

REVIEW ARTICLE

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Out-of-hospital cardiac arrest: Do we have to perform coronary angiography?

Wojciech Wańha^{1, 2}*, Michalina Kołodziejczak^{1, 3}*, Mariusz Kowalewski^{4, 5}, Rafał Januszek⁶, Łukasz Kuźma⁷, Miłosz Jaguszewski^{1, 8}, Mariusz Tomaniak^{1, 9}, Szymon Darocha^{1, 10}, Karolina Kupczyńska^{1, 11}, Piotr Dobrowolski^{1, 12}, Agata Tymińska^{1, 9}, Aleksandra Ciepłucha^{1, 13}, Justyna Sokolska^{1, 14}, Agnieszka Kapłon-Cieślicka^{1, 9}, Andrzej Kułach^{1, 15}, Maciej Wybraniec^{1, 16}, Tomasz Roleder^{2, 17}, Mateusz Tajstra¹⁸, Klaudiusz Nadolny^{19, 20}, Tomasz Darocha²¹, Katarzyna Sierakowska³, Tomasz Pawłowski²², Marek Gerlotka²³, Maciej Lesiak¹³, Krystian Wita¹⁶, Robert Gil^{1, 22}, Przemysław Trzeciak¹⁸

¹"Club 30", Polish Cardiac Society, Poland; ²Department of Cardiology and Structural Heart Diseases, Medical University of Silesia, Katowice, Poland; ³Department of Anesthesiology and Intensive Care, Ludwik Rydygier Collegium Medicum, Nicolaus Copernicus University, Antoni Jurasz University Hospital No. 1, Bydgoszcz, Poland; ⁴Department of Cardiac Surgery, Central Clinical Hospital of the Ministry of Interior, Center of Postgraduate Medical Education, Warsaw, Poland; ⁵Thoracic Research Center, Innovative Medical Forum, Collegium Medicum Nicolaus Copernicus University, Bydgoszcz, Poland; ⁶Second Department of Cardiology, Jagiellonian University Medical College, Krakow, Poland; ⁷Department of Invasive Cardiology, Medical University of Bialystok, Poland: ⁸First Department of Cardiology, Medical University of Gdansk, Poland; ⁹First Department of Cardiology, Medical University of Warsaw, Poland; ¹⁰Department of Pulmonary Circulation, Thromboembolic Diseases and Cardiology, Center of Postgraduate Medical Education Fryderyk Chopin Hospital in European Health Center Otwock, Poland; ¹¹Chair and Department of Cardiology, Medical University of Lodz, Poland; ¹²Department of Hypertension, National Institute of Cardiology, Warsaw, Poland; ¹³First Department of Cardiology, Poznan University of Medical Sciences, Poznan, Poland; ¹⁴Department of Cardiovascular Imaging, Institute of Heart Diseases, Wroclaw Medical University, Wroclaw, Poland; ¹⁵Department of Cardiology, Medical University of Silesia, Katowice, Poland; ¹⁶First Department of Cardiology, Medical University of Silesia, Katowice, Poland; ¹⁷Department of Cardiology, Regional Specialist Hospital in Wroclaw, Poland; ¹⁸Third Department of Cardiology, Faculty of Medical Sciences in Zabrze, Medical University of Silesia, Katowice, Poland; ¹⁹Faculty of Medicine, Katowice School of Technology, Katowice, Poland; ²⁰Department of Health Sciences, WSB University, Dabrowa Gornicza, Poland; ²¹Department of Anesthesiology and Intensive Therapy, Medical University of Silesia, Katowice, Poland; ²²Department of Invasive Cardiology, Central Clinical Hospital of the Ministry of Interior and Administration, Center of Postgraduate Medical Education, Warsaw, Poland; ²³Department of Cardiology, University Hospital, Institute of Medical Sciences, University of Opole, Poland

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*Authors contributed equally to this paper.

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Address for correspondence: Wojciech Wańha, MD, PhD, Department of Cardiology and Structural Heart Diseases, Medical University of Silesia, ul. Ziołowa 45, 40–635 Katowice, Poland, tel: +48 32 359 80 00, fax: +48 32 202 87 54, e-mail: wojciech.wanha@gmail.com

Abstract

Out-of-hospital cardiac arrest (OHCA) remains a leading cause of global mortality, while survivors are burdened with long-term neurological and cardiovascular complications. OHCA management at the hospital level remains challenging, due to heterogeneity of OHCA presentation, the critical status of OHCA patients reaching the return of spontaneous circulation (ROSC), and the demands of post ROSC treatment. The validity and optimal timing for coronary angiography is one important, yet not fully defined, component of OHCA management. Guidelines state clear recommendations for coronary angiography in OHCA patients with shockable rhythms, cardiogenic shock, or in patients with ST-segment elevation observed in electrocardiography after ROSC. However, there is no established consensus on the angiographic management in other clinical settings.

While coronary angiography may accelerate the diagnostic and therapeutic process (provided OHCA was a consequence of coronary artery disease), it might come at the cost of impaired post-resuscitation care quality due to postponing of intensive care management. The aim of the current statement paper is to discuss clinical strategies for the management of OHCA including the stratification to invasive procedures and the rationale behind the risk-benefit ratio of coronary angiography, especially with patients in critical condition. (Cardiol J 2023; 30, 6: 1026–1037)

Key words: out-of-hospital cardiac arrest, coronary angiography

Introduction

Recommendations for performing coronary angiography (CAG) in patients admitted after out-of-hospital cardiac arrest (OHCA) are limited to patients presenting with shockable rhythm, cardiogenic shock, or in patients with ST-segment elevation myocardial infarction (STEMI) on electrocardiography (ECG) after a return of spontaneous circulation (ROSC) (Table 1) [1-6]. As the majority of sudden cardiac arrests (CAs) are caused by non-shockable rhythms without underlying acute coronary lesion, they lack a clear indication for CAG [7, 8]. The 2021 update of European Resuscitation Council (ERC) and European Society of Intensive Care Medicine (ESICM) guidelines describe post-resuscitation care outlining emergent CAG strategy in the context of ST-elevation (STE) prevalence, as well as in patients without STE on the ECG but at a high probability of acute coronary occlusion [4]. The 2020 European Society of Cardiology (ESC) guidelines for the management of acute coronary syndromes in patients presenting without persistent STE recommend considering delayed, as opposed to immediate, CAG among hemodynamically stable patients without STE who were successfully resuscitated after OHCA [3]. The recommendations are to be altered by ongoing trials focusing on more detailed clinical settings to further define the possible benefit of an early invasive approach.

Etiology of OHCA

The timeline of OHCA management implies a number of pitfalls, and long-term clinical outcomes that are strictly determined by the promptness and quality of the measures undertaken during the initial period after CA. Sudden CA is characterized by a relatively low prevalence among the general population, challenging the development of an accurate individual risk prediction tool. It is particularly difficult among individuals without premonitory symptoms who remain at risk of sudden CAs as their first cardiac event [9–12]. Ischemic heart disease remains a dominant contributor to sudden CAs, albeit cardiomyopathies associated with myocardial fibrosis and left ventricular hypertrophy also significantly increases its prevalence [11]. Moreover, ischemic heart disease is less frequent among younger populations (where genetic structural disorders and cardiac channelopathies, myocarditis, and congenital heart disease are more widespread), but its prevalence increases with age which allows for the atherosclerotic burden to build up [13].

ST-elevation on ECG

Since the OHCA population is so diverse, it is necessary to implement a differential diagnosis as soon as possible after stabilizing the patient's condition. This allows for the ROSC status to be reached or maintained and the patient's prognosis to be improved. The simultaneous implementation

Guideline	Coronary angioplasty	Class, level
2017 ESC Guidelines for the management of acute	A primary PCI strategy is recommended in patients with resusci- tated CA and an ECG consistent with STEMI	I, B
myocardial infarction with ST-segment elevation [1]	In cases without STE on post-resuscitation ECG but with a high suspicion of ongoing myocardial ischemia, urgent CAG should be done within 2 h after a quick evaluation to exclude non-coronary causes. In all cases, the decision to perform urgent CAG should take into account factors associated with poor neurological outcome	IIa, C
2017 AHA/ACC/HRS Guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death [2]	In patients who have recovered from unexplained sudden CA, CT or invasive CAG is useful to confirm the presence or absence of ischemic heart disease and guide decisions for myocardial revascularization	I, C-EO
	Quickly identifying and treating patients with OHCA related to acute coronary occlusion is associated with improved survival and better functional recovery	NA
	Coronary occlusion as a cause of CA is not reliably predicted by clinical and ECG findings, and emergency CAG should be consid- ered (rather than later in the hospital stay or not at all) for unstable patients with a suspected cardiac etiology regardless of whether the patient is comatose or awake	I, B-NR
2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting with- out persistent ST-segment	The management of patients presenting with resuscitated CA and concomitant NSTE-ACS needs to be individualized according to their hemodynamic and neurological status. In comatose survivors, ECG should be performed immediately for further evaluation of differential diagnoses	NA
elevation [3]	Delayed as opposed to immediate CAG should be considered among hemodynamically stable patients without STE successfully resuscitated after OHCA	lla, B
2021 ACC/AHA/SCAI Guideline for coronary artery revascularization [5]	In patients with VF, polymorphic VT, or CA, revascularization of significant CAD (with CABG or PCI) is recommended to improve survival	I, B-NR
2021 ERC and ESICM Guidelines: post- -resuscitation care [4]	In patients with ROSC after OHCA without STE on the ECG, emergent cardiac catheterization laboratory evaluation should be considered if there is an estimated high probability of acute coronary occlusion (e.g., patients with hemodynamic and/or electrical instability)	NA
2022 ESC Guidelines for the management of	In electrically unstable patients after sudden CA, with suspicion of ongoing myocardial ischemia, a CAG is indicated	I, C
patients with ventricular arrhythmias and the prevention of sudden cardiac death [6]	Urgent CAG is recommended for patients presenting with STEMI	I

Table 1	. Guideline	recommendations for	coronary ar	ngioplastv	in	cardiac arrest pa	atients.
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REFERENCE FOR GUIDELINE RECOMMENDATIONS

ACC/AHA/HRS/SCAI Guidelines

Classes (STRENGTH) of Recommendation

Class I (STRONG) Benefit >>> Risk

Class IIa (MODERATE) Benefit >> Risk

Class IIb (WEAK) Benefit > Risk

Class III: No Benefit (WEAK) Benefit = Risk

Class III: Harm (STRONG) Risk > Benefit

Level (QUALITY) of Evidence

Level A

- High-quality evidence* from more than 1 RCT

- Meta-analyses of high-quality RCTs

- One or more RCTs corroborated by high-quality registry studies

Table 1 (cont.). Guideline recommendations for coronary angioplasty in cardiac arrest patients.

Level B-R (Randomized)

- Moderate-quality evidence* from 1 or more RCTs
- Meta-analyses of moderate-quality RCTs

Level B-NR (Nonrandomized)

- Moderate-quality evidence* from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies
- Meta-analyses of such studies

Level C-LD (Limited Data)

- Randomized or nonrandomized observational or registry studies with limitations of design or execution
- Meta-analyses of such studies
- Physiological or mechanistic studies in human subjects

Level C-EO (Expert Opinion)

- Consensus of expert opinion based on clinical experience

ESC Guidelines

Classes of Recommendation

Class I: Conditions for which there is evidence and/or general agreement that a given procedure or treatment is beneficial, useful, and effective

Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/ /efficacy of a procedure or treatment

Class IIa: Weight of evidence/opinion is in favor of usefulness/efficacy

Class IIb: Usefulness/efficacy is less well established by evidence/opinion

Class III: Conditions for which there is evidence and/or general agreement that a procedure/treatment is not useful/effective and in some cases may be harmful

Levels of Evidence

Level of Evidence A: Data derived from multiple randomized clinical trials or meta-analyses of such studies

Level of Evidence B: Data derived from one or more randomized trials or meta-analysis of such studies. Data derived from one or more non-randomized trials or meta-analysis of such studies

Level of Evidence C: Non randomized observational studies with limitations in design or execution or metanalysis of such studies. Consensus opinion of experts based on clinical experience

*The method of assessing quality is evolving, including the application of standardized, widely used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

ACC — American College of Cardiology; AHA — American Heart Association; CA — cardiac arrest; CABG — coronary artery bypass grafting; CAD — coronary artery disease; CAG — coronary angiogram; CT — computer tomography; ECG — electrocardiography; ERC — European Resuscitation Council; ESC — European Society of Cardiology; ESICM — European Society of Intensive Care Medicine; HRS — Heart Rhythm Society; NA — not available; NSTE-ACS — non-ST-elevation acute coronary syndrome; OHCA — out-of-hospital cardiac arrest; PCI percutaneous coronary intervention; RCT — randomized controlled trial; SCAI — Society of Cardiovascular Angiography and Interventions; STE — ST-elevation; STEMI — ST-segment elevation myocardial infarction; VF — ventricular fibrillation; VT — ventricular tachycardia

of various diagnostic elements enables a comprehensive assessment of the patient's condition and the determination of therapeutic priorities. One of the fastest, widely available, and cost-effective tools is the ECG, which is used in the initial stage of patient management before reaching ROSC. ECG is of additional importance in the context of high positive predictive value of STE for acute coronary lesions causing CA (85–96%), and OHCA being the first manifestation of coronary artery disease (CAD) [14–17]. International guidelines for decades gave strong recommendations on the timely

management of patients presenting with STE on post-ROSC ECG. Urgent (≤ 2 h) angiography with primary percutaneous coronary intervention (PCI) was the strategy of choice in this population [1]. As a consequence, for over 12 years (2000 vs. 2012) CAG and PCI were performed more frequently in patients after post-ROSC STEMI of ventricular tachycardia or ventricular fibrillation (VT/VF) of OHCA origin (53.7% vs. 87.2% and 29.7% vs. 77.3%, respectively). Additionally, patient survival to discharge has also improved (59.2% vs. 74.3%) [18, 19] over this period.

Non-ST-elevation myocardial infarction

The potential benefit or harm of urgent CAG in patients without STE is still a subject of debate. A question on the proper selection of patients for early CAG strategy is particularly important. An advantage of CAG in OHCA patients could only be present in the group with significant stenosis in the coronary artery who received PCI for reversing ongoing ischemia [20]. Thus, it is conceivable that the potential benefit of emergency CAG in patients with post-ROSC depends heavily on the presence of significant stenosis in the coronary arteries.

While the observational and registry data suggest improved survival with early CAG [21–24], randomized studies showed no such benefit when comparing emergency CAG with a delayed strategy [8, 25]. This was confirmed by a recent meta-analysis showing no difference in early vs. non-early CAG in terms of mortality, neurological status, and rate of PCI during 30 days among patients with OHCA without STE [26].

The obstructive coronary atherosclerosis and acute thrombotic occlusions in the post-OHCA population are not uncommon but can vary between different subgroups. In the PROCAT registry [16], the reported prevalence of acute CAD was 58%. while in TOMAHAWK randomized trial [25], authors claimed a 40% prevalence of coronary culprit lesions. In the EMERGE trial [8], the latest published randomized study, significant CAD was found only in 49.7% of patients. The highest number of CAD post-OHCA, reaching 65%, was observed in COACT trial [27]; however, patients with non-shockable rhythm were excluded from randomization. Other studies conducted in patients with CA without STE who underwent CAG report approximately 25% acute occlusions and nearly 60% significant obstructive lesions [28]. Despite the high prevalence of CAD in OHCA patients without STE, a high burden of comorbidities, including intracranial bleeding, is present in this population [29, 30], suggesting that the cause of CA in this setting may be due to non-cardiac causes. Additionally, the ECG changes originating from a brain injury can be present and mimic myocardial ischemia (widespread giant T-wave inversions, QT prolongation, bradycardia, STE/ST-depression, increased U wave amplitude) [31, 32]. Therefore, before the final decision to perform CAG, unfavorable features that potentially affect the survival of complicated OHCA patients should be assessed, preferably after consultation by a multidisciplinary team. In this population, the outcomes are driven by neurological complications or multiorgan failure, resulting in a 10-fold higher mortality rate compared to non–CA patients with STE [33]. Faced with numerous features indicating multiorgan and irreversible ischemia, the incremental benefit of restoring coronary perfusion would be marginal and clinically insignificant.

To address some of these controversies, a number of studies were conducted on patients without STE in order to quantify the potential role of CAG and intervention (Table 2) [8, 25, 27, 34-37]. The COACT trial [25] showed no significant difference in clinical outcomes after 1-year follow-up in OHCA patients with a shockable rhythm in the absence of STE treated with both strategies. These results suggested that CAG can be delayed until neurologic recovery. The data from the TOMAHAWK trial [23] point toward the lack of benefit of early CAG in clinical outcomes such as survival, bleeding, stroke, or renal failure. Moreover, the authors noted a slight increase in the composite outcome of death and severe neurologic deficit in the group treated with immediate CAG. Additionally, the most recent randomized clinical trial showed that a strategy of emergency CAG was not better than a strategy of delayed CAG with respect to 180-day survival rate and neurologic sequelae [8]. Immediate CAG may be warranted for a specific subgroup of OHCA patients with no significant comorbidities who are hemodynamically unstable and have an unknown cause of arrest at the time of admission, but who are likely to regain consciousness. These patients were excluded from previous trials, but are still at a high likelihood of having underlying CAD.

The choice to perform emergency CAG post--ROSC should also consider issues related to poor neurological outcome. The clear-cut benefit of immediate CAG in other settings is still a matter of debate. Coronary angiography holds both potential risks and benefits that, could either improve a patient's condition or result in a greater burden for complications. This would depend on the underlying cause of the OHCA and concomitant medical issues (Table 3). Urgent CAG may increase the risk of bleeding and procedural complications, especially in unstable and neurologically compromised patients after an extensive resuscitation, which can further decline chances of survival. On the other hand, primary revascularization of coronary occlusions increases myocardial viability, securing better cardiovascular and perfusion stability that might be of a paramount importance in patients with severe acute myocardial dysfunction. In cases where coronary revascularization is not feasible,

	Outcomes	AN	No significant dif- ference in clinical outcomes at 1 year between the two strategies CAG can be de- layed until after neurologic recov- ery without affect- ing outcomes	Survival rate at 180 days (emergency CAG, 36.2% [51 of 141] vs. delayed CAG, 33.3% [46 of 138]; HR 0.86; 95% CI 0.64–1.15; p = 0.31)
ardial infarction.	Timing of coronary angiography	Ą	2.1 h (IQR 1.5–2.8) vs. 121.4 h (IQR 50.4–201.4)	2 h (IOR 2–3) vs. 65.5 h (IOR 40.8–74.8)
nent elevation myoca	Main outcomes assessed (follow-up)	All-cause mortality (30 days, 3, 6, 12 months) Cerebral perfor- mance category score (30 days, 3 months) Modified Rankin Score (30 days, 3 months) EQ-5D-5L QoL (30 days)	Survival, MI, revas- cularization, ICD shock, QoL, hospi- talization for heart failure, and the com- posite of death or MI or revascularization (1 year)	180-day survival rate with no or minimal neurologic sequelae
ng with non-ST-segn	Arms	Direct transfer to CA center vs. Current standard of care (geographically closest ED)	Immediate CAG vs. Delayed CAG	Emergency CAG vs. Delayed CAG (sooner than 48 to 96 h)
with patients presentir	Inclusion criteria	OHCA with ROSC and absence of STE on ECG Absence of non- -cardiac cause (trauma, drowning, suicide, drug overdose) Prognostication is to be delayed in trial patients until ≥ 72 h post arrest	OHCA with a shock- able rhythm who reached ROSC in the absence of STEMI	OHCA with ROSC, without an obvious non-cardiac cause of arrest No evidence of STE on postresuscitation ECG
rdiac arrest	Number of patients	860 patients (planned)	552 patients	279 patients
in out-of-hospital ca	Years of enrollment Type of study	02.2018–09.2020 (planned) RCT	01.2015–07.2018 A prespecified analysis of RCT	01.2017–11.2020 RCT
Table 2. Studies	Study	ARREST [34]	COACT [27, 35] [NTR4973]	EMERGE [8] [NCT02876458]

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ion.	Outcomes	The primary end point 55.1% early CAG vs. 46.0% no early CAG beath at 6 months (early CAG vs. no early CAG; HR 0.93; 95% CI 0.55-1.95; p = 0.77)	~30% of OHCA patients without STE had a culprit coronary lesion requiring PCI Emergent PCI was associated with a nearly 2-fold in- crease in the rate of cerebral perfor- mance category An initial shockable rhythm was the sole independent indicator for PCI requirement
ı myocardial infarct	Timing of coronary angiography	1.5 h (IOR 0.8 to 2.0) vs. 2.5 days (IOR 0.6 to 7.2) 48% of patients had CAG	AN
ST-segment elevation	Main outcomes assessed (follow-up)	A composite of efficacy and safety measurements (efficacy measures of survival to discharge and favorable neuro- logic status at discharge and echo- cardiographic measures) within 24 h of admission 24 h of admission 24 h of admission 26 condary end points: — prevalence of acute coronary oc- clusion, survival and favorable neurologic function (30 \pm 15 and 180 \pm 30 days after hospital discharge) — LVEF, and regional wall motion scores (at hospital discharge and 180 \pm 30 days after hospital discharge and 180 \pm 30 days after hospital discharge and 180 \pm 30 days after hospital discharge	The best level on the cerebral performance category scale (at hospital discharge)
resenting with non-S	Arms	Early CAG (within 120 min of arrival at the PCI-capable center) vs. No early CAG (no CAG within 6 h of hospital arrival)	Not randomized Successful PCI vs. No culprit lesion
arrest with patients p	Inclusion criteria	Successfully resusci- tated and comatose after OHCA, without regard for initial rhythm Suspected cardiac etiology for their sudden CA ECG demonstrated no STE or new LBBB	OHCA patients with an emergent CAG No evidence of STE on the post-resuscitation ECG
oital cardiac	Number of patients	99 patients	695 patients
Studies in out-of-hosp	Years of enrollment Type of study	01.2016-10.2018 RCT	01.2004–12.2013 Registry
Table 2 (cont.). 5	Study	PEARL [NCT02387398] [36]	PROCAT II [37]

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Benefits	Risks
High prevalence of coronary artery occlusions despite the absence of ST-elevation on the first acute electrocardiography	Highly unstable patients at a high risk of coronary angiography complications (a need to identify patients that would benefit from the procedure by detection of other potential treatable causes of the arrest, provision of clinical optimization prior to angiography)
Exclusion of coronary artery disease leading to facilitated differential diagnosis towards alternative etiology of cardiac arrest	Procedure-related adverse events
Withdrawal of potentially harmful antithrombotic treatment in case of coronary artery disease exclusion	Suboptimal care during peri-catheterization period (intensive care management included)

Table 3. Benefits and risks of revascularization in out-of-hospital cardiac arrest patients.

the exclusion of underlying CAD can provide valuable insights into differential diagnosis of complicated OHCA cases and optimal pharmacological management. Some investigators believe that reorganization and facilitation of OHCA management could offer significant clinical benefit. The ongoing ARREST [34] trial assesses the impact of the facilitated organization of OHCA management (direct transfer to CA center) in patients without STE vs. the current standard of care. Notably, a consulting cardiologist should be aware of potential neurological compromise and questionable survival benefit when qualifying to CAG. As reported in the study by Laver et al. [38], regardless of initial rhythm or ECG findings, the main reason for death in patients with OHCA is due to anoxic brain injury and, secondly, due to a refractory post-arrest shock and multi-organ failure. It was also confirmed in the COACT trial [27], which demonstrated that neurological condition was the cause of death in more than 70% of cases.

Treatment algorithm for management of OHCA

While response time and quality of care in the "chain of survival" predominantly affect survival of OHCA patients, an access to certain specific treatments, such as early activation of emergency medical services and resuscitation or advanced post-admission care with a focus on treating the underlying cause of OHCA, improves chances of recovery [39–41]. Upon OHCA patient arrival to a hospital emergency department, rapid and detailed assessment is required to develop a tailored treatment plan to be implemented in the department specializing in intensive management (Central illustration) [28, 42, 43]. Notably, 80% of OHCA patients admitted alive to the hospital are unconscious [44, 45]. Considering the high frequency of CAD as a cause of OHCA, interventional cardiologists are consulted frequently to consider CAG. Although emergency CAG is recommended in post-resuscitation STEMI patients, there is a common belief among physicians about the alleged benefit of CAG in OHCA patients without STE, which is not supported by current evidence.

Timely introduction of post-ROSC care, including admission to cardiac intensive care unit (CICU) or intensive care unit (ICU), targeted temperature management, vital-organ support, and treatment of the underlying cause of the arrest improves neurological outcomes that are detrimental drivers of survival and quality of life after hospital discharge, with studies reporting the majority of non-survivors dying of neurologic complications after the CA [27, 38, 46–48]. Therefore, any procedures delaying the initiation of post-ROSC management should be accounting for the potential benefit-risk ratio of an individual patient. This, depends on the center's organization and team leader approach for a specific clinical presentation, that usually takes one of two forms — ordering advanced imaging procedures, and consults from the level of the emergency department, prior to the admission to CICCU/ /ICU, or timely admission to CICU/ICU, where additional procedures are conducted after a period of initial stabilization of the condition and initiation of post-ROSC care. The clinical condition of the patient and OHCA presentation remains a significant driver for diverse steps of treatment management. Unclear presentation requires the execution of not only general post-ROSC care but also an introduction of differential diagnosis and personalized management. Any concomitant conditions that contributed to OHCA or has complicated its presentation require urgent medical



Central illustration. Proposed algorithm for coronary catheterization. Based on Rab et al. [28], Jentzer et al. [42], and Kelly et al. [43]; I. Exclude non-cardiac reasons for arrest = (acute respiratory failure, non-cardiogenic shock) by surgical management of trauma, neurosurgical or vascular patients, and/or brain and chest computed tomography-scans with subsequent thrombectomy of cerebral arteries, pneumothorax dressing, etc.; ACO — acute coronary occlusion; ALS — advanced life support; CABG — coronary artery bypass grafting; CAD — coronary artery disease; CICU — cardiac intensive care unit; CPR — cardiopulmonary resuscitation; ECG — electrocardiography; ECLS — extracorporal life support; ED — emergency department; ETCO₂ — end tidal carbon dioxide; ICU — intensive care unit; LBBB — left bundle branch block; LV — left ventricle; OHCA — out-of-hospital cardiac arrest; PCI — percutaneous coronary intervention; ROSC — return of spontaneous circulation; STE — ST-elevation; TTM — targeted temperature management; VF — ventricular fibrillation; VT — ventricular tachycardia.

attention and are commonly prioritized in treatment plan development. This includes, but is not limited to, the treatment of reversible arrest causes (acute respiratory failure, non-cardiogenic shock), surgical management of trauma, neurosurgical or vascular patients, coronary angiography and/or brain and chest computed tomography — scans with subsequent thrombectomy of cerebral arteries, pneumothorax dressing, etc. Despite delaying patient admission to the ICU, these procedures can provide vital clinical reserves for stabilizing and subsequently improving a patients' condition and future outcomes.

Closing remarks

The facilitation and individualization of OHCA management remain a pivotal point of focus to assert improvement of clinical outcomes. With patients facing poor survival and requiring timely neurological- or cardiovascular-oriented management, there is an urgent need for data, especially in patients without STE who could benefit from either immediate or delayed angiography.

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