Coronary angiography after out-of-hospital cardiac arrest without ST-segment elevation: a systematic review and meta-analysis of randomised trials

Gonçalo Ferraz Costa[a,b,c], Iolanda Santos[d], João Sousa[d], Sofia Beirão[d] and Rogério Teixeira[a,b,c]

Background **Out-of-hospital cardiac arrest (OHCA) has a poor prognosis. The optimal timing and role of early coronary angiography (CAG) in OHCA patients without ST-segment elevation remains unclear. The goal of this study is to compare an early CAG versus delayed CAG strategy in OHCA patients without ST elevation.**

Methods **We systematically searched PubMed, Embase and Cochrane databases, in June 2022, for randomised controlled trials (RCTs) comparing early versus delayed early CAG. A random effects meta-analysis was performed.**

Results **A total of seven RCTs were included, providing a total of 1625 patients: 816 in an early strategy and 807 in a delayed strategy. In terms of outcomes assessed, our meta-analysis revealed a similar rate of all-cause mortality (pooled odds ratio [OR] 1.22 [0.99–1.50], $P = 0.06$, $I^2 = 0\%$), neurological status (pooled OR 0.94 [0.74–1.21], = 0.65, $I^2 = 0\%$), need of renal replacement therapy (pooled OR 1.11 [0.78–1.74], $P = 0.47$, $I^2 = 0\%$) and major bleeding events (pooled OR 1.51 [0.95–2.40], $P = 0.08$, $I^2 = 69\%$).**

Conclusion **According to our meta-analysis, in patients who experienced OHCA without ST elevation, early CAG is not associated with reduced mortality or an improved neurological status. *Coron Artery Dis* 35: 67–75 Copyright © 2023 The Author(s). Published by Wolters Kluwer Health, Inc.**

Coronary Artery Disease 2024, **35**:67–75

Keywords: coronary angiography, emergency medicine, out-of-hospital cardiac arrest

[a]Serviço de Cardiologia, Centro Hospitalar e Universitário de Coimbra, [b]Serviço de Medicina Intensiva, Centro Hospitalar e Universitário de Coimbra, [b]Faculdade de Medicina da Universidade de Coimbra, [c]Coimbra Institute for Clinical and Biomedical Research (iCBR), Coimbra and [d]Serviço de Medicina Intensiva, Centro Hospitalar e Universitário de Coimbra, Portugal

Correspondence to Gonçalo Ferraz Costa, MSc, Serviço de Cardiologia, Hospital Geral – Centro Hospitalar e Universitário de Coimbra, Quinta dos Vales, S. Martinho do Bispo, 3041-801 Coimbra, Portugal
Tel: +351911997603; e-mail: gnfcosta.93@gmail.com

Received 17 July 2023 **Accepted** 12 August 2023.

Introduction

Despite advancements in the treatment of post-cardiac arrest, out-of-hospital cardiac arrest (OHCA) remains a primary cause of mortality [1,2]. The percentage of hospital-discharged patients with no or minor neurological sequelae ranges from 2 to 18% [3]. Up to 80% of all causes of cardiac arrest are attributable to coronary artery disease, primarily acute coronary artery occlusion [4]. Nevertheless, the selection of patients for an invasive approach is still a matter of contention. If ST-segment elevation is found on a post-resuscitation electrocardiogram (ECG), the chance of detecting an acute coronary artery lesion during early coronary angiography (CAG) is substantial (70 to 80%) according to several retrospective investigations [5,6]. Therefore, guidelines propose doing an emergency CAG in sudden cardiac death survivors with no clear non-cardiac cause of arrest and ST elevation [7]. Regarding patients experiencing cardiac arrest without ST-segment elevation on post-resuscitation ECG, the utility of an emergency CAG remains debatable. In these patients, the incidence of an acute coronary artery lesion is considerably reduced (15–20%) [8]. This topic has been the subject of multiple trials and meta-analysis, but with several limitations [9–15]. Verma *et al*. analysis revealed no significant difference in mortality or neurological status [16]. However, recent published trials may further add to the body of evidence regarding this topic [17,18].

Therefore, the primary goal of this study is to conduct an updated systematic review and meta-analysis of clinical studies evaluating the efficacy and safety of early CAG in patients with cardiac arrest and no ST-segment elevation on their post-resuscitation ECG.

Methods

Protocol and registration

This study was designed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Supplementary Table 1, Supplemental digital content 1, *http://links.lww.com/MCA/A602*). This systematic review and meta-analysis was registered with the International Prospective

Supplemental Digital Content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website, www.coronary-artery.com.

DOI: 10.1097/MCA.0000000000001298

Key messages

(1) What is already known about this subject?
  (a) The timing and role of early coronary angiography in out-of-hospital cardiac arrest patients without ST-segment elevation remains unclear.
(2) What does this study add?
  (a) Routine early coronary angiography is not associated with reduced mortality, or an improved neurological status compared to a delayed strategy;
  (b) Early coronary angiography presented a similar a rate of major bleeding event and renal replacement therapy.
(3) How might this impact on clinical practice?
  (a) Change management of out-of-hospital cardiac arrest patients without ST-segment elevation

Register of Systematic Reviews Database (PROSPERO) (CRD42022321076). Ethical approval was not required because this study retrieved and synthesised data from already published studies.

Review questions

The review questions that drove this systematic review and meta-analysis using PICOST frame was: In patients who experienced OHCA without ST-segment elevation (Population), does early CAG (Intervention) compared to delayed CAG (Comparison) reduce all-cause mortality and/or improved neurological status (Outcomes)? Is this strategy associated with higher rate of periprocedural complication, as renal replacement therapy or major bleeding events?

Literature search

We systematically searched Pubmed, Embase and Cochrane databases from their inception to June 2022 for both full-length and randomised clinical trials that compared early and delayed CAG in patients with cardiac arrest and no ST-segment elevation on their post-resuscitation ECG. The definition of OHCA was based on those used in the included individual studies. The search was not limited by language. Supplementary Table 2, Supplemental digital content 1, *http://links.lww.com/MCA/A602* describes the search strategy in detail.

Eligibility criteria

Studies were included if they fulfilled the following criteria: 1) Patients older than 18 years who experienced an OHCA; 2) Return of spontaneous circulation (ROSC) without an obvious non-cardiac cause of arrest and without ST-segment elevation; 3) Studies compared early versus delayed CAG; 4) Information on outcomes during follow-up was reported; 5) Randomised clinical trial design or post-hoc analysis of clinical trials. We excluded retrospective studies, abstracts, reviews, case reports, meeting abstracts and editorial material.

Outcome measures

The primary endpoint was all-cause mortality. Subgroup analysis was performed regarding 30- and 180-day mortality. Neurological status, frequency of percutaneous coronary intervention (PCI) after CAG, major bleeding events and acute renal worsening were secondary outcomes. Neurological status was defined in terms of a cerebral performance category score. Scores of 1 and 2 were deemed to indicate good neurological status, and scores of 3 to 5 were defined to indicate poor neurological status. Major bleeding events were defined as major bleeding according to the Thrombolysis in Myocardial Infarction classification or types 2 to 5 on the Bleeding Academic Research Consortium scale [19]. Another safety outcome was the use of renal replacement therapy.

Data collection and management

Two investigators (G. Ferraz Costa, I. Santos) independently screened titles and abstracts of publications retrieved according to a search strategy in order to select studies that met the inclusion criteria outlined above. Secondly, identified articles were subjected to full-text review. Data was extracted on the study population, main demographic and baseline characteristics, interventions and the outcomes described above. We analysed studies with multiple publications in sequence, ensuring no duplication of results, and which collected the most recent data.

Risk of bias assessment

Two authors (G.C, I.S) independently assessed the risk of bias in the included articles, following the Cochrane Collaboration's 'Risk of bias' tool for randomised controlled trials (RCTs). RCTs were assessed as having a 'low', 'high' or 'unclear' risk for the following biases: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other biases. The quality assessment for each study is presented in a 'risk of bias summary'. Publication bias was assessed using funnel plots (Supplementary Figures 1–4, Supplemental digital content 1, *http://links.lww.com/MCA/A602*). The certainty of the evidence was evaluated using the (Grades of Recommendation, Assessment, Development and Evaluation approach.

Patient and public involvement

Patients and the public were not involved in this research study. The study was designed and conducted by researchers with expertise in the relevant field. The study was conducted in accordance with ethical guidelines and regulatory requirements to ensure that the rights and interests of participants were protected.

Statistical analysis

We pooled dichotomous data using odds ratios (OR) to describe effect sizes and a Mantel–Haenszel procedure in a random effects model. The mean effect was considered significant if its 95% confidence interval (CI) did not include zero. Heterogeneity was assessed statistically using an I^2 index (<25% low, 25–50% moderate, >50% high heterogeneity). Publication bias was assessed visually using funnel plots. A P value < 0.05 was considered statistically significant.

Results

Search results

A literature search identified 2928 articles relevant to this meta-analysis. After the removal of duplicates, we excluded 1879 publications according to title and abstract assessment, study type and study population. Seven randomised clinical trials were included [9,11,13,17,18,20], providing a total of 1625 patients: 816 in an early strategy and 807 in a delayed strategy. Figure 1 displays the PRISMA flow diagram for the study search and selection. Study characteristics relating to the included studies are described in Table 1 and baseline characteristics of the included patients are summarised in Table 2. CAG findings are summarised in Supplementary Table 3, Supplemental digital content 1, *http://links.lww.com/MCA/A602*.

In all trials, groups were balanced for key baseline characteristics. Two trials exclusively enrolled patients who had experienced witnessed OHCA [11,18]. The remaining trials included both witnessed and non-witnessed cases, despite the majority of included participants being witnessed. In the studies conducted by Lemkes *et al.* and Patterson *et al.* [12,18], all patients underwent Targeted Temperature Management (TTM) regimens. At the same time, the incidence of TTM varied between 50% and 90% in the remaining studies. In two trials, only patients with an initial shockable rhythm were included [12,18]. In the remaining studies, both types of rhythms were allowed. Coronary artery disease and PCI performance were similar between the two groups in all trials, but had a higher absolute number in the early angiography group. Viana-Tejedor *et al.* were underpowered due to a lower number of enrolled participants than the calculated sample size [17].

Primary outcome

Our meta-analysis of all included studies showed a similar all-cause mortality for an early CAG strategy compared with the delayed CAG group (pooled OR, 1.22 95% CI [0.99–1.50], P = 0.06; I^2 = 0%) (Fig. 2). Subgroup analysis of 180-day and 30-day survival maintained no significant all-cause mortality difference (pooled OR, 1.15; 95% CI [0.77–1.72], P = 0.50; I^2 = 0% and pooled OR, 1.21; 95% CI [0.90–1.62], P = 0.21; I^2 = 0%, respectively).

Secondary outcomes

Regarding secondary endpoints, an early CAG strategy demonstrated no significant difference concerning neurological status (pooled OR 0.94 [0.74–1.21], P = 0.65, I^2 = 0%), need for renal replacement therapy (pooled OR 1.11 [0.78–1.74], P = 0.47, I^2 = 0%), major bleeding events (pooled OR 0.97 [0.56–1.69], P = 0.92, I^2 = 0%) (Fig. 3) and primary coronary intervention (pooled OR 1.51 [0.95–2.40], P = 0.08, I^2 = 69%).

Risk of bias and evidence certainty

Overall, all included trials had a relatively low risk of bias. However, due to the nature of the interventions, there is a high risk of bias in the blinding of participants and personnel (Supplementary Table 4, Supplemental digital content 1, *http://links.lww.com/MCA/A602*). Therefore, in terms of the certainty of evidence, we consider moderate certainty for the outcomes assessed (Supplementary Table 5, Supplemental digital content 1, *http://links.lww.com/MCA/A602*).

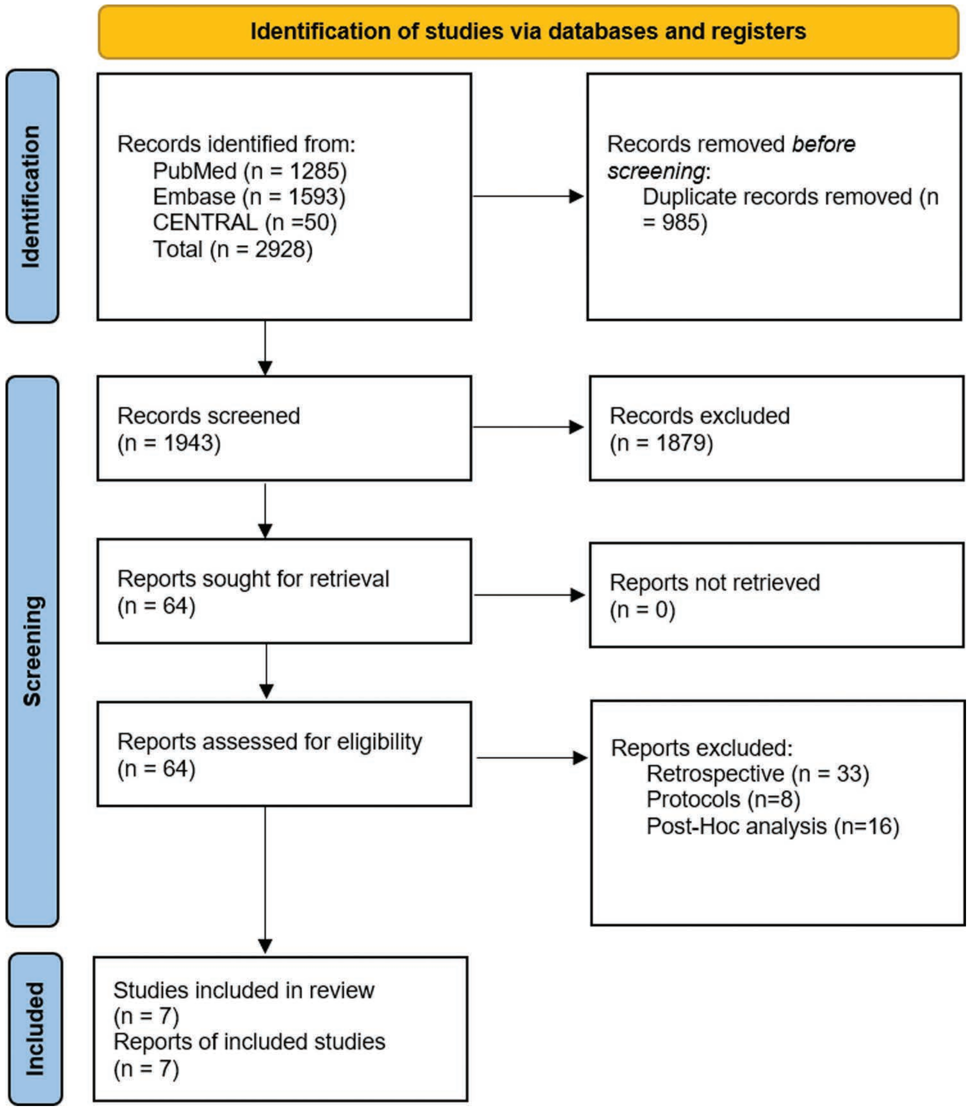
Discussion

This meta-analysis demonstrates that delaying CAG in patients following OHCA without ST elevation has no impact on all-cause mortality, both at 30- and 180-day follow-up. Additionally, no significant difference was identified in neurologic status, need for renal replacement therapy or major bleeding events.

Several findings may account for the doubtful benefit of rapid CAG. Forty percent of patients in the total group were determined to have a coronary culprit lesion that was responsible for initiating an incident. A possible advantage of CAG would only be anticipated in the subgroup of patients in whom coronary disease has been detected and revascularization has been considered for the treatment of persistent ischaemia. In all other patients, urgent, unselected CAG would raise the risk of procedural problems without benefit and might postpone the identification of the cause of the cardiac arrest and subsequent therapy. Therefore, identification of patients who have a severe coronary occlusion requires additional development.

An ECG is an important tool to triage patients after ROSC. The identification of acute occlusion myocardial infarction (OMI) patterns is essential for managing patients who will benefit from emergent reperfusion therapy [21]. Currently, guidelines recommend an ST-elevation vs. non-ST-elevation strategy [22]. However, 25–30% of non-ST-elevation myocardial infarctions (NSTEMI) present with OMI and are

Fig. 1



Flow diagram.

discovered only on delayed cardiac catheterisation [23]. Such subsets of patients have an increased incidence of major adverse events compared with NSTEMI without OMI [23]. Many authors have suggested that a new paradigm shift is needed in the classification of heart attacks from STEMI/NSTEMI to OMI/non-OMI. This is because OMI can be accurately identified by examining additional ECG features, including minor ST-elevations that do not meet STEMI criteria, disproportionate ST-elevations relative to preceding QRS, unusual patterns that show opposite ST deviations in contiguous leads, and some patterns that do not exhibit ST-elevation at all (such as subtle ST-segment elevation, reciprocal depression, hyperacute T-waves, and DeWinter's pattern) [24]. A recent clinical trial (NCT04022668) reliably detected OMI in patients with NSTEMI, resulting in better long-term mortality compared to a NSTEMI vs. STEMI approach [25].

Another tool to triage ROSC is a point-of-care ultrasound. It potentially identifies reversible causes of cardiac arrest, such as pericardial tamponade or right heart strain indicative of pulmonary embolism [26]. Additionally, it can accurately assess cardiac activity since variability exists in physicians' interpretations of cardiac activity [26]. However, the assessment of ejection fraction and contractility regional abnormalities may not be a reliable indicator of OMI because in survivors of OHCA, hemodynamic instability post-resuscitation is present frequently at admission, presenting as a severely depressed ejection fraction due to myocardial stunning [27]. In a study assessing haemodynamics in patients, post-resuscitation, immediate CAG was performed in all patients at admission. Severe but transient myocardial dysfunction was observed in 49.3% of patients (with no acute coronary occlusion) [28].

A risk prediction model for the existence of an acute coronary lesion in resuscitated individuals was created by Waldo *et al* [29]. They identified four variables: angina prior to cardiac arrest, congestive heart failure, shockable rhythm and STE, with the latter having the most points. However, few studies have focussed on the identification of CAG candidates based on a neurologic prognosis in OHCA survivors without STE. Except for those with ST-elevation myocardial infarction or cardiogenic shock, it is currently unknown which categories would benefit from early CAG [30,31]. A study utilising the International Cardiac Arrest Registry created a prediction model of CREST scores for circulatory-aetiology mortality based on data obtained at the time of ICU admission for OHCA patients without STE [32]. A history of coronary artery disease, non-shockable rhythm, initial left ventricular ejection fraction < 30%, shock upon presentation and total ischaemia duration >25 min correctly and pragmatically predicted the probability of death due to circulatory aetiology. The American College of Cardiology

Table 1 Study characteristics

Author	Trial name	Number of patients: Early CAG	Number of patients: Delayed CAG	Definition of early CAG	Definition of delayed CAG	Major bleeding criteria	Duration of follow-up, days
Patterson *et al.* (2017) [39]	ARREST	18	18	Directly after hospital admission	Within 48–72 h if not performed sooner	Not specified	30
Lemkes *et al.* (2019) [12]	COACT	273	265	Within 2 h after randomisation	After neurologic recovery	TIMI	90
Elfwén *et al.* (2019) [11]	DISCO	38	40	Within 2 h after admission	Not be performed earlier than 3 days	Bleeding with decrease in haemoglobin >50 g/L	4
Kern *et al.* (2020) [13]	PEARL	49	50	Within 120 min of arrival at the PCI-capable centre	After 6 h of hospital arrival	BARC	180
Desch *et al.* (2021) [9]	TOMA-HANK	265	265	As soon as possible after hospital admission	After a minimum delay of 24 h after cardiac arrest	BARC	30
Hauw-Berlemont *et al.* (2022) [14]	EMERGE	141	138	Immediately after admission	Performed after 48–96 h after admission	NR	180
Viana-Tejedor *et al.* (2022) [17]	COUPE	32	34	Within 2 h after admission	Performed after neurological recovery, when patient extubated, before hospital discharged	BARC	30

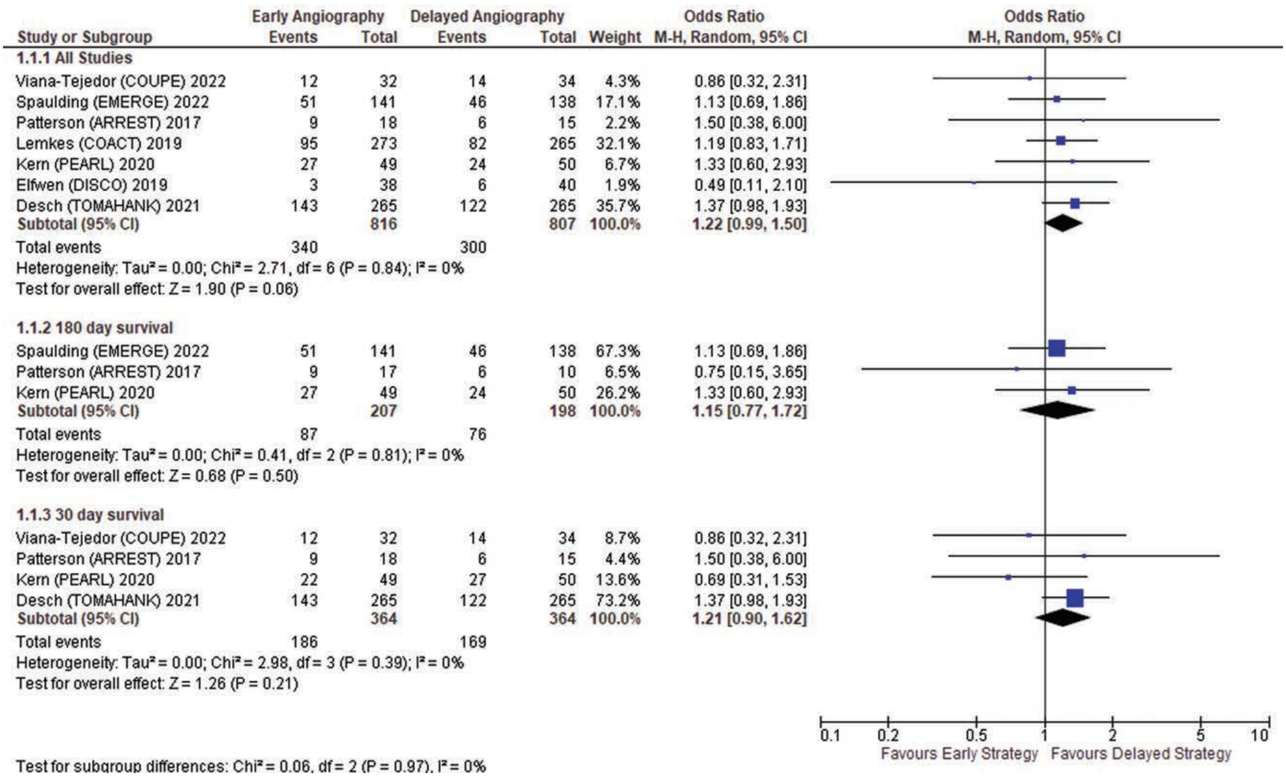
BARC, bleeding academic research consortium; CAG, coronary angiography; NR, not reported; OHCA, out-of-hospital cardiac arrest; TIMI, thrombolysis in myocardial infarction.

Table 2 Demographics and baseline characteristics of included patients

Author	Age, years: Early CAG	Age, years: Delayed CAG	Male gender, n (%): Early CAG	Male gender, n (%): Delayed CAG	Hypertension: Early CAG	Hypertension: Delayed CAG	Diabetes: Early CAG	Diabetes: Delayed CAG	Smoking: Early CAG	Smoking: Delayed CAG
Patterson *et al.* (2017) [39]	60 ± 17	61 ± 14	15 (83)	16 (89)	8 (44%)	7 (39%)	4 (22%)	2 (11%)	4 (22%)	3 (17%)
Lemkes *et al.* (2019) [12]	65.7 ± 12.7	64.9 ± 12.5	223 (82)	202 (76)	131 (49%)	126 (48%)	55 (20%)	44 (17%)	50 (20%)	67 (27%)
Elfwén *et al.* (2019) [11]	71 (62–78)	70 (61–77)	22 (58)	31 (78)	NR	NR	6 (16%)	10 (25%)	NR	NR
Kern *et al.* (2020) [13]	65.0 (57–73)	65.5 (59–72)	42 (85.7)	36 (72.0)	26 (53.1%)	29 (58%)	11 (22.4%)	16 (32%)	NR	NR
Desch *et al.* (2021) [9]	69 (59–78)	71 (60–79)	185 (69.8)	184 (69.4)	161 (67.1%)	162 (69.2%)	71 (29.1%)	74 (29.5%)	49 (29.9%)	59 (34.5%)
Hauw-Berlemont *et al.* (2022) [14]	65.4 ± 13.8	63.9 ± 15.4	103 (73.1)	92 (66.7)	NR	NR	NR	NR	NR	NR
Viana-Tejedor *et al.* (2022) [17]	66.5 (60–73.5)	60.5 (55–71)	26 (81.3)	25 (73.6)	22 (68.8%)	22 (66.7%)	5 (15.6%)	10 (30.3%)	7 (21.9%)	10 (29.4%)

CAG, coronary angiography; NR, not reported.

Fig. 2



Forest plot of all-cause mortality comparing early CAG strategy versus non-early CAG strategy. CAG, coronary angiography; CI, confidence interval; M–H, Mantel–Haenszel.

Interventional Council recommended triaging OHCA survivors based on 10 unfavourable resuscitation features, as determined by consensus: unwitnessed arrest, initial rhythm non-ventricular fibrillation, no bystander cardiopulmonary resuscitation, >30 min from collapse to ROSC (time-to-ROSC), ongoing cardiopulmonary resuscitation, pH 7.2, lactate > 7 mmol/L, age > 85 years, end-stage renal disease, and non-cardiac aetiology [33]. In addition, a recent study by Harhash *et al.* sought to identify resuscitated cardiac arrest patients with adverse clinical characteristics for whom invasive operations were unlikely to increase survival. The strongest predictors of unfavourable outcome were age >85 years, >30 min before recovery of spontaneous circulation, and initial non-shockable rhythm according to their findings. Some characteristics, such as age, length of cardiopulmonary resuscitation, shockable rhythm, and pH in a blood gas measurement, were also predictors of a substantial coronary lesion from machine learning (ML) [34]. Using data from 2344 patients, Noh *et al.* evaluated a ML strategy for selecting a high-risk group of patients with acute coronary syndrome requiring revascularisation. The derived prediction functions were applicable, with an AUROC of 0.866 for the prediction of acute coronary syndrome patients requiring revascularisation [35]. Additionally, neurologic impairment, rather than cardiac injury, may have the most significant impact on overall prognosis in many patients with cardiac arrest, hence diminishing the potential therapeutic effect of coronary revascularisation. Notably, brain injury was by far the most common cause of death among trial participants. Both reasons demonstrate the need for additional modifications in the selection of cardiac catheterisation candidates.

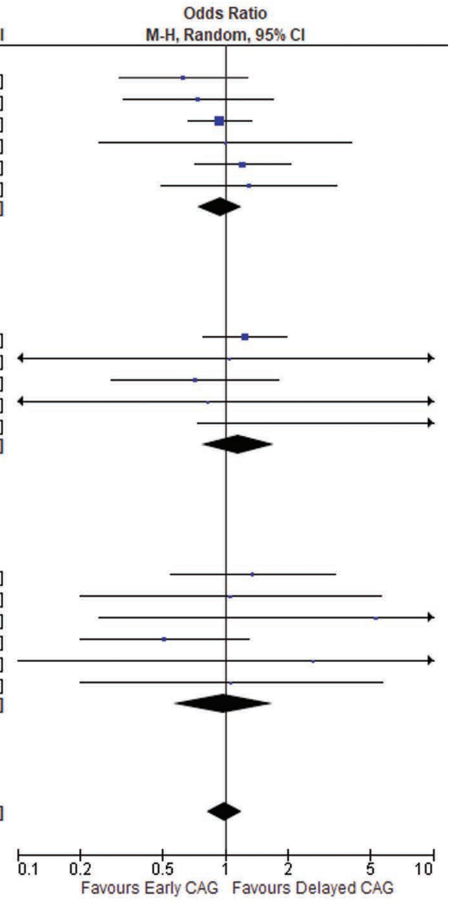
Several systematic reviews and meta-analysis were published on this topic. However, despite similar conclusions, most of them included fewer RCTs than our study due to date search limitation [36,37]. Additionally, other meta-analysis included non-randomised studies, as post-hoc analysis [15,38]. Therefore, we consider that our study was the most updated sum of evidence.

Limitations

Several limitations exist in our meta-analysis. First, the most significant drawback is the danger of bias originating

Fig. 3

Study or Subgroup	Early Angiography Events	Early Angiography Total	Delayed Angiography Events	Delayed Angiography Total	Weight	Odds Ratio M-H, Random, 95% CI
1.4.1 Neurological Satus (CPC<2)						
Desch (TOMAHANK) 2021	91	112	110	126	7.7%	0.63 [0.31, 1.28]
Kern (PEARL) 2020	30	49	34	50	5.6%	0.74 [0.33, 1.70]
Lemkes (COACT) 2019	171	272	170	264	31.0%	0.94 [0.66, 1.33]
Patterson (ARREST) 2017	9	18	7	14	2.0%	1.00 [0.25, 4.04]
Spaulding (EMERGE) 2022	40	141	34	138	13.5%	1.21 [0.71, 2.06]
Viana-Tejedor (COUPE) 2022	19	32	18	34	4.0%	1.30 [0.49, 3.45]
Subtotal (95% CI)		**624**		**626**	**63.9%**	**0.95 [0.74, 1.21]**
Total events	360		373			
Heterogeneity: Tau² = 0.00; Chi² = 2.84, df = 5 (P = 0.73); I² = 0%						
Test for overall effect: Z = 0.45 (P = 0.65)						
1.4.2 Need of Renal Replacement Therapy						
Desch (TOMAHANK) 2021	49	259	38	241	17.7%	1.25 [0.78, 1.99]
Elfwen (DISCO) 2019	1	38	1	40	0.5%	1.05 [0.06, 17.47]
Lemkes (COACT) 2019	8	244	11	243	4.5%	0.71 [0.28, 1.81]
Patterson (ARREST) 2017	1	18	1	15	0.5%	0.82 [0.05, 14.39]
Viana-Tejedor (COUPE) 2022	5	32	0	34	0.4%	13.80 [0.73, 260.54]
Subtotal (95% CI)		**591**		**573**	**23.6%**	**1.16 [0.78, 1.74]**
Total events	64		51			
Heterogeneity: Tau² = 0.00; Chi² = 3.98, df = 4 (P = 0.41); I² = 0%						
Test for overall effect: Z = 0.72 (P = 0.47)						
1.4.3 Major Bleeding						
Desch (TOMAHANK) 2021	12	260	8	232	4.6%	1.35 [0.54, 3.37]
Elfwen (DISCO) 2019	3	38	3	40	1.4%	1.06 [0.20, 5.59]
Kern (PEARL) 2020	2	49	0	50	0.4%	5.32 [0.25, 113.61]
Lemkes (COACT) 2019	7	273	13	265	4.4%	0.51 [0.20, 1.30]
Patterson (ARREST) 2017	1	18	0	15	0.4%	2.66 [0.10, 70.11]
Viana-Tejedor (COUPE) 2022	3	32	3	34	1.4%	1.07 [0.20, 5.73]
Subtotal (95% CI)		**670**		**636**	**12.5%**	**0.97 [0.56, 1.69]**
Total events	28		27			
Heterogeneity: Tau² = 0.00; Chi² = 3.91, df = 5 (P = 0.56); I² = 0%						
Test for overall effect: Z = 0.10 (P = 0.92)						
Total (95% CI)		**1885**		**1835**	**100.0%**	**1.00 [0.82, 1.21]**
Total events	452		451			
Heterogeneity: Tau² = 0.00; Chi² = 11.42, df = 16 (P = 0.78); I² = 0%						
Test for overall effect: Z = 0.04 (P = 0.96)						
Test for subgroup differences: Chi² = 0.74, df = 2 (P = 0.69), I² = 0%						



Forest plot of neurological status (cerebral performance category ≤2), renal replacement therapy and major bleeding comparing early CAG strategy versus non-early CAG strategy. CAG, coronary angiography; CI, confidence interval; M–H, Mantel–Haenszel.

both from the selection process due to the negative discrimination of individuals with a higher ischemic risk and from deviations from intended interventions resulting from the open-label design of all trials. Due to the subjective nature of the endpoint and the absence of blinding, measurement bias may also be present for the neurological result. Due to impracticality, however, it is unlikely that double-blind RCTs can be undertaken on this topic. Second, the definitions of the endpoints differed between trials, including the key endpoint of all-cause mortality, which ranged from 24 h to 180 days following OHCA, despite the fact that heterogeneity was minimal. Thirdly, the inclusion and exclusion criteria differed significantly between studies, particularly with regard to the initial rhythm and Glasgow Coma Scale. In addition, we were unable to account for possible differences in resuscitation-related parameters, such as immediate cardiopulmonary resuscitation, time required to achieve ROSC, and time required to transfer the patient to an acute care facility for further management. Finally, a significant heterogeneity existed in the definition of delayed angiography, varying between 6 h to 96 h.

Conclusion

According to our meta-analysis, in patients experiencing OHCA without ST elevation, early CAG was not associated with reduced mortality or an improved neurological status.

Acknowledgements

GC: Conceptualisation, Data curation, Formal analysis, Methodology, Project administration, Software, Writing – original draft; IS: Conceptualization, Data curation, Formal analysis, Methodology, Project administration, Software, Writing – original draft; JS: Supervision, Writing - review & editing; SB: Supervision, Writing - review & editing; RT: conception and design, interpretation of data, revision of the manuscript, final approval and is responsible for the overall content as guarantor.

Not applicable, as all studies included in our analysis have been individually evaluated by their respective ethical committee.

Availability of data and materials: All studies included are available online.

Conflicts of interest

There are no conflicts of interest.

References

1 Tsao CW, Aday AW, Almarzooq ZI, Alonso A, Beaton AZ, Bittencourt MS, *et al*. Heart Disease and stroke statistics-2022 update: a report from the American Heart Association. *Circulation* 2022; **145**:e153–e639.
2 Timmis A, Vardas P, Townsend N, Torbica A, Katus H, De Smedt D, *et al*.; Atlas Writing Group, European Society of Cardiology. European society of cardiology: cardiovascular disease statistics 2021. *Eur Heart J* 2022; **43**:716–799.
3 Wong CX, Brown A, Lau DH, Chugh SS, Albert CM, Kalman JM, *et al*. Epidemiology of sudden cardiac death: global and regional perspectives. *Heart Lung Circ* 2019; **28**:6–14.
4 Yannopoulos D, Bartos JA, Aufderheide TP, Callaway CW, Deo R, Garcia S, *et al*.; American Heart Association Emergency Cardiovascular Care Committee. The evolving role of the cardiac catheterization laboratory in the management of patients with out-of-hospital cardiac arrest: a scientific statement from the American Heart Association. *Circulation* 2019; **139**:e530–e552.
5 Berdowski J, Berg RA, Tijssen JGP, Koster RW. Global incidences of out-of-hospital cardiac arrest and survival rates: Systematic review of 67 prospective studies. *Resuscitation* 2010; **81**:1479–1487.
6 Byrne R, Constant O, Smyth Y, Callagy G, Nash P, Daly K, *et al*. Multiple source surveillance incidence and aetiology of out-of-hospital sudden cardiac death in a rural population in the West of Ireland. *Eur Heart J* 2008; **29**:1418–1423.
7 Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, *et al*.; ESC Scientific Document Group. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevationThe Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2018; **39**:119–177.
8 Dumas F, Cariou A, Manzo-Silberman S, Grimaldi D, Vivien B, Rosencher J, *et al*. Immediate percutaneous coronary intervention is associated with better survival after out-of-hospital cardiac arrest: insights from the PROCAT (Parisian Region Out of hospital Cardiac ArresT) registry. *Circ Cardiovasc Interv* 2010; **3**:200–207.
9 Desch S, Freund A, Akin I, Behnes M, Preusch MR, Zelniker TA, *et al*.; TOMAHAWK Investigators. Angiography after out-of-hospital cardiac arrest without ST-segment elevation. *N Engl J Med* 2021; **385**:2544–2553.
10 Yannopoulos D, Bartos J, Raveendran G, Walser E, Connett J, Murray TA, *et al*. Advanced reperfusion strategies for patients with out-of-hospital cardiac arrest and refractory ventricular fibrillation (ARREST): a phase 2, single centre, open-label, randomised controlled trial. *Lancet* 2020; **396**:1807–1816.
11 Elfwén L, Lagedal R, Nordberg P, James S, Oldgren J, Böhm F, *et al*. Direct or subacute coronary angiography in out-of-hospital cardiac arrest (DISCO)-an initial pilot-study of a randomized clinical trial. *Resuscitation* 2019; **139**:253–261.
12 Lemkes JS, Janssens GN, van der Hoeven NW, Jewbali LSD, Dubois EA, Meuwissen M, *et al*. Coronary angiography after cardiac arrest without ST-segment elevation. *N Engl J Med* 2019; **380**:1397–1407.
13 Kern KB, Radsel P, Jentzer JC, Seder DB, Lee KS, Lotun K, *et al*. Randomized pilot clinical trial of early coronary angiography versus no early coronary angiography after cardiac arrest without ST-segment elevation: the pearl study. *Circulation* 2020; **142**:2002–2012.
14 Hauw-Berlemont C, Lamhaut L, Diehl JL, Andreotti C, Varenne O, Leroux P, *et al*.; EMERGE investigators. EMERGEncy versus delayed coronary angiogram in survivors of out-of-hospital cardiac arrest with no obvious non-cardiac cause of arrest: Design of the EMERGE trial. *Am Heart J* 2020; **222**:131–138.
15 Abusnina W, Al-Abdouh A, Latif A, Alkhouli M, Alraies MC, Daggubati R, *et al*. Timing of coronary angiography in patients following out-of-hospital cardiac arrest without ST-segment elevation: a systematic review and meta-analysis of randomized trials. *Cardiovasc Revasc Med* 2022; **40**:92–98.
16 Verma BR, Sharma V, Shekhar S, Kaur M, Khubber S, Bansal A, *et al*. Coronary angiography in patients with out-of-hospital cardiac arrest without ST-segment elevation: a systematic review and meta-analysis. *JACC Cardiovasc Interv* 2020; **13**:2193–2205.
17 Viana-Tejedor A, Andrea-Riba R, Scardino C, Ariza-Solé A, Bañeras J, García-García C, *et al*. Coronary angiography in patients without ST-segment elevation following out-of-hospital cardiac arrest. *Rev Esp Cardiol (Engl Ed)* 2023; **76**:94–102.
18 Hauw-Berlemont C, Lamhaut L, Diehl JL, Andreotti C, Varenne O, Leroux P, *et al*.; EMERGE Investigators. Emergency vs delayed coronary angiogram in survivors of out-of-hospital cardiac arrest: results of the randomized, multicentric emerge trial. *JAMA Cardiol* 2022; **7**:700–707.
19 Mehran R, Rao SV, Bhatt DL, Gibson CM, Caixeta A, Eikelboom J, *et al*. Special report. Standardized bleeding definitions for cardiovascular clinical trials a consensus report from the bleeding academic research consortium. *Circulation* 2011; **123**:2736–2747.
20 Dankiewicz J, Nielsen N, Annborn M, Cronberg T, Erlinge D, Gasche Y, *et al*. Survival in patients without acute ST elevation after cardiac arrest and association with early coronary angiography: a post hoc analysis from the TTM trial. *Intensive Care Med* 2015; **41**:856–864.
21 Baldi E, Schnaubelt S, Caputo ML, Klersy C, Clodi C, Bruno J, *et al*. Association of timing of electrocardiogram acquisition after return of spontaneous circulation with coronary angiography findings in patients with out-of-hospital cardiac arrest. *JAMA Netw Open* 2021; **4**:e2032875–e2032875.
22 Collet J-P, Thiele H, Barbato E, Barthélémy O, Bauersachs J, Bhatt DL, *et al*.; ESC Scientific Document Group. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevationThe Task Force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2021; **42**:1289–1367.
23 Khan AR, Golwala H, Tripathi A, Bin Abdulhak AA, Bavishi C, Riaz H, *et al*. Impact of total occlusion of culprit artery in acute non-ST elevation myocardial infarction: a systematic review and meta-analysis. *Eur Heart J* 2017; **38**:3082–3089.
24 Meyers HP, Bracey A, Lee D, Lichtenheld A, Li WJ, Singer DD, *et al*. Comparison of the ST-Elevation Myocardial Infarction (STEMI) vs. NSTEMI and Occlusion MI (OMI) vs. NOMI Paradigms of Acute MI. *J Emerg Med* 2021; **60**:273–284.
25 Aslanger EK, Yıldırımtürk O, Şimşek B, Bozbeyoğlu E, Şimşek MA, Yücel Karabay C, *et al*. DIagnostic accuracy oF electrocardiogram for acute coronary OCClUsion resuLTing in myocardial infarction (DIFOCCULT Study). *Int J Cardiol Hear Vasc* 2020; **30**:100603.
26 Gardner KF, Clattenburg EJ, Wroe P, Singh A, Mantuani D, Nagdev A. The Cardiac Arrest Sonographic Assessment (CASA) exam – a standardized approach to the use of ultrasound in PEA. *Am J Emerg Med* 2018; **36**:729–731.
27 Gazmuri RJ, Weil MH, Bisera J, Tang W, Fukui M, McKee D. Myocardial dysfunction after successful resuscitation from cardiac arrest. *Crit Care Med* 1996; **24**:992–1000.
28 Laurent I, Monchi M, Chiche JD, Joly LM, Spaulding C, Bourgeois B, *et al*. Reversible myocardial dysfunction in survivors of out-of-hospital cardiac arrest. *J Am Coll Cardiol* 2002; **40**:2110–2116.
29 Waldo SW, Chang L, Strom JB, O'Brien C, Pomerantsev E, Yeh RW. Predicting the presence of an acute coronary lesion among patients resuscitated from cardiac arrest. *Circ Cardiovasc Interv* 2015; **8**:e002198.
30 Hosmane VR, Mustafa NG, Reddy VK, Reese CL IV, DiSabatino A, Kolm P, *et al*. Survival and neurologic recovery in patients with ST-segment elevation myocardial infarction resuscitated from cardiac arrest. *J Am Coll Cardiol* 2009; **53**:409–415.
31 Harhash AA, May TL, Hsu CH, Agarwal S, Seder DB, Mooney MR, *et al*. Risk stratification among survivors of cardiac arrest considered for coronary angiography. *J Am Coll Cardiol* 2021; **77**:360–371.
32 Bascom KE, Dziodzio J, Vasaiwala S, Mooney M, Patel N, McPherson J, *et al*.; International Cardiac Arrest Registry (INTCAR). Derivation and validation of the CREST model for very early prediction of circulatory etiology death in patients without ST-segment-elevation myocardial infarction after cardiac arrest. *Circulation* 2018; **137**:273–282.
33 Rab T, Kern KB, Tamis-Holland JE, Henry TD, McDaniel M, Dickert NW, *et al*.; Interventional Council, American College of Cardiology. Cardiac arrest: a treatment algorithm for emergent invasive cardiac procedures in the resuscitated comatose patient. *J Am Coll Cardiol* 2015; **66**:62–73.
34 Youn CS, Yi H, Kim YJ, Song H, Kim N, Kim WY. Early identification of resuscitated patients with a significant coronary disease in out-of-hospital cardiac arrest survivors without st-segment elevation. *J Clin Med* 2021; **10**:5688.
35 Noh YK, Park JY, Choi BG, Kim KE, Rha SW. A machine learning-based approach for the prediction of acute coronary syndrome requiring revascularization. *J Med Syst* 2019; **43**:1–8.

36 Aroney N, Tatavarty S, Mengel C, Walters D, Burstow D. When the TAVI stops humming - an indicator for thrombus. *Heart Lung Circ* 2017; **26**:S278.
37 Amartya Kundu M, Nakeya Dewaswala M, Huzefa Bhopalwala M, David J, Moliterno M. Immediate vs delayed coronary angiography for out-of-hospital cardiac arrest: a meta-analysis of randomized controlled trials. *Cardiovasc Interv* 2023; **16**:875–877.
38 Amacher SA, Bohren C, Blatter R, Becker C, Beck K, Mueller J, *et al*. Long-term survival after out-of-hospital cardiac arrest: a systematic review and meta-analysis. *JAMA Cardiol* 2022; **7**:633–643.
39 Patterson T, Perkins GD, Joseph J, Wilson K, Van Dyck L, Robertson S, *et al*. A randomised trial of expedited transfer to a cardiac arrest centre for non-ST elevation ventricular fibrillation out-of-hospital cardiac arrest: the ARREST pilot randomised trial. *Resuscitation* 2017; **115**:185–191.