Revascularization strategies in cardiogenic shock after acute myocardial infarction

Steffen Desch[a,b]

Purpose of review
Coronary revascularization compared with medical treatment alone leads to improved survival in patients with myocardial infarction (MI) and cardiogenic shock. Percutaneous coronary intervention (PCI) is the predominant mode of revascularization in clinical practice. This review discusses several aspects relevant to mechanical revascularization such as general indication, the roles of PCI and bypass surgery, percutaneous access site choice, strategy in multivessel disease and adjunctive antithrombotic therapy.

Recent findings
The recently published CULPRIT-SHOCK trial provided the first randomized evidence that in the vast majority of patients with infarct-related cardiogenic shock PCI should be confined to the culprit lesion, whereas nonculprit lesions should not be routinely treated in the emergency setting. Although randomized data are not available, a primary radial access for PCI is becoming more popular in the shock population. Cardiac surgery plays an indispensable, yet quantitatively only minor role in the management of infarct-related cardiogenic shock.

Summary
Coronary revascularization remains the cornerstone in the early management of patients with acute MI and cardiogenic shock. In patients with multivessel disease, a strategy of culprit lesion only PCI is the default approach.

Keywords
cardiogenic shock, myocardial infarction, revascularization

INTRODUCTION

Between 5 and 13% of patients with acute myocardial infarction (MI) will develop cardiogenic shock [1–4]. In the vast majority of patients, infarct-related cardiogenic shock results from acute left ventricular failure. Despite advances in interventional and medical treatment, cardiogenic shock remains a leading cause of death in MI with in-hospital mortality rates up to 50% [5▪▪,6]. Coronary revascularization has been the most significant treatment advance in the past decades. This review discusses several aspects relevant to revascularization therapy such as general indication, the roles of percutaneous coronary intervention (PCI) and coronary artery bypass surgery (CABG), percutaneous access site choice, PCI strategy in multivessel disease and adjunctive antithrombotic therapy.

General benefit of revascularization in infarct-related cardiogenic shock

The landmark SHOCK trial investigated the value of emergency revascularization in cardiogenic shock patients with ST-elevation MI (STEMI), new left bundle branch block or posterior infarction (with ST-depression in anterior leads) [7]. The study randomized a total of 302 patients to either emergency revascularization (152 patients) or initial medical stabilization (150 patients). The primary end point was all-cause mortality at 30 days. Revascularization was accomplished by either angioplasty (64% of first revascularization attempts) or CABG (36% of first attempts). Of note, a high percentage of patients received thrombolytic therapy (49% in the emergency revascularization group and 63% in the medical therapy group). The median time

[a]Department of Internal Medicine/Cardiology, Heart Center Leipzig at the University of Leipzig, Leipzig and [b]Deutsches Zentrum für Herz-Kreislauf-Forschung (DZHK), partner site Hamburg/Kiel/Lübeck, Lübeck, Germany

Correspondence to Steffen Desch, MD, Department of Internal Medicine/Cardiology, Heart Center Leipzig at the University of Leipzig, Strümpellstr. 39, 04289 Leipzig, Germany. Tel: +49 341 865 1428; fax: +49 341 865 1461; e-mail: steffen.desch@medizin.uni-leipzig.de

Curr Opin Crit Care 2019, 25:379–383
DOI:10.1097/MCC.0000000000000623

1070-5295 Copyright © 2019 Wolters Kluwer Health, Inc. All rights reserved.

Copyright © 2019 Wolters Kluwer Health, Inc. All rights reserved.

KEY POINTS

- Mechanical coronary revascularization predominantly by PCI remains the cornerstone in the early management of patients with acute MI and cardiogenic shock.
- Cardiac surgery plays an indispensable role in complex coronary anatomies and/or mechanical complications of infarction.
- Radial access has proven feasible in PCI of cardiogenic shock. The choice between radial and femoral access should be individualized.
- In patients with multivessel disease, a strategy of culprit lesion only PCI is the default approach while nonculprit lesions should not be routinely treated in the emergency setting.

from randomization to emergency angioplasty was 0.9 and 2.7 h for CABG. Compared with today's standards, stent use was low (36% among patients assigned to early revascularization and receiving percutaneous angioplasty). By protocol, delayed revascularization after a minimum of 54 h was allowed in the medical treatment arm and was finally attempted in 21%. Although the trial failed to meet its primary endpoint of lowering 30-day mortality with early revascularization in comparison with initial medical stabilization, there was a significant survival benefit in favor of revascularization at longer follow-up after 6 months, 1 and 6 years [7,8]. The number needed to treat to save on life was reported to be eight reflecting a large absolute survival benefit [8]. By protocol, the SHOCK trial did not enroll patients with non-ST-elevation MI (NSTEMI), a cohort which made up about one third of the randomized trial populations in the more recent studies IABP-SHOCK II and CULPRIT-SHOCK [5▪▪,6]. It is assumed that the mortality benefit of early revascularization observed in shock patients with STEMI also pertains to the NSTEMI population.

Based on the SHOCK trial, revascularization as early as possible by either PCI or CABG is now standard of care in infarct-related cardiogenic shock. Nonetheless, despite the existing body of evidence, the rate of early revascularization ranges from 50 to 70% and is thus still underused in clinical practice [1].

In general, mechanical revascularization is preferred over fibrinolysis. However, fibrinolysis should be considered in STEMI-related cardiogenic shock if timely PCI is not feasible (within 120 min from STEMI diagnosis according to European Society of Cardiology guidelines) and mechanical complications have been ruled out [9].

PERCUTANEOUS CORONARY INTERVENTION OR CORONARY ARTERY BYPASS SURGERY?

There are no direct randomized comparisons between PCI and CABG in the setting of infarct-related cardiogenic shock. Observational reports could not demonstrate an influence on outcome by the type of revascularization [10]. For reasons of availability and timeliness of reperfusion as well as lower invasiveness, PCI has therefore emerged as the predominant mode of revascularization with CABG rates less than 5% in registries and randomized trials [3,6]. However, this does not dismiss the interventional cardiologist from consultation with cardiac surgery. Complex patients such as those with severe multivessel or left main disease should be discussed ad hoc in the catheterization laboratory by the Heart Team. Next to coronary anatomy and associated procedural risks, relevant aspects to consider also include patient comorbidities, potential treatment delays, local expertise, patient preference or additional mechanical complications of infarction. A collaborative approach also proves to be extremely helpful in the setting of high-risk PCI with the potential need for rapid surgical bail-out. Current guidelines recommend PCI in infarct-related cardiogenic shock if coronary anatomy is amenable and CABG as an alternative treatment option if coronary anatomy is not suitable for PCI (class IB recommendation) [9].

Percutaneous coronary intervention strategy in multivessel disease

Approximately 70–80% of patients with cardiogenic shock subsequent to MI present with multivessel disease [11]. These patients display higher mortality compared with patients with single vessel disease [12]. Although PCI of the culprit lesion is established standard practice, the optimal management of additional nonculprit lesions has only recently been elucidated in the multicenter CULPRIT-SHOCK trial. CULPRIT-SHOCK randomly assigned 706 patients who had multivessel disease, acute MI and cardiogenic shock to one of two initial revascularization strategies: either PCI of the culprit lesion only, with the option of staged revascularization of nonculprit lesions, or immediate multivessel PCI [5▪▪]. There was a significant clinical benefit of a culprit-lesion only strategy with a reduction in the primary endpoint of 30-day mortality or renal replacement therapy [45.9% culprit-lesion-only PCI versus 55.4% immediate multivessel PCI; relative risk 0.83; 95% confidence interval (CI) 0.71–0.96; $P = 0.01$] which was mainly driven by an absolute 8.2% reduction in 30-day mortality (43.3 versus

Copyright © 2019 Wolters Kluwer Health, Inc. All rights reserved.

51.5%; relative risk 0.84; 95% CI 0.72–0.98, $P = 0.03$). The 30-day results of CULPRIT-SHOCK could recently be confirmed with a consistent reduction in the composite endpoint at 1-year follow-up for the culprit-lesion-only PCI with possible staged revascularization strategy [13▪]. The difference in all-cause mortality was slightly attenuated and as expected more patients underwent additional revascularization after culprit-lesion-only PCI. The CULPRIT-SHOCK results were consistent across all predefined subgroups [5▪▪,13▪]. Thus, except for individual patients, revascularization should be limited to the culprit lesion with possible staged revascularization of other lesions at a later point in time. This has recently been implemented in the ESC 2018 revascularization guidelines (class IIIB recommendation against immediate multivessel PCI) [14].

Access site

In acute coronary syndrome without cardiogenic shock, several large-scale clinical trials have shown superiority of radial over femoral access and the radial approach is now considered standard of care in operators experienced in radial catheterization [15–17]. The picture is, however, much less clear in infarct-related cardiogenic shock as there are yet no randomized data.

Femoral access is still preferred by many interventionalists. Arguments in favor of the traditional femoral access are centralization of circulation with faint or nonpalpable radial pulse, unstable patients with little tolerance for prolonged attempts of puncture or coronary access, oftentimes complex coronary interventions and the possible use of percutaneous mechanical circulatory support (which necessitates femoral access). On the other hand, the radial approach has undoubtedly proven superior with regard to access-site bleeding, a frequent complication in cardiogenic shock patients which may influence clinical outcome.

In a meta-analysis of observational trials in patients with cardiogenic shock undergoing PCI, transradial access was associated with a reduction in mortality and major adverse cardiac and cerebral events at 30 days [18]. However, the results must be treated with caution given the high likelihood of selection bias in the underlying studies. Until randomized trials become available, it is prudent to say that access site should predominantly be based on personal expertise with either technique and additional considerations based on the individual scenario. Operators inexperienced in radial technique should first master technical aspects of the radial approach in PCI of stable patients with or without acute coronary syndrome before moving to cardiogenic shock patients. For operators proficient in radial interventions, the threshold for a switch from radial to femoral access should be low in case the intervention proves to be difficult via the radial access. If percutaneous mechanical circulatory support via the femoral artery is planned following PCI, the femoral approach should be strongly considered. If mechanical circulatory support is started before PCI, a combination of radial and femoral access presents an option.

Adjunctive antiplatelet and anticoagulant therapy

Data on the use of antiplatelet agents specifically in the population of patients with infarct-related cardiogenic shock are limited. Cardiogenic shock is often accompanied by severely impaired enteral perfusion and a subsequent compromise in absorption of oral antiplatelet agents. This might theoretically translate into a delayed onset of platelet inhibition or an overall attenuated effect of antiplatelet agents with subsequent increased risk for acute stent thrombosis and cardiovascular morbidity and mortality. Further, cardiogenic shock often leads to acute kidney/liver failure and altered elimination kinetics.

In general, prasugrel or ticagrelor (clopidogrel if there are contraindications to the newer oral antiplatelets) are administered in addition to aspirin, a regimen adopted from patients with hemodynamically stable MI. In nonshock patients with MI crushed ticagrelor leads to faster inhibition of platelet aggregation compared with noncrushed tablets [19]. It appears therefore reasonable to administer crushed tablets in the setting of cardiogenic shock in case ticagrelor is used. The intravenous P2Y12 inhibitor cangrelor provides rapid onset of platelet inhibition and a short half-life and is therefore theoretically appealing. A randomized study of cangrelor in cardiogenic shock (DAPT-SHOCK-AMI) is currently recruiting patients [20]. Administration of P2Y12 inhibitors may be deferred until coronary anatomy is known, as emergent CABG could be indicated based on angiographic findings.

Glycoprotein IIb/IIIa inhibitors provide immediate onset of action and may also be used temporarily in cardiogenic shock. Observational data suggest a potential survival benefit with the use of glycoprotein IIb/IIIa inhibitors in cardiogenic shock [21]. However, a small randomized trial of 80 patients failed to confirm clinical benefit from routine upstream compared with optional abciximab [22]. In the subset of cardiogenic shock patients with high thrombus burden or slow flow after PCI, glycoprotein IIb/IIIa inhibitors should be considered as bail-out treatment.

1070-5295 Copyright © 2019 Wolters Kluwer Health, Inc. All rights reserved.

Copyright © 2019 Wolters Kluwer Health, Inc. All rights reserved.

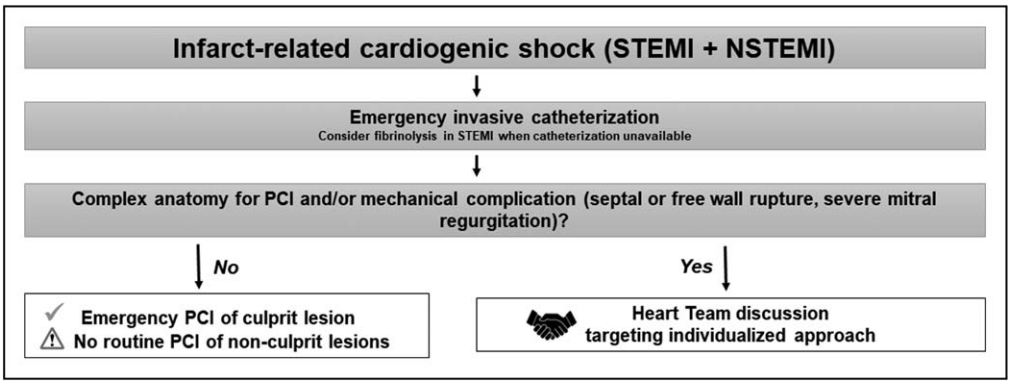


FIGURE 1. Proposed revascularization algorithm for patients with cardiogenic shock associated with myocardial infarction. NSTEMI, non-ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

Intravenous unfractionated heparin is usually administered in conjunction with reperfusion therapy although data specific to infarct-associated cardiogenic shock are missing. Similarly, there are only scarce scientific data for alternative anticoagulants such as bivalirudin, low-molecular-weight heparin or fondaparinux. Given the high prevalence of acute kidney and/or liver injury in cardiogenic shock, these may be less suited and may only be used with great caution and close monitoring. Subcutaneous administration may be unreliable in centralized circulation.

Guidance documents by professional societies

Guidance on revascularization in infarct-related cardiogenic shock can be found in diverse documents issued by professional societies [9,14,23–25]. A dedicated scientific statement document recently published on behalf of the American Heart Association specifically deals with the various aspects of cardiogenic shock management including detailed coverage of revascularization [26▪▪]. An analogous document is currently being prepared by the Heart Failure Association of the European Society of Cardiology.

CONCLUSION

Early revascularization is the evidence-based cornerstone of initial shock treatment. PCI plays a predominant role in today's clinical practice and for the majority of patients should be confined to the culprit lesion (with possible staged PCI of other significant nonculprit lesions at a later time point). Emergency cardiac surgery is reserved for patients with complex coronary anatomy not amenable to PCI and/or mechanical complications and should be discussed by the Heart Team. The transradial access in PCI of cardiogenic shock has recently gained popularity as an alternative to traditional femoral access although a direct randomized comparison is missing. Evidence for optimal antiplatelet therapy in cardiogenic shock is scarce. Crushed tablets of oral P2Y12 inhibitors or intravenous antiplatelet agents appear reasonable treatment options based on pharmacokinetic assumptions. Mechanical circulatory support will be discussed in another article of this issue. A treatment algorithm for revascularization in infarct-related cardiogenic shock is presented in Fig. 1.

Acknowledgements

None.

Financial support and sponsorship

None.

Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- ▪ of special interest
- ▪▪ of outstanding interest

1. Aissaoui N, Puymirat E, Tabone X, *et al.* Improved outcome of cardiogenic shock at the acute stage of myocardial infarction: a report from the USIK 1995, USIC 2000, and FAST-MI French Nationwide Registries. Eur Heart J 2012; 33:2535–2543.
2. Backhaus T, Fach A, Schmucker J, *et al.* Management and predictors of outcome in unselected patients with cardiogenic shock complicating acute ST-segment elevation myocardial infarction: results from the Bremen STEMI Registry. Clin Res Cardiol 2018; 107:371–379.
3. Jeger RV, Radovanovic D, Hunziker PR, *et al.* Ten-year incidence and treatment of cardiogenic shock. Ann Intern Med 2008; 149:618–626.
4. Rathod KS, Koganti S, Iqbal MB, *et al.* Contemporary trends in cardiogenic shock: incidence, intra-aortic balloon pump utilisation and outcomes from the London Heart Attack Group. Eur Heart J Acute Cardiovasc Care 2018; 7:16–27.

Copyright © 2019 Wolters Kluwer Health, Inc. All rights reserved.

5. Thiele H, Akin I, Sandri M, *et al.* PCI strategies in patients with acute ■■ myocardial infarction and cardiogenic shock. N Engl J Med 2017; 377:2419–2432.

Landmark study addressing percutaneous coronary intervention (PCI) strategy in infarct-related cardiogenic shock and multivessel disease. Culprit-lesion only proved to be superior to immediate multivessel PCI.

6. Thiele H, Zeymer U, Neumann F-J, *et al.* Intraaortic balloon support for myocardial infarction with cardiogenic shock. N Engl J Med 2012; 367:1287–1296.
7. Hochman JS, Sleeper LA, Webb JG, *et al.* Early revascularization in acute myocardial infarction complicated by cardiogenic shock. SHOCK Investigators. Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock. N Engl J Med 1999; 341:625–634.
8. Hochman JS, Sleeper LA, Webb JG, *et al.* Early revascularization and long-term survival in cardiogenic shock complicating acute myocardial infarction. JAMA 2006; 295:2511–2515.
9. Ibanez B, James S, Agewall S, *et al.* 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. The 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.
10. Mehta RH, Lopes RD, Ballotta A, *et al.* Percutaneous coronary intervention or coronary artery bypass surgery for cardiogenic shock and multivessel coronary artery disease? Am Heart J 2010; 159:141–147.
11. Thiele H, Ohman EM, Desch S, *et al.* Management of cardiogenic shock. Eur Heart J 2015; 36:1223–1230.
12. Sanborn TA, Sleeper LA, Webb JG, *et al.* Correlates of one-year survival in patients with cardiogenic shock complicating acute myocardial infarction: angiographic findings from the SHOCK trial. J Am Coll Cardiol 2003; 42:1373–1379.
13. Thiele H, Akin I, Sandri M, *et al.* One-year outcomes after PCI strategies in ■ cardiogenic shock. N Engl J Med 2018; 379:1699–1710.

One-year outcomes of landmark CULPRIT-SHOCK study addressing PCI strategy in multivessel disease.

14. Neumann F-J, Sousa-Uva M, Ahlsson A, *et al.* 2018 ESC/EACTS Guidelines on myocardial revascularization. Eur Heart J 2019; 40:87–165.
15. Jolly SS, Yusuf S, Cairns J, *et al.* Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes (RIVAL): a randomised, parallel group, multicentre trial. Lancet 2011; 377:1409–1420.
16. Romagnoli E, Biondi-Zoccai G, Sciahbasi A, *et al.* Radial versus femoral randomized investigation in ST-segment elevation acute coronary syndrome: the RIFLE-STEACS (Radial Versus Femoral Randomized Investigation in ST-Elevation Acute Coronary Syndrome) study. J Am Coll Cardiol 2012; 60:2481–2489.
17. Valgimigli M, Gagnor A, Calabro P, *et al.* Radial versus femoral access in patients with acute coronary syndromes undergoing invasive management: a randomised multicentre trial. Lancet 2015; 385:2465–2476.
18. Pancholy SB, Palamaner Subash Shantha G, Romagnoli E, *et al.* Impact of access site choice on outcomes of patients with cardiogenic shock undergoing percutaneous coronary intervention: a systematic review and meta-analysis. Am Heart J 2015; 170:353–361.
19. Parodi G, Xanthopoulou I, Bellandi B, *et al.* Ticagrelor crushed tablets administration in STEMI patients: the MOJITO study. J Am Coll Cardiol 2015; 65:511–512.
20. https://www.clinicaltrials.gov/ct2/show/NCT03551964?cond=NCT03551964&rank=1. [Accessed March 2019].
21. Antoniucci D, Valenti R, Migliorini A, *et al.* Abciximab therapy improves survival in patients with acute myocardial infarction complicated by early cardiogenic shock undergoing coronary artery stent implantation. Am J Cardiol 2002; 90:353–357.
22. Tousek P, Rokyta R, Tesarova J, *et al.* Routine upfront abciximab versus standard periprocedural therapy in patients undergoing primary percutaneous coronary intervention for cardiogenic shock: the PRAGUE-7 Study. An open randomized multicentre study. Acute Card Care 2011; 13:116–122.
23. Ibanez B, Halvorsen S, Roffi M, *et al.* Integrating the results of the CULPRIT-SHOCK trial in the 2017 ESC STEMI Guidelines: viewpoint of the Task Force. Eur Heart J 2018; 39:4239–4242.
24. Patel MR, Calhoon JH, Dehmer GJ, *et al.* ACC/AATS/AHA/ASE/ASNC/SCAI/SCCT/STS 2016 appropriate use criteria for coronary revascularization in patients with acute coronary syndromes: a report of the American College of Cardiology Appropriate Use Criteria Task Force, American Association for Thoracic Surgery, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and the Society of Thoracic Surgeons. J Am Coll Card 2017; 69:570–591.
25. Roffi M, Patrono C, Collet J-P, *et al.* 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. 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 2016; 37:267–315.
26. van Diepen S, Katz JN, Albert NM, *et al.* Contemporary management of ■■ cardiogenic shock – a scientific statement. Circulation 2017; 136:e232–e268.

Up-to-date and comprehensive guidance document on the management of cardiogenic shock (of various causes).

1070-5295 Copyright © 2019 Wolters Kluwer Health, Inc. All rights reserved.

Copyright © 2019 Wolters Kluwer Health, Inc. All rights reserved.