marked mortality gradient. This finding should be interpreted cautiously because death was not analyzed as a competing event. Patients with greater vulnerability had substantially higher mortality and therefore less opportunity to experience subsequent rehospitalization.

Treatment decisions in older patients with ACS should integrate acute clinical severity, functional and cognitive status, renal function, anemia, comorbidities, procedural and bleeding risk, life expectancy, coronary anatomy when available, and patient preferences [3–6]. Our findings also show the importance of separating the decision to perform coronary angiography from the subsequent decision regarding revascularization. Admission clinical vulnerability was associated with angiography selection and prognosis, while the association with chronological age was most evident before coronary anatomy was defined.

Study Limitations

First, the retrospective, single-center design limits causal inference and generalizability. The study was conducted at a tertiary referral center, and referral and treatment pathways may differ from those in other healthcare systems.

Second, treatment decisions were subject to confounding by indication, and individual reasons for performing or withholding coronary angiography or PCI were not systematically documented. The PCI analysis was restricted to patients already selected for angiography. Reliable information on whether CABG was actually performed was not available, precluding analysis of a combined PCI/CABG revascularization endpoint. Temporary restrictions on catheterization-laboratory access during the COVID-19 pandemic could not be evaluated at the patient level. Limited information on the timing of angiography and death precluded a reliable 24 or 48 h landmark analysis; excluding early deaths did not eliminate survival-related selection bias.

Third, primary multivariable analyses used complete cases, which differed from patients with incomplete covariate data in PCI use and mortality. Multiple-imputation analyses yielded similar age associations with angiography and subsequent PCI, although they remain dependent on assumptions about missing data (Supplementary Table S3, Part C). Separately, 111 patients without an explicit angiography code were classified as having no documented angiography; excluding these patients did not change the association between age and angiography (Supplementary Table S3, Part A).

Fourth, mobility and mental status were obtained from routine clinical records rather than formal geriatric assessments. SAF-75 combines admission clinical vulnerability and acute illness status using investigator-defined scoring rules and is not a validated frailty or treatment-selection instrument. Its prognostic performance was evaluated in the same cohort and may be optimistic; bootstrap internal validation does not replace external validation. A validated frailty instrument such as the Clinical Frailty Scale could not be reliably reconstructed from the available retrospective records.

Fifth, incomplete information on pre-transfer fibrinolysis, first-medical-contact-to-angiography times, and interhospital transfer intervals limited reconstruction of the STEMI reperfusion pathway. Patient-level reasons for not performing primary PCI could not be established in every case, limiting interpretation of the observed primary PCI rate.

Finally, cardiovascular rehospitalization was analyzed without accounting for death as a competing event, and cause-specific mortality was not systematically adjudicated. Some

covariate effects in the 1-year Cox model varied over time. The overall interpretation was unchanged in sensitivity analyses, but the reported hazard ratios should be interpreted as average associations over follow-up.

5. Conclusions

In patients aged ≥75 years with ACS, advancing age and greater admission clinical vulnerability were independently associated with lower odds of coronary angiography. Among patients already selected for angiography, neither age nor SAF-75 showed a statistically significant independent association with subsequent PCI in the complementary models. Greater vulnerability was strongly associated with in-hospital and 1-year mortality. These findings highlight prognostic heterogeneity and the distinction between angiography selection and subsequent treatment decisions. SAF-75 remains an exploratory indicator of admission vulnerability and acute illness status, which should be validated in independent cohorts. Further research is needed to better understand the factors guiding angiography selection before coronary anatomy is known.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/jcm15228830/s1, Figure S1: Mortality, discrimination, and PCI use according to SAF-75; Figure S2: Calibration of SAF-75 for 1-year all-cause mortality; Table S1: Data availability and characteristics according to inclusion in the complete-case multivariable analysis; Table S2: Clinical characteristics according to coronary angiography and PCI use in the overall cohort; Table S3: Sensitivity analyses for invasive management and 1-year mortality; Table S4: Invasive management, coronary anatomy, and clinical characteristics according to ACS presentation and primary PCI use; Table S5: Complementary multivariable logistic regression models including chronological age and SAF-75; Table S6: Completeness and exploratory prognostic performance of SAF-75 and GRACE; Table S7: Adjusted associations of age with coronary angiography and subsequent PCI in STEMI and NSTE-ACS.

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Abbreviations

The following abbreviations are used in this manuscript:

ACS	Acute coronary syndrome
AIC	Akaike information criterion
AUC	Area under the curve
CABG	Coronary artery bypass grafting
CI	Confidence interval
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration
COPD	Chronic obstructive pulmonary disease
CRP	C-reactive protein
eGFR	Estimated glomerular filtration rate
GRACE	Global Registry of Acute Coronary Events
HR	Hazard ratio
IPCW	Inverse probability of censoring weighted
IQR	Interquartile range
KDIGO	Kidney Disease: Improving Global Outcomes
LVEF	Left ventricular ejection fraction
NLR	Neutrophil-to-lymphocyte ratio
NSTE-ACS	Non-ST-segment elevation acute coronary syndrome
NSTEMI	Non-ST-segment elevation myocardial infarction
OR	Odds ratio
PCI	Percutaneous coronary intervention
SAF-75	Senior ACS Clinical Vulnerability Score
SD	Standard deviation
STEMI	ST-segment elevation myocardial infarction

References

1. Völschow, B.; Goßling, A.; Kellner, C.; Neumann, J.T. Frailty prevalence, invasive treatment frequency, and in-hospital outcome in patients hospitalized for acute coronary syndrome in Germany (2005–2022): A nationwide registry study. *Lancet Reg. Health Eur.* **2025**, *49*, 101168. [CrossRef] [PubMed]
2. Lawless, M.; Damluji, A.A.; Dirjayanto, V.J.; Mills, G.; Pompei, G.; Rubino, F.; Kunadian, V. Differences in treatment and clinical outcomes in patients aged ≥75 years compared with those aged ≤74 years following acute coronary syndromes: A prospective multicentre study. *Open Heart* **2023**, *10*, e002418. [CrossRef] [PubMed]
3. Damluji, A.A.; Forman, D.E.; Wang, T.Y.; Chikwe, J.; Kunadian, V.; Rich, M.W.; Young, B.A.; Page, R.L., II; DeVon, H.A.; Alexander, K.P.; et al. Management of acute coronary syndrome in the older adult population: A scientific statement from the American Heart Association. *Circulation* **2023**, *147*, e32–e62. [CrossRef] [PubMed]
4. Byrne, R.A.; Rossello, X.; Coughlan, J.J.; Barbato, E.; Berry, C.; Chieffo, A.; Claeys, M.J.; Dan, G.A.; Dweck, M.R.; Galbraith, M.; et al. 2023 ESC Guidelines for the management of acute coronary syndromes. *Eur. Heart J.* **2023**, *44*, 3720–3826. [CrossRef] [PubMed]
5. Damluji, A.A.; Nanna, M.G.; Mason, P.; Lowenstern, A.; Orkaby, A.R.; Washam, J.B.; Kolkailah, A.A.; Beckie, T.M.; Dangas, G.; Lawton, J.S.; et al. Coronary artery revascularization in the older adult population: A scientific statement from the American Heart Association. *Circulation* **2025**, *152*, e494–e525. [CrossRef] [PubMed]
6. Rao, S.V.; O'Donoghue, M.L.; Ruel, M.; Rab, T.; Tamis-Holland, J.E.; Alexander, J.H.; Baber, U.; Baker, H.; Cohen, M.G.; Cruz-Ruiz, M.; et al. 2025 ACC/AHA/ACEP/NAEMSP/SCAI guideline for the management of patients with acute coronary syndromes: A report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *J. Am. Coll. Cardiol.* **2025**, *85*, 2135–2237. [CrossRef] [PubMed]
7. Roman, M.; Miksza, J.; Lai, F.Y.-L.; Sze, S.; Poppe, K.; Doughty, R.; Squire, I.; Murphy, G.J. Revascularization in frail patients with acute coronary syndromes: A retrospective longitudinal study. *Eur. Heart J.* **2025**, *46*, 535–547. [CrossRef] [PubMed]
8. Christensen, D.M.; Strange, J.E.; Falkentoft, A.C.; El-Chouli, M.; Ravn, P.B.; Ruwald, A.C.; Fosbøl, E.; Køber, L.; Gislason, G.; Sehested, T.S.G.; et al. Frailty, treatments, and outcomes in older patients with myocardial infarction: A nationwide registry-based study. *J. Am. Heart Assoc.* **2023**, *12*, e030561. [CrossRef] [PubMed]
9. Gupta, A.; Tsang, S.; Hajduk, A.M.; Krumholz, H.M.; Nanna, M.G.; Green, P.; Dodson, J.A.; Chaudhry, S.I. Presentation, treatment, and outcomes of the oldest-old patients with acute myocardial infarction: The SILVER-AMI Study. *Am. J. Med.* **2021**, *134*, 95–103. [CrossRef] [PubMed]

10. Campo, G.; Maietti, E.; Tonet, E.; Biscaglia, S.; Ariza-Solé, A.; Pavasini, R.; Tebaldi, M.; Cimaglia, P.; Bugani, G.; Serenelli, M.; et al. The assessment of scales of frailty and physical performance improves prediction of major adverse cardiac events in older adults with acute coronary syndrome. *J. Gerontol. A Biol. Sci. Med. Sci.* **2020**, *75*, 1113–1119. [CrossRef] [PubMed]
11. Toshima, T.; Watanabe, T.; Goto, J.; Kobayashi, Y.; Otaki, Y.; Wanezaki, M.; Nishiyama, S.; Kutsuzawa, D.; Kato, S.; Tamura, H.; et al. Impact of activities of daily living on percutaneous coronary intervention and acute and long-term mortality in patients with acute myocardial infarction: Yamagata AMI registry. *J. Cardiol.* **2022**, *80*, 313–318. [CrossRef] [PubMed]
12. Molina-Ramos, A.I.; Doncel-Abad, V.; Carmona-Segovia, A.; Becerra-Muñoz, V.; García-Rodríguez, L.; Romero-Cuevas, M.; Segovia-Reyes, J.; Jiménez-Salva, M.; Robles-Mezcua, M.; Díaz-Ottaviano, M.; et al. Frailty and cognitive impairment are associated with early adverse clinical events and angiographic differences in older adults with acute coronary syndrome. *Eur. J. Cardiovasc. Nurs.* **2026**, zvag152. [CrossRef] [PubMed]
13. Briet, C.; Blanchart, K.; Lemaître, A.; Roux, I.; Lavergne, K.; Rocamora, A.; Bignon, M.; Ardouin, P.; Sabatier, R.; Roule, V.; et al. Bedside mental status and outcome in elderly patients admitted for acute coronary syndromes. *Heart* **2019**, *105*, 1635–1641. [CrossRef] [PubMed]
14. Thygesen, K.; Alpert, J.S.; Jaffe, A.S.; Chaitman, B.R.; Bax, J.J.; Morrow, D.A.; White, H.D.; ESC Scientific Document Group. Fourth universal definition of myocardial infarction (2018). *Eur. Heart J.* **2019**, *40*, 237–269. [CrossRef] [PubMed]
15. Inker, L.A.; Eneanya, N.D.; Coresh, J.; Tighiouart, H.; Wang, D.; Sang, Y.; Crews, D.C.; Doria, A.; Estrella, M.M.; Froissart, M.; et al. New creatinine- and cystatin C-based equations to estimate GFR without race. *N. Engl. J. Med.* **2021**, *385*, 1737–1749. [CrossRef] [PubMed]
16. Pruc, M.; Kubica, J.; Banach, M.; Swieczkowski, D.; Rafique, Z.; Peacock, W.F.; Siudak, Z.; Kurek, K.; Nanayakkara, P.; Szarpak, Ł. Diagnostic and prognostic performance of the neutrophil-to-lymphocyte ratio in acute coronary syndromes: A meta-analysis of 90 studies including 45,990 patients. *Kardiol. Pol.* **2024**, *82*, 276–284. [CrossRef] [PubMed]
17. Mamas, M.A.; Kwok, C.S.; Kontopantelis, E.; Fryer, A.A.; Buchan, I.; Bachmann, M.O.; Zaman, M.J.; Myint, P.K. Relationship between anemia and mortality outcomes in a national acute coronary syndrome cohort: Insights from the UK Myocardial Ischemia National Audit Project registry. *J. Am. Heart Assoc.* **2016**, *5*, e003348. [CrossRef] [PubMed]
18. De Rosa, R.; Morici, N.; De Servi, S.; De Luca, G.; Galasso, G.; Piscione, F.; Ferri, L.A.; Piatti, L.; Grosseto, D.; Tortorella, G.; et al. Impact of renal dysfunction and acute kidney injury on outcome in elderly patients with acute coronary syndrome undergoing percutaneous coronary intervention. *Eur. Heart J. Acute Cardiovasc. Care* **2021**, *10*, 1160–1169. [CrossRef] [PubMed]
19. Zhu, L.; Chen, M.; Lin, X. Serum albumin level for prediction of all-cause mortality in acute coronary syndrome patients: A meta-analysis. *Biosci. Rep.* **2020**, *40*, BSR20190881. [CrossRef] [PubMed]
20. World Health Organization. *Guideline on Haemoglobin Cutoffs to Define Anaemia in Individuals and Populations*; World Health Organization: Geneva, Switzerland, 2024.
21. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int.* **2024**, *105*, S117–S314. [CrossRef] [PubMed]
22. Granger, C.B.; Goldberg, R.J.; Dabbous, O.; Pieper, K.S.; Eagle, K.A.; Cannon, C.P.; Van de Werf, F.; Avezum, A.; Goodman, S.G.; Flather, M.D.; et al. Predictors of hospital mortality in the Global Registry of Acute Coronary Events. *Arch. Intern. Med.* **2003**, *163*, 2345–2353. [CrossRef] [PubMed]
23. Fox, K.A.A.; FitzGerald, G.; Puymirat, E.; Huang, W.; Carruthers, K.; Simon, T.; Coste, P.; Monsegu, J.; Steg, P.G.; Danchin, N.; et al. Should patients with acute coronary disease be stratified for management according to their risk? Derivation, external validation and outcomes using the updated GRACE risk score. *BMJ Open* **2014**, *4*, e004425. [CrossRef] [PubMed]
24. Tegn, N.; Abdelnoor, M.; Aaberge, L.; Endresen, K.; Smith, P.; Aakhus, S.; Gjertsen, E.; Dahl-Hofseth, O.; Ranhoff, A.H.; Gullestad, L.; et al. Invasive versus conservative strategy in patients aged 80 years or older with non-ST-elevation myocardial infarction or unstable angina pectoris (After Eighty study): An open-label randomised controlled trial. *Lancet* **2016**, *387*, 1057–1065. [CrossRef] [PubMed]
25. Kunadian, V.; Mossop, H.; Shields, C.; Bardgett, M.; Watts, P.; Teare, M.D.; Pritchard, J.; Adams-Hall, J.; Runnett, C.; Ripley, D.P.; et al. Invasive treatment strategy for older patients with myocardial infarction. *N. Engl. J. Med.* **2024**, *391*, 1673–1684. [CrossRef] [PubMed]
26. Sanchis, J.; Bueno, H.; Miñana, G.; Guerrero, C.; Martí, D.; Martínez-Sellés, M.; Domínguez-Pérez, L.; Díez-Villanueva, P.; Barrabés, J.A.; Marín, F.; et al. Effect of routine invasive vs conservative strategy in older adults with frailty and non-ST-segment elevation acute myocardial infarction: A randomized clinical trial. *JAMA Intern. Med.* **2023**, *183*, 407–415. [CrossRef] [PubMed]
27. Reddy, R.K.; Koeckerling, D.; Eichhorn, C.; Jamil, Y.; Ardissino, M.; Braun, V.; Abu Sharar, H.; Frey, N.; Howard, J.P.; Ahmad, Y. Early invasive or conservative strategies for older patients with acute coronary syndromes: A meta-analysis. *JAMA Intern. Med.* **2025**, *185*, 966–975. [CrossRef] [PubMed]
28. Ravindran, J.; Brieger, D.; Hyun, K.; Chow, V.; Yong, A.; Kritharides, L.; Ng, A.C.C. Impact of coronary intervention on in-hospital mortality in octogenarians and nonagenarians, compared to elderly patients aged <80 years with acute coronary syndromes. *CJC Open* **2025**, *7*, 897–906. [CrossRef] [PubMed]

29. Câlmâc, L.; Bătăilă, V.; Ricci, B.; Vasiljevic, Z.; Kedev, S.; Gustiene, O.; Trininic, D.; Knežević, B.; Miličić, D.; Dilic, M.; et al. Factors associated with use of percutaneous coronary intervention among elderly patients presenting with ST segment elevation acute myocardial infarction (STEMI): Results from the ISACS-TC registry. *Int. J. Cardiol.* **2016**, *217*, S21–S26. [CrossRef] [PubMed]
30. Pompei, G.; Rubino, F.; Jenkins, K.; Ratcovich, H.; Austin, D.; Banerjee, S.; Buchanan, G.L.; Junejo, S.; Nasser, A.; Hussein, N.; et al. Angiographic characteristics of older patients with non-ST elevation myocardial infarction undergoing invasive strategy: A pre-specified analysis from the SENIOR-RITA trial. *Eur. Heart J. Open* **2026**, *6*, oeag131. [CrossRef] [PubMed]
31. Llaó, I.; Ariza-Solé, A.; Sanchis, J.; Alegre, O.; López-Palop, R.; Formiga, F.; Marín, F.; Vidán, M.T.; Martínez-Sellés, M.; Sionis, A.; et al. Invasive strategy and frailty in very elderly patients with acute coronary syndromes. *EuroIntervention* **2018**, *14*, e336–e342. [CrossRef] [PubMed]
32. Spadafora, L.; Cacciatore, S.; Salvi, M.; Russo, F.; Lo Sasso, L.; Lauretti, A.; Perone, F.; Pierucci, N.; Sabouret, P.; Zangari, G.; et al. Exercise After Coronary Stenting: Potential Effects on in-Stent Restenosis. *Curr. Atheroscler. Rep.* **2026**, *28*, 82. [CrossRef] [PubMed]
33. Rubino, F.; Mossop, H.; Ripley, D.P.; Carter, J.; Twomey, D.; Cooke, J.; Austin, D.; Veerasamy, M.; Kelly, D.; Felmeden, D.; et al. Invasive vs conservative strategy for frail older patients with myocardial infarction: A secondary analysis of the SENIOR-RITA randomized clinical trial. *JAMA Netw. Open* **2026**, *9*, e267316. [CrossRef] [PubMed]
34. Dal Passo, B.; Tonet, E.; Lanzilotti, V.; Menozzi, M.; Scarsini, R.; Picchi, A.; Andò, G.; Sarti, A.; Farina, J.; Cantone, A.; et al. Consistent benefit of physiology-guided complete revascularization across the spectrum of frailty in older patients with myocardial infarction: A prespecified analysis of the FIRE trial. *Age Ageing* **2026**, *55*, afag078. [CrossRef] [PubMed]
35. Anand, A.; Cudmore, S.; Robertson, S.; Stephen, J.; Haga, K.; Weir, C.J.; Murray, S.A.; Boyd, K.; Gunn, J.; Iqbal, J.; et al. Frailty assessment and risk prediction by GRACE score in older patients with acute myocardial infarction. *BMC Geriatr.* **2020**, *20*, 102. [CrossRef] [PubMed]
36. Fernández-Bergés, D.; Degano, I.R.; Gonzalez Fernandez, R.; Subirana, I.; Vila, J.; Jiménez-Navarro, M.; Perez-Fernandez, S.; Roqué, M.; Bayes-Genis, A.; Fernandez-Aviles, F.; et al. Benefit of primary percutaneous coronary interventions in the elderly with ST segment elevation myocardial infarction. *Open Heart* **2020**, *7*, e001169. [CrossRef] [PubMed]

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