

ORIGINAL RESEARCH

Invasive Strategy With Intended Percutaneous Coronary Intervention Versus Conservative Treatment in Older People With ST-Segment–Elevation Myocardial Infarction: A Meta-Analysis

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BACKGROUND: Patients ≥ 80 years old were underrepresented or excluded from landmark trials demonstrating the superiority of primary percutaneous coronary intervention (PCI) in ST-segment–elevation myocardial infarction. The current meta-analysis assessed the effects of an invasive strategy with intended PCI compared with conservative treatment in older people (≥ 80 years) with ST-segment–elevation myocardial infarction.

METHODS: A structured literature search was performed. The primary outcome was overall survival. Secondary outcome analyses included but were not limited to 30-day and 1-year mortality.

RESULTS: Thirteen studies reporting on 102 158 older adults were included. Of these, 31 629 (31%) were assigned to PCI and 70 529 (69%) were treated conservatively. The overall survival was 76.5% in PCI and 67.2% in conservative treatment at the time of longest available follow-up (odds ratio [OR], 2.18 [95% CI, 1.79–2.66], $P < 0.001$, $I^2 = 88\%$, favoring PCI). The follow-up period ranged from 30 days to 26.5 months. The 30-day (OR, 0.39 [95% CI, 0.31–0.50], $P < 0.001$, $I^2 = 0\%$) and 1-year mortality (OR, 0.34 [95% CI, 0.25–0.46], $P < 0.001$, $I^2 = 0\%$), were lower in the PCI group.

CONCLUSIONS: This meta-analysis indicates a potential underuse of PCI in older adults with ST-segment–elevation myocardial infarction. PCI was advantageous in short- and long-term survival, but these results were affected by confounding. Nonetheless, every second patient not referred for invasive treatment survived at least 1 year. These findings have hypothesis generating implications, but they indicate ageism and emphasize that PCI should not be automatically withheld in older patients.

Key Words: centenarians ■ nonagenarians ■ octogenarians ■ optimal medical therapy ■ percutaneous coronary intervention ■ STEMI

Cardiovascular diseases and particularly ischemic heart disease significantly contribute to morbidity and reduce longevity of octogenarians, nonagenarians, and centenarians.¹ Even though the incidence of acute myocardial infarction (AMI) decreased within

the past 2 decades among the general population,^{2–4} longer estimated life spans contribute to a considerable number of AMIs in those older adults.^{5,6} Although recent evidence in older patients with non-ST-segment–elevation myocardial infarction (non-STEMI)

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CLINICAL PERSPECTIVE

What Is New?

- This meta-analysis indicates a potential under-use of primary percutaneous coronary intervention in older adults with ST-segment-elevation myocardial infarction; only one third of older patients were triaged to percutaneous coronary intervention.
- As expected, percutaneous coronary intervention was advantageous in short- and long-term survival, but even every second older patient who was conservatively treated was a long-term survivor; this calls into question the ad hoc triage decision.
- This practice might indicate ageism.

What Are the Clinical Implications?

- Real-world data from registries and observational studies indicate that percutaneous coronary intervention should not be automatically withheld in older patients.
- Patient triaged to conservative treatment might also be long-term survivors.

Nonstandard Abbreviations and Acronyms

CON	conservative treatment
NRSI	nonrandomized controlled studies of interventions
RoB	risk of bias

demonstrated that invasive management does not result in improved survival compared with conservative treatment,^{7–9} older patients with ST-segment elevation myocardial infarction (STEMI) are usually referred for invasive strategy.

In broader STEMI cohorts, there is robust evidence that primary percutaneous coronary intervention (PCI) is superior to fibrinolysis^{10–13} and that timely PCI is the preferred reperfusion strategy in patients with symptom onset within 48 hours.¹⁴ But in those historical studies assessing reperfusion strategies, patients ≥ 80 years were either excluded or underrepresented.^{15–18} No randomized controlled trial (RCT) exclusively enrolling patients with STEMI ≥ 80 years old has been conducted yet. As reperfusion strategies might be less effective or might even cause harm in this patient group with more morbidity,¹⁹ conservative treatment could represent a reasonable strategy following the “primum non nocere” principle. In depth, the authors of the current European Society of Cardiology guideline on acute

coronary syndrome emphasized that the optimal treatment strategy of older patients with STEMI—who often suffer from frailty or comorbidities—still represents a gap in the evidence.¹⁴ Targeted treatment algorithms considering specific needs and demands of older patients are required.

A meta-analysis of the available reports enrolling this understudied patient group is warranted, to further elucidate the efficacy of PCI compared with conservative treatment in older people.

METHODS

This meta-analysis was conducted using a protocol and reproducible plan for literature search and synthesis. The meta-analysis was prospectively registered (International Prospective Register of Systematic Reviews CRD42024551601). It was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines.²⁰ Data are available and can be extracted from studies included. We did not obtain ethical approval for this meta-analysis because we did not collect data from individual human subjects.

The systematic literature search was performed in three data bases including Medline (via PubMed), Web of Science, and Cochrane Library. The search strategy for each database is provided in the [Supporting Information Appendix](#). The first search was performed on May 27, 2024, and the last search update was performed on August 27, 2024. No restrictions on publication date, language, or study size were applied. After exclusion of duplicates and screening of titles and abstracts according to the eligibility criteria, full texts of the remaining articles were assessed. Additional hand-searching of screened references was performed. The study selection was independently performed by 2 reviewers (S.M., D.D.). In case of any disagreement, this was resolved by consensus with the senior authors (C.F., T.S.).

Controlled trials comparing invasive strategy with intended primary percutaneous coronary intervention (PCI group) to conservative strategy (CON group) in patients aged ≥ 80 years with STEMI were considered.

RCTs and nonrandomized controlled studies of interventions (NRSIs) were eligible. In NRSI adjusted data were preferred over crude data whenever eligible. Studies treating patients before Food and Drug Administration approval of coronary stents in 1994 were excluded as they underly an inherent risk of performance bias in the PCI group throughout.²¹ This criterion was added as a post hoc adjustment. No other restrictions were applied for specific interventional or conservative treatment strategies, follow-up duration, or timing of the intervention itself.

Double publications, case reports, case series without control groups, reviews, meta-analyses and conference abstracts, or posters were excluded. Studies grouping revascularization techniques (eg, PCI and emergent coronary artery bypass grafting) or studies with solely coronary artery bypass grafting revascularization were excluded. Studies including younger patients (<80 years) and without providing separate reports on outcomes of older patients were excluded.

Data were independently extracted by 2 investigators (S.M., D.D.) using a standardized prespecified data collection form. Main study reports as well as any Supporting Information Appendices and study protocols were reviewed. Prespecified data elements included study design, patient baseline characteristics, intervention, and follow-up data. In case of published follow-up reports or several reports of the same cohorts the longest available observational period was preferred, and event data were extracted accordingly.

The primary end point was overall survival calculated from the longest available follow-up of each individual study. Secondary outcomes included in-hospital, 30-day “short-term,” and 1-year “long-term” mortality—each defined as death from any cause. Additionally, cardiac mortality, heart failure hospitalization, repeated hospitalizations, and major bleeding were assessed as defined per individual trial.

Per protocol, the present meta-analysis should assess major adverse cardiac events (defined as a composite of cardiac mortality, MI, and target vessel/lesion revascularization), any bleeding and minor bleeding, but these were not thoroughly reported in the included trials. Consequently, these were eliminated from the present analysis.

Risk of bias (RoB) at study level would have been assessed using the Cochrane Collaborations risk-of-bias tool (RoB2, version August 22, 2019) for RCTs per protocol,²² but RCTs were not available. NRSIs were assessed using the Cochrane Collaborations Risk of Bias in Non-randomized Studies of Interventions (version October 20, 2016) tool.²³ RoB assessment was independently performed by 2 investigators (S.M., D.D.). In case of discrepancy a third independent investigator was consulted (T.S.). RoB assessment was performed with focus on the primary outcome.

Random-effects meta-analyses were performed using the DerSimonian-Laird’s method for dichotomous event data. Pooled odds ratios (ORs) and 95% CIs are given for each analysis with a 2-sided significance level of $P < 0.05$ (RevMan 5.3, Nordic Cochrane Centre, Cochrane Collaboration). The extent of heterogeneity was approximated by I^2 tests considering 0% to 40% as nonimportant, 30% to 60% as moderate, 50% to 90% as substantial and 75% to 100% as considerable heterogeneity.²⁴ Prespecified funnel plot analysis was performed for the primary outcome.

Additionally, quantitative funnel plot analysis by Egger’s regression test was added following a post hoc adjustment (R statistics, Metafor package, version 4.4-0).

Sensitivity meta-analysis of the primary outcome was performed according to RoB judgment. As all included NRSIs were judged to be at critical RoB in the confounding domain, sensitivity analysis would have lost its discriminative power. Therefore, the NRSIs with “serious” or “critical” RoB in any other domain were excluded from the modified sensitivity analysis. Again, this was a post hoc adjustment. An additional post hoc sensitivity meta-analysis was conducted using a fixed-effects model.

A further post hoc subgroup meta-analysis of the primary outcome was performed according to the follow-up duration: as long-term mortality data were included in secondary outcome analysis, those reports with a follow-up duration >12 months were considered to further assess long-term prognosis.

We did not obtain ethical approval for this meta-analysis because we did not collect data from individual human subjects.

RESULTS

Study Selection

A total of 1446 articles were identified by the first literature search (see [Figure 1](#)). After removing duplicates, the titles and abstracts of 1012 remaining references were screened. Of these, 955 were excluded, which left 57 references to assess full-text eligibility. Fourteen publications^{5,6,25–36} reporting on 13 patient cohorts were evaluated. Two publications^{25,26} had an overlap of study cohorts; the most recent report²⁶ was considered for further analysis. Ultimately, 13 studies were included in the quantitative analysis. The last search update from August 27, 2024, did not reveal further eligible studies.

Cohorts

Thirteen patient cohorts were considered (see [Table 1](#)).^{5,6,26–36} All of these were either registry analyses or retrospective case series with unadjusted comparisons of PCI to CON. Five studies^{28,29,33,34,36} followed a monocentric design, and the others were conducted as multicentric or even nationwide reports.

In total, 102 158 older adults were included. Of these, 31 629 (31%) were assigned to PCI and 70 529 (69%) were managed conservatively. The first patient was treated in 2003, and the last patient was managed in December 2019. Most patients (98%) were included in registries reporting on nonagenarians.^{5,6} The baseline characteristics are summarized in [Table 1](#).

The STEMI definitions met the criteria of contemporary classifications and were comparable to the

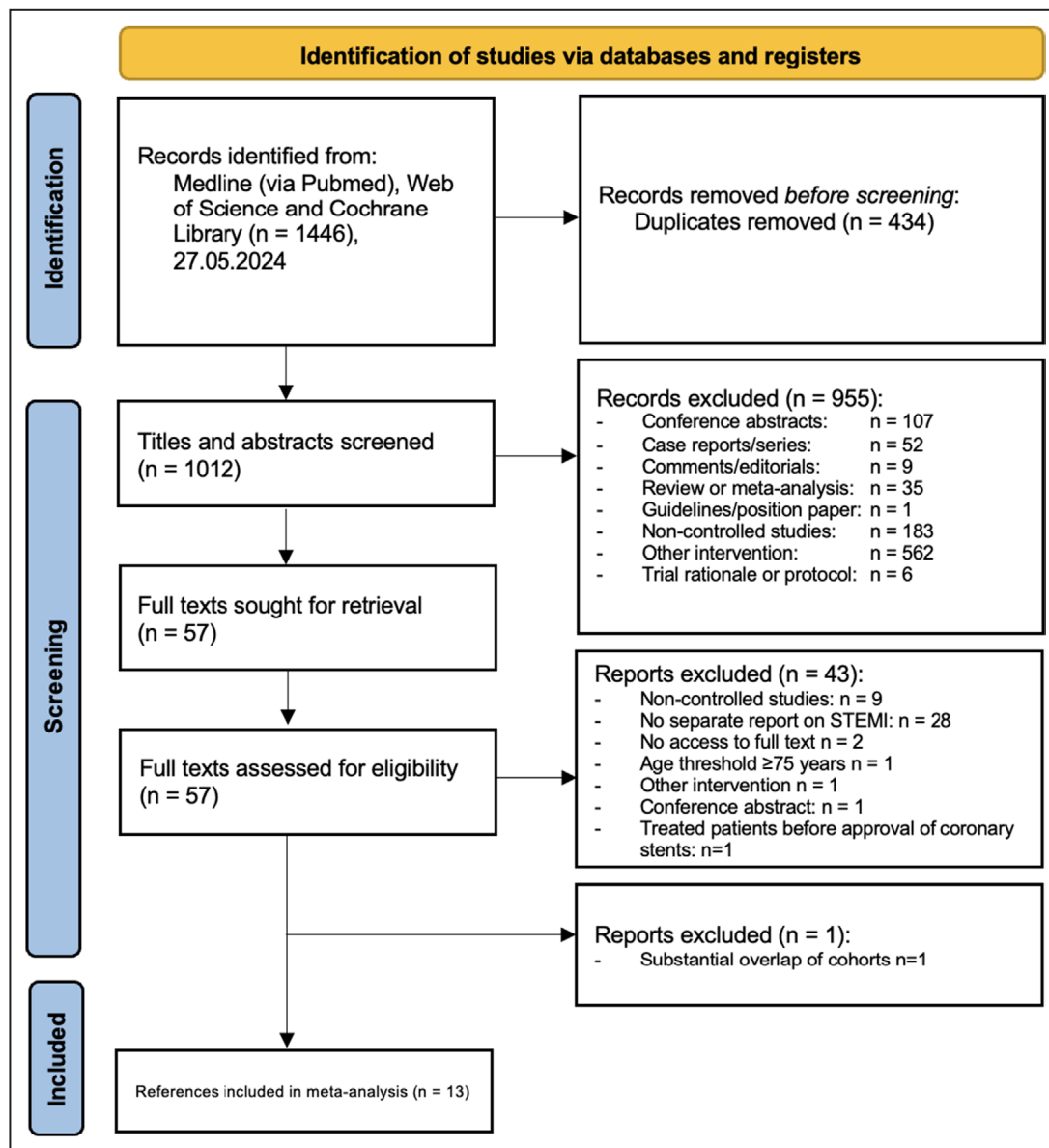


Figure 1. Flow chart diagram.

STEMI indicates ST-segment–elevation myocardial infarction.

greatest possible extent (see [Supporting Information Appendix, Table S1](#)). CON was defined as medical therapy on individual study level. Reported reasons to not perform PCI included but were not limited to refusal of the patient, absence of a culprit lesion, anatomy not suitable for PCI, cardiogenic shock, frailty, cognitive impairment, or significant comorbidities as judged by the treating interventional cardiologist. In 5 trials^{5,6,26,34,36} patients in the CON group were referred for coronary angiography but did not receive PCI.

In PCI group, the angioplasty rate varied from 82.2% to 100% whenever reported. Of these, 77.8% to 92.3% of patients were treated with stent implantation. Stent implantation data were given for only 318 patients in PCI group (1%) and were not reported for

remaining patients. In detail, 146 (45.9%) were treated with bare metal stents and 172 (54.1%) received drug-eluting stents.

Antithrombotic treatment regimens were sparsely reported, so direct comparison between CON and PCI was not feasible (see [Supporting Information Appendix, Table S2](#)). The follow-up period ranged from 30 days to 26.5 months.

Risk of Bias Assessment

The RoB assessment is summarized in [Table 2](#). All trials were judged to be at critical RoB in the “confounding” domain. This judgment based on severe imbalances in PCI and CON groups. For example, patients in CON

Table 1. Characteristics of Included Studies and Patients

Nonrandomized studies of interventions									
Trials	Cepas-Guillén et al.	Hu et al.	Ionescu et al.	Ismayl et al.	Kumar et al.	Pajjuru et al.	Piegza et al.	Ricci et al.	
Study characteristics									
Study period	2005–2018	January 2013–September 2014	January 2004–December 2008	2010–2018	January 2014–December 2019	2010–2017	2003–2018	October 2010–April 2016	
Study design	Retrospective CS, multicentric, Spain	Retrospective CS, nationwide registry, multicentric, China	Retrospective CS, monocentric, Italy	Retrospective CS, nationwide registry, multicentric, United States	Retrospective CS, monocentric, Ireland	Retrospective CS, nationwide registry, multicentric, United States	Retrospective CS, nationwide, multicentric registry, Poland	Retrospective CS, multicentric registry, South and Eastern Europe, Russia	
Included with STEMI patients	307	448	24	37 363	159	41 042	54	605	
Age group	≥90y	≥80y	≥90y	≥90y	≥80y	≥90y	≥100y	≥80y	
Invasive treatment									
Primary PCI	YES	YES	YES	YES	YES	YES	YES	YES	
Rescue PCI	-	NO	-	-	-	-	-	NO	
Exclusion of thrombolysis	-	YES	-	-	-	-	-	YES	
Exclusion of emergent CABG	-	YES	NO	-	NO	-	-	YES	
Inclusion of failed revascularization in PCI group Intention-to-treat principle	-	-	-	-	-	-	YES	-	
Comparator treatment									
General strategy	CON, CA possible, no PCI	CON, no CA	CON, no CA	CON, CA possible, no PCI	CON, no CA	CON, CA possible, no PCI	CON, no PCI	CON	
Patients with thrombolysis	Not reported	0 (0)	Not reported	Not reported	Not reported	Not reported	Not reported	0 (0)	
Follow-up period	1 y	2 y	21.7 mo, mean	30 d	1 y	In-hospital	1 y	30 d	
Baseline characteristics of patients included									
PCI	Patients, n	156 (51)	94 (21.0)	13 (54.2)	13 236 (35.4)	124 (78)	11 155 (27.2)	30 (55.6)	260 (43)
CON	Patients, n	151 (49)	354 (79.0)	11 (45.8)	24 127 (64.6)	35 (22)	29 877 (72.8)	24 (44.4)	345 (57)
PCI	Age, y, median	92.1 [2.4]‡	87.5 [2.4]‡	91.5 ¹⁷ ‡	-	83	-	-	-
CON	Age, y, median	93.0 [2.8]‡	87.6 [2.8]‡	92.5 [2.4]‡	-	85	-	-	-
PCI	Male patients, n	72 (46.2)	58 (61.7)	1 (7.7)	8378 (63.3)	65 (52.4)	3904 (35)	-	-
CON	Male patients, n	48 (31.8)	183 (51.7)	5 (45.5)	7286 (30.2)	16 (45.7)	9561 (32)	-	-
PCI	Hypertension, n	121 (77.6)	57 (60.6)	10 (76.9)	9411 (71.1)	71 (57.3)	-	-	-
CON	Hypertension, n	118 (78.1)	165 (46.6)	8 72.7	16 382 (67.9)	25 (71.4)	-	-	-
PCI	Diabetes, n	38 (24.4)	21 (22.3)	1 (7.7)	2885 (21.8)	11 (8.9)	-	-	-
CON	Diabetes, n	41 (27.2)	35 (9.9)	1 (9.1)	4801 (19.9)	4 (11.4)	-	-	-
PCI	Smoking, n	-	31 (33.3)	0 (0)	1152 (8.7)	65 (52.4)	-	-	-
CON	Smoking, n	-	97 (27.4)	2 (18.2)	1713 (7.1)	11 (31.4)	-	-	-
PCI	Dyslipidemia, n	-	13 (13.8)	3 (23.1)	6711 (50.7)	62 (50)	-	-	-
CON	Dyslipidemia, n	-	4 (1.1)	3 (27.3)	8999 (37.3)	21 (60)	-	-	-
PCI	Previous MI, n	13 (8.3)	5 (5.3)	-	-	19 (15.3)	-	-	-
CON	Previous MI, n	28 (18.5)	25 (7.1)	-	-	11 (31.4)	-	-	-
PCI	STEMI-arrest, n	-	-	-	-	-	-	-	-
CON	STEMI-arrest, n	-	-	-	-	-	-	-	-
PCI	Cardiogenic shock, n	12 (7.7)	8 (8.5)	5 (38.5)	-	17 (13.7)	-	-	-
CON	Cardiogenic shock, n	5 (3.3)	40 (11.3)	4 (36.4)	-	7 (20)	-	-	-

(Continued)

Table 1. Continued

Nonrandomized studies of interventions									
Trials		Cepas-Guillén et al.	Hu et al.	Ionescu et al.	Ismayl et al.	Kumar et al.	Pajjuru et al.	Piegza et al.	Ricci et al.
PCI	Anterior STEMI, n	-	-	9	-	62 (50)	-	-	-
CON	Anterior STEMI, n	-	-	7	-	-	-	-	-
PCI	Inferior STEMI, n	-	-	4	-	48 (38.7)	-	-	-
CON	Inferior STEMI, n	-	-	4	-	-	-	-	-
PCI	Posterior STEMI, n	-	-	-	-	2 (1.6)	-	-	-
CON	Posterior STEMI, n	-	-	-	-	-	-	-	-
PCI	Lateral STEMI, n	-	-	-	-	4 (3.8)	-	-	-
CON	Lateral STEMI, n	-	-	-	-	-	-	-	-
PCI	Other STEMI	-	-	-	-	7 (5.6)	-	-	-
CON	Other STEMI	-	-	-	-	-	-	-	-
Procedural aspects in PCI group									
Coronary angiographies, n		182	94	13	-	124	-	-	-
Initial TIMI flow 0, n		11 (6)	58 (61.7)	-	-	9 (8.4)	-	-	-
No culprit lesion identified, n		-	-	0 (0)	-	17 (13.7)	-	-	-
PCI performed, n		156 (85.7)	-	12 (92.3)	-	-	-	-	-
Stent implantation, n		156 (85.7)	81 (86.2)	12 (92.3)	-	97 (78.9)	-	-	-
DES		62 (39.7)	81 (100)	4 (33.3)	-	-	-	-	-
BMS		94 (60.3)	0 (0)	8 (66.6)	-	-	-	-	-
Radial access, n		130 (71.4)	78 (83.0)	-	-	95 (76.2)	-	-	-
Complete revascularization, n		75 (41.2)	-	-	-	-	-	-	-
Study characteristics									
Trials		Rymuza et al.	Sahin et al.	Sim et al.	Vandecasteele et al.	Yudi et al.			
Study period		2004–2007	January 2005–December 2014	2007–2012	January 2007–December 2010	November 2011–July 2015			
Study design		Retrospective CS, multicentric, Poland	Retrospective CS, monocentric, Turkey	Retrospective CS, monocentric, Australia	Retrospective CS, nationwide registry, multicentric, Belgium	Retrospective CS, monocentric, Australia			
Included patients with STEMI		100	73	73	1092 991 considered in the present analysis	101			
Age group		≥80 but ≤90 y	≥90 y	≥80 y	≥80 y	≥85 y			
Invasive treatment									
Primary PCI		YES	YES	YES	YES	YES			
Rescue PCI		-	NO	-	YES	-			
Exclusion of thrombolysis		NO	YES	-	YES	-			
Exclusion of emergent CABG		NO	-	-	-	-			
Inclusion of failed revascularization in PCI group Intention-to-treat principle		NO	NO	NO	-				
Comparator treatment									
General strategy		CON, no CA	CON, no CA	CON, CA possible, no PCI	CON, no CA	CON, CA possible, no PCI			
Patients with thrombolysis		20 (40)	0 (0)	Not reported	0 (0)	0 (0)			
Follow-up period		1 y	26.5 mo (mean)	30 d	In-hospital period	739 d PCI (mean) 330 d CON (mean)			

(Continued)

Table 1. Continued

Study characteristics						
Trials		Rymuza et al.	Sahin et al.	Sim et al.	Vandecasteele et al.	Yudi et al.
Baseline characteristics of patients included						
PCI	Patients, n	50 (50)	42 (57.5)	34 (46.6)	840 (84.8)	45 (44.6)
CON	Patients, n	50 (50)	31 (42.5)	39 (53.4)	151 (15.2)	56 (55.4)
PCI	Age, median	83.0 [2.3]‡	91.2 [2.4]‡	84 [3.4]‡	83	87.7 [3.4]‡
CON	Age, median	83.9 [2.7]‡	92.3 [4.0]‡	86 [4.3]‡	85	90 [3.4]‡
PCI	Male patients, n	21 (42)	10 (23.8)	19 (55.9)	399 (47.5)	14 (31.1)
CON	Male patients, n	14 (28)	9 (29.0)	13 (33.3)	100 (66.2)	23 (41.1)
PCI	Hypertension, n	32 (64)	26 (61.9)	-	512 (61.0)	34 (75.6)
CON	Hypertension, n	28 (56)	19 (61.3)	-	92 (60.9)	42 (75)
PCI	Diabetes, n	10 (20)	16 (38.1)	11 (32.4)	139 (16.5)	10 (22.2)
CON	Diabetes, n	9 (18)	14 (45.2)	17 (43.6)	29 (19.2)	14 (25)
PCI	Smoking, n	-	5 (11.9)	-	-	-
CON	Smoking, n	-	2 (6.5)	-	-	-
PCI	Dyslipidemia, n	-	6 (14.3)	-	-	16 (35.6)
CON	Dyslipidemia, n	-	3 (9.7)	-	-	21 (37.5)
PCI	Previous MI, n	13 (26)	5 (11.9)	-	-	11 (24.4)
CON	Previous MI, n	8 (16)	7 (22.6)	-	-	15 (26.8)
PCI	STEMI-arrest, n	-	-	-	-	2 (4.4)
CON	STEMI-arrest, n	-	-	-	-	2 (3.6)
PCI	Cardiogenic shock, n	-	-	-	-	6 (13.3)
CON	Cardiogenic shock, n	-	-	-	-	11 (19.6)
PCI	Anterior STEMI, n	26 (52)	-	14 (41.2)	421 (50.1)	19 (42.2)
CON	Anterior STEMI, n	25 (50)	-	23 (59)	65 (43.0)	41 (74.5)
PCI	Inferior STEMI, n	-	-	17 (50)	-	20 (44.4)
CON	Inferior STEMI, n	-	-	14 (35.9)	-	11 (20)
PCI	Posterior STEMI, n	-	-	-	-	2 (4.4)
CON	Posterior STEMI, n	-	-	-	-	0 (0)
PCI	Lateral STEMI, n	-	-	2 (5.9)	-	4 (8.9)
CON	Lateral STEMI, n	-	-	1 (2.6)	-	2 (3.6)
PCI	Other STEMI	-	-	1 (2.9)	16 (1.9)	0 (0)
CON	Other STEMI	-	-	1 (2.6)	15 (9.9)	1 (1.8)
Procedural aspects in PCI group						
Coronary angiographies, n		-	43	Unclear	-	45
Initial TIMI flow 0, n		-	-	-	-	-
No culprit lesion identified, n		-	0 (0)	9	-	4 (8.9)
PCI performed, n		-	42 (100)	34	-	37 (82.2)
Stent implantation, n		-	34 (81)	-	-	35 (77.8)
DES			16 (47.1)			9 (25.7)
BMS			18 (52.9)			26 (74.3)
Radial access, n		-	0 (0)	-	-	
Complete revascularization, n		-	-	-	-	

Dashes indicate explicitly reported; brackets indicate SD; parentheses indicate percentages; *: mean instead of median; †: median instead of mean; ‡: missing data considered. BMS indicates bare metal stent; CA: coronary angiography; CABG, coronary artery bypass grafting; CON, conservative treatment; CS, case series; DES, drug-eluting stent; MI, myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-segment–elevation myocardial infarction; and TIMI, thrombolysis in myocardial infarction.

were more morbid and frailer compared with PCI group. The clinical status mainly contributed to the decision for or against reperfusion, and this selection into treatment groups represents an inherent source of confounding automatically favoring PCI group.

In detailed view of the other domains, 3 trials were judged to be at serious RoB in the “patient selection” domain.^{5,6,32} Of these, 1 trial excluded patients treated in December,⁵ 1 trial excluded critically ill patients and those who died on the day of admission,⁶ and 1 study

excluded patients with unsuccessful PCI as well as those with serious comorbidities potentially affecting the outcome.³²

One study²⁹ excluded invasively managed patients without a culprit lesion from the PCI group. This indicates moderate-to-serious RoB in “classification of intervention” domain.

In analysis of the “deviations from intended intervention” domain 5 trials were judged to be at serious RoB.^{26,32,33,35,36} Crossover from patients with either failed PCI or without clear culprit lesions to the CON group and evidence of facilitated PCI in an unknown proportion of the CON group in 1 trial were the drivers of this judgment. In 1 other study 40% of CON patients were treated with fibrinolytic therapy as reperfusion strategy,³² and 8 trials did not specify whether patients received pharmacological reperfusion or not.

A source of “other bias” was present, as medical postinfarction therapy did differ between the CON and PCI groups in many studies with more guideline adherence in the PCI group. This might have contributed to both short- and long-term outcome.

Primary Outcome Analysis: Overall Survival

All 13 studies including 102 158 older patients were considered in the primary outcome analysis. Of these, 31 629 received PCI and 70 529 were managed conservatively. The overall survival was 76.5% in PCI and 67.2% in CON at the time of longest available follow-up (see Figure 2, OR, 2.18 [95% CI, 1.79–2.66], $P<0.001$, $I^2=88\%$, favoring PCI, considerable heterogeneity). Both visual and quantitative funnel plot analysis

showed asymmetry indicating publication bias (see Figure S1, Egger’s test P value 0.0086).

Sensitivity Analysis

The first sensitivity analysis was based on the RoB assessment and included all trials with $\leq$ moderate RoB in all other domains than confounding. Five studies were eligible. The overall survival was 76.2% in PCI and 57.6% in CON group (see Figure S2, OR 2.52 [95% CI, 1.88–3.38], $P<0.001$, $I^2=0\%$, favoring PCI, nonimportant heterogeneity).

The second post hoc sensitivity analysis excluded the 2 registries,^{5,6} including 98% of patients and contributing to a statistical weight of 37% in the primary outcome analysis. This test was performed to further assess validity of results and to overcome statistical heterogeneity detected in I^2 statistics. Ultimately, 2895 patients remained for this exploratory analysis. Of these, 1665 were treated with PCI and 1230 were managed conservatively. Consistently, the overall survival rate was 78.9% in the PCI and 56.9% in the CON group at the time of longest available follow-up (OR 2.38 [95% CI, 1.96–2.90], $P<0.001$, $I^2=3\%$, favoring PCI, nonimportant heterogeneity). The third sensitivity analysis was based on a fixed effects model and resulted in an OR of 1.67 with a narrower CI: 1.62 to 1.72 ($P<0.0001$, favoring PCI).

Subgroup Analysis

Subgroup analysis of studies with a follow-up duration exceeding the 1-year period included 3 reports.^{27,28,33} The mean follow-up varied from 21.7 to 26.5 months.

Table 2. Risk of Bias Assessment of Nonrandomized Controlled Studies of Interventions

	Confounding	Patient selection	Classification of intervention	Deviations from the intended interventions	Missing data	Outcome measurement	Selection of the reported results	Overall risk of bias
Cepas-Guillén et al.	Critical	Moderate	Moderate	Serious	Low	Low	Moderate	Critical
Hu et al.	Critical	Moderate	Moderate	Moderate	Low	Low	Moderate	Critical
Ionescu et al.	Critical	Moderate	Moderate	Moderate	Low	Low	Moderate	Critical
Ismayl et al.	Critical	Serious	Moderate	Moderate	Low	Low	Moderate	Critical
Kumar et al.	Critical	Moderate	Moderate to serious	Moderate	Low	Low	Moderate	Critical
Pajjuru et al.	Critical	Serious	Moderate	Moderate	Low	Low	Moderate	Critical
Piegza et al.	Critical	Moderate	Moderate	Moderate	Low	Low	Moderate	Critical
Ricci et al.	Critical	Moderate	Moderate	Moderate	Low	Low	Moderate	Critical
Rymuza et al.	Critical	Serious	Moderate	Serious	Low	Low	Moderate	Critical
Sahin et al.	Critical	Moderate	Moderate	Serious	Low	Low	Moderate	Critical
Sim et al.	Critical	Moderate	Moderate	Moderate	Low	Low	Moderate	Critical
Vandecasteele et al.	Critical	Moderate	Moderate to serious	Serious	Low	Low	Moderate	Critical
Yudi et al.	Critical	Moderate	Moderate	Serious	Low	Moderate	Moderate	Critical

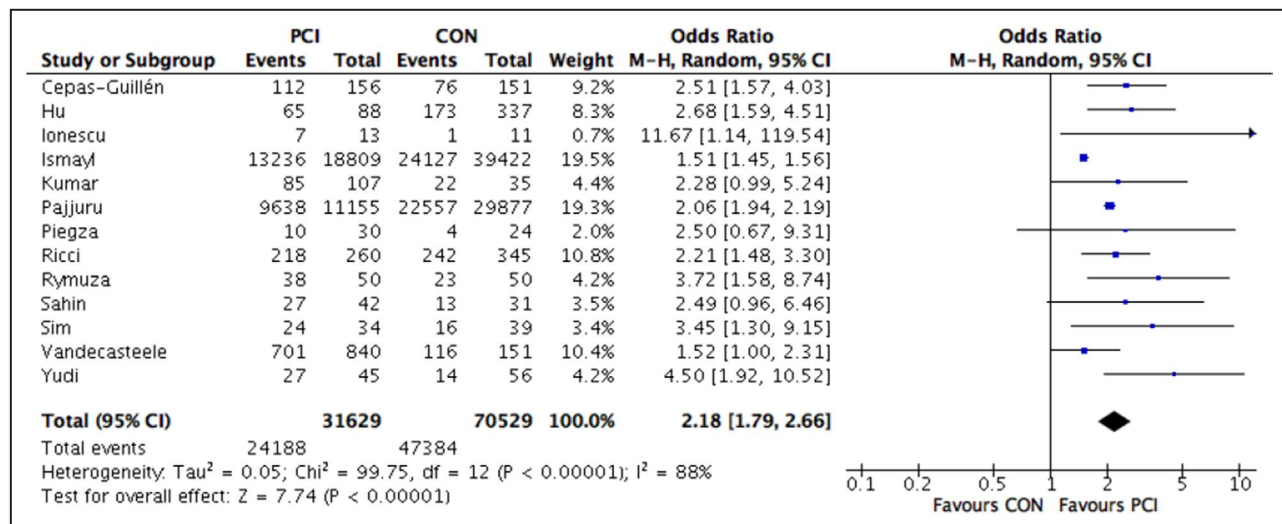


Figure 2. Forest plot of overall survival analysis.

CON indicates conservative treatment; M-H, Mantel-Haenszel; and PCI, percutaneous coronary intervention.

The overall survival was 69.2% in PCI and 49.3% in CON group (see Figure S3, OR, 2.78 [95% CI, 1.78–4.36], $P < 0.001$, $I^2 = 0\%$, favoring PCI, nonimportant heterogeneity).

Secondary Outcome Analyses

In-Hospital Mortality

Overall, 100832 patients from 8 studies were analyzed. The event rate was 15% in the PCI and 28.9% in the CON group (see Figure 3A, OR, 0.45 [95% CI, 0.38–0.54], $P < 0.001$, $I^2 = 80\%$, favoring PCI, considerable heterogeneity).

Short-Term 30-Day All-Cause Mortality

A total of 1511 patients from 7 studies were eligible. The event rate was 19.2% in the PCI and 35.4% in the CON group (see Figure 3B, OR, 0.40 [95% CI, 0.30–0.52], $P < 0.001$, $I^2 = 0\%$, favoring PCI, nonimportant heterogeneity).

Long-Term 1-Year All-Cause Mortality

Overall, 777 patients from 6 studies were analyzed. The event rate was 29.1% in the PCI and 54.4% in the CON group (see Figure 3C, OR, 0.34 [95% CI, 0.25–0.46], $P < 0.001$, $I^2 = 0\%$, favoring PCI, nonimportant heterogeneity).

Cardiac Mortality

A total of 671 patients from 2 studies were analyzed. The event rate was 18.0% in the PCI and 38.8% in the CON group (see Figure 3D, OR, 0.35 [95% CI, 0.23–0.52], $P < 0.001$, $I^2 = 0\%$, favoring PCI, nonimportant heterogeneity).

Major Bleeding

Overall, 893 patients from 6 studies were eligible. The event rate was 5.6% in the PCI and 4.1% in the CON group (see Figure 4, OR, 1.55 [95% CI, 0.77–3.12], $P = 0.22$, $I^2 = 0\%$, nonimportant heterogeneity).

Heart Failure Hospitalizations

A total of 37694 patients from 3 studies were analyzed. The event rate was 20.7% in the PCI and 18.4% in the CON group (OR, 1.17 [95% CI, 1.11–1.23], $P < 0.001$, $I^2 = 0\%$, favoring CON, nonimportant heterogeneity).

Repeated Hospitalizations of Any Cause

Overall, 37387 patients from 3 studies were analyzed. The event rate was 22.1% in the PCI and 16.2% in the CON group (OR 1.31 [95% CI 0.70–2.46], $P = 0.40$, $I^2 = 22\%$, nonimportant heterogeneity).

Sensitivity analyses for all secondary outcomes using a fixed effects model are presented in Figure S4.

DISCUSSION

The present meta-analysis comprehensively assessed efficacy and safety of an invasive triage with intended PCI compared with conservative treatment in older patients with STEMI. The main and novel findings were:

- The minority of the older patients with STEMI (31%) were triaged to invasive strategy with PCI; these data are dominated by all-comer registries with reduced quality of evidence

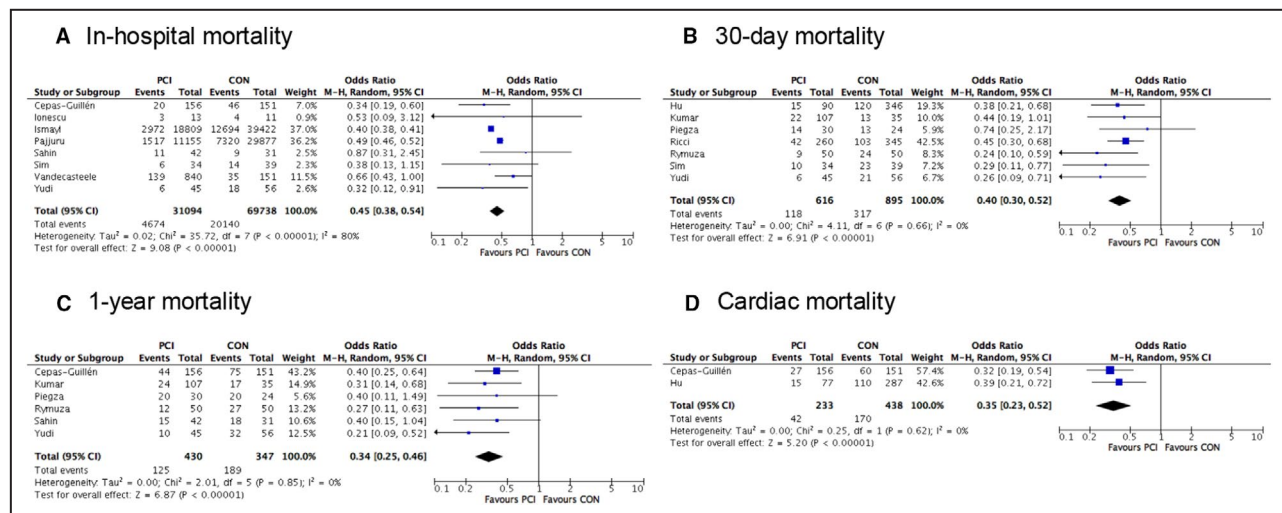


Figure 3. Secondary mortality analyses. A, In-hospital mortality. B, 30-day mortality. C, 1-year mortality. D, Cardiac mortality.

CON indicates conservative treatment; M-H, Mantel-Haenszel; and PCI, percutaneous coronary intervention.

- PCI was associated with a more favorable overall survival and short- and long-term mortality, but patients referred for PCI were specifically selected as candidates for reperfusion indicating confounding
- Every second patient in CON group survived for 1 year or longer despite the deprivation of PCI
- There was no difference in major bleeding between PCI and CON indicating an acceptable risk profile
- Heart failure hospitalizations and any hospitalizations were more likely in PCI group

In patients with STEMI the triage to invasive strategy including PCI represents the standard of care. This contemporary STEMI guideline recommendation is independent of age.¹⁴ Accordingly, preexisting observational reports proved technical feasibility of PCI and showed acceptable short- and midterm survival in older patients with STEMI.^{37–39} In addition, PCI was superior to fibrinolysis in older patients with AMI.⁴⁰ These findings support

that PCI might be preferred over other treatment strategies even in older patients with STEMI. Nonetheless, the present systematic analysis indicates an underuse of PCI in older patients in the published literature. This discrepancy was mostly driven by national registries reporting on nonagenarians.^{5,6} Ageism might be hypothesized, but the individual reasons against invasive management remain unclear in study-level meta-analysis. Some authors clarified the decision-making process. The predominant reasons to not triage older patients to invasive strategy were age,^{28,35} cognitive impairment,^{26,28,35,36} known comorbidities,^{28,29,32,35} cardiogenic shock, or resuscitation.^{29,32,35} Additionally, impaired functional status, frailty, impaired mobility, or admission from residential care were reported.^{26,34,36} This emphasized that the CON group had an inherent risk of worse outcome reflecting clinical variation between the groups. Consequently, the advantageous overall survival following invasive triage to PCI was an expected finding and the positive selection

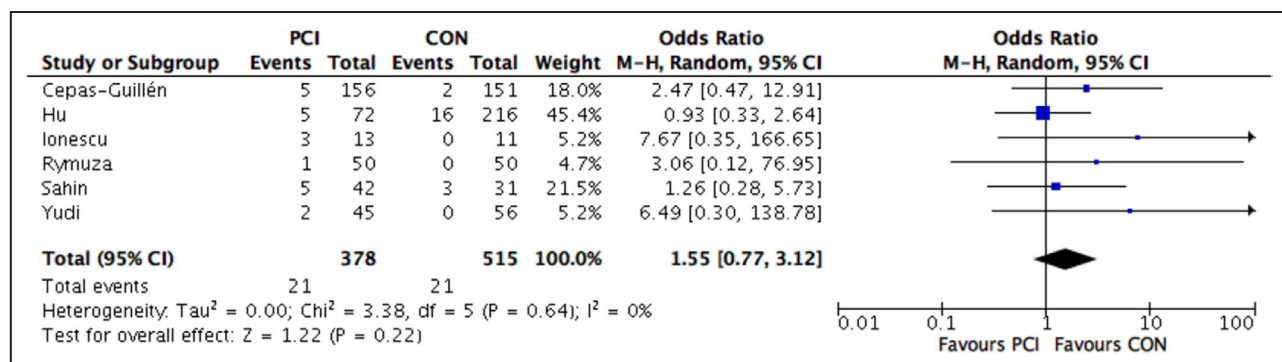


Figure 4. Forest plot of major bleeding.

CON indicates conservative treatment; M-H, Mantel-Haenszel; and PCI, percutaneous coronary intervention.

process in this group might have even intensified the observed outcome difference.

The survival advantage following PCI was not limited to the first year following STEMI. Instead, this advantage was even present in those trials with a longer follow-up duration.^{27,28,33} Surprisingly, the long-term overall survival was remarkably high in the CON group. Even though these patients were judged to be “not suitable” for primary PCI at index STEMI event, they had an acceptable long-term prognosis. This finding challenges the ad hoc triage to conservative management in this cohort with more morbidity as PCI represents a potentially life-saving intervention with acceptable procedural risk. The reasonable risk profile is further supported by the finding that there was no difference in major bleeding events in the present analysis. Major bleeding was the only safety end point, and other safety outcomes were not considered. Hence, the selection of those older patients with STEMI with an expected survival advantage following PCI requires further rework.

Timely treatment of AMI in older patients is challenging: they might present with unusual symptoms including dyspnea, syncope, or unexplained fall resulting in diagnostic delay.⁴¹ Moreover, clinical judgment should consider all dimensions, and ideally high prevalent geriatric syndromes like frailty, cognitive impairment, and comorbidities^{9,42,43} should be thoroughly assessed and weighed in decision making. These steps delay invasive treatment. On the other hand, structured recording of frailty and significant cognitive impairment might prevent this vulnerable cohort from unwanted and potentially harmful invasive management. In such patients, goal-oriented management might be preferred and shared decision making is required. Again, selection remains a frequent dilemma.

The present analysis showed that patients allocated to invasive strategy had a higher risk of subsequent heart failure hospitalization and of hospitalization from any cause. The increased hospitalizations might be attributed to the procedural risk of PCI itself or to pronounced awareness of caregivers for these patients who were recently suitable for interventional revascularization (positive selection). Notably, those selected for noninvasive management in clinical events with precise interventional treatment algorithms like STEMI will not be admitted to hospital for less impactful events like heart failure in the future. Potentially, treatment goals were redefined to avoid inappropriate therapy in these patients (“primum non nocere”) at end of life or with end-stage disease. As a result, undertreatment might have resulted in underestimation of hospitalizations in the CON group. Additionally, survivorship bias arising from the subgroup with more morbidity with higher mortality might contribute to increase hospitalization rate in the PCI group.

Ultimately, timely patient selection for invasive strategy in older people with STEMI remains a challenge in daily routine. Age itself should not per se determine the allocation to a treatment strategy as even older people might be long-term survivors.¹⁷ A prospective randomized controlled trial assessing the optimized treatment strategy of older patients with STEMI is desired. But recruitment could become an insuperable challenge^{8,40} and extensive screening efforts could be anticipated from comparable AMI trials in older patients.^{9,44} Beyond the well-established end points the use of patient-oriented outcomes might add further value because a potential gain or loss in quality of life might contribute to decision making.

Limitations

Confounders on individual study level and interstudy heterogeneity were acknowledged. The main concern was the evidence of significant imbalances in both confounding and selection into the study. Patients in the CON group suffered from negative selection as they were not suitable for catheterization or refused invasive strategy. The extracted data were restricted to study-level reports. As a result, adjusted analysis stratifying for these imbalances was not possible but would have offered further value.

Most patients were nonagenarians (98%), both octogenarians and centenarians were underrepresented, and generalizability to these subgroups is limited. This very old population is at risk of underlying survivorship bias which is an unmeasurable confounder in study-level meta-analysis.

Moreover, the authors were not able to analyze all prespecified outcomes. Major adverse cardiac events, minor bleeding, and overall bleeding were not thoroughly reported in the analyzed studies. Outcome analysis is further affected by variance in outcome definition. Precisely, cardiac mortality, heart failure hospitalizations, and major bleeding were assessed as defined in the individual trials which indicates heterogeneity.

In addition, the use of antithrombotics and revascularization therapy differed between the studies. The duration of antiplatelet therapy is a rapidly evolving research field, and stratified, patient-oriented deescalation strategies were recently proposed.^{14,45} The current evidence indicates that shorter duration of antiplatelets might be equally effective and associated with lower bleeding in older patients after PCI.⁴⁶ But high-quality studies to direct antithrombotic treatment in older patients with STEMI are pending.

The precise angioplasty strategy was extractable for only 1% of the PCI population. This is an inherent source of bias and mainly caused by the retrospective study design of included trials. Nonetheless, PCI using

bare metal stents was a prevalent strategy (45.9%) whenever the rate was reported. This might be related to the treatment periods with the first patient treated in 2003 and the last patient treated in 2019. To date, drug-eluting stents are explicitly preferred over bare metal stents, but again older people were underrepresented in these landmark trials, and further research is warranted.^{47,48}

CONCLUSIONS

The meta-analysis indicates a potential underuse of PCI in older patients with STEMI in the published literature. PCI was advantageous in short- and long-term survival compared with conservative treatment, but these results were affected by confounding with more unfavorable characteristics in conservatively managed patients.

Surprisingly, the half of the older patients with STEMI not referred for invasive management survived for at least 1 year or longer. This observation in combination with the comparable rate of major bleeding both challenge the ad hoc triage to conservative management in this cohort with more morbidity.

Ultimately, these findings have hypothesis-generating implications. But they emphasize the limited predictive value of age in the triage of STEMI and that PCI should not be automatically withheld in older patients. There is still demand for a RCT assessing efficacy of PCI in STEMI in older patients, but recruiting of representative patients might be an insuperable challenge.

ARTICLE INFORMATION

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Supplemental Material

Data S1

Tables S1–S2

Figures S1–S4

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