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Clinical paper

Coronary angiography and percutaneous coronary intervention in cardiac arrest survivors with non-shockable rhythms and no STEMI: A systematic review

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Abstract

Background: Emergency coronary angiography (CAG) and percutaneous coronary intervention (PCI) are thought to improve outcomes in cardiac arrest (CA) survivors with ST segment elevation myocardial infarction (STEMI) and those without STEMI but likely cardiac etiology (shockable rhythms). However, the role of CAG ± PCI in OHCA survivors with non-shockable rhythms and no STEMI post-resuscitation remains unclear.

Methods: We searched Ovid/MEDLINE, Embase, Scopus, the Cochrane Central Register of Controlled Trials, Web of Science, and ClinicalTrials.gov from inception to January 2019. Two reviewers independently screened titles and abstracts of all records retrieved in the database searches and full texts of all articles selected in the title/abstract screen, with disagreements resolved by consensus. Risk of bias was assessed using the Strobe checklist.

Results: Fourteen out of 1174 articles met criteria for full review. Only two studies including 152 patients with confirmed non-shockable rhythms and no STEMI post resuscitation met all criteria and were analyzed. One study reported 97 patients (of 1497 in the registry) underwent CAG and 24.7% underwent PCI. The second study reported 55 patients (of 545 in the cohort) underwent CAG and acute coronary lesions were found in 16.4% but only 9.1% underwent PCI and no survival benefit was demonstrated.

Conclusions: There is limited data describing the prevalence of CAD and the role of CAG ± PCI in CA survivors with non-shockable rhythms and no STEMI post-resuscitation. In the two studies meeting criteria for this systematic review, 16% of patients with non-shockable rhythms underwent PCI.

Keywords: Cardiac arrest, Non-shockable rhythm, Coronary angiography

Introduction

Cardiac arrest (CA) is common, with an incidence greater than 350,000 in 2016 in the United States alone, and remains associated with high morbidity and mortality worldwide[1,2] The most common etiology for CA is coronary artery disease (CAD), predominantly acute coronary occlusion.[3,4] Current European and American resuscitation guidelines recommend that emergency coronary angiography (CAG) and, if indicated, percutaneous coronary intervention (PCI), be performed in all patients with cardiac arrest who have evidence of ST-elevation myocardial infarction (STEMI) or (presumably) new left bundle branch block (LBBB).[5,6] Emergent CAG should also be considered in the presence of life-threatening ventricular arrhythmias.[7] Notably, both recommendations focus on the presence of ST segment elevation or clinical arrhythmias reflective of acute

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coronary syndrome. However, many studies have confirmed the unreliability of initial post-resuscitation electrocardiograms (ECGs) as predictors of acute coronary occlusion in cardiac arrest survivors.[8] Recently, the International Liaison Committee on Resuscitation (ILCOR) guidelines endorsed the referral of patients with clinical suspicion of acute coronary syndrome for immediate CAG even in the absence of ST elevation on the initial post-resuscitation ECG.[9] Despite this latest strong recommendation regarding the management of cardiac arrest survivors without ischemic changes on surface ECG and/or without evidence of ventricular tachyarrhythmias, the performance of cardiac angiography on these patients remains highly variable and based on local interventional cardiology practice culture, with real-life registry data reporting that only 26% patients with no STE actually undergo CAG.[10]

Multiple studies have addressed the question of whether CAG and, if indicated, PCI, improve clinical outcomes in cardiac arrest survivors. A large study from Arizona[11] reporting on the statewide regionalization of post-cardiac arrest care showed improvement in survival to discharge in patients with both shockable rhythms as well as those with non-shockable rhythms.[11] Staer-Jensen et al.[8] demonstrated that an acute culprit lesion may still be present even in the absence of initial ECG changes, and patients may benefit from emergent CAG. Similarly, Kern et al.[12] performed a retrospective evaluation of 746 comatose post-cardiac arrest patients and showed that early CAG was associated with improved functional outcomes among resuscitated patients both with and without STEMI.

Prior observational studies have confirmed the clinical importance of CAG in large groups of cardiac arrest survivors.[12,13] These studies included either all cardiac arrest patients requiring resuscitation, or divided patients based on the presenting rhythm (shockable vs. non-shockable), or on the presence or absence of STEMI on post resuscitation ECG. The majority of studies have focused on patients with shockable rhythms and the presence or absence of STE with growing evidence supporting the beneficial role of CAG in in those patients with STEMI and/or shockable rhythms on presentation.[12–14] There is less agreement on what constitutes the best management of cardiac arrest survivors who present with no evidence of STEMI post resuscitation and/or who have a non-shockable rhythm. The actual incidence of CAD in these patients and whether or not they should undergo urgent/emergent CAG are questions that are yet to be answered.

The authors of the COACT trial[15] recently reported the lack of superiority of immediate CAG (compared with delayed CAG) in out-of-hospital cardiac arrest (OHCA) survivors with shockable rhythms with no STEMI post ROSC. The PEARL (NCT02387398)[16] and DISCO trials (NCT02309151),[17] both prospective randomized multicenter trials evaluating the usefulness of emergent CAG in post-arrest patients without ST segment elevation (including those with non-shockable rhythms), have not yet published their results, though enrollment for both trials has finished. Therefore, we sought to perform a systematic review of previously published studies investigating the role of immediate CAG in cardiac arrest survivors with non-shockable rhythms and no evidence of STEMI on their post-resuscitation ECGs.

Methods

We planned and performed a systematic review, using the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement as our reporting guide.[18]

Table 1 – Summary of studies design.

Study	Registry	Cohort (IH/OH)	OHCA (%)	IHCA (%)	ROSC ECG	Total in registry	Shockable	Nonshockable	Nonshockable & STEMI	Nonshockable & NO STEMI
Wilson et al., Resuscitation 2017 [20]	PATH	Both	62	38	Yes- for all	1497 (only 1396 known rhythm)	517 (299 CAG)	879 (141 CAG)	44	97
Martinez-Losas et al., WJC 2017 [21]	Single Center-Spain	Both	66.7	33.3	Yes- for all	545 (excluded 314, STEMI, LBBB, shock, and 25 with incomplete CAG)	148	NA	NA	55

Eligibility criteria

Studies were included that looked at outcomes following coronary angiography in cardiac arrest survivors who initially had a non-shockable rhythm, namely, pulseless electrical activity (PEA) or asystole. Publications were excluded if they were not in English, were reviews, opinion pieces, or presented data about patients with non-shockable rhythms that could not be separated from those with shockable rhythms.

Search strategy

An information specialist (CH) conducted searches in Ovid/MEDLINE), Elsevier/Embase, Elsevier/Scopus, Wiley/Cochrane Central Register of Controlled Trials, Clarivate/Web of Science (WOS) and ClinicalTrials.gov, from the databases' dates of inception to January 28, 2019 when all the searches were completed. All search strategies are available in Appendix A. Reference lists of the articles finally selected for inclusion were also searched.

Study selection

All citations were exported into EndNote Versions X8 and X9 (Clarivate Analytics, Philadelphia, PA, USA) and duplicates were removed. Titles and abstracts of retrieved citations were screened for relevance by two independent reviewers (AH, JH) with discrepancies resolved by consensus. Similarly, the full text publications of the selected records were independently screened (AH, JH) and differences of opinion were resolved by consensus. The Strobe Checklist[19] was used to assess risk of bias in each of the selected publications.

Data collection

Two reviewers (AH, JH) worked independently to extract the following information from each included study: Study year; study design; outcomes and definitions; patient baseline characteristics; presence/absence of non-shockable rhythm; presence/absence of STEMI on post-resuscitation/return of spontaneous circulation (ROSC) ECGs; and crude and adjusted outcome estimates. Disagreements were resolved by consensus through discussion among both reviewers and the principal investigator (KK).

Statistical analysis

The PCI rate and the associated standard error were calculated for each study. The weighted average PCI rate based on all of the available studies was derived, in which the weight for each study was the inverse of variance for the PCI rate estimate. In addition, the associated 95% confidence interval was reported (Tables 1–4).

Results

Search results

We found 1957 results through database searches (Ovid/MEDLINE- 248; Cochrane Library-22; Embase-971; Scopus-502; WOS-180; ClinicalTrials.gov-34) and identified three additional publications in the reference lists of the most relevant articles. Of the 1174 publications that remained after duplicates (713) and non-English titles (73) were removed, 1160 were excluded as they did not meet criteria at title/abstract level (Fig. 1). Fourteen publications required screening at full text level to determine eligibility. Of these only two met the full set of inclusion criteria and are analyzed in this systematic review.[20,21] We excluded many large cardiac arrest studies because we were unable to isolate the data pertaining to patients with non-shockable rhythms from data of patients with shockable rhythms. Most studies made no clear distinctions between these two groups of patients. Table 5 highlights a sample of prior resuscitation work and the reason for exclusion from our analysis. Table 6 sheds light on the relative incidence of CAD, rates of CAG and PCI among all CA survivor cohorts for comparison.

Table 2 – Rates of coronary angiography among different groups of cardiac arrest survivors, based on their presenting rhythms and post arrest ECG finding.

Study	Overall CAG performed	CAG shockable	CAG shockable STEMI	CAG shockable NO STEMI	CAG nonshockable	CAG nonshockable STEMI	CAG nonshockable NO STEMI
Wilson et al.,[20]	440 (32%)	299 (58%)	NA since they subdivided after excluding those with no CAG	NA	141 (16%)	44 (31% of CAG)	97 (69% CAG)
Martinez-Losas et al.,[21]	ALL	NA	NA	ALL	NA	NA	All 55

Table 3 – Rates of percutaneous coronary intervention among different groups of cardiac arrest survivors, based on their presenting rhythms and post arrest ECG finding.

Study	PCI shockable all	PCI shockable STEMI	PCI shockable NO STEMI	PCI nonshockable all	PCI nonshockable STEMI	PCI nonshockable NO STEMI
Wilson et al., Resuscitation 2017[20]	147/ 299 (49%)	53/67 (79.1%)	94/232 (40.5%)	48/141 (34%)	24/44 (54.5%)	24/97 (24.7%)
Martinez-Losas et al., WJC 2017[21]	NA	NA	32 (21.6%)	NA	NA	5/55 (9.1%)

Table 4 – Summary of hospital outcomes.

Study	Hospital discharge all	Hospital discharge shockable	Hospital discharge nonshockable	Long term FU	Important notes
Wilson et al., Resuscitation 2017[20]	Multvariate analysis showed better odds in nonshockable if undergone CAG: OR: 0.38 (95% CI: 0.25–0.5)				
Martinez-Losas et al., WJC 2017[21]	151 (74.4%)	81.10%	56.40%	5-year data confirming worse prognosis in nonshockable (29.1%) vs. shockable (60%)	Ad hoc PCI improved outcomes in shockable but NOT in nonshockable rhythm

Summary of studies on final review

Study #1

Using the Penn Alliance for Therapeutic Hypothermia (PATH) registry, a multi-center US-based registry, Wilson et al.[20] investigated the prevalence of CAD in patients presenting with cardiac arrest. Of the 1497 patients in the registry who experienced either OHCA or in-hospital cardiac arrest (IHCA) with ROSC (62% OHCA and 38% IHCA), 1396 had post-resuscitation ECGs available for review. Of these, 879 (63%) presented with non-shockable rhythms, and 517 (37%) presented with shockable rhythms. Coronary angiography was performed in 440 (32%) out of the 1396 patients, including 16% (141 out of 879) of patients with non-shockable rhythms, compared to 58% (299 out of 517) with shockable rhythms. Among the 141 patients with non-shockable arrest who underwent CAG, 44 (31%) patients had evidence of STEMI on post ROSC ECG, leaving 97 patients who presented with non-shockable rhythm and did not have STEMI who underwent CAG.

Among 97 CA survivors with non-shockable rhythms and no evidence of STEMI, 24 patients (24.7%) underwent PCI for presumably acute coronary occlusion or significant CAD.

Study #2

Martinez-Losas et al.[21] investigated the prevalence of coronary disease in 545 cardiac arrest patients (single center, 66.7% OHCA and 33.3% IHCA) who underwent CAG after post-resuscitation ECGs confirmed the absence of STEMI. This study included 10% (55 out of 545) of patients with non-shockable rhythms and no STEMI who underwent CAG. They demonstrated acute coronary lesions in 16.4% (9 out of 55) of the patients and significant coronary lesions (defined as >50% stenosis) in 60% (33 out of 55) of the patients. However, the primary focus of the study was to compare patients based on their presenting rhythm. Patients with initial shockable rhythms showed a trend towards a higher incidence of acute coronary lesions (29.7%) compared with those with non-shockable rhythms, (16.4%) ($P = 0.054$) as well as higher rates of ad-hoc PCI (21.9% vs. 9.1%, $P = 0.03$). This study also demonstrated a trend towards better 5-year survival rates in those presenting with a shockable rhythm who underwent PCI. In contrast, those patients with a non-shockable rhythm undergoing PCI demonstrated no difference in 5-year survival compared with similar patients who did not undergo PCI.

Statistical analysis

In patients with CA presenting with non-shockable rhythms and no evidence of STEMI post resuscitation, Wilson, et al.[20] reported a PCI rate of: 24.74% with a standard error of 4.38% and Matinez-Losas, et al.[21] reported a PCI rate of 9% with a standard error of 3.88%.

Combining both studies, the weighted PCI rate was 16% with a standard error of 2.90% and a 95% confidence interval of (10.28%–21.64%).

Discussion

We performed a systematic review of published reports to investigate the incidence of acute coronary lesions in a selected and commonly under-represented subgroup of cardiac arrest survivors, those presenting with non-shockable rhythms who demonstrate no evidence of STEMI on post resuscitation ECG. Despite the prevalence of non-shockable cardiac arrest and no STEMI post resuscitation (36.4% of those with no STEMI and 21.5% among all OHCA survivors in the international resuscitation registry INTCAR),[22] there is a paucity of data with a very limited number of studies addressing this particular group of patients. After carefully reviewing the literature we only found two studies[20,21] that met our original inclusion criteria.

Cardiac arrest survivors with no obvious extra-cardiac etiology and no evidence of STEMI on ROSC ECG represent a very challenging group of patients. They are commonly overlooked from the invasive management standpoint, with only 1 in every 6 patients (16%) undergoing CAG compared to 58% in those with shockable rhythms and still no evidence of STEMI[20] and 90% in those with shockable rhythms and STEMI.[23] In our review, only two reports[20,21] included sufficient data to allow for statistical analysis. Combined data from these two reports demonstrated that 16% of patients with non-shockable rhythm and no STEMI on ECG underwent PCI for presumed significant CAD, potentially the cause of their cardiac arrests. This percentage seems important, especially when compared with the fact that there is only a 7–14% chance of finding an acutely occluded coronary artery in patients presenting to the ED with presumably new left bundle branch block[24,25] and 10% in those with ST elevations in lead aVR.[26] Yet in the latter scenarios activating the cardiac catheterization lab for emergency CAG based on ACCF/AHA recommendations has been the standard practice.[5]

The beneficial role of CAG and PCI have been well established in cardiac arrest in general.[27] Prior reports focusing on patients with no STE post ROSC did show a 30-day survival benefit, irrespective of the type of rhythm on presentation.[28] However, in our review, Wilson et al.[20] reported improved odds of survival in those who underwent CAG with no emphasis on PCI. The study by Martinez-Losas et al.[21] did not show survival benefits in those with non-shockable rhythms and no STEMI post resuscitation undergoing CAG and/or PCI. This finding could be related to the very small sub-selected population that underwent CAG.

Recently, there has been a shift towards performing CAG after cardiac arrest as soon as possible (<24 h) after ROSC, which has

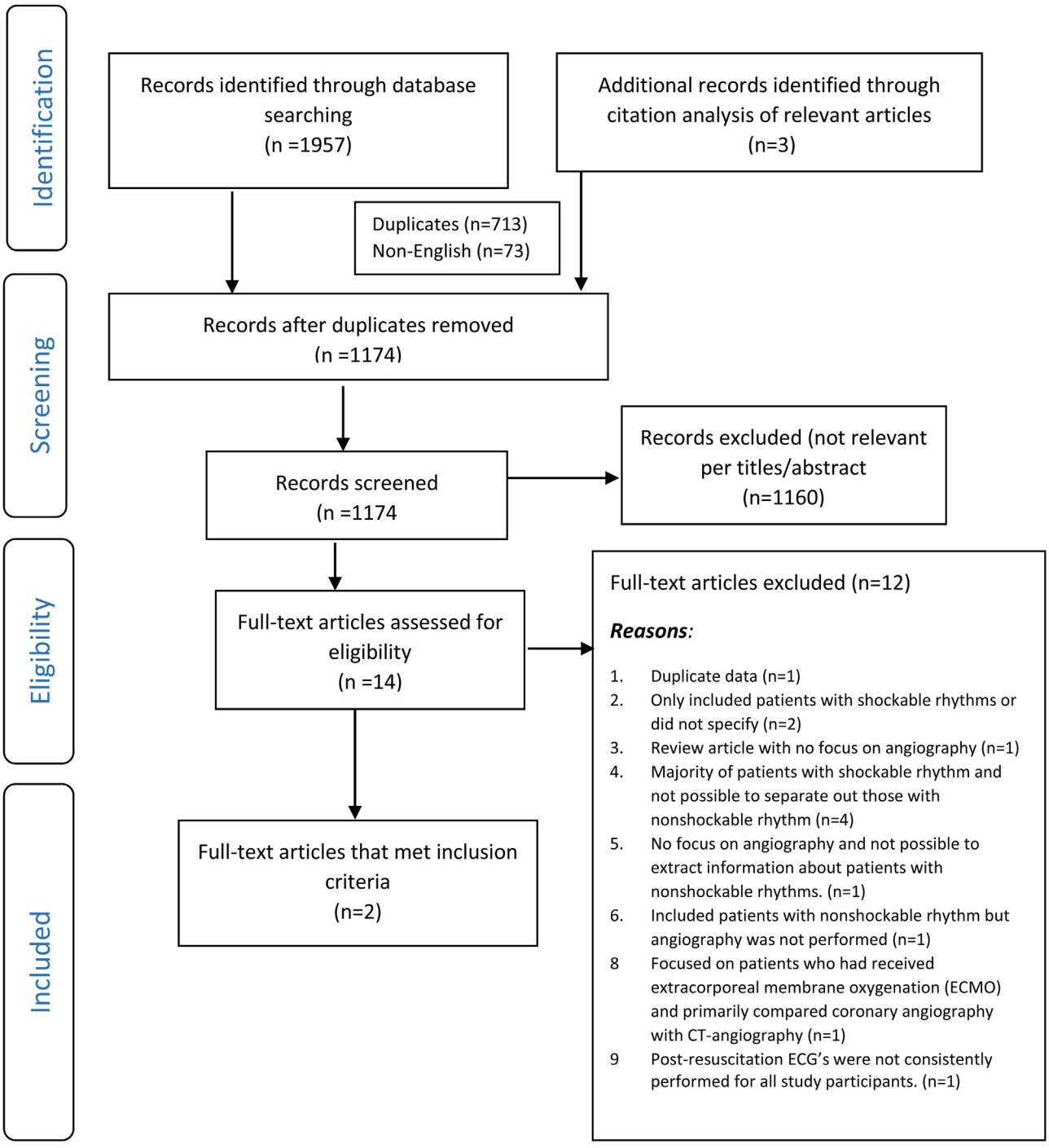

Fig. 1 – Flowchart of the process of literature search and extraction of studies meeting the inclusion criteria.

been shown to improve outcomes compared to late or no CAG.[29] Integrated management protocols involving multidisciplinary teams of cardiologists, intensivists, and emergency department physicians are currently advocated and have proven effective in improving the rates of performing CAG and Therapeutic Hypothermia (TH).[30] These team approaches can potentially address the subjective bias of individual care teams that may be hesitant to perform CAG in the absence of acute ECG changes. Team-based care could also quickly and effectively facilitate the accurate differential diagnosis of other etiologies for the cardiac arrest (stroke, dissection, etc.), potentially leading to faster care delivery and improvement in patient survival.[30] In this study by Akin et al, in which the authors described the additive value of standardized emergency protocol-based care, PCI rates in patients with no STEMI were very high (52%).[30] Although 73% of all OHCA patients had shockable rhythms on admission, and patients with STEMI had better outcomes than those with no STEMI, those with no STEMI who underwent PCI had comparable outcomes to the STEMI patients.[30] Another report by DeFilippis et al.[23] investigating

Table 5 – Summary of landmark studies investigating the utility of CAG ± PCI in cardiac arrest survivors and the reason for exclusion from the final meta-analysis.

Lemkes et al.[15]	COACT randomized controlled trial	Included only patients with shockable presenting rhythms and found lack of superiority to performing urgent/emergent CAG in patients with shockable rhythms and no STE post ROSC. Cannot separate our target group with non-shockable rhythms and no STE for further analysis
DeFilippis et al.[23]	YOUNG-MI Registry	Authors compared Type 1 MI with or without OHCA among those younger than 50 years of age. Those with OHCA had less chance of having CAG, BUT, those who had CAG had similar survival to those who did not have OHCA. Cannot separate our target group with non-shockable rhythms and no STE for further analysis
Akin et al.[30]	Single center prospective	All comers, 73% presented with shockable rhythms and about half had STE post ROSC. Cannot separate our target group with non-shockable rhythms and no STE for further analysis
Nogales-Romo et al.[33]	Hospital group database (San Carlos, Spain)	All had no significant ECG changes post ROSC, but >70% presented with shockable rhythm. Cannot separate our target group with non-shockable rhythms and no STE for further analysis
Jentzer et al.[29]	UPMC database	Early (<24) CAG had benefit in OHCA regardless of the ECG findings nor presenting rhythm, compared to late CAG. STE and/or VTA were associated with higher likelihood of performing CAG. Cannot separate our target group with non-shockable rhythms and no STE for further analysis
Waldo et al.[34]	Single Center (MGH)	Authors primary focus was to study differential characteristics between culprits and no culprits lesions. Cannot separate our target group with non-shockable rhythms and no STE for further analysis
Geri et al.[27]	Single Center (Paris)	Study included patients with different ECG findings and presenting rhythms. Cannot separate our target group with non-shockable rhythms and no STE for further analysis
Vyas et al.[13]	CARES	Study included CA survivors with VT and VF only
Lee et al.[35]		Cannot separate our target group with non-shockable rhythms and no STE for further analysis
Strote et al.[36]		Study included CA survivors with VT and VF only
Garcia-Tejada et al.[37]		Cannot separate our target group with non-shockable rhythms and no STE for further analysis
Redfors et al.[38]	RIKS-HIA and SCAAR Swedish Registries	Cannot separate our target group with non-shockable rhythms and no STE for further analysis
Dankiewicz et al.[39]	TTM	There was 20% no shockable with No STE. Cannot separate our target group with non-shockable rhythms and no STE for further analysis
Kern et al.[12]	INTCAR	58% with shockable rhythm, rest non-shockable. Cannot separate our target group with non-shockable rhythms and no STE for further analysis
Staer Johnson et al.[8]	Single Center- Oslo	Mostly VT/VF. Cannot separate our target group with non-shockable rhythms and no STE for further analysis
Kim et al.[40]		Included primarily shockable rhythms and focusing on other etiologies (SAH, etc.). Cannot separate our target group with non-shockable rhythms and no STE for further analysis
Zeyons et al.[41]	Single Center	Mostly VT/VF. Cannot separate our target group with non-shockable rhythms and no STE for further analysis
Bro Jeppessen et al.[42]	Single Center	Mostly VT/VF. Cannot separate our target group with non-shockable rhythms and no STE for further analysis
Zanuttini et al.[43]		Mostly VT/VF. Cannot separate our target group with non-shockable rhythms and no STE for further analysis
Sideris et al.[44]		Mostly VT/VF. Cannot separate our target group with non-shockable rhythms and no STE for further analysis
Hollenbeck et al.[45]		Study included CA survivors with VT and VF only
Dumas et al.[46]	PROCAT- Paris	Mostly VT/VF. Cannot separate our target group with non-shockable rhythms and no STE for further analysis
Dumas et al.[47]	PROCAT II	Mostly VT/VF. Cannot separate our target group with non-shockable rhythms and no STE for further analysis

Table 6 – Incidence of coronary artery disease, acute culprit occlusion, rates of PCI, and reported survival among all cardiac arrest survivors based on their presenting rhythm and post resuscitation ECG findings.

Group	CAG%	PCI	Survival
Shockable & STEMI[31]	87.2%	77.3%	78.9% (only 47% if no CAG)
Shockable & no STEMI[31]	33.9%	11.8%	80.3% (only 44.7% if no ACG)
No STEMI regardless of the presenting rhythm[32]	Acute culprit occlusion in 32.2% with PCI in 21.6%		
Nonshockable & STEMI[20]	PCI 54.5%		
Nonshockable & No STEMI	Our data demonstrated PCI rates of 15.96% with a standard error of 2.90% and a 95% confidence interval of (10.28%, 21.64%).		

younger (<50 years old) OHCA survivors enrolled in the YOUNG-MI registry, the authors divided young patients having type 1 MI based on whether they developed OHCA or not. OHCA survivors who underwent CAG had comparable survival rates to hospital discharge compared with those with MI and no cardiac arrest, further highlighting the potential life-saving effects of CAG in those selected patients.[23]

Many resuscitation reports have focused on patients with "cardiac arrest with presumed cardiac etiology" or have clearly selected those with shockable rhythms only. Both of these trends may contribute to the clinical bias towards patients with a clear cardiac etiology or shockable rhythms, resulting in significantly increased rates of CAG in patients with STE compared to those without.[31] Patients presenting with STEMI are 13 times more likely to undergo CAG.[32] Based on our research, cardiac arrest survivors presenting with non-shockable rhythms and no STEMI post ROSC have been overlooked in most landmark resuscitation studies.

Limitations

Our review has other significant limitations: First, we were inherently limited by the fact that only two studies of almost 1200 screened publications met selection criteria. Given the limited number of

patients in our combined analysis, care should be taken before drawing any definitive conclusions. Second, the true CAD incidence is not well defined since majority of patients with nonshockable rhythms and no STEMI did not undergo CAG and only a very small sub-selected group of cardiac arrest survivors underwent CAG. For example, Martinez-Losas et al.,[21] described the detailed coronary finding on those underwent CAG, yet more than two thirds of patients did not undergo CAG, and Wilson et al.,[20] did not include coronary findings with the focus on those who had PCI, additionally, only 16% of those with non-shockable rhythms in their cohort underwent CAG (including those with STEMI). This practice eliminates the real denominator for those with CAD, making it difficult to calculate the true incidence of CAD and draw clinical conclusions. Third, while studies reported rates of "PCI", it remained unclear whether those patients undergoing PCI had an acute coronary occlusion leading to their cardiac arrest, or stable severe CAD, which in fact, may or may not have led to their cardiac arrest. Lastly, because the end points of both studies were not similar, we were unable to draw final conclusions regarding long term outcomes. While these limitations may not allow us to draw definitive conclusions they highlight the clear paucity of data and the corresponding need for more studies addressing this group of cardiac arrest survivors.

Conclusions

Among cardiac arrest survivors presenting with non-shockable rhythms and no STEMI post ROSC, there was very little data describing the prevalence of CAD or culprit coronary occlusions. The rates of performing CAG was very low and the incidence of CAD necessitating PCI was significant among those who underwent CAG. The beneficial impact of CAG and, if indicated, PCI in those patients remains unclear. Whether CAG and PCI are beneficial for cardiac arrest survivors with non-shockable rhythms without obvious evidence of STEMI will need to be validated in larger registries and prospective cohort studies.

Source of funding

None.

Conflict of interest

None.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.resuscitation.2019.08.023.

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