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Outcomes of early versus delayed intervention in emergency department patients with non-ST elevation acute coronary syndrome: a systematic review

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ABSTRACT

Background: For non-ST elevation acute coronary syndrome (NSTE ACS), guidelines endorse an invasive strategy, but the optimal timing (immediate, early, or delayed) is debated, especially for emergency department (ED) pathways. We aimed to synthesize studies comparing early versus delayed invasive management in NSTE ACS, focusing on clinically relevant outcomes overall and within risk strata. Method: MEDLINE, PubMed, Embase, Cochrane CENTRAL, Web of Science, and Scopus (inception to 2025); ClinicalTrials.gov, WHO ICTRP; reference lists and forward citation tracking. Dual independent screening, data extraction with a piloted form, and PRISMA-aligned reporting. Risk of bias was assessed with RoB 2 (trials) and ROBINS I (cohorts). Owing to heterogeneity in timing cut-offs, therapies, and endpoints, a structured qualitative synthesis was performed. Results: In trials, routine immediate invasive management did not reduce major clinical events versus delayed approaches in unselected patients. Signals consistently favored earlier angiography among high-risk subgroups, particularly GRACE scores more than 140 and those with heart failure, while an isolated trial showed the benefit of immediate intervention. Observational data aligned with neutral overall effects but associated earlier procedures (within 24 to 48 h) with improved outcomes in higher risk patients. Major bleeding and procedural complications were generally similar between timing strategies. Conclusions: For ED care, a risk tailored approach is supported: immediate invasive management for very high risk features; early (less than 24 h) for high risk patients; and angiography within 24 to 72 h appears safe for stabilized intermediate risk patients.

Keywords: NSTE ACS; early invasive strategy; delayed invasive strategy; coronary angiography; percutaneous coronary intervention; time to treatment; risk stratification; GRACE risk score; emergency department; systematic review.

1. INTRODUCTION

Non-ST-segment elevation acute coronary syndrome (NSTE ACS) represents the majority of acute coronary presentations and carries short and long-term risk

despite advances in antithrombotic and revascularization strategies (Byrne et al., 2023). Guidelines recommend a routine invasive approach for most patients, with the timing of angiography and revascularization stratified by clinical risk: immediate (less than 2 h) for very high risk features (hemodynamic instability, refractory ischemia, malignant arrhythmias), early (less than 24 h) for high risk profiles (elevated troponin, dynamic ST and T changes, GRACE more than 140), and within 72 h for intermediate risk (Byrne et al., 2023; Collet et al., 2021).

The TIMACS trial found no difference between early (less than 24 h) and delayed strategies, although high-risk patients (GRACE score more than 140) benefit from early angiography (Mehta et al., 2009). The cooling off concept, deferring intervention to allow intensive antithrombotic pre-treatment, was not advantageous and increased early events in ISAR COOL (Neumann et al., 2003). ABOARD trial reported no superiority of immediate vs next day angiography (Montalescot et al., 2009). VERDICT showed that early strategy (less than 12 h) did not improve outcomes in all cases, with benefit only in the highest risk strata (Kofoed et al., 2018).

A large SWEDEHEART analysis suggested that within the first 24 to 72 h, earlier angiography had limited population level impact, though some subgroups differ (Eggers et al., 2022). Meta analyses synthesize these heterogeneous data, generally showing reduced recurrent ischemia and shorter length of stay with earlier invasive care, but inconsistent effects on mortality or myocardial infarction except in selected high-risk patients (Kite et al., 2022; Zhang et al., 2019). Our review focuses on emergency department pathways and clinically relevant outcomes across risk strata and time points.

2. REVIEW METHODS

Protocol and reporting

We conducted and report this systematic review in accordance with PRISMA 2020. The review protocol was developed a priori; we did not prospectively register it. Reporting follows PRISMA items on information sources, eligibility, selection, data collection, bias assessment, and synthesis (Page et al., 2021).

Eligibility criteria (PICOS)

Population: Adults evaluated in the emergency department or hospital with non ST elevation acute coronary syndrome (NSTE ACS) (unstable angina, NSTEMI). Intervention (Early strategy): Invasive management (coronary angiography ± PCI, CABG) performed as defined by each study (immediate-less than or equal 6 h, less than or equal 12 h, less than or equal 24 h).

Comparator (Delayed): Invasive management performed later (≥24-72 h, (next working day)) per study protocol.

Outcomes: All cause death, myocardial infarction, stroke, urgent revascularization, composite ischemic endpoints, hospital length of stay, and safety (major bleeding, procedure related complications).

Study designs: Original randomized controlled trials and observational cohorts. Case reports, narrative reviews, editorials, and non-original designs were excluded.

Information sources

We searched electronic databases from inception to August 19, 2025: MEDLINE, PubMed, Embase, Cochrane CENTRAL, Web of Science Core Collection, and Scopus. We also screened ClinicalTrials.gov and WHO ICTRP for ongoing trials, checked reference lists of included articles, and used forward citation tracking to identify additional studies.

Search strategy

Database strategies combined controlled vocabulary and keywords for NSTE ACS and timing of invasive management (NSTE ACS, NSTEMI, unstable angina, early, immediate, timing, invasive, angiography, PCI). Strategies were tailored to each database (field tags, filters). The full search strings and any limits (humans) are available upon request.

Selection process

Two reviewers screened titles and abstracts and full texts in duplicate using pre specified criteria. Disagreements were resolved by discussion. We documented reasons for full text exclusions and summarized study flow in a PRISMA diagram. 17 original studies met inclusion and were included in the synthesis (Fig 1).

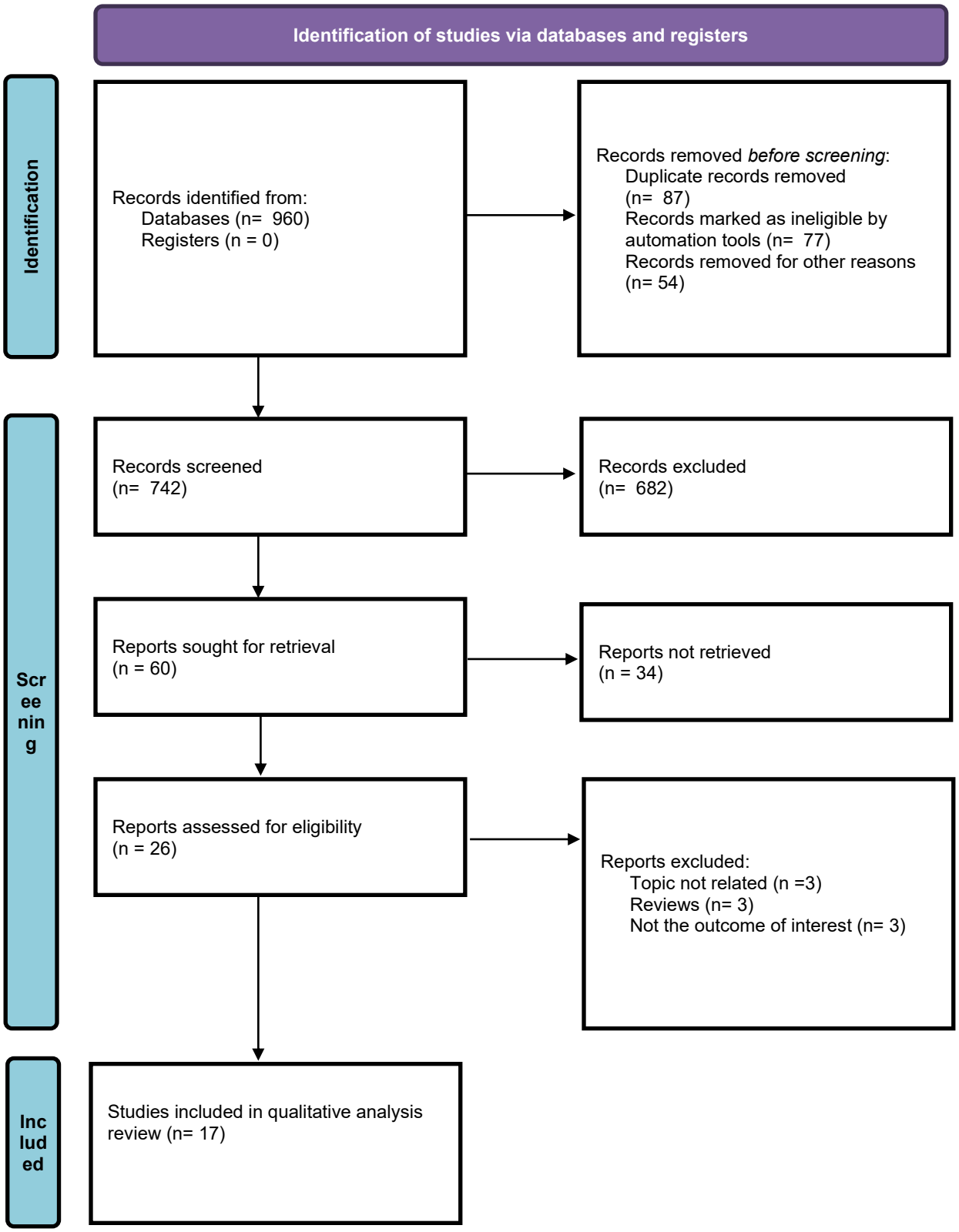

Figure 1: PRISMA consort chart

Data collection process

Using a piloted extraction form, two reviewers extracted: citation; country and setting; enrollment period; definitions of (early vs very early) and (delayed vs standard); inclusion, exclusion criteria; sample size and baseline risk (GRACE); antithrombotic background therapy; primary and secondary outcomes and definitions; follow up; and main findings. When multiple reports existed for the same cohort and trial, we reconciled them and used the most complete dataset (Oosterwerff et al., 2016).

Data items and outcome definitions

Primary clinical endpoints prioritized the study defined composite of death, MI, stroke, or urgent revascularization. Safety outcomes prioritized major bleeding (TIMI, BARC). Where studies used surrogate endpoints (peak CK MB, troponin AUC), these were recorded and classified as surrogate outcomes (Montalescot et al., 2009; Thiele et al., 2012; Fagel et al., 2021).

Risk of bias assessment

Two reviewers independently assessed risk of bias for randomized trials using Cochrane RoB 2 domains and for observational cohorts using ROBINS 1 and 2 (Tables 1 and 2). We summarized domain-level judgments (randomization, deviations, missing data, outcome measurement, reporting) and considered the risk of bias when interpreting results.

Effect measures

For dichotomous outcomes we extracted or calculated risk ratios (RR) or hazard ratios (HR) with 95% CIs, preferring adjusted estimates when available in observational studies (Lindholm et al., 2017; Bae et al., 2023). For continuous and surrogate outcomes, we extracted mean differences or study-reported measures.

Synthesis methods

Given heterogeneity in timing thresholds, background therapy eras, and endpoint definitions, we planned a random effect meta-analysis contingent on clinical, methodologic homogeneity. Because of substantial heterogeneity and variable reporting, we performed a structured qualitative synthesis in trials and cohorts, with risk stratified interpretation (GRACE more than 140, heart failure) (Mehta et al., 2009; Kofoed et al., 2018; Deharo et al., 2017; Yoshida et al., 2019). Where studies were sufficiently comparable, we narratively compared direction and magnitude of effect.

3. RESULTS

Study selection and characteristics

Seventeen original studies met eligibility, including multicenter RCTs (ISAR COOL, ABOARD, TIMACS, VERDICT, ELISA 3, LIPSIA NSTEMI, OPTIMA, OPTIMA 2, SISCA, RIDDLE NSTEMI), single-center RCTs (Sciahbasi), and large observational cohorts (SWEDEHEART, high-risk NSTEMI analyses). In studies, (early, very early) invasive timing ranged from immediate–less than or equal 6 h up to less than or equal 24 h; (delayed, standard) ranged from ≥24–72 h or (next working day). Detailed characteristics for all included studies are summarized in the result tables you provided (Table 1 and 2).

Table 1: Risk of Bias, ROBINS-I (non randomized studies)

Citation	Study type	Confounding	Selection of participants	Classification of interventions	Deviations from intended interventions	Missing data	Measurement of outcomes	Selection of reported results	Overall ROBINS-I judgment
Yoshida et al., 2019	Observational	Serious	Moderate	Low	Low	Moderate	Moderate	Moderate	Serious
Bae et al., 2023	Observational	Moderate	Moderate	Low	Low	Moderate	Moderate	Moderate	Moderate
Deharo et al., 2017	Observational	Serious	Low	Low	Low	Low Moderate	Low	Moderate	Serious
Lindholm et al., 2017	Observational	Serious	Moderate	Low	Low	Moderate	Low	Moderate	Serious

Table 2: Risk of Bias, RoB 2 for Randomized Trials

Citation	Randomization process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall RoB 2 judgment
Neumann et al., 2003	Low risk	Some concerns	Low risk	Low risk	Low risk	Some concerns
Montalescot et al., 2009	Low risk	Some concerns	Low risk	Low risk	Low risk	Some concerns
Mehta et al., 2009	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Kofoed et al., 2018	Low risk	Some concerns	Low risk	Low risk	Low risk	Some concerns
Fagel et al., 2021	Low risk	Some concerns	Low risk	Low risk	Low risk	Some concerns
Oosterwerff et al., 2016	Low risk	Some concerns	Low risk	Low risk	Low risk	Some concerns
Reuter et al., 2015	Some concerns	Some concerns	Low risk	Low risk	Some concerns	Some concerns
Badings et al., 2013	Low risk	Some concerns	Low risk	Low risk	Low risk	Some concerns
Thiele et al., 2012	Low risk	Some concerns	Low risk	Low risk	Low risk	Some concerns
Sciahbasi et al., 2010	Some concerns	Some concerns	Low risk	Some concerns	Some concerns	Some concerns
Riezebos et al., 2009	Low risk	Some concerns	Low risk	Low risk	Low risk	Some concerns

Primary clinical outcomes

Most RCTs reported no superiority of routine immediate invasive strategy versus a delayed approach for composite ischemic endpoints (Mehta et al., 2009; Kofoed et al., 2018; Thiele et al., 2012; Fagel et al., 2021; Badings et al., 2013; Reuter et al., 2015). RIDDLE NSTEMI showed a reduction in death or new MI with immediate (less than 2 h) intervention compared with 2–72 h delay (Milosevic et al., 2016). Long-term follow-up from OPTIMA did not show differences in 5-year death or spontaneous MI between immediate and deferred PCI (Oosterwerff et al., 2016). Observational evidence aligned with neutral effects but suggested potential advantages to earlier procedures in routine care depending on risk profile (Lindholm et al., 2017; Bae et al., 2023; Deharo et al., 2017; Yoshida et al., 2019).

High risk subgroups

Consistent signals favored earlier invasive timing among patients at high clinical risk. In TIMACS, patients with GRACE >140 benefited from early (less than or equal 24 h) versus delayed (≥36 h) intervention (Mehta et al., 2009). VERDICT reported a similar high-risk signal with very early timing (Kofoed et al., 2018). A large post-hoc analysis in high-risk NSTEMI (GRACE >140) showed lower 180-day death/MI with invasive management within 24 h, particularly less than or equal 12 h (Deharo et al., 2017). Patients with concomitant heart failure also appeared to benefit from earlier coronary angiography (Yoshida et al., 2019). Registry data (SWEDEHEART) associated PCI within 24–48 h with reduced mortality and recurrent MI, with the greatest effect in higher-risk strata (Lindholm et al., 2017).

Secondary and surrogate outcomes

Several RCTs used biomarker or infarct-size surrogates and found no reduction with immediate timing (Montalescot et al., 2009; Thiele et al., 2012; Fagel et al., 2021). A small physiologic study reported improved microvascular perfusion indices with immediate PCI, but was underpowered for clinical events (Sciahbasi et al., 2010). Operational endpoints, such as hospital stay, sometimes favored earlier strategies (Badings et al., 2013), but without consistent translation to major clinical benefit.

Safety outcomes

Major bleeding and procedural complications were broadly similar between earlier and delayed strategies (Neumann et al., 2003; Kofoed et al., 2018; Thiele et al., 2012; Fagel et al., 2021; Badings et al., 2013). No reproducible excess harm with earlier timing was observed in contemporary antithrombotic practice (Fagel et al., 2021).

Synthesis of direction of effect

Taken together, the weight of randomized evidence supports clinical equivalence overall between routine immediate and delayed invasive strategies for unselected NSTE ACS (Mehta et al., 2009; Kofoed et al., 2018; Thiele et al., 2012; Fagel et al., 2021; Badings et al., 2013; Reuter et al., 2015), while earlier intervention appears advantageous in high-risk phenotypes, especially GRACE >140, heart failure, or persistent ischemia (Mehta et al., 2009; Kofoed et al., 2018; Lindholm et al., 2017; Deharo et al., 2017; Yoshida et al., 2019). An isolated positive RCT (Milosevic et al., 2016) favors immediate timing, aligning with the broader risk-tailored interpretation rather than a universal mandate for immediacy. The study's characteristics and main findings were presented in Tables 3 and 4, respectively.

Table 3: Study Characteristics, Early vs Delayed Invasive Strategy in NSTE ACS

Citation (first author et al., year)	Study design	Sample size	Inclusion criteria	Method	Study aim
Neumann et al., 2003	Randomized controlled trial: early (less than 6 h) vs delayed (3-5 d pretreatment)	N 410	Unstable angina less than or equal 24 h + ST depression ≥0.1 mV (≥2 leads) or elevated troponin T, key exclusions (STEMI, shock, unsuitability)	Sealed envelope randomization, early angiography, PCI vs prolonged antithrombotic pretreatment	Does prolonged pretreatment reduce early ischemic events vs early intervention?
Montalescot et al., 2009	Multicenter RCT: immediate vs next working day angiography	N 352	Suspected NSTE ACS eligible for early invasive management	Immediate angiography (70 min) vs next working day, guideline pretreatment	Is immediate angiography superior to next day strategy?
Mehta et al., 2009	International RCT: early (less than or equal 24 h) vs delayed (≥36 h) invasive	N 3031	UA, NSTEMI within 24 h + ≥2 risk features (age ≥60, biomarkers, ischemic ECG changes)	Central randomization, angiography, PCI per group, blinded adjudication	Early vs delayed invasive outcomes
Kofoed et al., 2018	Randomized clinical trial: very early vs standard invasive	N 2147	NSTE ACS meeting trial criteria	Randomization to very early vs standard timing, blinded event adjudication	Does very early evaluation reduce composite events vs standard timing?
Fagel et al., 2021	RCT: immediate (0-12 h) vs early (12-24 h)	N 249 (stopped early)	Intermediate, high risk NSTE ACS planned for invasive, contemporary antiplatelets	Randomization to immediate vs early, CK-MB AUC primary endpoint, 1 year follow up	Immediate vs early strategy effects on infarct size and safety
Yoshida et al., 2019	Single center cohort: early less than 24 h vs delayed ≥24 h	N 160	NSTE ACS + CHF (Framingham), planned CAG during admission	Prospective identification, KM, Cox analyses	Does early invasive improve long term outcomes in NSTE ACS + CHF?
Bae et al., 2023	Multicenter retrospective cohort, propensity matched by timing	Matched n 240 (120 pairs)	NSTEMI undergoing angiography with symptom-to-catheter times	Grouped by less than or equal 24 h, 24-48 h, more than 72 h, matching + Cox, KM	Association between symptom-to-catheter timing and outcomes
Deharo et al., 2017	Post-hoc analysis of RCT cohort, timing groups (less than or equal 12 h, 12-24 h,	N 4,071 (GRACE more than 140)	NSTEMI with GRACE score more than 140, scheduled invasive within 72 h	Categorized by time from admission to CAG, composite death, MI at 180 days	Association of very-early vs later CAG with ischemic outcomes at 180

	≥24 h)				days
Oosterwerff et al., 2016	Long-term follow-up of RCT (OPTIMA): immediate vs deferred PCI	N 142 randomized, 5-year data n 133	Intermediate, high-risk NSTE-ACS from original OPTIMA trial	Kaplan-Meier and Cox models for death + spontaneous MI at 5 years	Long-term outcomes by PCI timing (immediate vs deferred)
Reuter et al., 2015	Randomized trial: early invasive (less than or equal 6 h, tirofiban, angiography) vs delayed	N 170	High-risk NSTE-ACS (ECG ischemia + ≥1 severity criterion or TIMI more than 5)	Prehospital, randomization, primary 30-day MACE (death, MI, urgent revasc)	Effectiveness of early invasive vs delayed in high-risk NSTE-ACS
Badings et al., 2013	Multicenter RCT: immediate (less than 12 h) vs delayed (more than 48 h)	N 542	NSTE-ACS with ≥2 high-risk features (ECG ischemia, TropTmore than 0.10, agemore than 65)	Randomization, primary 30-day death, MI, recurrent ischemia	Early vs delayed strategy in high-risk NSTE-ACS (elderly enriched)
Thiele et al., 2012	Multicenter RCT: immediate (less than 2 h) vs early (10-48 h) vs selective (67 h)	N 602	Stable NSTEMI after admission	Randomization to three strategies, primary peak CK-MB, 6-month clinical endpoints	Whether immediate is superior to early, selective regarding large infarction
Sciahbasi et al., 2010	Single-center RCT: immediate (less than or equal 6 h) vs early (7-72 h) PCI	N 54	First NSTEMI with ECG changes, eptifibatide used	Randomization, perfusion by MCE, biomarker peaks	Perfusion and infarct size markers by timing
Riezebos et al., 2009	Multicenter RCT: immediate PCI vs deferred PCI (24-48 h)	N 142 randomized (of 251 screened)	NSTE ACS eligible for PCI, protocol defined high risk features	Triple antiplatelet, 30 day death, MI, unplanned revasc, 6 mo follow up	Impact of immediate vs deferred PCI
Lindholm et al., 2017	Nationwide observational cohort (PCI treated NSTEMI), timing cut offs 1, 2, 3 days	N 40,494	Consecutive NSTEMI undergoing PCI in Sweden 2006-2013	Mixed effects Cox, 1-year outcomes (death, MI, stent thrombosis, bleeding)	Mortality, MI vs earlier PCI (real world)
Milosevic et al., 2016	Duplicate listing, consolidated with RIDDLE above	N 323	NSTEMI stabilized, invasive strategy planned	Immediate vs delayed, death, new MI endpoints	Impact of timing in NSTEMI

Table 4: Main Findings and Outcome, NSTE-ACS Early vs Delayed (less than or equal 40 words per cell)

Citation	Main findings	Outcome
Neumann et al., 2003	Prolonged antithrombotic pretreatment before PCI did not improve 30-day ischemic outcomes versus early intervention; early strategy reduced pre-PCI recurrent ischemia; bleeding rates were similar.	No overall advantage of delayed pretreatment; early strategy acceptable without excess harm.
Montalescot et al., 2009	Immediate angiography versus next working day showed no reduction in peak troponin or major adverse events; bleeding similar; logistics favored immediate for shorter pathway but without clinical superiority.	No significant clinical difference between immediate and next-day strategies.
Mehta et al., 2009	Overall composite (death, MI, stroke) similar between early less than or equal 24h and delayed ≥36h; predefined high-risk subgroup (GRACEmore than 140) benefited from early strategy.	Neutral overall; early improves outcomes in high-risk (GRACEmore than 140).

Kofoed et al., 2018	Very-early invasive versus standard timing had similar primary composite overall; benefit signal for very-early in GRACEmore than 140; bleeding and complications comparable.	Neutral overall; earlier timing beneficial in high-risk patients.
Fagel et al., 2021	Immediate (0-12h) versus early (12-24h) invasive strategy showed no difference in CK-MB AUC or one-year clinical events; safety similar in ticagrelor era.	No significant difference between immediate and early strategies.
Yoshida et al., 2019	In NSTE-ACS with heart failure, early angiography less than 24h associated with lower long-term death, MI after adjustment; benefits consistent in sensitivity analyses.	Early strategy favored in concomitant heart failure subgroup.
Bae et al., 2023	Shorter symptom-to-catheter times (less than or equal 24h) were associated with lower major adverse events versus more than 72h; adjusted analyses supported association; bleeding differences were not significant.	Earlier catheterization associated with improved outcomes.
Deharo et al., 2017	Among GRACEmore than 140 NSTEMI, invasive within 24h, especially less than or equal 12h, was associated with lower 180-day death, MI; no excess major bleeding observed.	Early, very-early strategy beneficial in high-risk patients.
Oosterwerff et al., 2016	Long-term follow-up of OPTIMA showed no significant difference in five-year death or spontaneous MI between immediate and deferred PCI groups.	Neutral long-term differences between timing strategies.
Reuter et al., 2015	Early less than or equal 6h strategy with tirofiban, early CAG did not significantly reduce 30-day MACE versus delayed; feasibility demonstrated; no major bleeding signal.	No significant short-term advantage of early strategy.
Badings et al., 2013	Immediate less than 12h versus delayed more than 48h showed similar 30-day death, MI, recurrent ischemia; hospital stay tended to be shorter with early approach; safety comparable.	Overall neutral; operational advantages without clear clinical superiority.
Thiele et al., 2012	Immediate less than 2h did not reduce infarct size versus early, selective strategies; clinical outcomes similar; potential for higher bleeding with immediate noted.	No clinical superiority of immediate strategy; safety trade-offs possible.
Sciahbasi et al., 2010	Small RCT: immediate less than or equal 6h improved microvascular perfusion indices; biomarkers similar; underpowered for clinical endpoints.	Physiologic perfusion benefit without proven clinical advantage.
Riezebos et al., 2009	Immediate PCI compared with deferred 24-48h showed similar 30-day death, MI, unplanned revascularization; length of stay differed slightly; safety similar.	Neutral short-term clinical differences between immediate and deferred PCI.
Lindholm et al., 2017	Registry: earlier PCI within 24-48h associated with lower mortality and recurrent MI, especially in high-risk; observational design limits causal	Earlier PCI associated with improved outcomes; strongest in high-risk.

	inference; bleeding not increased.	
Milosevic et al., 2016	Same trial population as above; immediate strategy consistently reduced death, MI without excess bleeding in reported analyses.	Confirms superiority of immediate approach within this trial.

4. DISCUSSION

Of the included studies, three themes emerge. First, deferring invasive evaluation to permit prolonged antithrombotic cooling off, is not beneficial and harmful due to pre catheterization events, an effect robustly shown in ISAR COOL (Neumann et al., 2003). This aligns with practice show rapid stabilization with guideline directed dual antiplatelet therapy and parenteral anticoagulation while preparing for angiography rather than postponing it (Byrne et al., 2023).

Immediate angiography (less than 2 h) for all comers with NSTE ACS has not improved hard outcomes versus an early (less than 24 h) plan. ABOARD and LIPSIA NSTEMI both showed no advantage for an immediate strategy over early approaches in unselected or semi selected cohorts (Montalescot et al., 2009; Thiele et al., 2012). VERDICT found no benefit of less than 12 h vs standard care timing, with signals favoring very early invasive care confined to the highest risk patients (GRACE more than 140, extensive ischemia) (Kofoed et al., 2018). These findings suggest that faster is not always better once patients are stabilized and protected with potent antithrombotic therapy.

Risk stratification modifies timing effects, TIMACS trial show that early angiography reduced the composite of death, MI and refractory ischemia in patients with GRACE more than 140, whereas lower risk patients derived little difference from earlier vs delayed strategies (Mehta et al., 2009). A meta-analyses support this interaction, earlier invasive care lower recurrent ischemia and length of stay, with possible mortality benefit in high-risk subgroups, and neutral effects (Kite et al., 2022; Zhang et al., 2019). Large registry data from SWEDEHEART indicate limited incremental population level benefit of less than 24 h angiography in careful selection, while hinting at heterogeneity by sex, diabetes, or troponin amplitude (Eggers et al., 2022).

Clinical implications for the emergency department are pragmatic, patients with very high-risk features (shock, refractory ischemia, malignant arrhythmias) warrant immediate invasive management (Byrne et al., 2023). For high risk NSTE ACS (positive troponin, dynamic ST, T changes, GRACE more than 140), early angiography within 24 h is reasonable and guideline endorsed, balancing bed capacity and catheter lab logistics (Byrne et al., 2023; Collet et al., 2021). For stabilized intermediate risk patients, angiography within 24-72 h appears safe, with careful attention to recurrent symptoms and biomarker; routine cooling off is not supported (Neumann et al., 2003; Eggers et al., 2022). Institutions should hardwire ED pathways that couple rapid risk scoring (including GRACE), high-sensitivity troponin algorithms, and early antithrombotic loading to minimize pre-catheterization events while targeting early access for those most likely to benefit.

5. CONCLUSION

Early invasive management within 24 h does not improve hard outcomes versus delayed strategies in unselected NSTE ACS; high-risk patients (GRACE score more than 140, heart failure, dynamic ischemia) benefit from earlier angiography. For stabilized intermediate risk patients, angiography within 24-72 h is safe without excess bleeding or complications. ED pathways operationalize risk-based triage: immediate for very high risk, early for high risk, routine within 72 h for others, avoiding cooling-off delays. Evidence is limited by heterogeneous timing thresholds and evolving adjunctive therapy. Future trials standardize timing definitions and prioritize patient-important outcomes, including quality of life and time to symptom resolution.

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Informed consent

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Ethical approval

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Conflict of interest

The authors declare that they have no conflicts of interests, competing financial interests or personal relationships that could have influenced the work reported in this paper.

Data and materials availability

All data associated with this study will be available based on reasonable request to the Corresponding Author.

REFERENCES

1. Badings EA, The SH, Dambrink JH, van Wijngaarden J, Tjeerdsma G, Rasoul S, Timmer JR, van der Wielen ML, Lok DJ, van 't Hof AW. Early or late intervention in high-risk non-ST-elevation acute coronary syndromes: results of the ELISA-3 trial. Euro Intervention 2013;9(1):54-61. doi: 10.4244/EIJV9I1A9.
2. Bae S, Cha JJ, Lim S, Kim JH, Joo HJ, Park JH, Hong SJ, Yu CW, Lim DS, Kim Y, Kang WC, Cho EJ, Lee SY, Kim SW, Shin ES, Hur SH, Oh SK, Lim SH, Kim HS, Hong YJ, Ahn Y, Jeong MH, Ahn TH. Early Invasive Strategy Based on the Time of Symptom Onset of Non-ST-Segment Elevation Myocardial Infarction. JACC Cardiovasc Interv 2023;16(1):64-75. doi: 10.1016/j.jcin.2022.09.039.
3. Byrne RA, Rossello X, Coughlan JJ, Barbato E, Berry C, Chieffo A, Claeys MJ, Dan GA, Dweck MR, Galbraith M, Gilard M, Hinterbuchner L, Jankowska EA, Jüni P, Kimura T, Kunadian V, Leosdottir M, Lorusso R, Pedretti RFE, Rigopoulos AG, Rubini Gimenez M, Thiele H, Vranckx P, Wassmann S, Wenger NK, Ibanez B; ESC Scientific Document Group. 2023 ESC Guidelines for the management of acute coronary syndromes. Eur Heart J 2023;44(38):3720-3826. doi: 10.1093/eurheartj/ehad191. Erratum in: Eur Heart J 2024;45(13):1145. doi: 10.1093/eurheartj/ehad870.
4. Collet JP, Thiele H, Barbato E, Barthélémy O, Bauersachs J, Bhatt DL, Dendale P, Dorobantu M, Edvardsen T, Folliguet T, Gale CP, Gilard M, Jobs A, Jüni P, Lambrinou E, Lewis BS, Mehilli J, Meliga E, Merkely B, Mueller C, Roffi M, Rutten FH, Sibbing D, Siontis GCM; ESC Scientific Document Group. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J 2021;42(14):1289-1367. doi: 10.1093/eurheartj/ehaa575.
5. Deharo P, Ducrocq G, Bode C, Cohen M, Cuisset T, Mehta SR, Pollack C Jr, Wiviott SD, Elbez Y, Sabatine MS, Steg PG. Timing of Angiography and Outcomes in High-Risk Patients With Non-ST-Segment-Elevation Myocardial Infarction Managed Invasively: Insights From the TAO Trial (Treatment of Acute Coronary Syndrome With Otamixaban). Circulation 2017;136(20):1895-1907. doi: 10.1161/CIRCULATIONAHA.117.029779.
6. Eggers KM, Lindholm D, Melka S, Jernberg T. Timing of coronary angiography in patients with non ST elevation acute coronary syndrome: long term clinical outcomes from the nationwide SWEDEHEART registry. Eur Heart J Qual Care Clin Outcomes 2022;8(4):350 358. doi:10.1093.ehjqcco.qcac025.
7. Fagel ND, Amoroso G, Vink MA, Slagboom T, van der Schaaf RJ, Herrman JP. An immediate or early invasive strategy in non ST elevation acute coronary syndrome: the OPTIMA 2 randomized controlled trial. Am Heart J 2021;234:42 50.
8. Kite TA, Mohee K, Gale CP, Kontopantelis E, Deanfield J, de Belder M. Timing of invasive strategy in patients with non ST elevation acute coronary syndrome: a meta analysis. Eur Heart J 2022;43(33):3148 3161. doi:10.1093, eurheartj.ehac250.
9. Kofoed KF, Kelbæk H, Hansen PR, Torp Pedersen C, Löfgren B, Kløvgaard L. Early versus standard care invasive examination and treatment of patients with non-ST-segment elevation acute coronary syndrome (VERDICT). Lancet 2018;391(10134):1769 1778. doi:10.1016, S0140 6736(18)31123 7.
10. Lindholm D, Alfredsson J, Angerås O, Böhm F, Calais F, Koul S. Timing of PCI and outcomes in NSTEMI: a SWEDEHEART study. Eur Heart J Qual Care Clin Outcomes 2017;3(1):53 60. doi:10.1093.ehjqcco.qcw044.
11. Mehta SR, Granger CB, Boden WE, Steg PG, Bassand J P, Faxon DP. Early vs delayed invasive intervention in acute coronary syndromes (TIMACS). N Engl J Med 2009;360(21):2165 2175. doi:10.1056.NEJMoa0807986.
12. Milosevic A, Vasiljevic Pokrajcic Z, Milasinovic D, Marinkovic J, Vukcevic V, Stefanovic B. Immediate versus delayed invasive intervention in NSTEMI (RIDDLE NSTEMI). JACC Cardiovasc Interv 2016;9(6):541 549. doi:10.1016.j.jcin.2015.11.018.

13. Montalescot G, Cayla G, Collet J P, Elhadad S, Beygui F, Le Breton H. Immediate vs delayed intervention for acute coronary syndromes (ABOARD). JAMA 2009;302(9):947 954. doi:10.1001.jama.2009.1260.
14. Neumann FJ, Kastrati A, Pogatsa-Murray G, Mehilli J, Bollwein H, Bestehorn HP, Schmitt C, Seyfarth M, Dirschinger J, Schömig A. Evaluation of prolonged antithrombotic pretreatment ("cooling-off" strategy) before intervention in patients with unstable coronary syndromes: a randomized controlled trial. JAMA 2003;290(12):1593-9. doi: 10.1001/jama.290.12.1593.
15. Oosterwerff EF, Fagel ND, Slagboom T, Tijssen JG, Herrman JP, Smits PC, Suttorp MJ, Ronner E, Laarman GJ, Patterson MS, Amoroso G, Vink MA, van der Schaaf RJ, Verheugt FW, Riezebos RK. Impact of percutaneous coronary intervention timing on 5-year outcome in patients with non-ST-segment elevation acute coronary syndromes. The 'wait a day' approach might be safer. Neth Heart J 2016;24(3):173-80. doi: 10.1007/s12471-016-0803-0.
16. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71.
17. Reuter PG, Rouchy C, Cattan S, Benamer H, Jullien T, Beruben A, Montely JM, Assez N, Raphael V, Hennequin B, Boccara A, Javaud N, Soulat L, Adnet F, Lapostolle F. Early invasive strategy in high-risk acute coronary syndrome without ST-segment elevation. The Sisca randomized trial. Int J Cardiol 2015;182:414-8. doi: 10.1016/j.ijcard.2014.12.089.
18. Riezebos RK, Ronner E, ter Bals E, Slagboom T, Smits PC, ten Berg JM. Immediate versus deferred coronary angioplasty in non ST segment elevation acute coronary syndromes. Heart 2009;95(10):807 812. doi:10.1136.hrt.2008.154815.
19. Sciahbasi A, Madonna M, De Vita M, Agati L, Scioli R, Summaria F. Immediate vs early invasive strategy in first acute NSTEMI. Clin Cardiol 2010;33(10):650 655. doi:10.1002.clc.20785.
20. Thiele H, Rach J, Klein N, Pfeiffer D, Hartmann A, Hambrecht R. Optimal timing of invasive angiography in stable non-ST elevation myocardial infarction (LIPSIA NSTEMI). Eur Heart J 2012;33(16):2035 2043. doi:10.1093.eurheartj.ehs014.
21. Yoshida R, Saito S, Iwashita S, Yamamoto R, Nakano M, Kodani E. Potential of early invasive strategy in selected patients with non ST segment elevation acute coronary syndrome and congestive heart failure: a retrospective cohort study. J Cardiol 2019;74:320-327. doi:10.1016.j.jjcc.2019.03.006.
22. Zhang MB, Hu Q, Yin YJ, Zhang JW. Comparison of early and delayed invasive strategies in NSTE ACS: a meta analysis of randomized clinical trials. PLoS One 2019;14(7):e0220847. doi:10.1371.journal.pone.0220847.