RESEARCH ARTICLE

DOI: 10.4274/ijca.2026.80774
Int J Cardiovasc Acad 2026;12(2):114-126

Clinical Characteristics, Treatment Strategies, and Short-term Outcomes in Octogenarian Patients with Acute Coronary Syndrome

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Abstract

Background and Aim: Octogenarians (≥80 years) with acute coronary syndrome (ACS) represent a high-risk group due to comorbidities, frailty, and atypical clinical presentations, which pose significant management challenges. There is limited evidence to guide optimal management, especially regarding the choice between conservative and invasive strategies. This study examines the clinical characteristics, treatment approaches, and short-term outcomes in this population.

Materials and Methods: In this multi-center observational study, 197 octogenarian ACS patients were enrolled between January 2022 and August 2024. Patients were categorized into conservative (57.4%) and invasive (42.6%) management groups. Demographics, comorbidities, clinical presentation, and geriatric assessments (Fried Frailty Scale, Confusion Assessment Method, Geriatric Depression Scale) were collected. Outcomes assessed included in-hospital and 30-day mortality, reinfarction, bleeding (Bleeding Academic Research Consortium ≥3), and target vessel revascularization (TVR).

Results: The cohort was predominantly non-ST-elevation ACS (88.3%) with high frailty (53.8%). Selection bias was notable: the conservative group had more peripheral vascular disease (38.9% vs. 19.0%, $P = 0.003$) and delirium (42.5% vs. 26.2%, $P = 0.02$), while the invasive group had higher Global Registry of Acute Coronary Events scores ($P = 0.039$) and body mass index ($P = 0.028$). In-hospital (5.9% vs. 7.9%) and 30-day mortality (9.6% vs. 15.9%) were lower in the invasive group, though these differences were not statistically significant. The invasive group had a higher TVR rate (13.1% vs. 0.0%, $P < 0.001$) and a trend toward lower reinfarction (3.5% vs. 10.6%, $P = 0.12$). Major bleeding rates were similar (13.1% vs. 9.7%, $P = 0.61$).

Conclusion: Geriatric syndromes have a substantial impact on ACS management in octogenarians. Frailty and delirium are associated with a preference for conservative care. In appropriately selected patients, invasive treatment appears safe and associated with numerical reduction of recurrent ischemic events without increasing short-term risk. Comprehensive geriatric assessment is essential for individualized treatment planning.

Keywords: Octogenarian, frailty, acute coronary syndrome

To cite this article: Mahmoud K, Nagah H, Louka E, Ammar W, Abdelghany M. Clinical characteristics, treatment strategies, and short-term outcomes in octogenarian patients with acute coronary syndrome. Int J Cardiovasc Acad. 2026;12(2):114-126

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Received: 25.01.2026
Accepted: 28.04.2026
Publication Date: 22.06.2026

INTRODUCTION

Ischemic heart disease (IHD) is the top global cause of death, and advanced age is its main non-modifiable risk factor linked to higher morbidity and mortality.[1,2] Acute coronary syndrome (ACS) in the elderly, especially octogenarians (≥80 years), is rising and presents a growing challenge.[3,4]

Octogenarian patients with ACS represent a distinct and highly vulnerable population. They have more comorbidities, frailty, polypharmacy, and face higher complications from both disease and treatment. Compared to younger patients, octogenarians often present with atypical symptoms, such as dyspnea, dizziness, or syncope. These atypical symptoms delay ACS diagnosis and increase rates of conservative management.[5-7] This management disparity is exacerbated by the underrepresentation of the elderly in major clinical trials, resulting in gaps in evidence-based guidelines.[8] Early invasive strategies are associated with better outcomes in ACS but also with higher complication rates in this subgroup. Management choice depends on comorbidities, functional status, and life expectancy.[9,10]

Given these challenges, a thorough understanding of clinical characteristics, treatment patterns, and outcomes in this cohort is essential for optimizing management. This study investigates the clinical profiles, treatment strategies (conservative versus invasive), and short-term outcomes of octogenarian patients with ACS. The findings aim to inform evidence-based, individualized decision-making for this high-risk group.

METHODS

Study Design

This multi-center observational study provides real-world insights into the management and outcomes of octogenarians with ACS by comparing invasive and conservative management strategies. Conducting a randomized controlled trial (RCT) in this high-risk population presents significant ethical and practical challenges; therefore, an observational design was chosen to reflect actual clinical practice.

Objective

To investigate the characteristics, treatment approaches, and outcomes of octogenarian patients hospitalized with ACS.

Population of Study

A total of 212 patients aged 80 and older presenting with ACS were evaluated for eligibility. Of these, 197 were enrolled between January 2022 and August 2024. Fifteen patients were excluded—seven declined to participate, and eight could not be reached after discharge. Patients or their representatives provided written consent to the study. Data from the included patients were collected during the study period, and a complete case analysis was performed. The study was approved by the Local Research Ethics Committee, Cairo University Faculty of Medicine (approval no: MD-371-2021, date: 04.10.2022).

Inclusion Criteria

Age ≥80 years old. Patients presented with ACS [non-ST-segment elevation (NSTE)-ACS or ST-segment elevation myocardial infarction (STEMI)].

Exclusion Criteria

1. Patient refusing to participate in the study.

2. Patients who presented with elevated cardiac troponin levels due to non-ischemic causes such as renal impairment, heart failure (HF), myocarditis, sepsis, or rhabdomyolysis were excluded.

Methodology

All the patients were subjected to the following during the index hospitalization:

- Demographics and risk factors: Age, gender, hypertension [systolic blood pressure (SBP) ≥140 and diastolic blood pressure (DBP) ≥90 mmHg],[11] diabetes mellitus (HbA1c > 6.5 and FBS >126),[12] smoking, dyslipidemia [low-density lipoprotein (LDL) cholesterol >70 mg/dL, triglycerides >150 mg/dL][13], family history of IHD,[14] previous coronary artery bypass grafting (CABG), history of percutaneous coronary intervention (PCI).

- Comorbidities: Chronic kidney disease,[15] hepatic impairment,[16] peripheral vascular disease (PVD),[17] cerebrovascular disease (ischemic stroke or transient ischemic attack),[18] chronic obstructive pulmonary disease.[19]

- ACS data:
    - Clinical presentation: Symptom characteristics (typical vs. atypical chest pain, diaphoresis, nausea, vomiting, dyspnea, syncope).
    - ACS type: NSTE-ACS and STEMI.
    - Timing: Duration of chest pain, time from first medical contact to revascularization.
    - Hemodynamic support: Use of vasopressors, intra-aortic balloon counterpulsation (IABP), in-hospital or out-of-hospital resuscitation.
    - Management strategy: The choice between conservative and invasive strategies was made at the discretion of

the treating physician, based on assessment of patient characteristics, comorbidities, geriatric syndromes, and clinical presentation, rather than following predefined standardized criteria. This approach reflects real-world clinical practice in this complex patient population.

- Conservative strategy: A management approach in which coronary angiography is not routinely performed, but is reserved for patients with refractory symptoms or objective evidence of recurrent ischemia, despite optimal medical therapy. The initial focus is on pharmacological stabilization.
- Invasive strategy: This approach involves routine coronary angiography within a recommended timeframe, with the intention to perform PCI or, less commonly, CABG if the coronary anatomy is suitable.[20]

• Electrocardiographic (ECG): Rhythm, ST-segment changes, and conduction abnormalities.

• Transthoracic echocardiography: The echocardiographic studies were performed during the first 48 hours of hospitalization.[21]

• Laboratory assessment: Including cardiac enzymes [creatine kinase-MB, high-sensitivity troponin, glomerular filtration rate (GFR), creatinine, hemoglobin, total leucocytic count, platelets count, alanine aminotransferase, aspartate aminotransferase, HbA1c, total cholesterol, high-density lipoprotein, LDL, and triglycerides].

• Coronary angiographic assessment: This included evaluation of single versus multivessel disease, left main (LM) coronary artery or equivalent involvement, lesion characteristics (type, length, calcification), and access site complications. We also recorded the incidence of contrast-induced acute kidney injury.[22,23]

• Frailty was assessed using the Fried Frailty Scale. Additional evaluations included the Confusion Assessment Method (CAM) and the Geriatric Depression Scale (GDS).

- Fried Frailty Phenotype Scale:[24]
    - Administration: Patients were assessed across five predefined criteria: unintentional weight loss, self-reported exhaustion, low physical activity (Minnesota leisure time activity questionnaire), slow walking speed (4-meter walk), and weak handgrip strength (dominant hand, measured with a Jamar dynamometer).
    - Scoring and Interpretation: Each criterion present was scored as 1 point. Patients were categorized as follows:
- Robust (not frail): 0 criteria present.
- Pre-frail: 1-2 criteria present.
- Frail: ≥3 criteria present.
- CAM:[25]
    - Administration: The CAM was administered daily throughout hospitalization by the attending nurse to screen for acute delirium. The assessment evaluated: (1) acute onset and fluctuating course, (2) inattention, (3) disorganized thinking, and (4) altered level of consciousness.
    - Scoring and interpretation: A patient was diagnosed with delirium (CAM-positive) if they displayed both features (1) and (2) plus either feature (3) or (4).
- GDS-15:[26]
    - Administration: The 15-item short form of the GDS was used. Patients were asked to answer "yes" or "no" to 15 questions about how they felt over the past week.
    - Scoring and interpretation: Each answer suggestive of depression scores 1 point. The total score was interpreted as:
- Normal (no significant depression): 0-5 points.
- Suggestive of mild/moderate depression: 6-10 points.
- Suggestive of severe depression: 11-15 points.

In this study, a score of ≥6 was used to define clinically significant depressive symptoms.

Patient Outcomes

- Primary outcome:
    - In-hospital mortality: Death from any cause during hospital admission.
- Secondary outcomes:
    - Target vessel revascularization (TVR): A repeat revascularization procedure (either PCI or CABG) performed on the original culprit vessel treated during the index ACS event.[27]
    - Reinfarction: According to the fourth universal definition of myocardial infarction:[28]

- In patients with PCI for the index myocardial infarction: A recurrence of symptoms and new ECG changes plus a re-elevation of cardiac troponin values by >20% from the previous trough level, with a peak value exceeding the 99th percentile upper reference limit (URL).
- In patients without PCI (conservative arm): The detection of a rise and/or fall of cardiac troponin values with at least one value above the 99th percentile URL and with at least one of the following: (1) symptoms of ischemia, (2) new ischemic ECG changes, (3) development of pathological Q-waves, or (4) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.
- In-hospital HF: The development of new or worsening symptoms and signs of HF (e.g., dyspnea, orthopnea, pulmonary edema, hypoperfusion) requiring intensification of diuretic therapy or the initiation of intravenous vasoactive agents (e.g., diuretics, inotropes, vasopressors) during the index hospitalization.
- Bleeding Academic Research Consortium (BARC) type 3 or 5 bleeding:[29]
    - BARC 3a: Overt bleeding with a hemoglobin drop of 3 to <5 g/dL odds ratio (OR) transfusion of whole blood or packed red blood cells.
    - BARC 3b: Overt bleeding with a hemoglobin drop ≥5 g/dL OR cardiac tamponade OR bleeding requiring surgical intervention or intravenous vasoactive drugs.
    - BARC 3c: Intracranial hemorrhage OR subcategories confirmed by autopsy, imaging, or lumbar puncture.
    - BARC 5: Fatal bleeding.
- Stroke: Rapidly developing clinical signs of focal (or global) disturbance of cerebral function lasting >24 hours or leading to death, with no apparent non-vascular cause, confirmed by a neurologist and neuroimaging (computed tomography or magnetic resonance imaging).[30]
- Readmission: An unplanned admission to any hospital for any cause within a specified timeframe after the index discharge (30 days).

Medical Follow-up

Throughout the one-month follow-up period after discharge, all patients remained on guideline-directed medical therapy. This included antithrombotic and anti-ischemic agents, with additional HF medications as clinically indicated. The therapeutic regimen typically consisted of antithrombotic agents, statins, beta-blockers, nitrates, and renin-angiotensin-aldosterone inhibitors.[20] Survival was assessed at one month following hospital discharge.

Statistical Analysis

A formal sample size calculation was not performed a priori for this study. The final sample size of 197 participants was determined based on feasibility and convenience sampling over a defined enrollment period.

This approach was justified for the following reasons:

- Real-world constraints in a specific population: This study focused exclusively on octogenarians (≥80 years) presenting with ACS. This population is distinct and challenging to enroll due to higher mortality, more complex comorbidities, and frequent exclusion from clinical trials. A consecutive sample over 30 months was the most pragmatic approach to obtain a meaningful, real-world cohort representative of this demographic at our institution.
- Explorative and hypothesis-generating nature: As an observational study, its primary aim was to describe characteristics, management patterns, and associated outcomes, rather than to test a single prespecified hypothesis with a definitive effect size. The sample size is sufficient to provide precise estimates of prevalence (e.g., frailty, depression) and to identify clinically relevant trends and associations that can inform the design of future, larger-scale or randomized studies.
- Post-hoc evaluation of precision: Despite the lack of a prior power calculation, the obtained sample provides measurable precision. For example, with 197 participants, the proportion of a given outcome (e.g., the overall 30-day mortality rate of 13.4%) has a 95% confidence interval (CI) of approximately ±4.8%. This indicates a reasonable level of precision for estimating event rates within this cohort.

Therefore, although this sample may be underpowered to detect small differences in less common endpoints, it constitutes a clinically relevant effort to characterize the presentation and care of a critically important, understudied patient group in a real-world setting. A complete case approach was utilized in this study; patients with missing data for any variable included in a specific analysis were excluded from that analysis.

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Descriptive statistics were used to summarize the demographic and clinical characteristics of patients. Continuous variables were presented as mean with standard deviation for normally distributed data or median with interquartile range for skewed data, while categorical variables were expressed as percentages. The normality of continuous data was assessed using the Shapiro-Wilk test. Additionally, histogram charts and measures of central tendency and dispersion were examined to further assess the distributions' normality. Group comparisons were conducted using Student's t-test for normally distributed continuous variables and the Mann-Whitney U-test for skewed continuous variables. Categorical variables were compared between groups using the chi-square (χ^2) test, as appropriate. Variables with a *P*-value <0.2 in univariate analysis, along with clinically relevant factors such as age, sex, and type of ACS, were considered for inclusion in the multivariable logistic regression model. A backward stepwise selection method was employed to identify independent predictors of mortality. A two-sided *P*-value of less than 0.05 was considered statistically significant. For the comparison of clinical outcomes between the invasive and conservative management groups, OR with 95% CIs were calculated to estimate the effect size and precision of the treatment strategy. All statistical analyses were performed using SPSS (Statistical Package for Social Sciences, SPSS Inc., Chicago, IL), Version 27.0 for Windows.

RESULTS

This multicenter observational study enrolled 197 octogenarian patients (range: 80-95 years) who were diagnosed with ACS between January 2022 and August 2024. The study aimed to assess their clinical characteristics, treatment approaches, and in-hospital and short-term outcomes. The study also compared conservative (57.4%) vs. invasive (42.6%) management among the study patients. All patients in the invasive arm received PCI.

Table 1 shows the baseline characteristics of the studied patients. The mean age in this study was 84.8±3.9, with 56% of the patients were male. The studied patients showed NSTE-ACS dominance, accounting for 88.3% of cases, and it was significantly more frequent in the conservative group (*P* = 0.004). The management strategy was invasive management in 73.9% of STEMI patients (17 out of 23) and in 38.5% of NSTE-ACS patients (67 out of 174). The decision to proceed with either coronary intervention or conservative management was made individually for each patient based on their clinical condition.

There were differences between the two management strategies in baseline characteristics (Table 1). The invasive group had a significantly higher average body mass index (BMI) (30.45±3.52 kg/m²) compared to the conservative group (29.33±3.45 kg/m²) (*P* = 0.028). Patients in the conservative group had a significantly higher history of PVD (38.9%) compared to the invasive group (19.0%) (*P* = 0.004).

Octogenarians presented with atypical ACS symptoms rather than classic chest pain. Only one-fifth of the patients presented with chest pain. There was a trend of late presentation of patients presenting with chest pain, with a chest pain duration of 10.0±16.1. The conservative group showed a non-significantly longer duration of chest pain (11.2±18.6 vs. 8.4±12.0, *P* = 0.23). The other presenting symptoms included dyspnea, diaphoresis, nausea, vomiting, syncope, and cardiac arrest. While the difference between groups in individual symptoms is not statistically significant, the overall trend suggests a higher likelihood of conservative management for these patients (Table 2). DBP is relatively low in the whole group (66.2±15.2); however, the conservative group exhibited a significantly higher DBP (67.96±16.40 mmHg) upon admission compared to the invasive group (63.68±12.99 mmHg) (*P* = 0.049). Cardiac resuscitation on presentation (out-of-hospital or in-hospital) was numerically higher in the invasive group. The use of vasopressors and IABP was also higher in the invasive group; however, the *P*-values were not significant.

The invasive group showed a statistically higher incidence of Q-wave myocardial infarction (42.4% vs. 54.7%, *P* = 0.03). All patients with anterior STEMI were treated invasively (*P* < 0.001). On the contrary, some patients with inferior (3 patients) and lateral (3 patients) STEMI were treated conservatively.

The overall ejection fraction in the study was 50.6±14.1 with no significant difference between the two groups. Significant aortic stenosis and left ventricular thrombus were detected in 9.4% and 4.1% of the study patients, respectively. The conservative group had a significantly higher prevalence of mitral regurgitation (57.5%) compared to the invasive group (42.8%) (*P* = 0.045) (Table 3).

Interestingly, the majority of patients were frail (53.8%) and prefrail (46.2%) according to the Fried Frailty Scale. There was a trend of increased frailty in the conservative group (58.4% vs. 47.6%). Delirium was significantly higher in the conservative group (42.5%) compared to the invasive group (26.2%) (*P* = 0.019). The invasive group had significantly higher GRACE scores (*P* = 0.039), indicating a higher overall risk profile in patients selected for invasive management. Patients with GRACE scores ≥140 were predominantly treated invasively (Table 4).

Regarding the laboratory, the mean GFR in the study was 49.0±22.7. There was a trend of lower creatinine (1.7±1.1 vs. 1.4±0.9, *P* = 0.09) in the invasive group. The invasive group also showed a trend of higher HbA1c (6.1±1.2 vs. 6.5±1.3, *P* = 0.05) and lower total cholesterol values (183.4±50.6 vs. 170.7±42.5, *P* = 0.07) (Table 5).

Table 1. Baseline criteria, comorbidities, and baseline medications for the total, conservative, and invasive patients [data are expressed as mean ± SD or count (percentage)]

	Total (n=197)	Conservative (n=113)	Invasive (n=84)	*P*-value
Age (years)	84.8±3.9	84.8±3.9	84.2±3.6	0.27
Male gender	111 (56.3)	67 (59.3)	44 (52.4)	0.33
BMI (kg/m^2)	29.8±3.5	29.3±3.5	30.5±3.5	**0.03**
Smoker	50 (25.4)	31 (27.4)	19 (22.6)	0.66
Dyslipidemia	169 (85.8)	95 (84.1)	74 (88.1)	0.42
Hypertension	170 (86.3)	97 (85.8)	73 (86.9)	0.83
Diabetes mellitus	101 (51.3)	55 (48.9)	46 (54.8)	0.40
Ischemic heart disease	144 (73.1)	84 (74.3)	60 (71.4)	0.65
History of PCI	60 (30.5)	40 (35.4)	20 (23.8)	0.08
Previous CABG	13 (6.6)	8 (7.1)	5 (6.0)	0.75
Family history for IHD	51 (25.9)	29 (25.7)	22 (26.2)	0.93
Atrial fibrillation	57 (28.9)	35 (31.0)	22 (26.2)	0.56
PVD	60 (30.5)	44 (38.9)	16 (19.0)	**0.003**
CVD	51 (25.9)	30 (26.5)	21 (25.0)	0.81
CKD	79 (40.1)	45 (39.8)	34 (40.5)	0.93
COPD	52 (26.4)	33 (29.2)	19 (22.6)	0.30
Liver disease	9 (4.6)	4 (3.5)	5 (6.0)	0.42
Medications				
Aspirin	127 (64.5)	77 (68.1)	50 (59.5)	0.27
Clopidogrel	145 (73.6)	83 (73.4)	62 (73.8)	1.00
Ticagrelor	9 (4.6)	4 (3.5)	5 (6.0)	0.50
Beta blocker	63 (32.0)	33 (29.2)	30 (35.7)	0.42
ACEI	38 (19.3)	23 (20.3)	15 (17.8)	0.80
ARB	37 (18.8)	18 (15.9)	19 (22.6)	0.32
ARNI	39 (19.8)	26 (23.0)	13 (15.4)	0.26
Diuretics	56 (28.4)	33 (29.2)	23 (27.3)	0.90
CCB	49 (24.9)	25 (22.1)	24 (28.5)	0.39
PPI	43 (21.8)	22 (19.4)	21 (25.0)	0.45
Insulin	43 (21.8)	25 (22.1)	18 (21.4)	0.99
Oral hypoglycemic drugs	62 (31.5)	31 (27.4)	31 (36.9)	0.21
Vasopressors	29 (14.7)	14 (12.4)	15 (17.8)	0.39
IABP	4 (2.0)	1 (0.8%)	3 (3.5%)	0.42

SD: Standard deviation, CABG: Coronary artery bypass grafting, ACEI: Angiotensin-converting enzyme inhibitor, ARB: Angiotensin receptor blocker, ARNI: Angiotensin receptor-neprilysin inhibitor, BMI: Body mass index, CCB: Calcium channel blocker, CKD: Chronic kidney disease, COPD: Chronic obstructive pulmonary disease, CVD: Cerebrovascular disease, IABP: Intra-aortic balloon counterpulsation, IHD: Ischemic heart disease, PCI: Percutaneous coronary intervention, PPI: Proton pump inhibitor, PVD: Peripheral vascular disease

Based on the data from the invasive strategy group (n=84), coronary angiography revealed significant and severe coronary artery disease. The vast majority of patients (98%) had at least one diseased vessel, with multi-vessel disease being common; 31.0% had one-vessel disease, 28.6% had two-vessel disease, and 38.1% had three or more diseased vessels. The lesions were complex, predominantly type B (42.9%) or type C (39.3%), with a high prevalence of moderate or greater calcification (65.5%). The LM artery and its equivalent were frequently affected (26.2% and 20.2%, respectively). Following angiography, the invasive group patients underwent an intervention as follows: 67.9% received stents (most requiring stents longer than 15 mm and larger than 2.5 mm), and 11.9% were referred for CABG. The invasive procedures were associated with a 16.7% rate of access site complications and a 15.5% incidence of contrast-induced nephropathy.

Table 2. Clinical presentation and ECG findings for the total, conservative, and invasive patients [data are expressed as mean ± SD or count (percentage)]

	Total (n=197)	Conservative (n=113)	Invasive (n=84)	*P*-value
NSTE-ACS	174 (88.3)	107 (94.7)	67 (79.8)	**0.004**
STEMI	23 (11.7)	6 (5.3)	17 (20.2)	
Chest pain	45 (22.8)	24 (21.2)	21 (25.0)	0.65
Chest pain duration	10.0±16.1	11.2±18.6	8.4±12.0	0.23
Dyspnea	74 (37.6)	44 (38.9)	30 (35.7)	0.75
Diaphoresis	53 (26.9)	29 (25.6)	24 (28.6)	0.77
Nausea/vomiting	45 (22.8)	27 (23.9)	18 (21.4)	0.81
Syncope	17 (8.6)	9 (8.0)	8 (9.5)	0.90
OHCA	2 (1.0)	0 (0.0)	2 (2.3)	0.35
In-hospital resuscitation	9 (4.6)	3 (2.6)	6 (7.1)	0.25
SBP (mmHg)	120.6±25.3	123.3±25.0	117.0±25.4	0.08
DBP (mmHg)	66.2±15.2	68.0±16.4	63.7±13.0	0.049
Heart rate (bpm)	82.3±19.6	82.8±17.4	81.7±22.4	0.72
Killip class	1.9±0.9	1.8±0.8	2.0±0.9	0.19
ECG				
Pathological Q-wave	94 (47.7)	48 (42.4)	46 (54.7)	**0.03**
Anterior STEMI	14 (7.1)	0 (0.0)	14 (16.7)	**<0.001**
Lateral STEMI	4 (2.0)	3 (2.6)	1 (1.2)	0.83
Inferior STEMI	4 (2.0)	3 (2.6)	**1 (1.2)**	0.83
LBBB	1 (0.5)	0 (0%)	1 (1.2)	0.88

SD: Standard deviation, DBP: Diastolic blood pressure, LBBB: Left bundle branch block, NSTE-ACS: Non-ST segment elevation-acute coronary syndrome, ECG: Electrocardiographic, OHCA: Out of hospital cardiac arrest, SBP: Systolic blood pressure, STEMI: ST-segment elevation myocardial infarction

Table 3. Echocardiographic data for the total, conservative, and invasive patients [data are expressed as mean ± SD or count (percentage)]

	Total (n=197)	Conservative (n=113)	Invasive (n=84)	*P*-value
Aortic root diameter (cm)	3.3±1.6	3.2±0.7	3.4±2.2	0.45
Left atrial diameter (cm)	4.6±2.8	4.7±1.2	4.6±3.9	0.97
LVED (cm)	5.1±0.7	5.2±0.7	5.1±0.8	0.47
LVES (cm)	3.6±0.8	3.6±0.8	3.5±0.9	0.51
Ejection fraction (%)	50.6±14.1	50.0±14.4	51.3±13.6	0.53
WMSI	1.4±0.5	1.5±0.5	1.4±0.5	0.38
Mitral incompetence	101 (51.3)	65 (57.5)	36 (42.8)	**0.045**
Significant aortic stenosis	18 (9.4)	9 (7.9)	9 (10.7)	0.62
LV thrombus	8 (4.1)	5 (4.4)	3 (3.5)	0.99

SD: Standard deviation, LV: Left ventricle, LVED: Left ventricular end-diastole, LVES: Left ventricular end-systole, WMSI: Wall motion systolic index

No significant difference was found between the two groups regarding discharge medications. Aspirin was the most commonly used antiplatelet (77.2%), followed by clopidogrel (64%), with ticagrelor prescribed in only 4.6%. 31.5% of the patients received direct oral anticoagulants on discharge, with the main indications being atrial fibrillation and LV thrombus. 85.3% of the patients received statins (Table 6).

The in-hospital and 30-day mortality were 7.1% and 13.2%, respectively. The in-hospital and 30-day mortality were numerically higher in the conservative group (7.9% vs. 5.9%; OR: 0.73, 95% CI 0.24-2.27; *P* = 0.79, and 15.9% vs. 9.6%; OR: 0.56, 95% CI 0.23-1.35; *P* = 0.27, respectively). More than 10% of the invasive patients had TVR. Reinfarction was less frequent in the invasive group (10.6% vs. 3.5%), while bleeding (BARC ≥3) was more frequent in the invasive group (9.7% vs. 13.1%), though

Table 4. Geriatric assessment and GRACE risk score for the total, conservative, and invasive patients [data are expressed as mean ± SD or count (percentage)]

	Total (n=197)	Conservative (n=113)	Invasive (n=84)	*P*-value
Frailty				
Pre-frail	91 (46.2)	47 (41.6)	44 (52.4)	0.13
Frail	106 (53.8)	66 (58.4)	40 (47.6)	
Delirium				
Delirium by CAM	70 (35.5)	48 (42.5)	22 (26.2)	**0.02**
Geriatric Depression Scale				
Suggestive	63 (32)	34 (30.1)	29 (34.5)	0.78
Indicative	60 (30.5)	36 (31.9)	24 (28.6)	
GRACE risk score				
Low	91 (46.2)	60 (53.1)	31 (36.9)	**0.04**
Moderate	83 (42.1)	44 (38.9)	39 (46.4)	
High	23 (11.7)	9 (8.0)	14 (16.7)	

SD: Standard deviation, CAM: Confusion assessment method

Table 5. Laboratory for the total, conservative, and invasive patients [data are expressed as mean ± SD or count (percentage)]

	Total (n=197)	Conservative (n= 113)	Invasive (n=84)	*P*-value
GFR (mL/min)	49.0±22.7	47.8±23.9	50.5±21.0	0.41
Creatinine (mg/dL)	1.6±1.0	1.7±1.1	1.4±0.9	0.09
CK-MB (U/L)	48.1±56.6	49.1±61.8	46.8±49.2	0.79
High-sensitive troponin (pg/mL)	402.5±696.9	424.7±840.3	373.5±439.1	0.62
Hemoglobin (gram/dL)	11.8±1.9	11.6±2.0	11.9±1.6	0.33
Total leucocytic count (x10^3/cmm)	10.5±5.7	10.8±5.8	10.2±5.6	0.53
Platelets count (x10^3/cmm)	266.8±35.3	243.5±21.7	297.3±25.0	0.25
ALT (U/L)	47.9±181.6	59.4±238.4	32.6±27.2	0.31
AST (U/L)	43.0±130.2	50.3±170.1	33.3±28.2	0.37
Albumin (g/dL)	3.6±0.5	3.5±0.5	3.6±0.4	0.08
Hemoglobin A1c (%)	6.3±1.2	6.1±1.2	6.5±1.3	0.05
Cholesterol (mg/dL)	178.0±47.6	183.4±50.6	170.7±42.5	0.07
Low-density lipoprotein (mg/dL)	105.2±39.9	108.9±42.6	100.2±35.6	0.13
High-density lipoprotein (mg/dL)	43.3±10.2	43.7±10.2	42.9±10.2	0.59
Triglycerides (mg/dL)	141.8±66.0	145.6±67.3	136.7±64.3	0.35

SD: Standard deviation, GFR: Glomerular filtration rate, CK-MB: Creatine kinase-MB, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase

neither difference was statistically significant (Supplementary Table 1 and Figure 1). On the other hand, the invasive group exhibited a higher incidence of hospital stays, which tended to be longer in the conservative group (6.4±3.9 vs. 5.4±4.0, $P = 0.08$).

Multiple logistic regression analysis showed that SBP <100 mmHg, Killip II, GFR, low EF, and HF were positively associated with mortality. STEMI diagnosis was associated with a reduction in the odds of mortality (Supplementary Table 2 and Figure 2).

DISCUSSION

ACS in octogenarians presents a major clinical challenge due to the high prevalence of comorbidities, frailty, and neuropsychiatric disorders, as well as the risks associated with both invasive and conservative treatments.[3] This prospective observational study of 197 octogenarians with ACS provides real-world data on clinical characteristics, treatment pathways, and short-term outcomes in this vulnerable population.

Consistent with contemporary literature, our cohort demonstrated a high burden of NSTE-ACS, accounting for 88.3%

Table 6. Discharge medications for the total, conservative, and invasive patients [data are expressed as mean ± SD or count (percentage)]

	Total (n=197)	Conservative (n=113)	Invasive (n=84)	*P*-value
Aspirin	152 (77.2)	84 (74.3)	68 (81.0)	0.36
Clopidogrel	126 (64.0)	68 (60.2)	58 (69.1)	0.26
Ticagrelor	9 (4.6)	4 (3.5)	5 (6.0)	0.50
DOAC	62 (31.5)	38 (33.6)	24 (28.6)	0.55
Statin	168 (85.3)	93 (82.3)	75 (89.3)	0.24
Beta blocker	125 (63.5)	73 (64.6)	52 (61.9)	0.81
RAAS blocker	75 (38.1)	39 (34.5)	36 (42.9)	0.30
Nitrates	61 (31.0)	34 (30.1)	27 (32.1)	0.88
CCB	30 (15.2)	16 (14.2)	14 (16.7)	0.78

SD: Standard deviation, CCB: Calcium channel blocker, DOAC: Direct oral anticoagulant, RAAS: Renin-angiotensin-aldosterone system

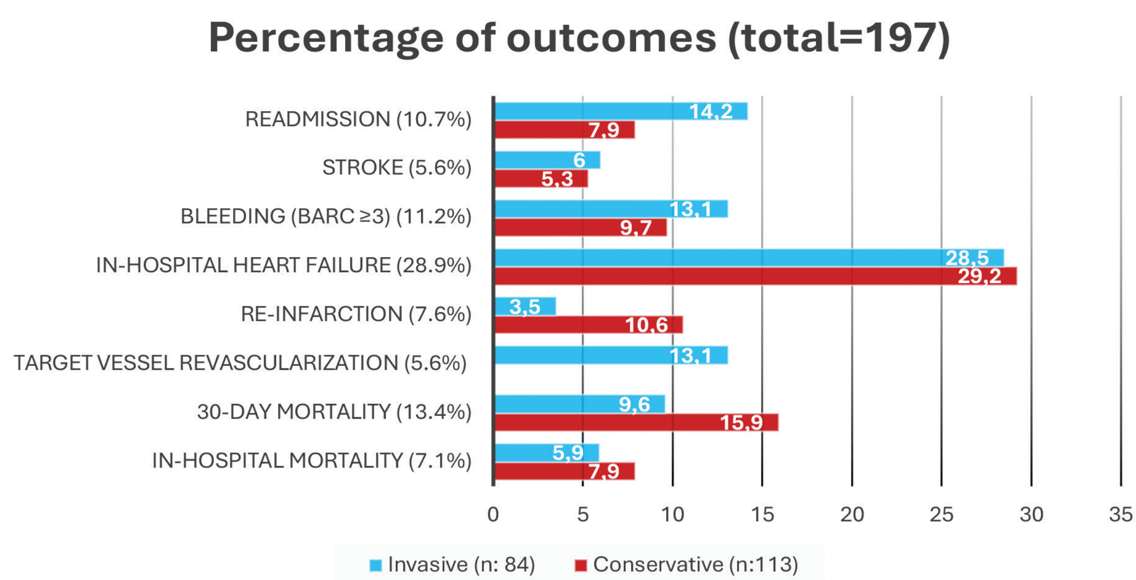

Figure 1. The outcome data for total patients (presented on the vertical axis) with comparison between the conservative and invasive arms regarding the different outcome data

BARC: Bleeding Academic Research Consortium

of all ACS presentations, a finding that was significantly more frequent in the conservative group (94.7% vs. 79.8%, $P = 0.004$). This observation is explained by the complex chronic coronary artery disease in the elderly progressing into ACS rather than acute plaque rupture, leading to STMEI that is commonly encountered in the younger patients.[31,32]

The decision to pursue an invasive strategy was not random but reflected a careful selection process guided by clinical judgment and risk stratification. Patients in the invasive group, despite a higher proportion of high-risk features (such as higher GRACE scores and a greater incidence of anterior STEMI), demonstrated characteristics indicative of better overall functional reserve. Compared to the conservative group, the invasive group had significantly higher BMI (30.5±3.5 vs. 29.3±3.5, $P = 0.03$), lower prevalence of PVD (19.0% vs. 38.9%, $P = 0.003$), and lower rates of delirium (26.2% vs. 42.5%, $P = 0.02$), with a trend toward lower frailty rates (47.6% vs. 58.4%, $P = 0.13$). Conservative management appears to be favored in octogenarian patients with a higher burden of comorbidities, including low BMI, PVD, and cognitive impairment, despite the potential for favorable long-term outcomes with an invasive approach. Comprehensive geriatric assessment is therefore critical in decision-making for elderly patients with ACS.[3,33,34]

The primary outcome of in-hospital mortality was numerically lower in the invasive group (5.9% vs. 7.9%, $P = 0.79$). Similarly, the 30-day mortality was lower in the invasive group (9.6% vs. 15.9%), but this difference was not statistically significant ($P = 0.27$). This lack of a significant short-term mortality

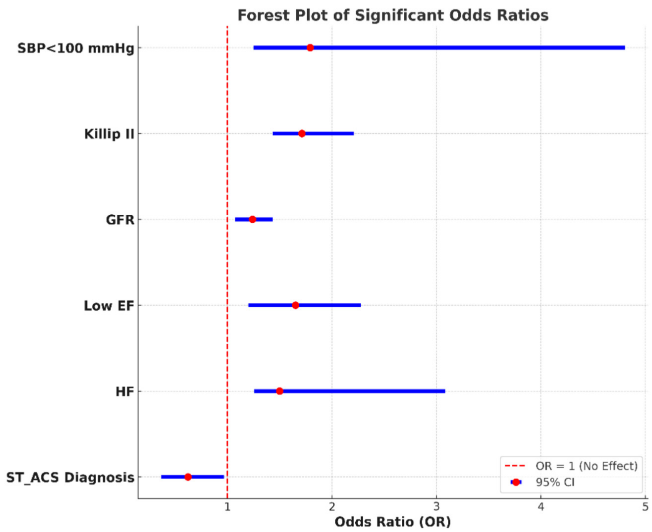

Figure 2. Forest plot for the significant predictors of mortality. Bars represent the ORs for each variable. Red lines indicate the 95% confidence intervals (CIs)

EF: Ejection fraction, GFR: Glomerular filtration rate, HF: Heart failure, SBP: Systolic blood pressure, ST-ACS: ST-segment elevation acute coronary syndrome

benefit aligns with the primary outcome of the SENIOR-RITA trial, the largest RCT to date in this population, which found no difference in the composite endpoints of cardiovascular death and myocardial infarction between routine invasive and conservative strategies.[35,36]

This study provides evidence supporting the benefit of the invasive strategy in reducing future ischemic events. The invasive group had a significantly higher rate of TVR (13.1% vs. 0.0%, $P < 0.001$), as expected since the conservative group did not undergo the initial procedure. Additionally, the invasive group demonstrated a numerical trend toward a lower reinfarction rate (3.5% vs. 10.6%, $P = 0.12$). These findings are consistent with major RCTs and meta-analyses. Our findings, particularly the numerical but non-significant reduction in mortality with an invasive strategy, resonate with observations from key RCTs in similar elderly populations. The After Eight study[37] was an open-label RCT involving patients aged 80 years or older with NSTE-ACS, which showed that the invasive strategy significantly reduced a composite endpoint of myocardial infarction, urgent revascularization, stroke, and death. However, like our study, the After Eight trial did not find a statistically significant difference in all-cause mortality between the invasive and conservative groups. This suggests that while an invasive approach may improve overall cardiovascular outcomes, the mortality benefit in these vulnerable patients remains challenging, even in a randomized setting. A meta-analysis by Kotanidis et al.[9] reported that the invasive strategy was associated with a significant reduction in the one-year risk of recurrent myocardial infarction (hazard ratio 0.62, 95% CI 0.44-0.87) and urgent revascularization (hazard ratio 0.41, 95% CI 0.18-0.95). These data support the benefit of an invasive approach in reducing future ischemic events and the need for repeat procedures, even among octogenarians.

A critical finding is the absence of a significant difference in major bleeding complications (BARC bleeding >3) between the invasive (13.1%) and conservative (9.7%) groups ($P = 0.61$). This finding can suggest that the increased bleeding risk imposed by the invasive approach can be decreased by proper patient selection, procedural planning, and adjustment of antithrombotic drugs. This is further supported by the non-significant difference in the use of high-risk medications such as glycoprotein IIb/IIIa antagonists and the similar rates of discharge medications between the two groups. The comparable rates of in-hospital HF and stroke also indicate that the invasive strategy did not introduce a disproportionate risk of these major complications.

The length of hospital stay was numerically shorter in the invasive group (5.4±4.0 days) than in the conservative group (6.4±3.9 days). This trend toward shorter hospital stays with the invasive strategy suggests that it may lead to more rapid stabilization and discharge than conservative management.

Our study highlights the profound influence of geriatric syndromes on treatment selection and outcomes. As mentioned earlier, conservative management was associated with higher delirium and frailty rates. Frailty is increasingly recognized as a powerful, independent predictor of adverse outcomes, including mortality, functional decline, and bleeding, often surpassing the predictive power of chronological age or traditional risk scores.[38,39] This association between cognitive disorder and conservative approach denotes selection bias against the intervention approach in such patients, which may lead to increased long-term adverse cardiac events. A retrospective analysis by Roman et al.[40] compared revascularization rates between frail and non-frail patients. The study showed that revascularization is associated with a reduction in cardiovascular mortality in frail patients, suggesting that they could benefit from an invasive approach.[40] On the other hand, the MOSCA-FRAIL study[41] included frail elderly patients (≥70 years) with NSTEMI. This trial found no significant difference in the primary composite outcome of death or new myocardial infarction at one year between the two groups. The MOSCA-FRAIL study highlighted the impact of frailty on outcomes and showed that comorbidities, such as frailty, can dilute the benefits of revascularization. Our observational findings, showing a trend towards lower mortality in the invasive group but without statistical significance, are consistent with the nuanced and often challenging results observed in this trial.

We suggest that a comprehensive geriatric assessment guide the individualized decision-making in such high-risk patients.

The counterintuitive finding that STEMI diagnosis was associated with a reduction in the odds of mortality in our regression analysis could be explained by the increased use of invasive management in octogenarian STEMI patients. In our study, more STEMI patients (73.9%) received invasive management compared to NSTE-ACS patients (38.5%). The early aggressive invasive management in STEMI patients may mitigate the high risk imposed by STEMI presentation compared to NSTE-ACS patients, who had more conservative management.

Study Limitations

This study is underpowered to detect statistically significant differences in less frequent outcomes, such as mortality. This limitation is due to the observational design and the challenges of recruiting a large cohort of octogenarian ACS patients. The absence of an a priori sample size or power calculation represents a significant methodological limitation. Consequently, our study may be susceptible to type I or II errors. This study should therefore be viewed as primarily descriptive and hypothesis-generating, providing real-world insights to inform future, adequately powered research. Our 30-day follow-up period provided insights into short-term outcomes, but limited the assessment of long-term morbidity and mortality, which are crucial considerations in this elderly population. Furthermore, although we assessed frailty and delirium, using a single frailty scale (Fried Frailty Scale) may not capture the full spectrum of functional decline. Despite using logistic regression to adjust for confounders, the authors acknowledge that a more robust method, such as propensity score matching, could mitigate baseline imbalances in future observational studies. The observational design of this study carried a potential limitation in the form of unmeasured confounders that influenced the treatment decision, such as subjective assessments of frailty and overall prognosis (e.g., the "eyeball assessment") that may not have been fully captured by the objective geriatric assessment conducted in this study. We described that the selection bias was evident in this descriptive study due to multiple comorbidities of the octogenarians. Finally, as a multicenter trial, multicenter heterogeneity may introduce variability in the management of such patients. This growing patient population requires future studies with large sample sizes, longer follow-up, and formal geriatric assessment to better inform optimal management strategies for these high-risk patients.

CONCLUSION

This study describes the characteristics of octogenarian patients presenting with ACS, a high-risk population with increased ischemic and bleeding risks. Several key findings emerged. First, selection bias was evident, as the choice between invasive and conservative management was strongly influenced by geriatric factors beyond traditional risk scores. Patients managed conservatively had a significantly higher prevalence of geriatric syndromes, particularly delirium, and a greater burden of comorbidities such as PVD. In contrast, the invasively managed group, despite higher GRACE scores, demonstrated better functional reserve indicators, such as higher BMI. These findings indicate that clinical decision-making in this population is appropriately guided by comprehensive geriatric assessment. Second, the invasive strategy was associated with a trend toward lower reinfarction rates. Randomized trials are required to support the effectiveness of invasive therapy in reducing recurrent ischemic events in this high-risk population. Third, the safety profile of the invasive strategy was acceptable, with no statistically significant increase in short-term adverse outcomes, including in-hospital or 30-day mortality or major bleeding complications.

In summary, current ACS management practices in octogenarians vary and are influenced by individual characteristics and comorbidities. Early invasive strategy shows a numerical trend towards reduced recurrent ischemic events; however, geriatric syndromes such as frailty and delirium remain strong determinants of conservative management. Future research should prioritize the development of standardized, validated geriatric risk assessment tools.

Ethics

Ethics Committee Approval: The study was approved by the Local Research Ethics Committee, Cairo University Faculty of Medicine (approval no: MD-371-2021, date: 04.10.2022).

Informed Consent: Patients or their representatives provided written consent to the study.

Data Availability

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Footnotes

Authorship Contributions

Surgical and Medical Practices: W.A., Concept: M.A., Design: E.L., M.A., Data Collection or Processing: H.N., Analysis or Interpretation: K.M., E.L., W.A., Literature Search: H.N., Writing: K.M., H.N.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

Supplementary Tables 1-2. https://d2v96fxpocvxx.cloudfront.net/cf9d60d6-523c-458a-a2e6-78728d3ffbb0/content-images/b7d9ce90-b725-4545-8d09-2a4843782dcb.pdf

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