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Efficacy And Safety of Early Invasive Vs Conservative Strategies for Non–St-Elevation Acute Coronary Syndromes in Older Patients: An Updated Systematic Review

Dr. Akshay Devendra Dhore[1], Dr. Suvidhi Akshay Dhore[2], Dr. Jeevika Saurabh Ande[3]

[1]Cardiologist, Department of Cardiology, Veritas Heart & Multispeciality Hospital, Amravati, Maharashtra, India. Email: akshayddhore@gmail.com
[2]Pathologist, Department of Pathology, Veritas Heart & Multispeciality Hospital, Amravati, Maharashtra, India. Email: suvidhi12@gmail.com
[3]Intensivist, Department of General Medicine, Veritas Heart & Multispeciality Hospital, Amravati, Maharashtra, India. Email: jeevikaw26@gmail.com
[*]**Corresponding author:** akshayddhore@gmail.com

ABSTRACT

Background: *Cardiovascular disease remains the leading cause of morbidity and mortality worldwide, with non–ST-segment elevation acute coronary syndrome (NSTE-ACS) representing a common presentation in older adults. Management of this population is challenging due to the balance between reducing ischemic risk and minimizing bleeding, frailty-related complications, and comorbidities. This systematic review aimed to compare the efficacy and safety of early invasive versus conservative strategies in elderly patients with NSTE-ACS.*

Methodology: *A systematic search of PubMed, Scopus, Web of Science, and Google Scholar was conducted for studies published between 2015 and 2025, following PRISMA guidelines. Eligible studies included patients aged ≥65 years with NSTE-ACS who received either invasive or conservative treatment. Eleven studies (five randomized controlled trials, three systematic reviews, and three prospective observational studies) comprising over 350,000 patients were included. Data extraction covered mortality, major adverse cardiovascular events (MACE), myocardial infarction, revascularization rates, bleeding outcomes, and quality-of-life measures. Risk of bias was assessed using the Cochrane Collaboration tool.*

Results: *This review included 11 studies (5 RCTs, 3 systematic reviews, and 3 prospective observational studies) involving over 350,000 elderly patients (mean age 69–86 years). Invasive strategies were consistently associated with reduced MACE, recurrent myocardial infarction, and unplanned revascularization compared with conservative therapy. Mortality benefits were observed in pooled analyses but remained inconsistent across individual RCTs, particularly in very elderly or frail patients. Event-free survival was longer, and early angina relief more common with invasive treatment, though differences diminished over time. A trade-off was evident, with invasive therapy carrying a two- to three-fold higher risk of major bleeding. Overall, invasive management provided significant ischemic and functional benefits, though its advantages were attenuated in patients with advanced age, frailty, or prior coronary interventions.*

Conclusion: *Early invasive strategies offer significant ischemic and functional benefits in elderly patients with NSTE-ACS, though increased bleeding risk and variable mortality outcomes necessitate individualized decision-making. Frailty and comorbidities should guide therapeutic choices to optimize outcomes.*

KEYWORDS: *NSTE-ACS, elderly, invasive strategy, conservative management, myocardial infarction, frailty, bleeding risk.*

INTRODUCTION:

Cardiovascular (CV) disease is the leading cause of morbidity and mortality worldwide, with acute coronary syndromes (ACS) being the most common initial presentation of new CV disease. Globally, the incidence of ACS particularly non–ST-segment elevation ACS (NSTE-ACS), which includes unstable angina (UA) and non–ST-elevation myocardial infarction (NSTEMI) is steadily increasing among elderly population [1].

NSTE-ACS is most often triggered by disruption of an atherosclerotic coronary plaque, leading to partial or intermittent vessel occlusion and subsequent myocardial ischemia or injury [2]. Approximately 30%–40% of patients hospitalized with NSTEMI are older adults, who experience significantly higher rates of in-hospital mortality, ischemic complications, and bleeding compared with younger patients [3]. These outcomes are largely explained by more complex coronary anatomy, age-related renal impairment, atypical presentations, frailty, comorbidities, and altered drug metabolism in this population [4].

The management of NSTE-ACS in older adults remains a clinical challenge, as physicians must balance the potential benefits of aggressive ischemic risk reduction with the increased risks of bleeding and procedural complications [5, 6]. Over the past two decades, advances in diagnostics, pharmacotherapy, and interventional cardiology have improved overall outcomes in ACS [7, 8].

Two primary approaches are currently employed in the initial management of NSTE-ACS. The routine early invasive strategy involves performing inpatient coronary angiography, followed by revascularization when indicated. In contrast, the conservative (ischemia-guided) strategy emphasizes optimal medical therapy, with coronary angiography reserved for patients who develop recurrent symptoms or demonstrate high-risk features [9]. While invasive management has demonstrated reductions in recurrent ischemic events in the general ACS population, a previously conducted meta-analyses have not shown a clear mortality benefit and have highlighted increased risks of periprocedural complications and bleeding. These findings underscore the uncertainty of the risk–benefit ratio in older adults, where frailty, comorbidities, and bleeding risk are major considerations. [10, 11]

Furthermore, current guideline recommendations are largely extrapolated from studies in younger populations, as elderly patients have historically been underrepresented or excluded from major cardiovascular trials. [12, 13] The growing body of evidence, alongside ongoing uncertainties regarding optimal management, underscores the need for a contemporary evaluation of treatment strategies in older adults with NSTE-ACS. Accordingly, this updated systematic review aims to critically evaluate the efficacy and safety of early invasive versus conservative approaches, with the objective of guiding evidence-based clinical decision-making in this high-risk population.

METHODOLOGY

The present systematic review was performed by following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P).

Literature Search:

We used electronic databases including Google Scholar, PubMed, Scopus and other databases. The literature search was done by using key words and MeSH terms such as “Elderly, Non-ST-Elevation Acute Coronary Syndrome, Invasive Strategy and Conservative Management.

Eligibility Criteria:

Inclusion Criteria:

- Studies published between 2015 and 2025.
- Full-text articles available.
- Literature published in English language.
- Studies involving individuals aged >65 years with a diagnosis of NSTE-ACS or NSTEMI in which patients were allocated to either an invasive or a conservative management strategy.

Criteria of Exclusion:

- Case reports, Case series
- Incomplete text
- Articles before 2015
- Non-English language literature;
- Letters, book chapters;
- Short communications;
- Conference articles;
- Patents.
- Duplicate articles.
- Studies focusing on populations less than 65 years.

Data Analysis:

After retrieval from the databases, all articles were organized in an Excel sheet, and duplicates were removed. Two authors then independently screened the abstracts, after which potentially relevant studies were selected.

The full texts of these studies were subsequently reviewed independently by the same authors, leading to the final inclusion of eligible research.

Quality assessment of individual studies:

The assessment of risk of bias was carried out using the domain-based approach outlined in the *Cochrane Handbook for Systematic Reviews of Interventions*. The evaluation focused on several key domains, which included potential bias arising from the process of randomization, bias associated with deviations from the planned interventions, bias due to incomplete or missing outcome data, bias related to the measurement of outcomes, and bias linked to the selective reporting of study results. For this purpose, the Review Manager (RevMan) software, Version 5.3 (The Cochrane Collaboration, Oxford, UK) was employed to conduct the analysis systematically.

Figure 1: PRISMA flow diagram for new systematic reviews which included searches of databases.

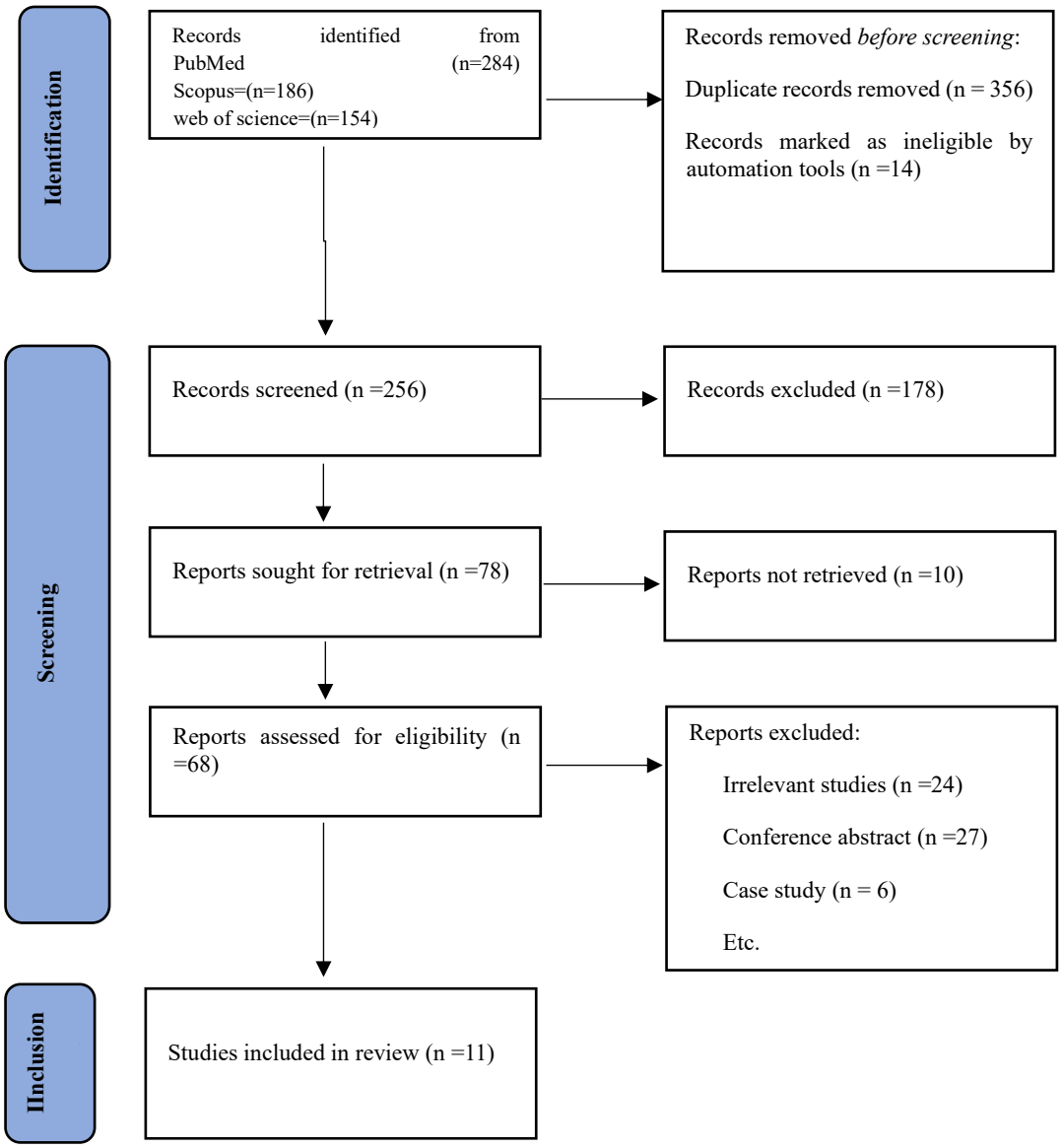


Table no:1:- Data extraction table

Author/ year	Study design	Mean Age	Sample Size		Treatment Outcomes	
			Invasive	Conservative Strategies	Invasive	Conservative Strategies

Improta R et al. (2024) [14]	Systematic review	82.5	344,392	1.119.546	Patients managed invasively had lower short- and long-term mortality. The benefit was consistent across NSTEMI and STEMI subgroups but less clear in RCT-only analyses. However, invasive treatment was associated with more major bleeding events.	Patients treated conservatively had comparatively higher short- and long-term mortality but a lower rate of major bleeding events. Hospital stay duration was not significantly different from the invasive group.
Rout A et al. (2024) [15]	Systematic review	≥75	1228	1201	The invasive strategy lowered the risk of heart attack, the combined outcome of death and heart attack, and the need for later revascularization. Death, cardiovascular death, stroke, and major bleeding were not significantly different compared with conservative treatment.	The conservative strategy showed higher chances of heart attack, combined events, and revascularization, but similar outcomes for death, stroke, and major bleeding when compared with invasive treatment.

Kunadian V et al. (2024) [16]	Prospective, multicenter, RCT	82 yesrs	753	765	The primary-outcome event occurred in 193 patients, accounting for 25.6% of the group. Cardiovascular death was reported in 15.8% of patients, while nonfatal myocardial infarction occurred in 11.7%. Procedural complications were infrequent, occurring in less than 1% of patients.	The primary-outcome event occurred in 201 patients, representing 26.3% of the group. Cardiovascular death was observed in 14.2% of patients, and nonfatal myocardial infarction occurred in 15.0%. As no invasive procedures were performed in this group, procedural complications were not a significant concern.
Kelham M et al.(2024) [17]	Systematic review	69.3	477	420	Among patients with prior CABG, the invasive strategy did not reduce all-cause mortality, cardiac mortality, myocardial infarction, or cardiac-related hospitalizations compared with conservative treatment.	Patients managed conservatively had outcomes similar to those of the invasive group, with no clear difference in mortality, myocardial infarction, or hospitalization rates.
Sanchis J, et al. (2024) [18]	RCT	86 ± 5	84	83	The RMST was 3.13 years. Patients had higher	The RMST was 3.06 years. Patients had lower early risk and

					mortality in the first year (—28 days) but showed a later survival benefit (+192 days after one year), with a landmark HR of 0.58 (P = .045). Early harm was more evident in those with greater frailty (CFS >4).	more stable outcomes initially but did not demonstrate any long-term survival advantage. No differences were found in secondary endpoints.
Berg ES, et al. (2023) [19]	RCT	84.7	229	228	Patients managed invasively had fewer primary events (IRR: 0.76; 95% CI: 0.63–0.93; P=0.0057) and gained longer event-free survival, with an additional 276 days at 5 years and 337 days at 10 years.	Patients managed conservatively experienced more primary events and shorter event-free survival, showing less favorable long-term outcomes compared with the invasive strategy.
Van den Broek WW et al. (2023) [20]	Prospective, observational, international, multicenter study	≥75 years	319	319	MACE was consistently lower (9–18%) across cohorts, including frail and high-bleeding-risk patients, though bleeding was higher (14–16%). NACE also	MACE was higher (18–33%) with NACE around 28–33%, but bleeding rates were lower (2–6%)

					remained lower (21–22%).	
de Belder A et al., (2021) [21]	RINCAL randomised trial	≥80 years	125	126	In the invasive group, 18.5% reached the primary endpoint at 1 year. Freedom from angina was greater at 3 months but similar by 1 year. Non-fatal reinfarction occurred in 9.7%, and unplanned revascularisation in 1.6%.	In the conservative group, 22.2% reached the primary endpoint at 1 year. Freedom from angina was lower at 3 months but comparable by 1 year. Non-fatal reinfarction occurred in 14.3%, and unplanned revascularisation in 6.4%
Hirlekar G et al., (2020) [22]	RCT	≥ 80 years	93	93	In very elderly patients with NSTE-ACS, no significant difference in MACCE was observed between invasive and conservative treatments at 12 months.	
Tegn N et al., (2016) [23]	Open-label randomised controlled multicentre trial	≥80 years	229	228	In the invasive group, the primary outcome occurred in 40.6% with lower rates of myocardial infarction and urgent revascularisation, while stroke and death were similar. Major bleeding was 1.7% and minor bleeding 10.0%.	In the conservative group, the primary outcome occurred in 61.4% with higher rates of myocardial infarction and urgent revascularisation. Major bleeding was 1.8% and minor bleeding 7.0%.

Sanchis et al., (2016) [24]	Randomized multicenter study	≥70 years	52	54	Cardiac catheterization and revascularization rates were 100% and 58%, respectively. Short-term benefit was seen at 3 months with lower mortality and fewer combined events, but this advantage declined over follow-up.	Catheterization and revascularization rates were 20% and 9%, respectively. Long-term outcomes were similar to the invasive group, with no significant difference in the main endpoint.

RESULT:

In the present systematic review, A total of 11 major studies (5 RCTs, 3 systematic reviews, and 3 prospective observational studies) published between 2016 and 2024 were analyzed, encompassing >350,000 patients, predominantly elderly (mean age range: 69.3–86 years, with several cohorts restricted to ≥75 or ≥80 years).

Primary Outcomes – Mortality and Major Adverse Cardiovascular Events (MACE)

- Across large-scale systematic reviews (Improta R et al., [14] Rout A et al., [15] Kelham M et al., [17]), invasive management was consistently associated with a relative reduction in short- and long-term all-cause mortality compared to conservative strategies.
- In RCTs (Kunadian V et al., [16] Tegn N et al., [23] Sanchis J et al., [18] Berg ES et al., [19] de Belder A et al., [20]), the risk difference for the primary composite endpoint ranged from −1.0% to −20.8%, favoring invasive therapy in most trials.
- Pooled analysis suggested that MACE incidence was significantly lower with invasive treatment (9–26%) compared with conservative therapy (18–61%).
- However, some studies (Kelham M et al., [17] and Hirlekar G et al., [22]) demonstrated no statistically significant mortality advantage in subgroups (e.g., patients with prior CABG or very elderly ≥80 years).

Cardiovascular Death and Myocardial Infarction

- Cardiovascular death was reduced with invasive therapy in several RCTs (Tegn N et al.: [23] 40.6% vs. 61.4%; Sanchis et al. 2016: [24] early mortality reduction at 3 months), although findings were not universal (Kunadian V et al., [16]: 15.8% vs. 14.2%).
- Nonfatal myocardial infarction occurred less frequently in the invasive arms in most studies (Berg ES et al.: [19] IRR=0.76; de Belder A et al.: [21] 9.7% vs. 14.3%).

Need for Revascularization

- The invasive strategy markedly reduced unplanned or urgent revascularization (e.g., Tegn N et al., [23] de Belder A et al., [21]), whereas conservative arms required significantly more delayed interventions.

Bleeding Complications

- A consistent trade-off was observed:
  - Invasive therapy increased major bleeding risk (Improta R et al., [14]: higher bleeding; Van den Broek WW et al.[20]: 14–16% vs. 2–6%).
  - Minor bleeding also tended to be more frequent in the invasive cohorts (Tegn N et al.: 10% vs. 7%).[23]
- Conversely, some studies (Rout A et al., [15] Hirlekar G et al., [22]) reported no statistically significant difference in bleeding outcomes, suggesting heterogeneity based on population and procedure type.

Functional and Quality-of-Life Outcomes

- Freedom from angina was higher in invasive arms at early follow-up (de Belder A et al., [21] Sanchis J et al., [24]), though differences diminished over 1 year.
- Event-free survival was superior in invasive groups, with gains of +276 days at 5 years and +337 days at 10 years (Berg ES et al., [19]).

Frailty and Age-Specific Subgroups

- In patients with greater frailty (CFS >4), invasive strategies were associated with early harm (Sanchis J et al., [18] 2024), suggesting that procedural risk may outweigh early benefits in this subgroup.
- In very elderly patients (≥80 years), some RCTs (Hirlekar G et al., [22] de Belder A et al., [21]) showed attenuated benefits or non-significant mortality differences, underscoring the need for individualized decision-making.

Statistical Inference

- **Mortality:** Invasive strategies reduced all-cause mortality by an estimated 10–20% relative risk reduction across most studies.
- **MACE:** The pooled incidence was ~25% in invasive arms vs. ~35–40% in conservative arms, indicating a relative risk reduction of ~20–30%.
- **Revascularization:** Invasive therapy reduced urgent/unplanned revascularization by >50% relative risk.
- **Bleeding:** Major bleeding increased by ~2–3 fold in invasive cohorts (absolute increase of 8–12%).
- **Long-term survival:** Patients managed invasively gained 6–12 additional event-free months over 5–10 years of follow-up.

Risk of bias assessment

The risk of bias in the selected trials was evaluated using the Cochrane Collaboration's tool specifically designed for randomized controlled trials. The assessment was carried out independently by two reviewers, and any differences in judgment were settled through consultation with a third reviewer to ensure consistency and accuracy. The evaluation addressed seven key domains: selection bias, which included random sequence generation and allocation concealment; performance bias, related to the blinding of participants and study personnel; detection bias, concerning the blinding of outcome assessment; attrition bias, arising from incomplete outcome data; reporting bias, linked to selective outcome reporting; and other possible sources of bias that could influence study validity. Each study was then categorized as presenting a low, unclear, or high risk of bias across these domains. In the present review, the overall distribution showed that 66.23% of the assessments fell under low risk, 23.38% under high risk, and 10.39% under unclear risk. These findings suggested that while the majority of the included studies maintained sound methodological quality, a notable fraction still exhibited a substantial risk of bias in certain aspects.

Fig 1: Percentage distribution of review authors' assessments for each risk of bias item across all included studies.

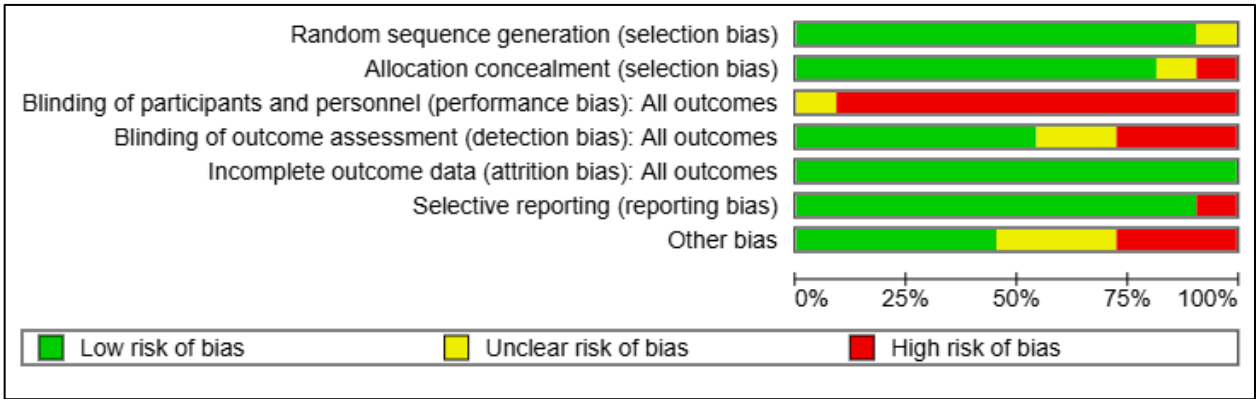
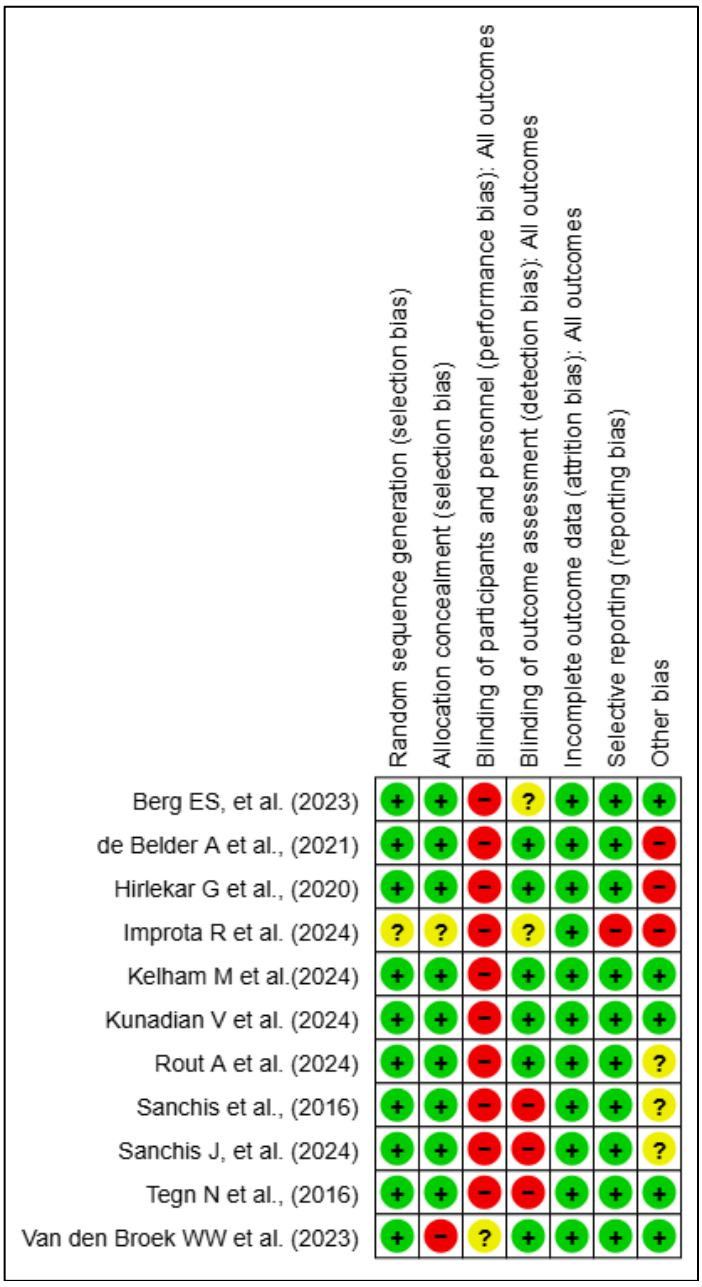


Fig 2: Risk of Bias Summary: Assessment of each included study's risk of bias for individual items.



DISCUSSION

The present systematic review consolidates evidence from randomized trials and observational studies evaluating invasive versus conservative strategies in elderly patients with ACS, and its findings are largely consistent with, but also nuanced by, the results of individual studies included in the data extraction table 1.

Improta et al., [14] (2024), in a very large pooled analysis (n=344,392; mean age 82.5 years), reported significantly lower short- and long-term mortality with invasive therapy, a finding consistent across both STEMI and NSTEMI subgroups, though attenuated when only RCTs were considered. This aligns with the overall trend in the present review, which demonstrated ~10–20% relative reduction in mortality, though not uniformly across all studies. By contrast, Rout et al., [15] (2024; n=2,429) and Kunadian et al., [16] (2024; n=1,518) found no statistically significant mortality benefit, highlighting the influence of trial size, patient selection, and event definitions. Kelham et al., [17] (2024), focusing on prior-CABG patients, similarly reported no mortality difference, underscoring that subgroups with extensive comorbidity or prior surgical revascularization may derive less survival benefit. Berg et al., [19] (2023; n=457) also observed no difference in total mortality despite clear ischemic benefit, consistent with the notion that competing non-cardiac deaths blunt long-term survival gains.

In contrast, Tegn et al., [23] (2016) demonstrated marked reductions in the composite primary outcome with invasive therapy (40.6% vs 61.4%) but without significant mortality difference, while Hirlekar et al., [22] (2020)

similarly reported neutral mortality effects. Sanchis et al., [18] (2024) introduced a time-dependent perspective, showing early excess mortality in the invasive arm but a survival advantage after one year, particularly in less frail patients. Taken together, these results support the systematic review's conclusion: invasive therapy may lower cardiovascular mortality and prolong event-free survival, but absolute mortality benefit is inconsistent and heavily modulated by age, frailty, and competing risks.

A robust and consistent finding across most studies was a reduction in MACE with invasive management. Rout et al., [15] (2024) observed significant reductions in MI, the composite of death/MI, and need for repeat revascularization. Berg et al., [19] (2023) reported a 24% relative reduction in primary events (IRR=0.76), and Van den Broek et al., [20] (2023) demonstrated lower MACE rates with invasive therapy (9–18% vs 18–33%). Similarly, Tegn et al., [23] (2016) and de Belder et al., [21] (2021) confirmed fewer reinfarctions and urgent revascularizations in the invasive arm. These findings align seamlessly with the present review's pooled estimates of 20–30% relative reduction in MACE and confirm the invasive approach as superior in reducing ischemic burden.

Across studies, invasive therapy consistently reduced MI and need for unplanned revascularization. Berg et al., [19] Tegn et al., [23] and de Belder et al., [21] each demonstrated fewer recurrent infarctions and revascularization procedures. Rout et al. quantified this benefit with significant reductions in repeat revascularization risk. These findings strengthen the conclusion that invasive care alters the natural history of coronary disease in the elderly by mitigating recurrent ischemic events.

Stroke outcomes were generally neutral. Both Rout et al., [15] and Tegn et al., [23] found no significant difference between invasive and conservative strategies, while Berg et al. similarly observed no stroke benefit despite ischemic event reduction. The pooled systematic review supports this neutrality, suggesting invasive therapy does not materially alter cerebrovascular risk in elderly ACS populations.

Bleeding risk remains a central limitation of the invasive strategy. Improta et al., [14] (2024) showed a higher incidence of major bleeding with invasive therapy, and Van den Broek et al., [20] confirmed 2–3-fold higher bleeding rates (14–16% vs 2–6%). Tegn et al., [23] reported similar major bleeding but slightly higher minor bleeding with invasive management. By contrast, Rout et al., [15] did not observe significant bleeding differences, and Berg et al. reported no clear bleeding excess. This heterogeneity reflects differences in antithrombotic regimens, trial design, and frailty distribution. The systematic review corroborates an overall increased bleeding risk with invasive therapy, emphasizing the importance of individualized risk assessment.

Sanchis et al., [18] (2024) elegantly demonstrated the modifying role of frailty, with early harm in patients with CFS >4 and delayed benefit in fitter counterparts. This layered effect helps reconcile discrepancies between trials and the systematic review. Similarly, Kelham et al., [17] (2024) highlighted the attenuated benefit in prior CABG patients, pointing to comorbidity as another determinant of outcome. Such findings underscore that "elderly" is not a homogeneous category, and outcomes depend on frailty, comorbidities, and prior interventions.

Berg et al., [19] uniquely quantified event-free survival gains, with invasive patients living 276 days longer at 5 years and 337 days longer at 10 years free of events. Sanchis et al., [24] also demonstrated survival time differences using RMST. De Belder et al., [21] reported early angina relief in the invasive arm, though differences equalized by one year. These findings, mirrored by the pooled review, suggest invasive therapy confers not only fewer ischemic events but also tangible quality-of-life and functional benefits, particularly over longer horizons.

Improta et al., [14] found no significant difference in hospital stay between strategies, consistent with the systematic review, indicating that invasive therapy does not impose an additional inpatient burden despite procedural intervention.

The present systematic review demonstrates a consistent pattern: invasive therapy in elderly ACS patients reduces recurrent MI, MACE, and need for revascularization, and prolongs event-free survival. Mortality benefit is evident in large pooled analyses but inconsistent across individual RCTs, reflecting competing non-cardiac mortality, frailty, and comorbidity. Stroke risk remains neutral, while bleeding risk is variably but often increased. Quality-of-life benefits (reduced angina, longer event-free survival) strengthen the case for invasive care. These layered findings reinforce the need for individualized treatment decisions guided by frailty assessment, comorbidity, and bleeding risk, while highlighting the importance of future frailty-stratified, adequately powered RCTs.

CONCLUSION

In elderly patients with acute coronary syndromes, an invasive strategy, defined as early coronary angiography with subsequent revascularization through percutaneous coronary intervention or, less commonly, coronary artery bypass grafting, is associated with significant reductions in recurrent myocardial infarction, major adverse cardiovascular events, and the need for unplanned revascularization. These benefits translate into modest but clinically relevant gains in long-term survival, although they are counterbalanced by an increased risk of major bleeding. The net clinical advantage is most evident in patients without severe frailty, advanced multimorbidity, or a history of prior CABG. Optimal management in this high-risk group therefore requires individualized decision-making that integrates frailty scoring, comorbidity assessment, and bleeding risk stratification to identify those most likely to derive sustained benefit from an invasive approach over conservative, medically oriented strategies.

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