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Interventional Therapies for Post-Cardiac Arrest Patients Suffering from Coronary Artery Disease

Michael Behnes, Philipp Kuche, Ibrahim Akin and Kambis Mashayekhi

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Abstract

Acute myocardial infarction and coronary artery disease (CAD) are the most common causes for the development of malignant arrhythmia often leading to cardiogenic shock and cardiac arrest. Structural heart disease represents the main pathology in older patients, whereas young adults mostly suffer from cardiomyopathies and channelopathies. This book chapter delineates modern interventional therapies for patients with cardiogenic shock or aborted cardiac arrest. Epidemiological data on the incidence of malignant arrhythmia depending causing cardiac arrest depending on the presence or absence of CAD and myocardial infarction are presented. Realistic difficulties within clinical decision-making are counterbalanced for and against an early, aggressive and invasive therapeutic approach including early coronary angiography with percutaneous coronary intervention (PCI), targeted temperature management and mechanical cardiac assist devices, depending on the individual clinical presentation and underlying cardiac arrhythmia.

Keywords: cardiac arrest, assist device, shock, ventricular fibrillation, ventricular tachycardia, coronary artery disease

1. Introduction

In recent decades, cardiovascular mortality has been reduced by effective prevention of risk factors and development of coronary heart disease (CAD) or progressive heart failure syndrome [1]. Nevertheless, cardiovascular disease accounts for 17 million deaths per year, of which 25% are related to cardiac arrest with consecutive sudden cardiac death (SCD) [1]. The risk of SCD was shown to be higher in men and increasing age, alongside with an increasing age-dependent

prevalence of CAD. European guidelines estimate SCD occurring in about 1.40/100,000 person-years in women, and even higher in about 6.68/100,000 person-years in men. Accordingly, the estimated annual death rate ranges in between 1100 and 9000 in Europe [1].

There are multiple varying causes for development of cardiac arrest. Structural heart diseases are present at older age, including CAD, heart valve diseases and heart failure syndrome, whereas in younger adults, cardiac arrest is more often caused by cardiomyopathies, channelopathies, myocarditis and substance abuse [1].

This chapter summarizes current knowledge of patients with cardiac arrest and concomitant CAD. Current knowledge about epidemiological data on the incidence of malignant arrhythmias causing cardiac arrest depending on the presence or absence of CAD is presented. Furthermore, the potential benefits of an early coronary revascularization as well as of a prompt complete coronary revascularization compared to treatment of coronary culprit lesion only are outlined. Finally, the advantages of invasive therapies for patients surviving cardiac arrest, such as targeted temperature management and mechanical cardiac assist devices, are elucidated.

2. Prevalence of CAD in patients with malignant cardiac arrhythmia

This chapter subsumes asystole, ventricular tachycardia, ventricular storming and ventricular fibrillation under the term malignant arrhythmia.

Prior structural heart disease may be present in almost 50% of patients suffering from cardiac arrest, whereas an even higher rate of subclinical CAD is suspected in these patients. Over decades, medical research has focused on the detection of reliable risk markers for the development of malignant arrhythmia in order to reliably estimate the chance for their individual occurrence. The most robust indicator represents the degree of left ventricular (LV) dysfunction according to LV ejection fraction (LVEF). In addition, screening includes all known cardiovascular risk factors, such as increases of low-density lipoprotein (LDL) cholesterol, smoking status, presence of diabetes mellitus, arterial hypertension and obesity. The implementation of screening methods to assess patients' individual cardiovascular risk, as well as effective diagnostics and treatment of CAD and heart failure has helped to prevent approximately 40% of SCD cases [2].

The overall rate of primary ventricular fibrillation or pulseless ventricular tachycardia (pVT) as the initial documented heart rhythm in clinical arrest settings varies between 25 and 79% in US registries in 2007, especially when occurring in public daily life [3]. In contrast, an increase of pulseless electrical activity (PEA) and asystole was documented alongside with a decrease of ventricular fibrillation and pVT. This inversion may be explained by improved medical care including improved guideline-based drug treatment for CAD and heart failure, percutaneous coronary intervention (PCI), implantable cardioverter-defibrillators (ICD), and the associated increasing prevalence of end-stage heart failure syndrome, which is associated with a higher prevalence of combined PEA or asystole at final disease stages [4, 5]. Survival rates are higher after cardiac arrest when a shockable ventricular arrhythmia (pVT or ventricular fibrillation) is documented (30.5%), whereas survival is lower in the presence of PEA or asystole (only 7.5–8%) [6].

-
- The risk of SCD is higher for men and increases with age.
 - Incidence of SCD: approx. 1.40/100,000 person-years in women, whereas 6.68/100,000 person-years in men.
 - The annual death rate of SCD ranges from 1100 to 9000 in Europe.
 - Causes:
 - Young adults: cardiac channelopathies, cardiomyopathies, myocarditis and substance abuse.
 - Older adults: degenerative heart disease such as CAD, valvular heart disease and heart failure.
 - Structural heart disease is already known in about 50% of patients.
 - Active screening for cardiovascular risk factors and early detection and treatment of CAD and heart failure prevents 40% of SCD cases.
 - A shockable initial rhythm (VF, pVT) is associated with a higher survival rate compared to asystole and PEA.
 - The rates of asystole and PEA as initial arrhythmia in cardiac arrest are increasing.
 - CAD requiring intervention is present in up to 75% of patients with survived cardiac arrest.
 - Patients with persistent coma after cardiac arrest are associated with a higher mortality of up to 50%.
-

Table 1. Empirical data on coronary artery disease (CAD), malignant cardiac arrhythmia and cardiac arrest.

Clinically relevant CAD with critical coronary arterial stenoses requiring PCI was shown in approximately 75% of patients with cardiac arrest [7, 8]. In the presence of an acute coronary syndrome, about 6% of these patients sustain pVT or ventricular fibrillation within the first 24 h after symptom onset [1]. There is currently no detailed information available on the exact prevalence of CAD depending on the different types of malignant arrhythmia. This is partly due to lack of representative prospective studies or registries including either preselected cohorts with smaller patient numbers and short follow-up periods. Currently running registries are:

- Parisian Region Out of Hospital Cardiac Arrest (PROCAT; [9]),
- Minnesota Resuscitation Consortium (MRC; [10]),
- Resuscitation Outcomes Consortium (ROC; [11]),
- Emergency Cardiopulmonary Bypass (ECPB; [12, 13]),
- Registry of Malignant Arrhythmias and Sudden Cardiac Death – Influence of Diagnostics and Interventions (RACE-IT; clinicaltrials.gov identifier: NCT02982473),
- Extracorporeal Life Support Organization (ELSO; <https://www.elseo.org>).

Furthermore, empirical data about the influence of CAD specific therapies on the different malignant arrhythmia are inconclusive. This implies in particular the influence of coronary revascularization by PCI or aortocoronary bypass surgery (CABG), targeted catheter-based ablation of ventricular tachycardia or supply by ICD on long-term course of patients with aborted cardiac arrest. Accordingly, mortality data depending on the underlying cardiac arrhythmia in patients being treated by modern cardiological therapies are not well represented in recent studies [1]. **Table 1** summarizes the most important empirical data on CAD, malignant arrhythmia and cardiac arrest.

3. Value of early invasive coronary diagnostics and therapies after cardiac arrest

The biological processes that cause an arrested heart either to regain a regulated sinus rhythm with sufficient myocardial contraction and stroke volume or not to recover adequately after an acute myocardial infarction are still unclear [4]. The reperfusion-damage theory is often debated, which has to be prevented by coronary revascularization and reperfusion. Still vital myocardium is threatened not only by cell death under circumstances of ongoing ischemia, but also by changes in cell metabolism and the sudden resupply of oxygen and other substrates after reperfusion [14]. Whether re-exposure to normal concentrations of oxygen, calcium or a balanced pH value may have beneficial or even fatal effects following successful reperfusion of a closed coronary artery is poorly understood and very controversial [15, 16]. It is assumed that the reperfusion damage is subject to temporal dynamics. After a prolonged ischemic phase, there is a critical time frame in which reperfusion may cause even more harm than benefit [17]. This has been proven in studies investigating ischemic preconditioning. Here, repetitive periods of iatrogenic induced complete ischemia may reveal myocardial protection and may reduce the reperfusion damage [18].

Today, emergency PCI combined with an extracorporeal bypass is one of the favored revascularization strategies. Emergency bypass requires rapid cannulation of a large central artery and vein, typically femoral artery and vein, and can be inserted out-of-hospital already [12, 19]. Since 2000, those concepts have been pushed forward. For instance, more than 30 cardiac arrest centers were created in Japan to establish full cardiovascular support and emergency PCI support within 15 min, achieving a survival rate of more than 15% in cardiac arrest patients with good neurological function [7]. The administration of additional intravenous drug combinations as a so-called “anti-perfusion-damage cocktail” is another concept that has so far only been evaluated in experimental work [4, 20].

In case of an established emergency bypass protected emergency PCI can be performed safer. Emergency PCI represents the decisive therapy in cardiac arrest patients, which may prevent ongoing myocardial necrosis. In addition, the baseline neurological status of each individual patient is directly related to mortality after cardiac arrest. About two-thirds of all patients with out-of-hospital cardiac arrest caused by ST segment elevation myocardial infarction (STEMI) are in a comatose state. In particular, this group of patients is associated with a significantly higher mortality of 50%, compared with a mortality of only 5% in awake patients after being successfully resuscitated [21].

About 50% of patients surviving out-of-hospital cardiac arrest and with proven CAD reveal acute coronary artery occlusion [7]. Therefore, European guidelines recommend primary PCI in patients with a successfully restored spontaneous circulation (ROSC) after cardiac arrest, cardiopulmonary resuscitation (CPR) in the presence of STEMI, regardless of baseline neurological status (recommendation class I, level of evidence B) [1, 7, 9]. In contrast, coronary angiography should also be performed independently of ECG findings in survivors of cardiac arrest with an intermediate pretest probability, which is estimated on the basis of age, gender and symptoms (recommendation grade IIa, level of evidence B-C [1, 22, 23]. This also includes patients with “ventricular storming” (recommendation grade IIa, level of evidence C [22]). According to various mostly nonrandomized studies, early invasive coronary

angiography may lead to increasing one-year survival in up to 60%. Still 58% of patients without ST-segment elevation reveal a critical coronary arterial stenosis (“culprit lesion”) [6, 9, 24, 25]. Again, most studies investigating patients suffering from acute coronary syndrome and malignant arrhythmia were observational and heterogeneous including both patients with STEMI and NSTEMI [26]. Invasive coronary angiography with PCI should be performed either immediately or as early as possible based on careful clinical assessment [6]. This concept is also supported by animal studies demonstrating an improvement of both survival and neurological function after immediate reperfusion therapy in pigs with induced ischemia-driven ventricular fibrillation [27]. A fortiori, further clinical parameters become considerably important, which in turn may limit the use of an early PCI in the individual (**Table 2**).

These parameters include the following: [6]

- unwitnessed cardiac arrest;
- absence of ventricular fibrillation as primary arrhythmia;
- absence of bystander CPR;
- prolonged or repeated CPR;
- CPR period longer than 30 min;
- lactate value >7 mmol/L, pH value <7.2 both being associated with severe tissue hypoxia and multiple organ failure;
- age > 85 years;
- terminal renal failure requiring renal replacement therapy; and
- presence of noncardiac causes leading to cardiac arrest.

-
- Unwitnessed cardiac arrest
 - Absence of ventricular fibrillation as primary arrhythmia
 - Absence of bystander CPR
 - Prolonged or repeated CPR
 - CPR period longer than 30 min
 - Lactate value >7 mmol/L, pH value <7.2 both being associated with severe tissue hypoxia and multiple organ failure
 - Age > 85 years
 - terminal renal failure requiring renal replacement therapy
 - Presence of noncardiac causes leading to cardiac arrest
 - Patients with noncardiac causes of cardiac arrest
 - Advanced dementia
 - Persistent ventilation
 - Frailty
 - Multisystem disorders
-

Table 2. Important clinical parameters limiting prognosis and the additional benefit of an early aggressive invasive treatment strategy by PCI.

Other factors to consider include comorbidities such as advanced dementia, persistent mechanical ventilation, respiratory failure, frailty, physical or neurological disability and multisystemic disorders. All these factors should be taken into account independently of the documented primary arrhythmia on ECG because they postpone the indication for early invasive diagnostics and therapies.

Figures 1 and 2 show two emergency complex multiple PCIs in two patients in cardiogenic shock after impending or survived cardiac arrest using two different cardiac/ventricular assist devices (VAD) as extracorporeal life support (ECLS).

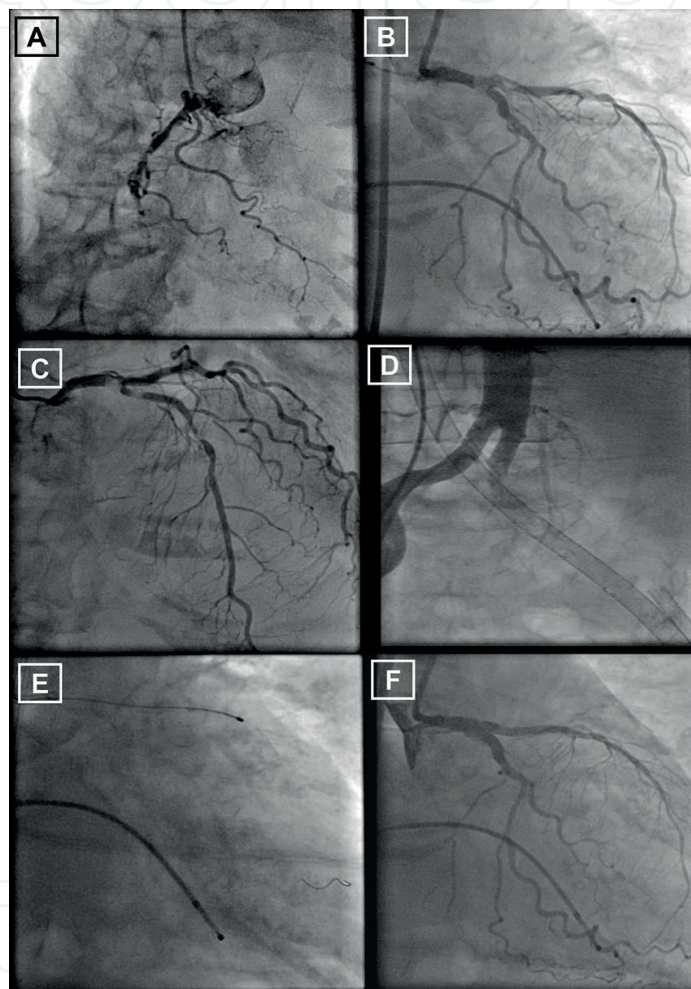


Figure 1. Emergency coronary angiography of a 82-year-old female patient surviving out-of-hospital cardiac arrest with immediate nonprofessional resuscitation. Ventricular fibrillation was documented as primary arrhythmia, with consecutive 15-min of CPR, multiple external electrical defibrillations and final ROSC. Severe coronary 3-vessel disease was found, with a chronic total occlusion of the right coronary artery (CTO) with ipsilateral and contralateral retrograde collateral connections (A). The left coronary artery shows a critical 99% stenosis at the distal main trunk (LMT), progressing into the central left circumflex (CX) (B) and left artery descending (LAD). LAD additionally shows sequential high-grade 99% proximal and mid-stenoses (C). By implantation of a venous-arterial extra-corporeal membrane oxygenation (VA-ECMO) via the left femoral artery and vein hemodynamic collapse was rapidly stabilized and complex multivessel PCI could have been initiated (D). First, rotablation (1.25 mm burr) from the LMT into the middle LAD (E). Secondly, single PCI/DES implantation was performed at mid-LAD (Boston Syndrome II 2.5/16 mm). Finally, bifurcational PCI of LMT-CX-RIVA T-stenting with antegrade protrusion (TAP) technique and final balloon kissing was performed (LMT in CX, Boston Synergy 4.0 / 24 mm; LMT in LAD protruded, Boston Synergy II 3.0/16 mm; final kissing with non-compliant balloons, Boston Emerge 4.0/20 and 3.5/15 mm) (F). Weaning from VA-ECMO and mechanical ventilation succeeds on the following day and the patient could have been discharged from hospital at day 9 in stable neurological and cardiopulmonary status.

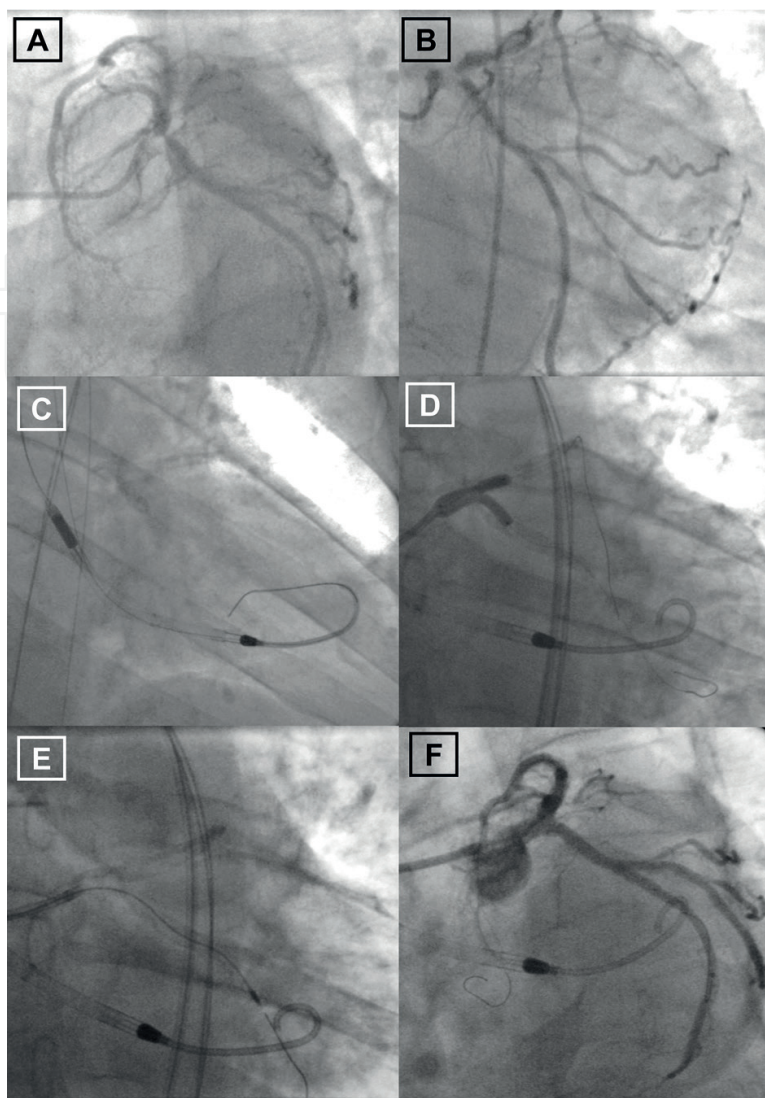


Figure 2. Severe coronary artery disease of a 50-year-old male patient with ST segment elevation myocardial infarction (STEMI) of the anterior wall, consecutive cardiogenic shock and prolonged cardiac arrest. Coronary angiography showed a subtotal stenosis of the mid and distal LMT, LAD showed long and critical stenosis, CX and first marginal branch were also highly stenosed (A&B). Right coronary artery was normal (not shown). Firstly, percutaneous and central intracardiac LVAD (Impella 2.5) was inserted into the left ventricle (C). Secondly, the LMT-LAD-CX bifurcation was predilated by a kissing balloon technique (D). Thirdly, rotablation (1.25 mm burr) of the mid CX was performed (E). Finally, complex multivessel PCI of marginal branch, CX and LAD. Final result showed sufficient TIMI-III flow with complete emergency revascularization (F). Impella device was removed after PCI due to recovery of circulation.

4. Emergency PCI with complete coronary revascularization or treatment of the coronary “culprit lesion” only?

European guidelines recommend immediate coronary revascularization in patients with recurrent ventricular tachycardia or fibrillation, in order to prevent suspected myocardial ischemia. However, graduation of recommendation is based on expert consensus only (grade of recommendation I, level of evidence C; [1, 22]). On the other hand, the SYNTAX trial demonstrated that complete compared to incomplete coronary revascularization (either by PCI or CABG) significantly improves long-term survival of patients with coronary three-vessel

disease [28]. In cardiogenic shock, early coronary revascularization was associated with improved long-term survival compared to drug therapy [29, 30]. However, early PCI in cardiogenic shock or in patients with aborted cardiac arrest is applied in 50–70% of patients only [31], although most of these patients reveal coronary multivessel disease being associated with significantly higher mortality compared to coronary one-vessel disease [32, 33]. Depending on hemodynamic instability and complexity of multivessel coronary disease according to the SYNTAX level, either a PCI or CABG may be the recommended treatment option in cardiogenic shock (Grade I, Level B evidence) [22]. The “CULPRIT-SHOCK” study recently demonstrated a prognostic benefit for a staged PCI of the “culprit lesion” at first in patients with cardiogenic shock and coronary multivessel disease compared to “ad-hoc” multivessel PCI directly at presentation. This prognostic benefit was attributed to fewer amount of contrast use and consecutive fewer rates of renal failure, when the culprit lesion was treated at first presentation and all other critical coronary artery stenoses underwent PCI some days later after hemodynamic recovery [34, 35]. Comparative studies evaluating CABG versus PCI in patients suffering from cardiac arrest or cardiogenic shock are lacking [36]. However, the advantages for immediate PCI consist of a better accessibility of cardiac catheterization laboratories compared to cardiac surgery units, including rapid feasibility of PCI with minimally invasive access. This has led to an almost lower prevalence of emergency CABG in post-cardiac arrest patients of less than 5% [31].

5. Additional benefit of interventional and surgical treatment options after cardiac arrest

Beside revascularization therapy of all critical coronary artery stenoses or occlusion, further interventional and surgical therapeutic option have become available for patients after cardiac arrest. These advanced therapies reveal two main therapeutic goals:

1. cerebral neuroprotection and myocyte protection after episodes of ongoing hypoxemia during cardiac arrest; and
2. restoration of hemodynamic stability in cardiogenic shock.

5.1. Targeted temperature management

Cerebral and myocardial protection can be achieved by myocardial reperfusion and targeted temperature management (TTM). The TTM may attenuate various signaling pathways leading to cell death by revealing anti-apoptotic and anti-inflammatory effects [37]. Smaller cohort studies demonstrated that invasive treatment after cardiac arrest including TTM and coronary angiography with reperfusion therapy by PCI can reduce myocardial infarction size [38]. In addition, it could have been shown that TTM alone without reperfusion reveals adverse effects because the extent of myocardial infarction was comparable independently of treatment with TTM. TTM plus reperfusion resulted in the best recovery

of cardiac function with the lowest myocardial infarction size [39]. This experimental evidence confirms the disadvantage of delayed coronary revascularization and limits the benefit of sole TTM after cardiac arrest.

In contrast, Mooney et al. demonstrated that delayed initiation of TTM in patients with out-of-hospital cardiac arrest was associated with a 20% increase of mortality. However, the rate of invasive coronary angiography was 72% with a PCI rate of 40% only [40]. It is well documented from several cohort studies that a combined PCI plus TTM improves survival and neurological outcome in patients with cardiac arrest and persistent coma [6].

TTM consists of controlled intravenous infusion systems (e.g., Bogard XP® Temperature Management System, ZOLL Medical Corporation, Asahi Kasei Corp, Japan) in combination with cool packs. TTM may not be initiated out-of-hospital only in order to achieve potentially best possible prognostic and neurological outcome [41, 42]. The target temperature is aimed between 32 and 36°C, whereas even lower target temperatures were shown to have no additional prognostic or neurological benefit [37, 43, 44]. Regardless of the documented primary arrhythmia, TTM is always recommended for at least 24 h duration in patients with persistent coma [37].

5.2. Cardiac assist devices for extracorporeal life support (ECLS)

Despite successful CPR and consecutive ROSC, there are still 30–40% of patients revealing hemodynamic instability and prolonged cardiogenic shock. In this situation, cardiac ventricular assist devices (VAD) may achieve stabilization or normalization of circulation. Cardiac index may be normalized, myocardial oxygen consumption and perfusion of secondary organs including brain and kidneys will be improved [25]. The presence of the acute emergency, in which post-cardiac arrest patients with prolonged cardiogenic shock are situated, favors minimally invasive or percutaneous VAD. Depending on the device type, each individual VAD increases cardiac output either with left (LV) or right ventricular (RV) mechanical support.

Currently available VAD systems for percutaneous access include the following:

- Intra-aortic balloon pump (IABP);
- LVAD – central:
 - LV to aorta: non-pulsatile axial Impella® 2.5/5.0 (Abiomed Europe, Aachen, Germany; Abb. 3a),
 - Left atrium (LA) to aorta: TandemHeart® LVAD KIT (CardiacAssist, Inc., Pittsburgh, USA; Abb. 3b);
- RVAD – central:
 - Vena cava inferior (VCI) to pulmonary artery (PA): non-pulsatile axial Impella RP® (Abiomed Europe, Aachen, Germany; 3a),

- RA to PA: TandemHeart® RVAD KIT with 2 cannulas (CardiacAssist, Inc., Pittsburgh, USA; Abb. 3c),
- RA to PA: TandemHeart® RVAD PROTEKDuo® double lumen cannula (CardiacAssist, Inc., Pittsburgh, USA; Abb. 3d);
- Extracorporeal membrane oxygenation (VA [veno-arterial]-ECMO) – peripheral:
 - V. femoralis to A. femoralis (VA): CARDIOHELP system (MAQUET GETINGE GROUP, Rastatt, Germany) or LIFEBRIDGE® 2.0 Systemccar- dio (ZOLL Medical Deutschland GmbH; Abb. 3e).

Unfortunately, scientific evidence about clinical benefits of the various VAD in patients with cardiogenic shock, aborted cardiac arrest or persistent ventricular tachycardia or fibrillation (“ventricular storming”) is still insufficient and not sound [1, 22, 25, 45]. Recommendation for mechanical circulatory support in cardiogenic shock caused by myocardial infarction is based purely on expert opinion (grade of evidence IIb, level of evidence C; [22]). VAD were shown to stabilize patients suffering from hemodynamically unstable ventricular tachycardia. In contrast, VAD may also complicate the therapeutic management in emergency situations because clinical application of VAD demands more members of staff. Additionally, mechanical assist devices were also shown to alleviate the incidence of ventricular tachycardia by the VAD itself [1].

Combining PCI with IABP was not associated with a significant reduction of infarct size [46]. In particular, IABP was not associated with a reduction of 30-day or 1-year mortality in patients surviving cardiogenic shock due to myocardial infarction [47, 48]. Therefore, the use of IABP is recommended only in case of mechanical complications in order to bridge the patient for cardiac surgery [22, 49].

More and more meta-analyses have recently been published, which conclusively analyzed smaller studies evaluating the benefit of VAD in patients after cardiac arrest or with cardiogenic shock. Ouweneel et al. [50] demonstrated that, after cardiac arrest, the use of VA-ECMO significantly improves both survival and neurological outcome at 30 days compared to patients treated with IABP or Impella® (n = 219). Even after cardiogenic shock, patients treated with VA-ECMO showed a higher survival rate at 30 days compared to patients with IABP or Impella® (n = 151) [50]. In contrast, the direct comparison between IABP and Impella® showed differences of survival in patients with acute myocardial infarction and cardiogenic shock [51, 52]. However, it could have been shown that the earliest possible use of Impella® reveals an independent prognostic factor for improved survival after cardiogenic shock [53–55]. Vase et al. described in a small case series (n = 8) that the use of the Impella® after cardiac arrest and mean CPR duration with “low-flow-time” of about 50 min is associated with a comparable survival rate to cardiogenic shock [56, 57].

Data for VAD between LA and aorta, such as TandemHeart®, are not available for patients surviving cardiac arrest or cardiogenic shock. Therefore, no evidence-based recommendation can be given. However, TandemHeart® was shown as a safe and feasible

mechanical circulatory support during high-risk PCI [45]. Specifically, for TandemHeart® a transseptal puncture is needed during implantation with trans-septal sheath diameters ranging from diameters of 15–16 French. However, transseptal puncture is rarely performed on a regular basis and only by a smaller number of interventional cardiologists. This makes the application of TandemHeart® limited for a widespread use in clinical practice especially in emergency situations of patients with cardiac arrest and cardiogenic shock [45]. In addition, dislocation of the LA cannula into pulmonary veins or left atrial appendage during relocation maneuvers or during intensive care transports are potential complications.

Data on VA-ECMO in cardiac arrest or cardiogenic shock patients are based on many smaller cohort studies published in 2006 in cardiac surgery settings. Here, a meta-analysis demonstrated a survival rate of 50% [11]. The abovementioned ELSO registry reports about a survival rate of 27% post cardiac arrest [58]. In 2013, Takayama et al. reported on 50% survival rate for patients with cardiac arrest or cardiogenic shock after implantation of VA-ECMO. Half of these patients needed a permanent surgical VAD at follow-up. Also in this cohort, prolonged duration of CPR was associated with increased mortality despite the use of VA-ECMO [59].

Modern medical technologies have been developed in recent years, which make VAD applicable for percutaneous access in critical and unstable situations. It should be emphasized that mechanical support after cardiac arrest and consecutive cardiogenic shock is not limited to the left heart only. In principle, and always depending on the underlying individual clinical condition, RV support can also be performed by another RVAD at the same time. The femoral access route is usually preferred for implantation of the LVAD. For RVAD, both the femoral and the transjugular access routes are possible. Direct and central unload of the congested heart is always recommended, but depends on technical applicability in each individual clinical situation. In contrast, insertion of cannulas at peripheral femoral vessels will always provide indirect unload for the congested heart because extracorporeal blood re-circulated to peripheral vessels. As a result, contrary effects were recently demonstrated for peripheral assist devices (**Figure 3d, e, left**; [45]). The increasing amount of peripherally recirculated blood volume automatically raises wall tension in the peripheral arterial system. In turn, this leads to considerable increase of afterload, which may be harmful for the congested, severely impaired LV after cardiac arrest. Therefore, the implantation of peripheral VA-ECMO systems additionally requires the placement of LA transseptal cannulas, which leads to “central unload” at the level of left atrium and the left ventricle (**Figure 3e, middle**; [60]). “Central unload” within the LA was more effective compared to RA because LV filling can be reduced from the left atrial level, while at the same time systemic perfusion is maintained more effectively. In contrast, unloading at the right atrium was associated with a significant increase of LV wall tension and LV unloading becomes even less effective [60]. Direct unloading within LA or LV (e.g., in the TandemHeart®) therefore represents the most effective way for mechanical circulatory support by VAD [49]. Additional unloading is usually achieved by an additionally inserted cannula, which is positioned in the LA after transseptal puncture, while it can be integrated into the peripheral VA-ECMO circuit via Y-connectors (**Figure 3e, right**).

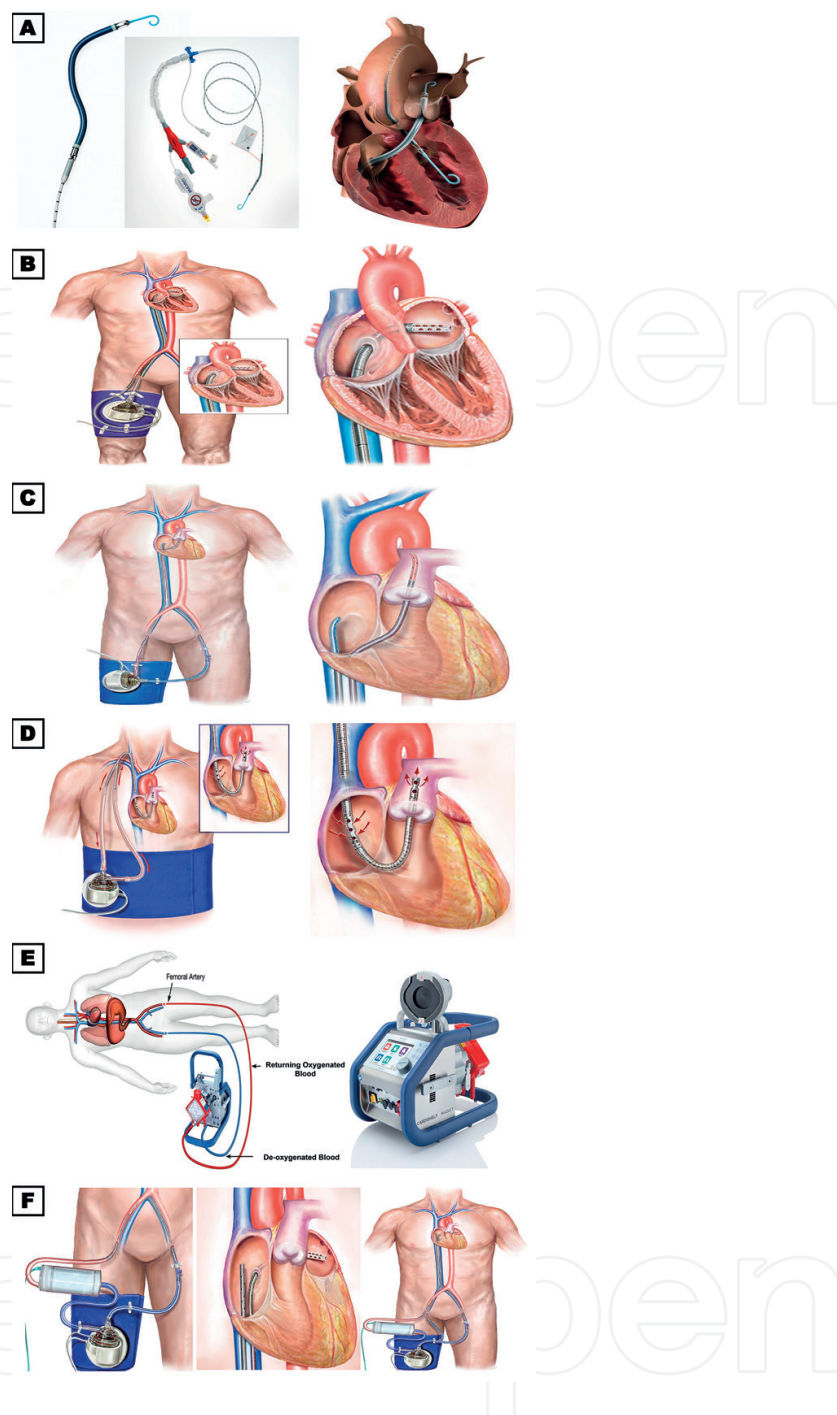


Figure 3. Graphical illustration of different ventricular assist devices (VAD) for extracorporeal life support (ECLS): Central left ventricular assist device (LVAD): (A) LV (left ventricular) to aorta: non-pulsatile axial Impella® 2.5/5.0 (Abiomed Europe, Aachen, Germany). (B) LA (left atrial) to aorta: Tandem Heart® VLAD KIT (Cardiac Assist, Inc., Pittsburgh, USA). Central right ventricular assist device (RVAD): (A) Vena cava inferior (VCI) to PA: nonpulsatile axial Impella RP® (Abiomed Europe, Aachen, Germany). (C) RA (right atrial) to PA (pulmonary artery): Tandem Heart® RVAD KIT with 2 cannulas (Cardiac Assist, Inc., Pittsburgh, USA). (D) RA to PA: Tandem Heart® RVAD PROTEK Duo® dual lumen cannula (Cardiac-Assist, Inc., Pittsburgh, USA). Peripheral ECLS: (E) extracorporeal membrane oxygenation (VA [veno-arterial] - ECMO): peripheral femoral vein to femoral artery (VA) - ECLS: CARDIOHELP System (MAQUET GETINGE GROUP, Rastatt, Germany). (F) Placement of LA cannula (trans-septal) in addition to the VA-ECMO: improved “unload” of the congested heart, the additional cannula can be integrated into the VA-ECMO circuit via Y-connectors. Unfavorable effects on the cardiovascular system due to peripherally placed assist devices can be reduced.

6. Conclusions for daily clinical practice

- The grade of recommendation for early invasive coronary angiography with immediate PCI in post cardiac arrest patients is still based only on non-randomized cohort studies or expert opinions, depending on the pretest probability and on the type of myocardial infarction (i.e., NSTEMI or STEMI).
- Decision-making for either an interventional-invasive or surgical approach should always include important prognostic cofactors.
- A staged PCI including emergency PCI of the coronary “culprit lesion” only in the emergency setting was shown to be safer and associated with improved survival compared to “ad-hoc” emergency PCI of all critical coronary stenoses in patients suffering from cardiogenic shock and coronary multivessel disease.
- The benefit of emergency CABG compared to emergency PCI after cardiac arrest requires further evaluation.
- Advanced interventional and operative therapies include targeted temperature management in combination with coronary revascularization and extracorporeal mechanical cardiac support systems, which include intra-aortic counter pulsation (IABP), central LVAD and RVAD, as well as peripheral ECMO systems.
- Randomized prospective studies comparing the use of VAD in post cardiac arrest patients is lacking. Use of VAD is still limited to specialized centers and a widespread routine application is still a long way off.

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