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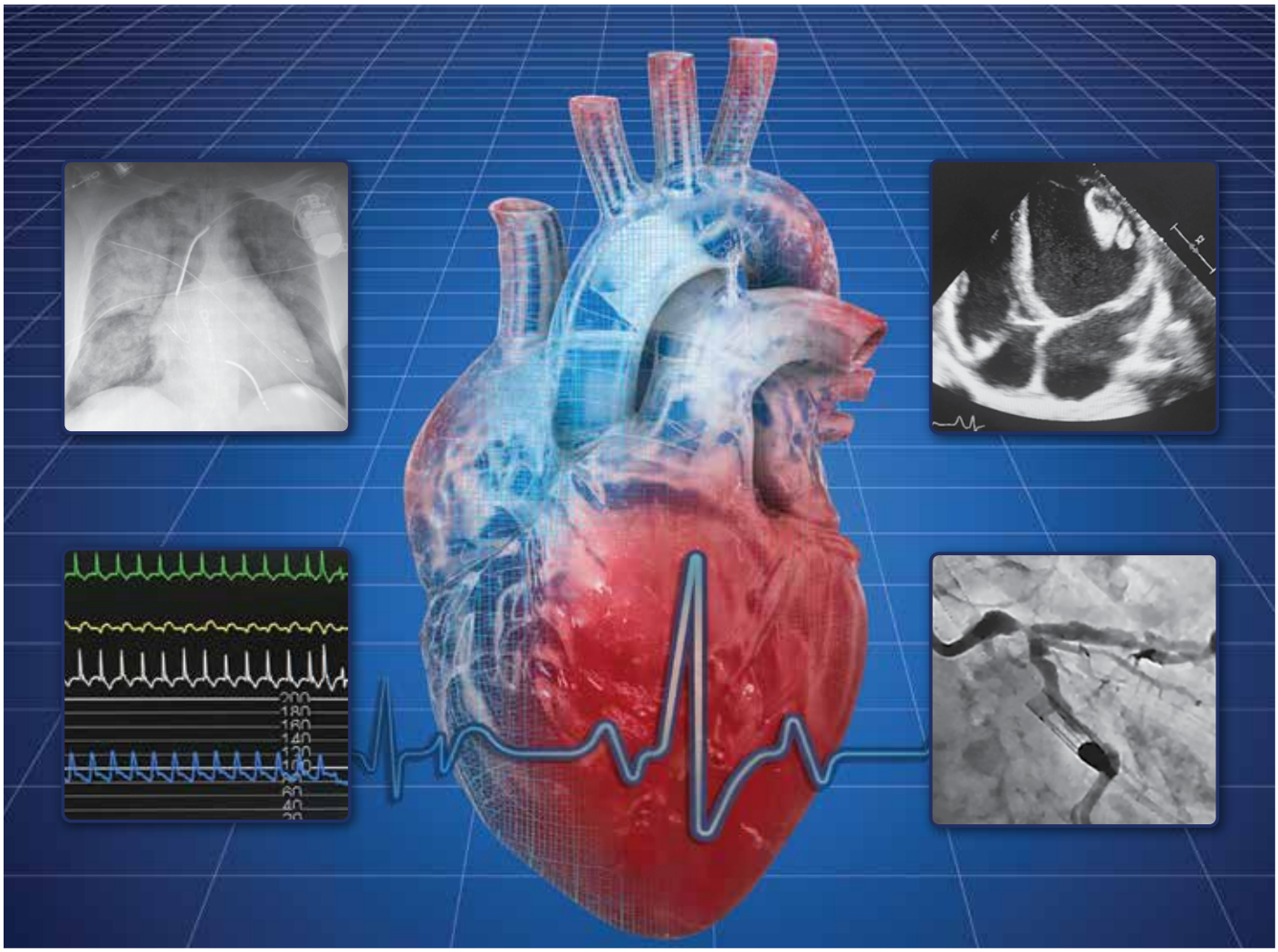

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General Information

Cardiogenic shock mortality remains unacceptably high despite advances in medical management and the widespread use of percutaneous mechanical circulatory support device therapy. Its mortality rate has been largely stagnant in the past two decades. This is partly because cardiogenic shock is a disease state that is occasionally elusive to recognize. Its severity is a spectrum that often fluctuates in the same patient, and its definitive therapies have not been protocolized. Further, septic shock is currently the leading cause of mortality in intensive care units, and clear guidance beyond initial fluid and antimicrobial therapy is lacking.

The ***Journal of Shock and Hemodynamics (JoSH)*** will publish original research manuscripts, review articles, and case reports related to all aspects of shock, including cardiogenic, septic, neurogenic, and vasodilatory circulatory collapse. Additionally, we will seek papers emphasizing invasive and non-invasive hemodynamic assessments that span the entire field of cardiovascular medicine. ***JoSH*** is an open-access publication that is the official journal of the Annual Houston Shock Symposium (www.HoustonShock.org).

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Target Audience: Cardiologists, cardiovascular surgeons, interventionalists, intensivists, neuro-intensivists, nurses, and others interested in critical care, hemodynamics, and cardiovascular medicine.

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2022 Symposium Presentation

Role of Invasive Hemodynamics in Shock Management:

Is a Pulmonary Artery Catheter Always Necessary?

Ajay J. Kirtane, MD, SM
Columbia University Medical Center, New York

Email: ak189@cumc.columbia.edu

Abstract

The pulmonary artery (PA) catheter can be a useful tool in the management of patients with cardiogenic shock; however, there are challenges with the use of this catheter, and clinicians must balance the risks and benefits. In addition, clinicians must properly interpret data generated from a PA catheter in the context of other data to optimize a patient's hemodynamics.

Keywords: pulmonary artery catheter, cardiogenic shock, hemodynamics

Background

The pulmonary artery (PA) catheter can be a useful tool in the management of patients with cardiogenic shock. It allows for direct and accurate measurements of hemodynamic parameters during insertion and serially over time. Serial observations are very useful for patient monitoring as the measurements (central venous pressure, right ventricle [RV] pressures, PA pressures, pulmonary capillary wedge pressure, saturations) can be used to calculate certain critical data (cardiac output, vascular resistance, stroke volume, oxygen delivery, shunt fractions, PA pulsatility index). Beyond this, PA catheters can even incorporate data simulation to calculate stress blood volume and other measurements useful in patient management. Most importantly, data generated from the PA catheter can provide information on the etiology of shock. It can detail the type of issue (eg, volume, output, what side) and what to do next (volume, pressors, mechanical circulatory support).

Challenges to PA Catheter Use

The challenge with the PA line by itself is that it gives the clinical team several numbers, and the team then has to actively integrate and analyze the readings to figure out what to do. Further, the use of a PA catheter requires time, effort, and cost—not just with the insertion, but the maintenance of the catheter. If the catheter is inserted for too long, the patient can develop a line infection. Data from a PA catheter can be misinterpreted, misleading, or simply not used. Thus, the clinical program must regularly educate team members on how to appropriately use the catheter and the resulting data. Of note, the information gathered from the PA catheter could additionally be redundant to other tests (eg, echocardiogram, central venous pressure measurement alone). Finally, complications are always a risk.

Despite the challenges, many clinicians caring for patients with shock insist upon a PA catheter. For each patient, the team must balance the risks and benefits of the procedure. With the advent of checklists and their integration into electronic health records, a team can ensure the PA catheter is placed in shock patients; however, it is not of value unless the team goes beyond checking the box and understands what to do with the data once the catheter is put in to be able to then manage the patient. Using Medicare data, Ikuta and colleagues showed that, overall, the use of the PA catheter is declining over time.[1] However, for patients with heart failure, there's an inflection point, and the use of catheters started to increase after 2005.[2]

A key trial to mention is the ESCAPE trial, which prospectively gathered data from 433 patients with heart failure at 26 sites and determined that the use of the PA catheter was not beneficial in patients who did not need it.[2] Importantly, shock patients were not included in the ESCAPE Trial. Many patients with decompensated heart failure at a variety of stages that are not that severe can, in fact, be managed without a PA catheter. The question that remains is, if the patient is in shock, should you use the catheter? Cardiogenic shock patients have very little reserve, so if the wrong decision is made, the patient could decompensate. On the other hand, inappropriately placed PA catheters could also lead to complications or suboptimal treatment decisions.

Use of PA Catheter Data

To optimize hemodynamics with a PA catheter, variables should not be interpreted (or overinterpreted) in isolation. Serial observations must be interpreted in the context of other data, and trends are generally more useful than isolated variables at a single point in time. Integration of measurements with the clinical situation increases the accuracy of the assessment. Thus, in a way, the best mantra for shock management could be summarized as “Keep calm and check, check, and recheck again on how patients are doing.” If one does not integrate serial measurements into the clinical picture, one might end up with a scenario where an agent such as an inotrope is given to a patient with active ischemia, which could induce ventricular tachycardia. The blame should not be on the agent but rather on the team for making the wrong decision in terms of what to give that patient. Clinicians can overreact to numbers, and that overreaction can result in unfavorable outcomes.

Clinical Studies

Studying patients with severe cardiogenic shock is difficult. However, when an invasive therapy is used in the sickest patients, and a benefit is still seen in observational studies of that therapy, that is a powerful outcome. Studies of the sickest populations usually show worse outcomes because the patients were so sick to begin with. Even if it is observational data, beneficial outcomes in these sick populations are rare. Thus, any benefit signal from observational studies in severely sick populations should be further explored in randomized trials. An excellent example is from the Cardiogenic Shock Working Group which observed that PA catheter use was associated with lower mortality rates in patients with cardiogenic shock.[3]

Another study compared PA catheter-based assessments of volume optimization and cardiac index to clinical judgment and found that clinical assessments had low accuracy across all training levels.[4] Thus, clinical teams need to understand the importance of using objective data derived from helpful tools, like a PA catheter. PA catheter measurements can also help the team determine the ideal device selection[5] and volume optimization.[6] Similarly, both sides of the heart must be assessed to determine the best treatment, as a significant proportion of patients have biventricular congestion.[7] Emerging data has shown how PA catheter measurements can be used to identify RV dysfunction.[8] Ultimately, PA catheter assessments have been useful in determining device weaning protocols.[9] While the PA catheter measurements cannot be used alone, they have been shown to be a valuable tool in the clinical toolbox.

Randomized trials of PA catheters in cardiogenic shock are currently being planned by the Cardiogenic Shock Working Group. However, the proposed PAC-CS Trial has the potential for failure if it is not done right; just placing the PA catheter alone is unlikely to be associated with improved outcomes. Specific guidance is needed to detail what should be done after the PA catheter is placed. Optimization and regulation of monitoring the readings from the catheter are vital for the success of the study.

History of the Swan Catheter

I had the privilege of hearing James Forrester present a talk on the development of the Swan catheter at the Transcatheter Cardiovascular Therapeutics meeting in 2019.[10] The following story is excerpted and paraphrased from his talk, which to me was awe-inspiring.

“Dr. Jeremy Swan was inspired by watching sailboats in the ocean off the coast of California. He hypothesized that a balloon-tipped catheter could enable a device to go into the PA or other vessel. As a favor, folks from Edwards Lifesciences used an infant feeding tube with a balloon and gave it to Swan to test, and the first animal catheterization by Diamond and Forrester was completed in 1969. They put the catheter into the venous system and saw an unusual waveform. In fact, the catheter had traversed the right heart and was advanced into the PA. As today’s institutional review board processes were not in place, they sterilized the catheter and then used it in a patient admitted to the medical intensive care unit. Unfortunately, once the catheter was placed, the patient had a horrific run of ventricular tachycardia that was induced by the catheter tip flailing wildly within the RV. A later modification to move the balloon on the tip of the catheter increased the safety of this catheter. Likewise, today as clinicians work with really sick patients, it always behooves us to think about how the placement of a PA catheter could cause complications.

Dr. Willie Ganz was 49 years old and abandoned all his worldly possessions and fled communism. Philanthropy enabled his journey to the United States, and through serendipity, the unknown lab researcher developed a way to measure cardiac output through thermistors in an animal laboratory. Through collaboration with Dr. Swan and the team that had developed the PA catheter, the Swan-Ganz catheter was born.”

In some ways, this is how we must take care of our sick patients; everyone with individual expertise and experiences must come together to manage the patients with an individualized treatment plan.

Disclosures

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References

[1] Ikuta K, Wang Y, Robinson A, Ahmad T, Krumholz HM, Desai NR. National Trends in Use and Outcomes of Pulmonary Artery Catheters Among Medicare Beneficiaries, 1999-2013. *JAMA Cardiol*. 2017;2(8):908-913. doi: 10.1001/jamacardio.2017.1670.

[2] Binanay C, Califf RM, Hasselblad V, et al. Evaluation study of congestive heart failure and pulmonary artery catheterization effectiveness: the ESCAPE trial. JAMA. 2005;294(13):1625-33. doi: 10.1001/jama.294.13.1625. DOI:10.1161/CIRCHEARTFAILURE.120.007405.

[3] Garan AR, Kanwar M, Thayer KL, et al. Complete Hemodynamic Profiling With Pulmonary Artery Catheters in Cardiogenic Shock Is Associated With Lower In-Hospital Mortality. *JACC Heart Fail*. 2020;8(11):903-913. doi: 10.1016/j.jchf.2020.08.012.

[4] Narang N, Chung B, Nguyen A, et al. Discordance Between Clinical Assessment and Invasive Hemodynamics in Patients With Advanced Heart Failure. *J Card Fail*. 2020;26(2):128-135. doi: 10.1016/j.cardfail.2019.08.004.

[5] Whitehead EH, Thayer KL, Sunagawa K, et al. Estimation of Stressed Blood Volume in Patients With Cardiogenic Shock From Acute Myocardial Infarction and Decompensated Heart Failure. *J Card Fail*. 2021;27(10):1141-1145. doi: 10.1016/j.cardfail.2021.04.002.

[6] Fincke R, Hochman JS, Lowe AM, et al. Cardiac power is the strongest hemodynamic correlate of mortality in cardiogenic shock: a report from the SHOCK trial registry. *J Am Coll Cardiol*. 2004;44(2):340-8. doi: 10.1016/j.jacc.2004.03.060.

[7] Thayer KL, Zweck E, Ayouty M, et al. Invasive Hemodynamic Assessment and Classification of In-Hospital Mortality Risk Among Patients With Cardiogenic Shock. *Circ Heart Fail*. 2020;13(9):e007099. doi: 10.1161/CIRCHEARTFAILURE.120.007099.

[8] Jain P, Thayer KL, Abraham J, et al. Right Ventricular Dysfunction Is Common and Identifies Patients at Risk of Dying in Cardiogenic Shock. *J Card Fail*. 2021;27(10):1061-1072. doi: 10.1016/j.cardfail.2021.07.013.

[9] Randhawa VK, Al-Fares A, Tong MZY, et al. A Pragmatic Approach to Weaning Temporary Mechanical Circulatory Support: A State-of-the-Art Review. *JACC Heart Fail*. 2021;9(9):664-673. doi: 10.1016/j.jchf.2021.05.011.

[10] Forrester J. Reflections from a Rich Interventional History: A Series of Featured Lectures. Transcatheter Cardiovascular Therapeutics Conference 2019.

2022 Symposium Presentation

Surviving Sepsis Campaign: Strategies to Implement in Cardiogenic Shock Management

James Burke, MD, PhD, FACC
Lehigh Valley Heart and Vascular Institute

Email: James.Burke@lvhn.org

Abstract

The Surviving Sepsis Guidelines can serve as a structure to help educate and create a set of recommendations on how to care for patients through this complicated pathway of shock. Designing a cardiogenic shock bundle could reduce the variability of care and possibly improve survival. Also, a more standard protocol would allow a review of the outcomes and a system to change practice nationally when new data or technology becomes available. This could create a continuous quality improvement cycle. Creating a "Surviving Cardiogenic Shock" system could help provide awareness for recognition of cardiogenic shock and advanced management alternatives needed at level one and two hospitals. The creation of cardiogenic shock systems of care would support smaller hospitals with a Hub and Spoke structure. Cardiogenic shock is not septic shock, but those in cardiology and cardiac critical care can and should take lessons from the Surviving Sepsis Campaign.

Keywords: Surviving Sepsis Campaign, cardiogenic shock, management

Background

The Surviving Sepsis Campaign is an international set of guidelines for the management of sepsis and septic shock. It provides guidance on the care of hospitalized adult patients with, or at risk of, sepsis. The goals are early identification and appropriate management in the initial hours after the development of sepsis to improve outcomes. To achieve that goal, *sepsis bundles* are used to improve program performance by integrating sepsis scoring, education, metrics, and patient outcomes. Meta-analysis and clinical trials have shown that using sepsis bundles improves mortality rates for patients with sepsis and septic shock. All bundles use sepsis screening tools, and the debate continues about which one is best for each situation. The most common include the quick sequential organ failure assessment (qSOFA), modified sequential organ failure assessment (mSOFA), national early warning score (NEWS), and modified early warning score (MEWS). Indeed, the EPIC electronic health record system has the MEWS already built in.

Recommendations

First published in 2004,[1] the guidelines put forth by the Surviving Sepsis Campaign have had several revisions, with the most recent being at the end of 2021.[2] Most recently, over 20 recommendations have been updated. One recommendation supports the use of the SOFA score over MEWS or NEWS. Another recommendation is to give crystalloid (30 mL/kg) to patients with hypoperfusion or shock within 3 hours. There is also a recommendation to use dynamic measures to guide fluid resuscitation over physical examination or static parameters. A suggestion for this is to use capillary refill as a guide for resuscitation. However, the new guidelines do not emphasize measuring central venous pressure; they do recommend looking at volume loading through some of those techniques. A mean arterial pressure of 65 mmHg is the recommended target pressure. The reality, though, is that there are not a lot of hemodynamic parameters included in the recommended sepsis bundle.

Cardiogenic Shock vs Septic Shock

While cardiogenic shock is not septic shock, the guidelines for septic shock do inform care. Sepsis has a relatively common etiology, including infection or inflammation. It has low-tech initial therapies that include intravenous (IV) fluids, IV antibiotics, IV vasopressors, and basic hemodynamic monitoring such as heart rate, blood pressure, and electrocardiogram. All therapies are available in acute care hospitals. Alternatively, cardiogenic shock has various etiologies and phenotypes that make the initial therapy variable as well. Treatment of cardiogenic shock involves advanced therapies that are not cheap and are not available in all hospitals.

The goal of the septic bundles is to cut down on variations, which is helpful for escalation and de-escalation. Thus, can a bundle be adapted to help inform cardiogenic shock therapy and reduce the huge variability in practice?

Critical Care Cardiology Trials

Clinical registries, such as the Critical Care Cardiology Trials Network (CCCTN), have looked at variations in care in the management of cardiogenic shock. This includes the use of pulmonary artery (PA) catheters to assess and guide management, acute mechanical circulatory support devices such as the intra-aortic balloon pump (IABP), and the Impella percutaneous ventricular assist device (pVAD) (Abiomed).

Utilization of the IABP in all care centers, tertiary or quaternary, varied and was dependent upon whether a shock team was present or not.[3,4] The presence of a shock team correlated with less IABP use and more Impella implantations. One of the key issues is that only 42% of patients who had advanced circulatory support and Impella or extracorporeal membrane oxygenation (ECMO) had a PA catheter placed. In the CCCTN registry, the use of a PA catheter was associated with improved survival. However, the use of PA catheters varied significantly among the different centers. This may be in part due to the perceived risk associated with use and cost. Surprisingly, many of the patients who received advanced mechanical circulatory support did not have PA catheter monitoring. While there are currently no randomized clinical trials demonstrating that PA catheters improve outcomes in conjunction with AMCS, current registries such as the CCCTN and the National Cardiogenic Shock registries demonstrate a strong correlation with survival in cardiogenic shock when a PA catheter is utilized to guide care. While there is literature on protocols for the management of cardiogenic shock and shock teams, there currently is no national consensus, similar to the Surviving Sepsis Bundles. It is likely that a consensus of best practice guidelines for the management of cardiogenic shock or care bundles may allow for a structure to further improve outcomes.

Conclusion

The Surviving Sepsis Guidelines can serve as a structure to help educate and create a set of recommendations on how to care for patients through this complicated pathway of shock. Designing a cardiogenic shock bundle could reduce the variability of care and possibly improve survival. Also, a more standard protocol would allow a review of the outcomes and a system to change practice nationally when new data or new technology becomes available. This could create a continuous quality improvement cycle. Creating a "Surviving Cardiogenic Shock" system could help provide awareness for recognition of cardiogenic shock and advanced management alternatives needed at level one and two hospitals. The creation of cardiogenic shock systems of care would support smaller hospitals with a Hub and Spoke structure. Cardiogenic shock is not septic shock, but those in cardiology and cardiac critical care can and should take lessons from the Surviving Sepsis Campaign.

References

[1] Dellinger RP, Levy MM, Rhodes A, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock, 2012. Intensive Care Med. 2013;39(2):165-228. doi: 10.1007/s00134-012-2769-8.

[2] Evans L, Rhodes A, Alhazzani W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Intensive Care Med. 2021;47(11):1181-1247. doi: 10.1007/s00134-021-06506-y.

[3] Berg DD, Barnett CF, Kenigsberg BB, et al. Clinical Practice Patterns in Temporary Mechanical Circulatory Support for Shock in the Critical Care Cardiology Trials Network (CCCTN) Registry. Circ Heart Fail. 2019;12(11):e006635. doi: 10.1161/CIRCHEARTFAILURE.119.006635.

[4] Tehrani BN, Truesdell AG, Psotka MA, et al. A Standardized and Comprehensive Approach to the Management of Cardiogenic Shock. JACC Heart Fail. 2020;8(11):879-891. doi: 10.1016/j.jchf.2020.09.005.

2022 Symposium Presentation

Hemodynamic Goals in Shock Management: Is There One Target for All?

Maya Guglin, MD, PhD
Indiana University

Email: mguglin@iu.edu

Abstract

The current guidelines for managing cardiogenic shock lack specificity and clarification. The main criterion for cardiogenic shock is low cardiac output, and the most important goal is to achieve adequate output from a shock state. Because of the complex nature of cardiogenic shock, a “one-size-fits-all" outline may not be the best solution. Historically, hemodynamic goals in cardiogenic shock are copied from septic shock. Because septic shock and cardiogenic shock are different hemodynamic entities, the goals should be different.

Keywords: cardiogenic shock, hemodynamics, management

Background

In a statement from the American Heart Association on critical care unit monitoring, there is only one paragraph that outlines the hemodynamic goals to manage cardiogenic shock. It states:

The optimal [mean arterial pressure] MAP likely differs from patient to patient, and the risks of hypoperfusion with lower MAPs must be balanced (and individualized) with the potentially deleterious impact of vasoactive agents on myocardial oxygen demand, ischemia, and arrhythmia associated with higher MAP targets.[1]

While certainly appropriate, the guidelines lack direct and specific goals for managing cardiogenic shock. Any recommendations come from studies of septic shock. In contrast, guidelines on septic shock are clear and specific.

The guidelines from the Surviving Sepsis Campaign[2] state similar goals:

- Central venous pressure (CVP) of 8-12 mmHg
- Mean arterial pressure (MAP) greater than 65 mmHg
- Mixed venous saturation (SvO_2) greater than 65%
- Urine output greater than 0.5 mL kg h^{-1}

Septic and cardiogenic shock studies in the context of guideline refinement will be reviewed.

Studies Related to Septic Shock

The Surviving Sepsis Campaign referenced a randomized trial comparing goal-directed therapy to standard therapy.[3] The in-hospital mortality for goal-directed therapy was 30.5% versus 46.5% with standard therapy.

A post hoc data analysis of a multicenter trial investigated the association of MAP and vasopressor load in septic shock patients.[4] Similar mortality rates were seen when patients were grouped into quartiles based on MAP (from 70-100 mm Hg). When the quartiles were based on vasopressor load and dose, there was a stepwise increase in mortality with each increasing quartile.

In a retrospective study evaluating arterial blood pressure during sepsis and outcome, the best results were seen in patients with a MAP between 60 and 65 mmHg.[5] The time spent below these values correlated with increased mortality risk, with an odds ratio of 2.96.

Septic Shock versus Cardiogenic Shock

Septic shock and cardiogenic shock are hemodynamically different. They share some common features, such as end-organ hypoperfusion, tissue hypoperfusion, and cardiac index but differ in cardiac output, wedge pressure, CVP, etc. Because they are entirely different entities, the hemodynamic goals for septic shock should not be applied to the cardiogenic shock setting. This is especially important since not all cardiogenic shock cases are created equal.

Cardiogenic shock can be caused by a pulmonary embolism and acute right ventricular failure with an underfilled ventricle that creates low cardiac output.[6] Cardiogenic shock can result from acute myocardial infarction with left ventricular failure, high wedge pressure, and normal right atrial pressure. Depending on ideology, there are differences in how patients go into cardiogenic shock. Hypertension, hypoperfusion, decreased cardiac output, and possible congestion are all commonly seen after the immediate impact of arterial occlusion in acute myocardial infarction-related shock. The same can also be seen in cardiogenic shock caused by heart failure; however, the process is gradual rather than acute. To curate more specific priorities and hemodynamic goals for managing cardiogenic shock, the differences between cardiogenic shock and septic shock, and even the different etiologies of cardiogenic shock, need to be further explored through prospective studies.

There are different mortality profiles depending on the type of congestion.[7] Right ventricular congestion, left ventricular congestion, and bi-ventricular congestion exist, and all are seen in patients with cardiogenic shock. Right ventricular and bi-ventricular congestion carry higher mortality risks than left ventricular congestion. In the setting of acute myocardial infarction, left ventricular congestion carries a higher risk of mortality than heart failure-related shock.

We need to design and conduct randomized trials in patients with cardiogenic shock to define appropriate hemodynamic goals for each type of shock of cardiogenic origin. For any type of shock, the specific goals should provide guidance to achieve normal cardiac output, adequate perfusion of end organs, and an euvolemic state.

Conclusion

The main criterion for cardiogenic shock is low cardiac output, and the most important goal is to achieve adequate cardiac output from a shock state. There may not be a “one size fits all” solution because of the variety of cardiogenic shock types; however, the current guidelines for goal-directed management need further clarification and specificity. For any type of cardiogenic shock, we need to achieve normal cardiac output, adequate perfusion of end organs, and an euvolemic state. Prospective studies comparing and investigating different sets of goals are needed.

References

[1] van Diepen S, Katz JN, Albert NM, et al. Contemporary Management of Cardiogenic Shock: A Scientific Statement From the American Heart Association. *Circulation*. 2017;136(16):e232-e268. doi: 10.1161/CIR.0000000000000525.
[2] Dellinger RP, Levy MM, Rhodes A, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock, 2012. *Intensive Care Med*. 2013;39(2):165-228. doi: 10.1007/s00134-012-2769-8.
[3] Rivers E, Nguyen B, Havstad S, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med*. 2001;345(19):1368-77. doi: 10.1056/NEJMoa010307.
[4] Dünser MW, Ruokonen E, Pettilä V, et al. Association of arterial blood pressure and vasopressor load with septic shock mortality: a post hoc analysis of a multicenter trial. *Crit Care*. 2009;13(6):R181. doi: 10.1186/cc8167.
[5] Dünser MW, Takala J, Ulmer H, et al. Arterial blood pressure during early sepsis and outcome. *Intensive Care Med*. 2009;35(7):1225-33. doi: 10.1007/s00134-009-1427-2.
[6] Abraham J, Blumer V, Burkhoff D, et al. Heart Failure-Related Cardiogenic Shock: Pathophysiology, Evaluation and Management Considerations: Review of Heart Failure-Related Cardiogenic Shock. *J Card Fail*. 2021;27(10):1126-1140. doi: 10.1016/j.cardfail.2021.08.010.
[7] Thayer KL, Zweck E, Ayouty M, et al. Invasive Hemodynamic Assessment and Classification of In-Hospital Mortality Risk Among Patients With Cardiogenic Shock. *Circ Heart Fail*. 2020;13(9):e007099. doi: 10.1161/CIRCHEARTFAILURE.120.007099.

2022 Symposium Presentation

Racial Variations in Shock Presentation and Outcome

Steven Bailey, MD, MSCAI, MACP, FACC, FAHA
Department of Internal Medicine, LSU Heath School of Medicine, Shreveport, LA

Email: Steven.Bailey@lsuhs.edu

Abstract

Working toward inclusive strategies for data sampling, trials, and triage is essential. Whatever the approach, it is important to do better than what has been done in the past when considering race and ethnicity in patient care. Although there may be limited publications with information on this topic, they have shown clear differences in patient outcomes with possible associations with gender, race, and ethnicity. It is critical to view the implications of this on socioeconomic status, access, resources, patient phenotypes, and patient desires and expectations. The disparities must first be recognized before any treatment options can be identified.

Keywords: racial variation, cardiogenic shock, outcome

Background

Discussing racial variation is difficult when our understanding of cardiogenic shock is evolving. Based on retrospective data, we know disparities exist. Patient demographics such as race, ethnicity, sex, and socioeconomic status are important determinants of health care, access, delivery, and outcomes. Significant racial and sex disparities have been documented in patients with heart failure, stroke, acute myocardial infarction, and transcatheter aortic valve replacement (TAVR). Further evaluation of access, quality of care, and health system biases is essential and requires investigation as, at present, their impacts are uncertain.

TAVR and Shock Stages

According to the Woodlands data, a key area of care that is costly but has a high impact is TAVR treatment.[1] Most individuals undergoing TAVR are Medicaid-funded, which is typical of cardiogenic shock, but they are not in communities or regions with a high concentration of Black or Hispanic individuals. It is important to consider how we categorize individuals, phenotype severity, risk, etc. This is even more true when we talk about race and ethnicity.

We understand that mortality risk rates depend on the patient's ranking in the Society for Cardiovascular Angiography and Interventions (SCAI) stage of shock. It is important to note the differences between where non-White patients present and their assessment. In terms of outcomes, some questions to consider are:

- How precise is our assessment of shock among physicians?
- How good are physicians at assessing shock?
- Do patients present with different shock phenotypes based on race and ethnicity?

We can make assumptions, but the data to support these assumptions is unavailable.

There are three programs with variable interpretations and assessments of the SCAI stages of shock.[1] This complicates patient assessment when we bring race and ethnicity into the equation. The data from these programs do not reflect the differences in assessment based on race and ethnicity, and this is a subject that should be addressed. However, it is important to note that data may identify some phenotypes that are associated with mortality. Using artificial intelligence could be an interesting approach to patient assessment.

The Data

Based on retrospective data from 2012 to 2017 on cardiogenic shock, another part of the population that must be considered is the race category of *other*—many of whom cross-identify as Black. In 2020, 12% of Americans self-identified as Black, and 14% identified as a mixed race, including being Black. When looking at national inpatient samples (NIS) of multiorgan failure, respiratory failure, hepatic failure, renal failure, and need for dialysis, Black and Hispanic individuals have the highest risk defined by phenotype.

Dhruva et al. reported that medical therapy use was lower by a small but significant margin in African American individuals and those identifying as *other* race categories.[2] Use of the microaxial left ventricular assist device was the same or higher in those same categories than among individuals self-identifying in the White category. The same trend was true for other mechanical therapies, indicating differences in usage among racial groups. This begs the question: is more mechanical support being used because this population is genuinely sicker?

Randomized data on outcomes exists through the National Cardiovascular Data Registry (NCDR) and administrative databases, but these data often underrepresent categories that are non-White race and ethnicity. The trial populations are also small, typically including a couple hundred patients. In a 2016 publication from NCDR, only 7% of enrolled patients self-identified as Black.

Retrospective data from the Mayo Clinic is available with trial populations of several thousand patients.[3] With this large sample size, we can begin teasing out information that reflects access to care and social determinants. The Charlson Comorbidity Index predicts 10-year survival and produces varied results; however, it could be used to evaluate outcomes and risk categories when comparing studies.

Considering interventions for cardiogenic shock, invasive procedures such as angiography, right heart catheterization, hemodialysis, and ventilation were disproportionately lower in non-White men and women.[4] However, noninvasive ventilation was higher in non-White males and females.

In a study over a 15-year period, there was a marked increase in admissions of White men for cardiogenic shock at 37.9%; the increase was not as high in White women at 21.6%.[4] Admission of non-White males and non-White females was 25.5% and 15.0%, respectively. In addition, there was a significant difference in in-hospital mortality, with a reported 20% increase in non-White male and non-White female groups. Not enough data on out-of-hospital mortality exists.

NIS Data

The same differences in mortality can be noted when analyzing data focused on patients with acute ST-elevation myocardial infarction. As compared to white men, a nearly 20% difference in Black men and ~30% difference in Black women has been reported.[5] Specifically, mortality was broken down to include the likelihood of revascularization support and right heart catheterization. The relationship between improved mortality in patients who were identified as having right heart catheterization and revascularization should be investigated more closely in future randomized trials that stratify patients by race and sex.

The caveat to this data is that it is from the NIS data bank. The NIS bank draws from a sampling frame that consists of discharge data submitted by partner groups, which means that data from nonpartner groups is missing entirely. Aside from that, data sent by partner groups is sometimes incomplete because of differing state reporting requirements. The sampling frame is also designed to draw from several hospitals that must net to a total of 20% of hospitals nationally. It is in four regions with three categories of hospital ownership, including a category for urban-rural locations, teaching status, and bed size. As a result, it is unlikely that the data from NIS hospitals are representative of all hospitals in the nation.

Conclusion

Working toward more inclusive strategies for data sampling, trials, and triage might be beneficial. Whatever the approach, it is important to do better than what has been done in the past when considering race and ethnicity in patient care. Although there may be limited publications with information on this topic, they have shown clear differences in patient outcomes with possible associations with gender, race, and ethnicity. It is critical to view the implications of this on socioeconomic status, access, resources, patient phenotypes, and patient desires and expectations. The disparities must first be recognized before any treatment options can be identified.

References

[1] Nathan AS, Yang L, Yang N, et al. Racial, Ethnic, and Socioeconomic Disparities in Access to Transcatheter Aortic

Valve Replacement Within Major Metropolitan Areas. *JAMA Cardiol*. 2022;7(2):150-157. doi: 10.1001/jamacardio.2021.4641.

[2] Dhruva SS, Ross JS, Mortazavi BJ, et al. Use of Mechanical Circulatory Support Devices Among Patients With Acute Myocardial Infarction Complicated by Cardiogenic Shock. *JAMA Netw Open*. 2021;4(2):e2037748. doi: 10.1001/jamanetworkopen.2020.37748.

[3] Jentzer JC, van Diepen S, Barsness GW, et al. Cardiogenic Shock Classification to Predict Mortality in the Cardiac Intensive Care Unit. *J Am Coll Cardiol*. 2019;74(17):2117-2128. doi: 10.1016/j.jacc.2019.07.077.

[4] Patlolla SH, Shankar A, Sundaragiri PR, Cheungpasitporn W, Doshi RP, Vallabhajosyula S. Racial and ethnic disparities in the management and outcomes of cardiogenic shock complicating acute myocardial infarction. *Am J Emerg Med*. 2022;51:202-209. doi: 10.1016/j.ajem.2021.10.051.

[5] Ya'qoub L, Lemor A, Dabbagh M, et al. Racial, Ethnic, and Sex Disparities in Patients With STEMI and Cardiogenic Shock. *JACC Cardiovasc Interv*. 2021;14(6):653-660. doi: 10.1016/j.jcin.2021.01.003.

2022 Symposium Presentation

Reperfusion Injury in Acute Myocardial Infarction Shock- Role of Mechanical Circulatory Support Devices

Finn Gustafsson, MD, PhD, DMSci, FHFA
University of Copenhagen, Department of Cardiology, Rigshospitalet, Denmark

Email: Finn.Gustafsson@regionh.dk

Abstract

The efficacy of mechanical circulatory support in acute myocardial infarction is dependent upon the size of the infarct. If applied early, mechanical support to reduce reperfusion injury appears to be effective in reducing infarct size in animal studies. The optimal timing of reperfusion is uncertain and requires further investigation. Efficient unloading appears to be essential in increasing the efficacy of the type of mechanical support and may favor one over another.

Keywords: myocardial infarction, cardiogenic shock, mechanical circulatory support

Background

When considering the management of shock, the topic of reperfusion injury in acute myocardial infarction (AMI) is challenging. Management must balance preventative cardiology and critical care, as the initial problem lies with the infarction rather than the shock.

There is a clear relationship between the size of an infarct and the prognosis after myocardial infarction. Data from ten randomized clinical trials where magnetic resonance imaging was done after an infarction show a clear correlation between all-cause mortality and heart failure hospitalization with the size of the infarction.[1] Importantly, in patients where the final size was 8% or less of area at risk, there was little to no mortality and very little morbidity.

The management solution for patients with AMI shock is to re-perfuse early in the treatment process. However, even if the patient presentation, treatment plan, and procedure are the same, patients can have very different hearts after reperfusion, and this is a consequence of reperfusion injury.

The pathophysiology behind reperfusion injuries is complex, but there is an understanding that cardiomyocyte death due to necrosis and apoptosis is important in the process. Changes in microcirculation, such as microvascular stasis and hemorrhage, tissue edema, and capillary compression, are also important. Clearly, strategies to address these mechanisms and minimize reperfusion injury would have a great impact on outcomes in AMI and, in turn, the development and prognosis of cardiogenic shock in this setting. There have been several studies that aimed to reduce reperfusion injury utilizing pharmacological strategies and remote ischemia by the use of blood pressure cuffs in ambulances en route to the hospital. Thus far, the results have been inconsistent.[2]

Use of Mechanical Circulatory Support

These inconsistencies led to the proposal that mechanical circulatory support (MCS) might be an efficient way to reduce reperfusion injury. In the setting of an AMI, MCS increases collateral coronary perfusion pressure and decreases left ventricular pressure, diastolic pressure, wall stress, and, consequently, myocardial oxygen consumption. The efficacy is dependent on the size of the infarct. Because of this, the question becomes: can MCS in AMI shock reduce reperfusion injury **and** infarct size? If so, how does it do it? How should reperfusion be timed with respect to the onset of unloading?

Animal Studies

MCS and infarct size were investigated in a study on sheep with left anterior coronary artery (LAD) occlusion.[3] The control group had reperfusion after 60 minutes of ischemia, while the group treated with an Impella CP (Abiomed) had immediate reperfusion. The group with full support from the onset had a lower myocardial oxygen extraction than the control group; however, both groups showed decreased infarct size.[3]

Another study in a pig model investigated MSC efficacy after 90 minutes of LAD occlusion with a balloon.[4] Four groups were evaluated: a reperfusion-only group (Group 1), a group that received an Impella CP device for 15 minutes before reperfusion (Group 2), a group that had an Impella CP on for 30 minutes before reperfusion (Group 3), and a group that had immediate reperfusion followed by circulatory support (Group 4). Group 3 had the smallest infarction.[4]

This same study also investigated different molecules related to the reperfusion process.[4] Specifically, stromal cell-derived factor 1-alpha (SDF1-alpha) was reduced in the group that did not receive MCS (Group 1). The group treated with unloading before reperfusion (Group 2) had a more normal level of SDF1-alpha. In addition, scar tissue formation was negatively associated with plasma SDF1-alpha, indicating that the molecule might be secreted by the heart to reduce reperfusion injury. This was further investigated in a model where SDF1-alpha was blocked, showing an attenuated effect of reperfusion.[4] The results challenge the understanding that "time is muscle," as a strong indication that delaying reperfusion by 30 minutes with circulatory unloading onboard was associated with improved outcomes.

A similar study using a pig model contested these results.[5] The effects of 60 minutes of ischemia and MCS were investigated in 3 groups: Group 1 with conventional ischemia with reperfusion, Group 2 with upfront unloading with an Impella for 30 minutes before reperfusion, and Group 3 where unloading and reperfusion were done simultaneously after 60 minutes of ischemia. Group 3 had the smallest infarct size, but no difference existed between Groups 1 and 2.[5] While there may be differences between these studies, the most important being the duration of ischemia, there is still a need for further understanding.

In a meta-analysis of several animal studies investigating the effects of MCS and unloading in AMI, there appears to be a 2.2% absolute reduction in infarct size, which corresponds to a relative reduction of ~10%.[6]

With the understanding that MCS works in the setting of AMI, the next step is to investigate which type of support works best. A study involving LAD occlusion for 120 minutes in pigs explored MCS type and efficacy in reducing infarct size in 3 groups.[7] Group 1 had continued occlusion with Impella support, Group 2 had re-perfusion, and Group 3 had veno-arterial extracorporeal membrane oxygenation (V-A ECMO) re-perfusion. Group 3 was associated with the largest infarct size, while Group 1 showed a decreased infarct size. Group 1 also showed a reduction in left ventricular (LV) stroke work, while Group 3 showed no change.[7] The study also examined collateral coronary perfusion by measuring the coronary collateral flow index and focusing on wedge pressure. Wedge pressure was positively influenced by unloading with an Impella.[7] No change was noticed with V-A ECMO, suggesting that collateral perfusion is essential and may improve the microvascular environment, leading to smaller infarcts.

It is essential to acknowledge the limitations of using animal models. These studies use 100% controlled occlusion with no disease of other vessels, and the time of occlusion is known. In contrast, patients often have partial reflow due to heparin administration, and occlusion time is rarely known for certain. In addition, reocclussion or distal embolization are always risks. Concomitant coronary disease must be considered as it can limit collateral flow and induce preconditioning that can potentially be beneficial for reperfusion injury. Arrhythmias can also play a significant role in these patients.

Clinical Studies

There is limited clinical data available exploring AMI shock and MCS efficacy. The CRISP AMI randomized trial compared percutaneous coronary intervention (PCI) alone to PCI with an intra-aortic balloon pump (IABP) in 337 patients not in cardiogenic shock.[8] The primary endpoint was infarct size. There was no difference between the two groups; in fact, there was a trend toward a larger infarct in the group with the IABP.[8]

The DTU STEMI pilot trial included 50 patients unloaded with an Impella CP and tested the hypothesis that delaying reperfusion by 30 minutes after starting unloading with an

Impella CP was feasible.[9] The trial results showed that this strategy was feasible and did not increase infarct size. However, there appeared to be no difference in the outcomes.[9] The DTU STEMI trial is ongoing, testing whether unloading with an Impella and delaying reperfusion compared to conventional therapy will help.

Conclusion

In conclusion, if applied early in animal studies, percutaneous MCS to reduce reperfusion injury can effectively reduce infarct size. Effective unloading appears essential so that left ventricular assist devices, such as the Impella, are more efficient than ECMO and possibly balloon pumps. The optimal timing of reperfusion is uncertain and is being further investigated in clinical trials. There is still little information on the development of acute heart failure and cardiogenic shock. However, MCS serves other purposes for cardiogenic shock patients, such as supplying blood flow to the brain and kidneys.

References

[1] Stone GW, Selker HP, Thiele H, et al. Relationship Between Infarct Size and Outcomes Following Primary PCI: Patient-Level Analysis From 10 Randomized Trials. *J Am Coll Cardiol*. 2016;67(14):1674-1683. doi:10.1016/j.jacc.2016.01.069

[2] Hausenloy DJ, Yellon DM. Myocardial ischemia-reperfusion injury: a neglected therapeutic target. *J Clin Invest*. 2013;123(1):92-100. doi:10.1172/JCI62874

[3] Meyns B, Stolinski J, Leunens V, Verbeken E, Flameng W. Left ventricular support by catheter-mounted axial flow pump reduces infarct size. *J Am Coll Cardiol*. 2003;41(7):1087-1095. doi:10.1016/s0735-1097(03)00084-6.

[4] Esposito ML, Zhang Y, Qiao X, et al. Left Ventricular Unloading Before Reperfusion Promotes Functional Recovery After Acute Myocardial Infarction. *J Am Coll Cardiol*. 2018;72(5):501-514. doi:10.1016/j.jacc.2018.05.034

[5] Ko B, Drakos SG, Ibrahim H, et al. Percutaneous Mechanical Unloading Simultaneously With Reperfusion Induces Increased Myocardial Salvage in Experimental Acute Myocardial Infarction. *Circ Heart Fail*. 2020;13(1):e005893. doi:10.1161/CIRCHEARTFAILURE.119.005893

[6] Miyashita S, Kariya T, Yamada KP, et al. Left Ventricular Assist Devices for Acute Myocardial Infarct Size Reduction: Meta-analysis. *J Cardiovasc Trans Res*. 2021;14(3): 467–475. https://doi.org/10.1007/s12265-020-10068-7

[7] Briceno N, Annamalai SK, Reyelt L, et al. Left Ventricular Unloading Increases the Coronary Collateral Flow Index Before Reperfusion and Reduces Infarct Size in a Swine Model of Acute Myocardial Infarction. *J Am Heart Assoc*. 2019;8(22):e013586. doi:10.1161/JAHA.119.013586

[8] Patel MR, Smalling RW, Thiele H, et al. Intra-aortic balloon counterpulsation and infarct size in patients with acute anterior myocardial infarction without shock: the CRISP AMI randomized trial. *JAMA*. 2011;306(12):1329-1337. doi:10.1001/jama.2011.1280

[9] Kapur NK, Alkhouli MA, DeMartini TJ, et al. Unloading the Left Ventricle Before Reperfusion in Patients With Anterior ST-Segment-Elevation Myocardial Infarction. *Circulation*. 2019;139(3):337-346. doi:10.1161/CIRCULATIONAHA.118.038269

2022 Symposium Presentation

Profound Vasoplegia after Coronary Artery Bypass Grafting

Subhasis Chatterjee, MD, FACS, FACC, FCCP
Divisions of Trauma and Acute Care Surgery & Cardiothoracic Surgery, Michael E. DeBakey
Department of Surgery, Baylor College Medicine, Houston, Texas
Department of Cardiovascular Surgery, Texas Heart Institute, Houston, Texas

Email: subhasis.chatterjee@bcm.edu

Abstract

Vasoplegic shock after cardiac surgery is characterized by a high cardiac output, low systemic vascular resistance, refractory hypotension, and ongoing need for vasopressors. In this case, management considerations are discussed, including vasoactive medications and other adjuncts to sustain a satisfactory mean arterial pressure and improve outcomes.

Keywords: vasoplegic shock, vasopressors, steroids

Case

A 63-year-old man with stage III chronic kidney disease presented with a non-ST elevation myocardial infarction. He was diagnosed with three-vessel coronary artery disease and recommended for urgent coronary artery bypass grafting (CABG). He underwent a difficult CABG x 4 with a long operation; the cardiopulmonary bypass time was 152 minutes, and the cross-clamp time was 123 minutes. Upon coming off cardiopulmonary bypass, he had a mean arterial pressure (MAP) in the 50s mmHg and a cardiac output of 7 L/min. Despite multiple vasoactive medications, his shock was refractory. The best strategies to improve his blood pressure are discussed.

Introduction

High cardiac output, low systemic vascular resistance, and ongoing need for vasopressors characterize post-cardiotomy vasoplegic shock or vasoplegia. With a reported incidence ranging from 10-45% due to heterogeneity in how it is clinically defined, vasoplegic shock is associated with increased mortality. The established risk factors include prolonged cardiopulmonary bypass and cross-clamp time, renal failure, reoperative cardiac surgery, and increased transfusion.[1]

Vasopressors

Most of our knowledge regarding vasopressor use has come from the sepsis literature. The only dedicated randomized trial in cardiac surgery, the Vasopressin versus Norepinephrine in Patients with Vasoplegic Shock after Cardiac Surgery (VANCS) trial, demonstrated that vasopressin as a primary vasopressor compared to norepinephrine showed no survival difference; however, the trial demonstrated a reduced incidence of postoperative atrial fibrillation and renal replacement therapy in the vasopressin group.[2] A large meta-analysis demonstrated that a combination of norepinephrine and vasopressin was generally more beneficial than norepinephrine alone.[3] Vasopressin may be the preferred agent in right ventricular dysfunction due to avoiding increased pulmonary vascular resistance.[4] Moreover, when treating patients with vasopressin, one should consider that about 45% of individuals were characterized as responders while 55% were

not; mortality in the non-responders (72%) was much higher than in the responders (57%).[5] This data favors the early concomitant use of vasopressin with first-line norepinephrine.

For patients with refractory hypotension, angiotensin II has been FDA approved since 2017. In the Angiotensin II for the Treatment of High-Output Shock (ATHOS-3) study of 321 patients, the use of angiotensin II compared to standard vasopressors was superior in achieving the primary endpoint of a 10mmHg increase or increase to > 75mmHg for three hours.[6] In a sub-study analysis of ATHOS-3 among cardiac surgery patients, angiotensin II demonstrated a higher likelihood of achieving the MAP goals and reduced vasopressors over the placebo.[7] It should be noted that in a multicenter trial of real-world use, approximately 67% of patients were angiotensin II responders with better survival than nonresponders (41% vs. 25%).[8] Further insights from recent studies demonstrate that patients with high plasma renin levels responded most favorably to angiotensin II with a greater survival advantage.[9]

Adjunctive Measures

A systematic review of 15 studies and 832 patients demonstrated methylene blue (MB) use in vasoplegic shock halved (OR = 0.54) mortality.[10] Typically, a 2 mg/kg IV bolus followed by an infusion of 0.5 mg/kg for 12 hours is initiated early.[11] Care should be taken to avoid MB in patients taking selective serotonin reuptake inhibitors due to the risk of serotonin syndrome. High-dose hydroxycobalamin or Vitamin B12 has been successfully used as a single 5-gram IV infusion.[12] In patients on hemodialysis, the deep red color of B12 may cause false detection of a "blood leak" on hemodialysis machines requiring temporary conversion to continuous renal replacement therapy.

Using both glucocorticoids[13] and mineralocorticoids[14] for vasoplegic shock has demonstrated hemodynamic and survival benefits. The standard regimen is 200-300 mg of IV hydrocortisone daily and 100 mg of fludrocortisone daily for 5-7 days. Finally, Vitamin C is administered as a 1500 mg dose every six hours with positive hemodynamic effects.[15] Our previous algorithm for vasoplegic shock went from norepinephrine to vasopressin, followed by multiple adjuncts with inconsistent results. (Figure 1).

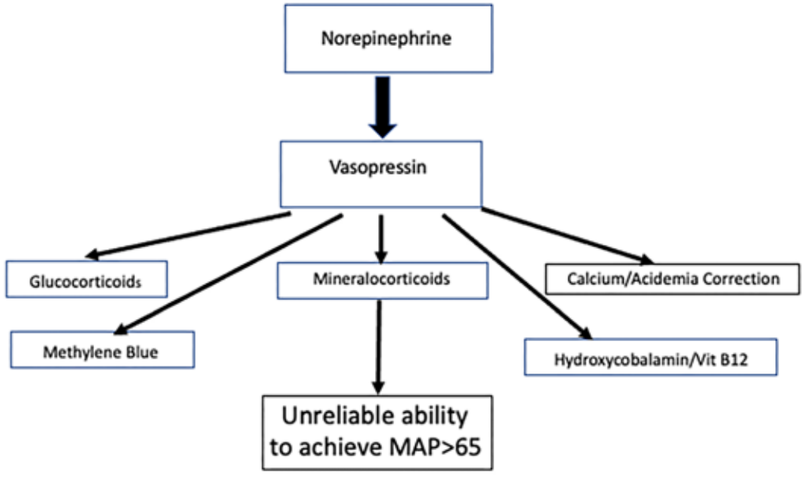

Figure 1: Old strategy for vasoplegic shock. Simultaneous utilization of vasoactive medications and pharmacologic adjuncts with inconsistent ability to achieve a satisfactory mean arterial pressure.

Perioperative Management

For those patients at high risk of vasoplegia, there is mixed evidence on whether angiotensin converting enzyme inhibitors (ACEI) or angiotensin receptor blocker (ARB) medications should be stopped before surgery. The only randomized trial consisted of 121 patients assigned to stopping ACEI/ARBs 48 hours before surgery versus continuation and found no difference in postoperative use of vasoactive medications or incidence of vasoplegic shock.[16] Moreover, vasoactive (milrinone) or sedation (propofol) agents that may exacerbate vasoplegia are discontinued in the intensive care unit. Aggressive management of hypocalcemia and metabolic acidosis should be corrected.

In this patient, after standard norepinephrine and vasopressin were initiated, angiotensin II was administered in the operating room at 20 ng/kg/min with a satisfactory MAP achieved at 40 ng/kg/min. Afterward, MB, hydrocortisone, and fludrocortisone were administered. The patient was weaned off vasopressors in 36 hours and had an unremarkable postoperative course.

Our updated algorithm (Figure 2) uses vasopressors to achieve a satisfactory MAP. Next, adjuncts are individualized to help resolve vasoplegia more quickly.

Conclusion

Vasoplegic shock after cardiac surgery is a common complication. A systematic approach using multiple vasopressors and systemic adjuncts can provide favorable outcomes.

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Disclosures

Dr. Chatterjee has served on advisory boards for Edwards Lifesciences, Eagle Pharmaceuticals, La Jolla Pharmaceutical Company, and Baxter Pharmaceuticals.

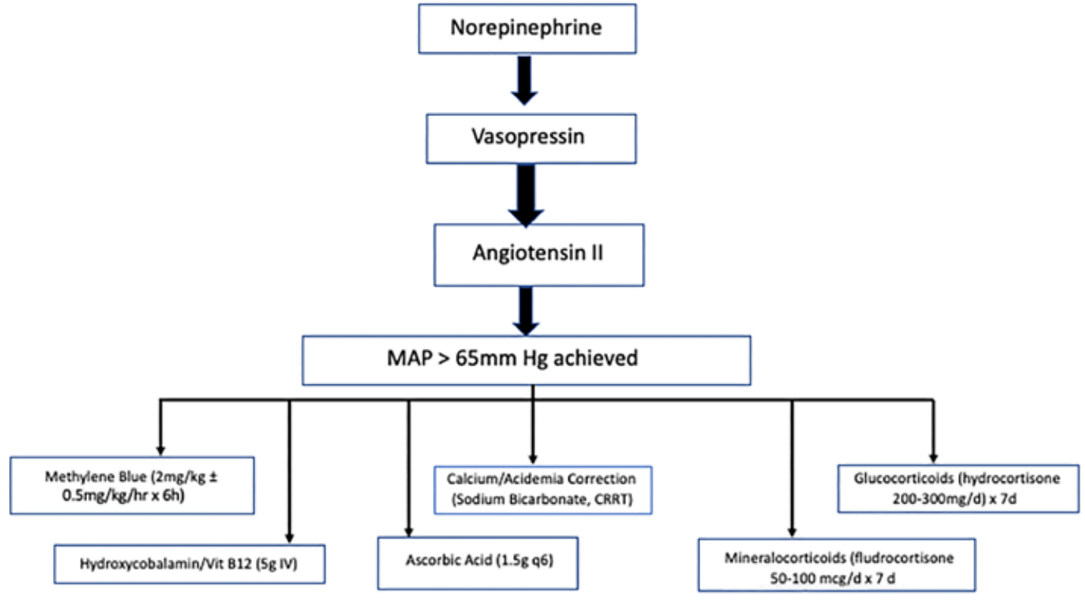

Figure 2: New strategy for vasoplegic shock. Initial escalation of vasoactive medications to achieve a satisfactory mean arterial pressure followed by pharmacologic adjuncts to reduce the period of vasoplegia.

References

[1] Dayan V, Cal R, Giangrossi F. Risk factors for vasoplegia after cardiac surgery: a meta-analysis. *Interact Cardiovasc Thorac Surg*. 2019;28(6):838-844. doi: 10.1093/icvts/ivy352.

[2] Hajjar LA, Vincent JL, Barbosa Gomes Galas FR, et al. Vasopressin versus Norepinephrine in Patients with Vasoplegic Shock after Cardiac Surgery: The VANCS Randomized Controlled Trial. *Anesthesiology*. 2017;126(1):85-93. doi: 10.1097/ALN.0000000000001434.

[3] McIntyre WF, Um KJ, Alhazzani W, et al. Association of Vasopressin Plus Catecholamine Vasopressors vs Catecholamines Alone With Atrial Fibrillation in Patients With Distributive Shock: A Systematic Review and Meta-analysis. *JAMA*. 2018;319(18):1889-1900. doi: 10.1001/jama.2018.4528.

[4] Jeon Y, Ryu JH, Lim YJ, et al. Comparative hemodynamic effects of vasopressin and norepinephrine after milrinone-induced hypotension in off-pump coronary artery bypass surgical patients. *Eur J Cardiothorac Surg*. 2006;29(6):952-6. doi: 10.1016/j.ejcts.2006.02.032.

[5] Sacha GL, Lam SW, Duggal A, et al. Predictors of response to fixed-dose vasopressin in adult patients with septic shock. *Ann Intensive Care*. 2018;8(1):35. doi: 10.1186/s13613-018-0379-5.

[6] Khanna A, Ostermann M, Bellomo R, et al. Angiotensin II for the Treatment of Vasodilatory Shock. *N Engl J Med*. 2017;377(26):2604. doi: 10.1056/NEJMc1714511.

[7] Klijian A, Khanna AK, Reddy VS, et al. Treatment With Angiotensin II Is Associated With Rapid Blood Pressure Response and Vasopressor Sparing in Patients With Vasoplegia After Cardiac Surgery: A Post-Hoc Analysis of Angiotensin II for the Treatment of High-Output Shock (ATHOS-3) Study. *J Cardiothorac Vasc Anesth*. 2021;35(1):51-58. doi: 10.1053/j.jvca.2020.08.001.

[8] Wieruszewski PM, Wittwer ED, Kashani KB, et al. Angiotensin II Infusion for Shock: A Multicenter Study of Postmarketing Use. *Chest*. 2021;159(2):596-605. doi: 10.1016/j.chest.2020.08.2074.

[9] Bellomo R, Forni LG, Busse LW, et al. Renin and Survival in Patients Given Angiotensin II for Catecholamine-Resistant Vasodilatory Shock. A Clinical Trial. *Am J Respir Crit Care Med*. 2020;202(9):1253-1261. doi: 10.1164/rccm.201911-2172OC.

[10] Zhao CC, Zhai YJ, Hu ZJ, Huo Y, Li ZQ, Zhu GJ. Efficacy and safety of methylene blue in patients with vasodilatory shock: A systematic review and meta-analysis. *Front Med (Lausanne)*. 2022;9:950596. doi: 10.3389/fmed.2022.950596.

[11] Mehaffey JH, Johnston LE, Hawkins RB, et al. Methylene Blue for Vasoplegic Syndrome After Cardiac Operation: Early Administration Improves Survival. *Ann Thorac Surg*. 2017;104(1):36-41. doi: 10.1016/j.athoracsur.2017.02.057.

[12] Shapeton AD, Mahmood F, Ortoleva JP. Hydroxocobalamin for the Treatment of Vasoplegia: A Review of Current Literature and Considerations for Use. *J Cardiothorac Vasc Anesth*. 2019;33(4):894-901. doi: 10.1053/j.jvca.2018.08.017.

[13] Venkatesh B, Finfer S, Cohen J, et al. ADRENAL Trial Investigators and the Australian–New Zealand Intensive Care Society Clinical Trials Group. Adjunctive Glucocorticoid Therapy in Patients with Septic Shock. *N Engl J Med*. 2018;378(9):797-808. doi: 10.1056/NEJMoa1705835.

[14] Annane D, Renault A, Brun-Buisson C, et al. CRICS-TRIGGERSEP Network. Hydrocortisone plus Fludrocortisone for Adults with Septic Shock. *N Engl J Med*. 2018;378(9):809-818. doi: 10.1056/NEJMoa1705716.

[15] Wieruszewski PM, Nei SD, Maltais S, et al. Vitamin C for Vasoplegia After Cardiopulmonary Bypass: A Case Series. *A A Pract*. 2018;11(4):96-99. doi: 10.1213/XAA.0000000000000752.

[16] van Diepen S, Norris CM, Zheng Y, et al. Comparison of Angiotensin-Converting Enzyme Inhibitor and Angiotensin Receptor Blocker Management Strategies Before Cardiac Surgery: A Pilot Randomized Controlled Registry Trial. *J Am Heart Assoc*. 2018;7(20):e009917. doi: 10.1161/JAHA.118.009917.

2022 Symposium Presentation

Why is Epinephrine Not the Drug of Choice in Cardiogenic Shock?

Esther Vorovich, MD, MSCE, FACC
Feinberg School of Medicine, Northwestern University, Chicago, IL

Email: Esther.Vorovich@nm.org

Abstract

Through the years, epinephrine has been the drug of choice for patients with cardiogenic shock. However, epinephrine was clinically inferior to norepinephrine in comparison studies because of the negative patient outcomes, which were statistically significant. These effects include type B lactic acidosis, tachycardia, increased myocardial oxygen demand, and arrhythmias.

Keywords: cardiogenic shock, epinephrine, norepinephrine

Background

In theory, epinephrine is good for clinical use. It is a catecholamine with a high affinity for alpha-1, beta-1, and beta-2 receptors and is commonly used in ~20-40% of patients with cardiogenic shock.[1] However, it is important to note that because of the high affinity for beta-1 and beta-2 receptors, the use of epinephrine can lead to increased chronotropy and inotropy. These increases, along with vasoconstriction, cause an increase in mean arterial pressure (MAP) and coronary blood flow relative to an increased duration in diastole. Ironically, even though it is sometimes known as “high dose” norepinephrine, epinephrine in high doses can cause even stronger effects due to its alpha-receptor affinity.

The Downsides

From a hemodynamic perspective, one of the downsides of epinephrine use is increased afterload, which can cause decreased cardiac output. High-dose usage of epinephrine causes increased pulmonary vascular resistance, increasing right ventricular afterload. Epinephrine also results in an increased heart rate and stroke work, which increases myocardial oxygen demand. Unsurprisingly, this stimulation of the heart can cause arrhythmias. Other downsides include cardiac toxicity with arterial wall damage and necrosis, stimulation of myocyte apoptosis, hyperglycemia, insulin resistance, and type B lactic acidosis.

Comparison Studies

In a study of the hemodynamic effects of epinephrine, norepinephrine, and phenylephrine in rats, epinephrine use showed a significant increase in heart rate and an increase in cardiac output and myocardial oxygen demand.[2] A mechanism common with these characteristics is tachycardia.

In a randomized trial of under 300 patients, with approximately half with cardiogenic shock, epinephrine and norepinephrine had similar effects on MAP.[3] However, as seen in the rat model, there was still an increase in heart rate, lactate, and insulin dose needed.

A smaller study of 30 randomized patients with cardiogenic shock compared epinephrine to norepinephrine-dobutamine. MAP and cardiac index were similar for both

drugs, but higher lactate and heart rates were seen with epinephrine use. In addition, epinephrine appeared to cause less diuresis.[4]

Epinephrine versus Norepinephrine

Following this small trial, a larger randomized study compared epinephrine to norepinephrine and included 57 patients with acute myocardial infarction complicated by cardiogenic shock. As seen with the other studies, MAP was similar between the two groups.[5] In addition, the epinephrine groups had higher lactate, a higher incidence of tachycardia, and increased myocardial oxygen demand. The trial was stopped early because there was a statistically significant signal of harm seen with the use of epinephrine; the incidence of refractory shock was 37% vs. 7% in the epinephrine vs. the norepinephrine groups, respectively.

Conclusion

In conclusion, epinephrine use in cardiogenic shock is associated with excess lactic acid (mainly type B lactic acidosis), tachycardia, increased myocardial oxygen demand, and increased arrhythmias. In small trials, norepinephrine seems clinically superior to epinephrine for patients with cardiogenic shock, and larger observational studies have demonstrated higher mortality rates with epinephrine use. Despite this data, epinephrine is still widely used.

References

[1] Léopold V, Gayat E, Pirracchio R, et al. Epinephrine and short-term survival in cardiogenic shock: an individual data meta-analysis of 2583 patients. *Intensive Care Med*. 2018;44(6):847-856. doi: 10.1007/s00134-018-5222-9.

[2] Ducrocq N, Kimmoun A, Furmaniuk A, et al. Comparison of equipressor doses of norepinephrine, epinephrine, and phenylephrine on septic myocardial dysfunction. *Anesthesiology*. 2012;116(5):1083-91. doi: 10.1097/ALN.0b013e31824f9669.

[3] Myburgh JA, Higgins A, Jovanovska A, et al. A comparison of epinephrine and norepinephrine in critically ill patients. *Intensive Care Med*. 2008;34(12):2226-34. doi: 10.1007/s00134-008-1219-0.

[4] Levy B, Perez P, Perny J, Thivilier C, Gerard A. Comparison of norepinephrine-dobutamine to epinephrine for hemodynamics, lactate metabolism, and organ function variables in cardiogenic shock. A prospective, randomized pilot study. *Crit Care Med*. 2011;39(3):450-5. doi: 10.1097/CCM.0b013e3181ffe0eb.

[5] Levy B, Clere-Jehl R, Legras A, et al. Epinephrine Versus Norepinephrine for Cardiogenic Shock After Acute Myocardial Infarction. *J Am Coll Cardiol*. 2018;72(2):173-182. doi: 10.1016/j.jacc.2018.04.051.

2022 Symposium Presentation

The Challenges of Conducting Clinical Trials for Patients with Cardiogenic Shock

Sunil V. Rao, MD
NYU Langone Health System, New York, NY

Email: Sunil.Rao@nyulangone.org

Abstract

Cardiogenic shock due to ST-segment elevation myocardial infarction is associated with high morbidity and mortality. Patients in shock are acutely ill, and clinicians may lack equipoise, thus presenting a challenge to developing high-quality evidence to guide practice. This review will summarize these challenges and offer possible solutions.

Keywords: cardiogenic shock, STEMI, clinical trials

Background

Observational data is vital to research efforts; however, relying on observational data can often lead to incorrect conclusions about treatment strategies. For example, three large propensity-matched analyses compared different mechanical support devices but were potentially confounded by indication.[1-3] Thus, prospective clinical trials are needed to test hypotheses and verify theories. While there are challenges to doing clinical trials in the cardiogenic shock population, they are essential for determining the appropriate management of these patients. It is important to recognize that randomized clinical trials also have weaknesses, and their findings may not be applicable to every patient. Thus, nuance must be used when interpreting any results from observation or randomized trials.

Incidence, Prognosis, and Functional Outcomes

Despite the availability and adoption of primary percutaneous coronary intervention (PCI) for acute ST-segment elevation myocardial infarction (STEMI), data from the National Cardiovascular Data Registry indicate that the incidence of cardiogenic shock is increasing in the United States.[4]

In addition, the prognosis for patients with cardiogenic shock remains unchanged. In-hospital mortality and 30-day mortality have stayed around 30% to 50%.[4] The acuity and severity of the clinical presentation make studying cardiogenic shock a challenge. Enrollment into clinical trials is difficult in STEMI patients due to the urgency of the door-to-balloon time metric. Given that patients in shock are in extremis, enrollment into clinical trials seems prohibitive.

Though important, mortality is not the only outcome of interest. To date, functional outcomes are understudied. For those who survive hospitalization, there are no data detailing disability in patients presenting with AMI shock. Moreover, there are no studies showing how many of these patients transition to long-term care or the effects of their recovery on their caregivers.

Pathophysiology and Hemodynamics of AMI Shock

Occlusion of an epicardial coronary artery leads to myocardial ischemia, which prompts the spiraling cascade of events that leads to end-stage shock and often mortality. This chain of events guides the clinical priorities when treating these patients, which involves immediately trying to open the occluded artery and support end-organ perfusion. There are several points along the care continuum that lend themselves to research questions. One of which is: will supporting the patient before opening the artery improve outcomes or vice versa?

The hemodynamics of AMI shock, which are hypotension, increased left ventricular end-diastolic pressure, and reduced cardiac output,[5] lend themselves to another important research question: is a strategy of inotropes or mechanical circulatory support better for patient outcomes?

Big Data, Phenotypes, and Clinical Decision-Making

One of the benefits of the contentious use of electronic health record (EHR) systems is that a tremendous amount of information is automatically collected during the course of clinical care. It has long been the promise of EHR systems that patient information could be used to create support for clinical decision-making.

In a recent study, machine learning was applied to three EHR datasets of patients with cardiogenic shock—the Cardiogenic Shock Working Group MI cohort (CSWG-MI), the Cardiogenic Shock Working Group CHF cohort (CSWG-CHF), and the Danish Retroshock Registry (DRR)—to cluster potential phenotypes.[6] The results of this analysis identified three clusters of phenotypes: noncongested shock, cardiorenal shock, and cardiometabolic shock.

All phenotypes shared clinical features indicative of cardiogenic shock (eg, decreased blood pressure). However, each showed distinct differences, which warrant further study. As the name suggests, the noncongestive phenotype showed no evidence of congestion. The cardiorenal phenotype had mostly left ventricular dysfunction, while the cardiometabolic had mostly right ventricular dysfunction. Applying machine learning techniques to ascertain the phenotypes of our clinical populations could open many research possibilities.

Interestingly, each of the three phenotypes has a distinct relationship with mortality. Compared to patients with noncongested shock, patients with cardiometabolic shock had the highest mortality. Although this might be a marker of when these patients sought medical attention, this phenotypic finding supports the clinical convention of treating these patients emergently. EHR data and resultant phenotypic understanding hold the potential to validate the timing of interventions and guide clinical best practices.

Treatment Strategies for Acute MI

Without standardized guidelines, interventional cardiologists rely on empirical decision-making in light of what would be best for the patient. Decisions are based on results from the catheterization laboratory, with revascularization as the priority. Ruling out any mechanical complications (eg, free wall rupture, papillary muscle rupture, ventricular septal defect) also informs the treatment approach, as do options for hemodynamic support (eg, vasopressors, mechanical circulatory support). However, most of these decisions are not supported by randomized trial data. Given the promise of big data and the consistently poor outcomes in shock, developing randomized trials for patients with cardiogenic shock has become a priority.

Clinical Studies

Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock (SHOCK) Trial

Some randomized trials have been conducted. Perhaps the most noteworthy study—the SHOCK trial—randomly assigned patients with cardiogenic shock (N = 302) with either STEMI or non-STEMI to receive revascularization or medical therapy. The results showed no difference in treatment response at 30 days.[7]

Other mechanical support studies also showed no benefit at 30 days, suggesting that 30 days after PCI may be too soon to measure a meaningful benefit of a therapeutic strategy in shock patients.[8-9] Fortunately, patients in the SHOCK trial were followed for 10 years, which highlighted the difference between the treatment arms (P = .03). So, when considering the study design, the conventional 30-day endpoint might not be an ideal time point for a randomized trial.

Culprit Lesion Only PCI versus Multivessel PCI in Cardiogenic Shock (CULPRIT-SHOCK) Trial

The CULPRIT-SHOCK trial set out to test a class 2B recommendation to perform multivessel PCI in patients with cardiogenic shock (N = 699). The researchers contended that upon opening the culprit artery, other compromising coronary diseases would be discovered in the patient. To prevent more ischemia, the subsequent opening of the other affected vessels was tested as potentially helpful to the patient. Unfortunately, this approach proved worse for patients that received multivessel PCI; they had worse relative risks of death, renal replacement therapy, and bleeding (relative risk 0.83 [95% CI 0.71 to 0.96], P = .01).[10]

This was a distinctly different outcome from what has been demonstrated in the COMPLETE trial for patients with STEMI who do not have cardiogenic shock, where multivessel PCI reduced major adverse cardiovascular events compared with culprit artery PCI alone.[11] This dichotomy underscores the importance of understanding the interplay between clinical presentation and treatment strategy, especially in patients with cardiogenic shock.

Other Randomized Trials

The Dobutamine Compared with Milrinone (DOREMI) Trial compared milrinone with dobutamine in patients with cardiogenic shock (N = 192).[12] No significant differences were reported in the primary composite outcome of in-hospital death from any cause, resuscitated cardiac arrest, receipt of a cardiac transplant or mechanical circulatory support, nonfatal myocardial infarction, transient ischemic attack or stroke diagnosed by a neurologist, or initiation of renal replacement therapy. Similarly, another study (N = 1679) randomly assigned patients with various types of shock to receive one of these vasopressor agents. For the 280 patients with cardiogenic shock, norepinephrine was associated with a better outcome than dopamine.[13] These data challenged the conventional practice of using dopamine as the first-line vasopressor for patients with shock.

The same level of randomized evidence does not exist for mechanical circulatory support devices (MCS). Conducting trials of MCS is tremendously challenging, particularly in the United States. In Germany, the Intraaortic Balloon Pump (IABP) SHOCK II trial randomly assigned patients with cardiogenic shock to either IABP intervention or control.[14] This trial showed no difference in outcomes for patients with cardiogenic shock and STEMI between using IABP and not using IABP. As a result, the European guidelines have downgraded the use of balloon pumps. Practice patterns have changed, particularly in Germany, where the use of balloon pumps has plummeted since the publication of this study.[14] It is not clear if patterns of IABP use in other countries have followed suit.

A number of multicenter trials have been designed and opened to evaluate the Impella device (Abiomed).[15] Many of these trials were discontinued because of a lack of enrollment. The trials that were completed had very small sample sizes (N < 20) and were not informative to clinical practice. To address the evidence gap, a large randomized trial called RECOVER IV has been planned to compare the Impella device to the standard of care, including the IABP.

What Are the Challenges to Conducting Trials In Cardiogenic Shock?

The challenge to conduct cardiogenic shock trials—and enhance evidence-based practice—sits squarely on the shoulders of clinicians. Due to historical practice patterns, the severity of the patient's clinical situation, and the dearth of randomized data, clinicians may be unwilling to randomize patients because of the perceived lack of equipoise.

To develop robust, scientifically sound guidelines, there must be a willingness to randomize patients in shock. Shock is a heterogeneous disease with multiple etiologies; therefore, it is imperative to clearly and consistently define the clinical trial population. Further, shock has a relatively low prevalence. While the diagnosis of shock may be increasing, it still accounts for a small proportion of patients with AMI. Large networks are needed to ensure that enough patients are recruited in a reasonable timeframe. In addition, the devices and trials themselves are very expensive, and funding has been and will continue to be a challenge. Attaining patient consent for enrollment can be difficult as many cases are emergent and the patient and/or family is not in a position to provide full consent. Delayed and proxy consent are two possibilities that have been tried. Exemption from informed consent is a mode used in trauma trials that may offer another alternative. Emergency consent has been used in cardiac arrest trials, and other creative consent mechanisms may be needed. Finally, a good trial must have equipoise; thus, we must figure out a way to separate ourselves from our own lack of equipoise so that we can actually get truly randomized data to guide our field.

Conclusion

A statement from the American Heart Association explored the different types of cardiogenic shock presentations and the different strategies that can be used to manage and treat patients.[16] While the clinical community awaits more randomized data, these guidelines will serve to inform clinical practice.

References

[1] Léopold V, Gayat E, Pirracchio R, et al. Epinephrine and short-term survival in cardiogenic shock: an individual data meta-analysis of 2583 patients. *Intensive Care Med*. 2018;44(6):847-856. doi: 10.1007/s00134-018-5222-9.

[2] Ouweneel DM, Schotborgh JV, Limpens J, et al. Extracorporeal life support during cardiac arrest and cardiogenic shock: a systematic review and meta-analysis. *Intensive Care Med*. 2016;42(12):1922-1934. doi: 10.1007/s00134-016-4536-8.

[3] Tam DY, Vo TX, Wijeysundera HC, et al. Transcatheter vs Surgical Aortic Valve Replacement for Aortic Stenosis in Low-Intermediate Risk Patients: A Meta-analysis. *Can J Cardiol*. 2017;33(9):1171-1179. doi: 10.1016/j.cjca.2017.06.005.

[4] Wayangankar SA, Elgendy IY, Xiang Q, et al. Length of Stay After Transfemoral Transcatheter Aortic Valve Replacement: An Analysis of the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry. *JACC Cardiovasc Interv*. 2019;12(5):422-430. doi: 10.1016/j.jcin.2018.11.015.

[5] Rihal CS, Naidu SS, Givertz MM, et al. 2015 SCAI/ACC/HFSA/STS Clinical Expert Consensus Statement on the Use of Percutaneous Mechanical Circulatory Support Devices in Cardiovascular Care: Endorsed by the American Heart Assocation, the Cardiological Society of India, and Sociedad Latino Americana de Cardiologia Intervencion; Affirmation of Value by the Canadian Association of Interventional Cardiology-Association Canadienne de

Cardiologie d'intervention. *J Am Coll Cardiol*. 2015;65(19):e7-e26. doi: 10.1016/j.jacc.2015.03.036.
[6] Zweck E, Thayer KL, Helgestad OKL, et al. Phenotyping Cardiogenic Shock. *J Am Heart Assoc*. 2021;10(14):e020085. doi: 10.1161/JAHA.120.020085.
[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(9):625-34. doi: 10.1056/NEJM199908263410901.
[8] O'Neill WW, Kleiman NS, Moses J, et al. A prospective, randomized clinical trial of hemodynamic support with Impella 2.5 versus intra-aortic balloon pump in patients undergoing high-risk percutaneous coronary intervention: the PROTECT II study. *Circulation*. 2012;126(14):1717-27. doi: 10.1161/CIRCULATIONAHA.112.098194.
[9] Perera D, Stables R, Thomas M, et al. Elective intra-aortic balloon counterpulsation during high-risk percutaneous coronary intervention: a randomized controlled trial. *JAMA*. 2010;304(8):867-74. doi: 10.1001/jama.2010.1190.
[10] 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(25):2419-2432. doi: 10.1056/NEJMoa1710261.
[11] Mehta SR, Wood DA, Storey RF, et al. Complete Revascularization with Multivessel PCI for Myocardial Infarction. *N Engl J Med*. 2019;381(15):1411-1421. doi: 10.1056/NEJMoa1907775.
[12] Mathew R, Di Santo P, Jung RG, et al. Milrinone as Compared with Dobutamine in the Treatment of Cardiogenic Shock. *N Engl J Med*. 2021;385(6):516-525. doi: 10.1056/NEJMoa2026845.
[13] De Backer D, Biston P, Devriendt J, et al. Comparison of dopamine and norepinephrine in the treatment of shock. *N Engl J Med*. 2010;362(9):779-89. doi: 10.1056/NEJMoa0907118.
[14] Thiele H, Zeymer U, Neumann FJ, et al. Intraaortic balloon support for myocardial infarction with cardiogenic shock. *N Engl J Med*. 2012;367(14):1287-96. doi: 10.1056/NEJMoa1208410.
[15] Pahuja M, Johnson A, Kabir R, et al. Randomized Trials of Percutaneous Microaxial Flow Pump Devices: JACC State-of-the-Art Review. *J Am Coll Cardiol*. 2022;80(21):2028-2049. doi: 10.1016/j.jacc.2022.08.807.
[16] Henry TD, Tomey MI, Tamis-Holland JE, et al. Invasive Management of Acute Myocardial Infarction Complicated by Cardiogenic Shock: A Scientific Statement From the American Heart Association. *Circulation*. 2021;143(15):e815-e829. doi: 10.1161/CIR.0000000000000959.

2022 Symposium Presentation

Coronary Flow and Unloading in Acute Myocardial Infarction Shock

Kiyo Ishikawa, MD, PhD
Icahn School of Medicine at Mount Sinai, New York

Email: kiyotake.ishikawa@mssm.edu

Abstract

In patients with cardiogenic shock that undergo successful coronary intervention, there are still factors complicating myocardial recovery. There is room for improvement in coronary flow using mechanical circulatory devices, specifically by left ventricular unloading. This idea was further explored in a research study using pigs. Results showed that subjects with acute myocardial infarction who have reduced cardiac contractility and/or high diastolic pressure would benefit from support strategies targeting left ventricular unloading.

Keywords: left ventricular unloading, myocardial infarction, coronary flow, Impella

Background

Previous studies showed that multivessel percutaneous coronary intervention (PCI) might not be an ideal treatment for acute myocardial infarction (AMI). For patients with ST-segment Elevation Myocardial Infarction (STEMI) and multivessel disease, non-culprit PCI with complete revascularization was superior to culprit lesion-only PCI.[1] In contrast, for patients with AMI and cardiogenic shock, culprit lesion PCI was a better treatment option than multivessel PCI.[2] Therefore, alternative strategies are needed to improve the outcomes of patients with AMI and cardiogenic shock.

In patients with cardiogenic shock, multiple factors impair coronary flow even after a successful PCI: 1) decreased cardiac output reduces coronary perfusion pressure, 2) increased diastolic pressure causes vasculature compression, and 3) lung congestion leads to hypoxia. All contribute to myocardial ischemia and can progressively worsen cardiogenic shock, creating a positive feedback loop. To break this loop, there is room for improvement in mechanical circulatory device use.

Left Ventricular Unloading with Impella in Pigs

An experimental pig study investigated the effects of left ventricular (LV) support on coronary flow (unpublished data). In one case, the pig underwent 90 minutes of the left anterior descending artery (LAD) balloon occlusion followed by reperfusion for 2 hours. A coronary flow/pressure wire was then placed into the LAD, together with LV pressure monitoring using a pressure catheter. There was a significant decrease in LV diastolic pressure with Impella (Abiomed) support. Meanwhile, it increased coronary pressure and led to an increase in driving pressure, which can be calculated by subtracting LV pressure from coronary pressure. Coronary flow was also increased by Impella support. The results from this case suggested that mechanical LV support increases coronary pressure and improves flow.

These results are unlikely to be limited to the Impella since all support devices can improve systemic flow by replacing cardiac output. However, one device that complicates this assumption is the intra-aortic balloon pump (IABP), which is known to increase coronary diastolic

pressure and flow but does not improve clinical outcomes.[3,4] The reason for the discrepancy might be that newer devices may provide more adequate support for LV diastolic pressure than the IABP.

Following an AMI, LV diastolic pressure increases because of insufficient pumping action, compressing the ischemic wall that prevents coronary flow during diastole. By unloading the LV via mechanical support, the goal is to improve flow by reducing the compression on the wall. To demonstrate this concept, porcine models underwent the previously described procedure and were monitored for pressure and volume during LV unloading.[5] Impella support reduced end-diastolic volume and pressure, resulting in a significant reduction in wall stress during diastole. In this study, the flow was measured with a microsphere technique instead of a coronary wire; millions of spheres were mixed with blood and injected into the left atrium. These spheres are large enough to get trapped in the capillaries of the myocardium, allowing quantitation of the tissue flow by counting the spheres in retrieved tissues.[5]

LV unloading resulted in an increase in infarct tissue perfusion, but not in the border or remote areas. This is likely due to the autoregulation that takes place in normal tissue to maintain a normal range of flow. This mechanism is disrupted in infarct tissues, allowing the flow to become reliant on external factors. Based on the infarct perfusion results and diastolic wall stress, the relationship indicated a reliance on this LV wall stress.

The study was expanded to identify factors that could predict infarct flow improvement with LV unloading.[6] Univariate analysis in data from 15 pigs identified cardiac output, mean pulmonary arterial wedge pressure, mean left arterial pressure, minimum LV pressure, end-diastolic LV pressure, end-diastolic pressure-volume relationship (EDPVR), and maximum ventricular contractility (dP/dt) to be the significant factors predicting flow improvement. Multivariate analysis showed that reduced dP/dt maximum and higher EDPVR were associated with improved infarct flow.[6] These results suggest that patients with reduced cardiac contractility, high diastolic pressure, or AMI shock benefit the most from mechanical LV unloading strategies.

Another study showed improved outcomes in patients treated with a combination of extracorporeal membrane oxygenation (ECMO) and Impella compared to those individuals treated with ECMO alone.[7] This data further supports the importance of LV unloading as a key factor in recovery from cardiogenic shock.

Conclusion

In conclusion, LV unloading in AMI shock improves myocardial perfusion by increasing coronary arterial pressure and decreasing LV diastolic wall stress. However, there is currently not enough data to prove the clinical benefit, so further research should focus on flow during support in AMI shock.

References

[1] Mehta SR, Wood DA, Storey RF, et al. Complete Revascularization with Multivessel PCI for Myocardial Infarction. *N Engl J Med*. 2019;381(15):1411-1421. doi: 10.1056/NEJMoa1907775.

[2] 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(25):2419-2432. doi: 10.1056/NEJMoa1710261.

[3] Takeuchi M, Nohtomi Y, Yoshitani H, et al. Enhanced coronary flow velocity during intra-aortic balloon pumping assessed by transthoracic Doppler echocardiography. *J Am Coll Cardiol*. 2004;43(3):368-76. doi: 10.1016/j.jacc.2003.08.047.

[4] Thiele H, Zeymer U, Thelemann N, et al. Intraaortic Balloon Pump in Cardiogenic Shock Complicating Acute Myocardial Infarction: Long-Term 6-Year Outcome of the Randomized IABP-SHOCK II Trial. *Circulation*. 2019;139(3):395-403. doi: 10.1161/CIRCULATIONAHA.118.038201.

[5] Watanabe S, Fish K, Kovacic JC, et al. Left Ventricular Unloading Using an Impella CP Improves Coronary Flow and Infarct Zone Perfusion in Ischemic Heart Failure. *J Am Heart Assoc*. 2018;7(6):e006462. doi: 10.1161/JAHA.117.006462.

[6] Sakata T, Watanabe S, Mazurek R, et al. Impaired Diastolic Function Predicts Improved Ischemic Myocardial Flow by Mechanical Left Ventricular Unloading in a Swine Model of Ischemic Heart Failure. *Front Cardiovasc Med*. 2022;8:795322. doi: 10.3389/fcvm.2021.795322.

[7] Schrage B, Becher PM, Bernhardt A, et al. Left Ventricular Unloading Is Associated With Lower Mortality in Patients With Cardiogenic Shock Treated With Venoarterial Extracorporeal Membrane Oxygenation: Results From an International, Multicenter Cohort Study. *Circulation*. 2020;142(22):2095-2106. doi: 10.1161/CIRCULATIONAHA.120.048792.

2022 Symposium Presentation

Right Ventricular Hemodynamics in COVID-19 Patients

Steven Hollenberg, MD
Director, Cardiac Intensive Care, Emory University School of Medicine, Atlanta, GA

Email: Steven.Hollenberg@emory.edu

Abstract

The right ventricle is highly sensitive to afterload, and pulmonary compromise can increase pulmonary vascular resistance and lead to right ventricular dysfunction. Pulmonary hypertension can also be exacerbated by mechanical ventilation. Patients with COVID-19 pneumonia and respiratory failure, especially those ventilated with positive end-expiratory pressure, are prone to pulmonary hypertension. Understanding their right ventricular hemodynamics can have therapeutic and prognostic implications.

Keywords: RV dysfunction, positive end-expiratory pressure, cardiac output, cardiac index

Background

There are four questions to consider when treating patients with COVID-19 pneumonia and acute respiratory distress syndrome (ARDS):

- Is there evidence of right ventricular (RV) dysfunction?
- Is this mediated by the heart, lungs, or a combination?
- Does this have independent prognostic significance?
- Does it have therapeutic implications?

The right ventricle is highly sensitive to afterload and, as such, may be affected by pulmonary pathophysiology, including hypoxia, hypercarbia, atelectasis, and overdistension. Hypoxia increases pulmonary vascular resistance because of hypoxic pulmonary vasoconstriction, which shunts blood away from deoxygenated areas. Hypercarbia also increases pulmonary vascular resistance.[1] Atelectasis leads to hypoxia and hypercarbia and decreases the number of perfused alveoli, increasing pulmonary resistance.[2,3] Overdistension of alveoli also increases pulmonary vascular resistance. All of these factors can cause increased pulmonary vascular resistance and right-sided afterload.

Effects of Ventilation on Respiratory Failure

Positive end-expiratory pressure (PEEP) is intended to minimize hypoxia and hypercarbia. The optimal PEEP decreases atelectasis without causing overdistension. The goal is to minimize lung stress and decrease pulmonary vascular resistance. The effects of PEEP on the heart depend on right and left ventricular function. PEEP decreases venous return in a normal heart, but this decrease is generally responsive to fluid administration. In left ventricular failure, PEEP decreases afterload since the positive pressure is applied to the chest and thus increases the gradient between the heart and the peripheral vasculature. This can increase cardiac output (CO) since failing left ventricles are afterload-dependent. In contrast, PEEP increases RV afterload in acute RV dysfunction, which can shift the septum to the left and cause a decrease in CO that does not respond to fluid administration. Ideally, tidal volume and PEEP should be limited to avoid hypercapnia, acidosis, hypoxia, and hypoxic vasoconstriction. Achieving all of these goals may be difficult for severely ill patients. These difficulties may be especially prominent in patients with COVID-19 and severe respiratory failure.

Clinical Data

In a prospectively collected database including 1,997 patients hospitalized in our institution for COVID-19 pneumonia from March 2020 to March 2021, 368 had shock requiring vasopressors. Of these, 327 had echocardiography to assess ventricular function and stroke volume based on clinical indications. Left ventricular ejection fraction and RVFAC (RV fractional area change) were measured; 187 patients had evaluable data on all parameters. Patients were divided into groups with low or preserved RVFAC (cutoff ≤ 35%) and low or normal cardiac index (cutoff ≤ 2.2 L/min/m^2).

The mean right ventricular systolic pressure (RVSP) was 38.8 ± 12.2 mm Hg, and the mean PEEP was 11.0 ± 3.7 cm H_2O. RVSP was higher in patients with low RVFAC than normal RVFAC regardless of cardiac index (CI) (40.5 ± 1.4 mm Hg versus 37.4 ± 1.1 mm Hg, respectively; P = .037). PEEP was higher in patients with low CI than normal CI regardless of RVFAC (11.9 ± 0.4 cm H_2O versus 10.2 ± 0.3 cm H_2O, respectively; P = .037). Hospital mortality was 80% in this group with COVID-19 pneumonia and shock and did not differ among the groups (P = .19).

RV contractile function correlated with RV pressure and not CI in this group, whereas CO correlated with PEEP and not contractile function. Although RV dysfunction has been associated with a worse prognosis, these results suggest a mechanism linked to afterload and pulmonary pathology rather than contractility. Low CI may be related less to impairment of RV contractile function than to right-sided filling influenced by positive pressure ventilation.

Conclusion

In conclusion, RV dysfunction is common in patients with severe COVID-19 and shock and appears to be driven by pulmonary insufficiency and positive pressure ventilation. Whether treatment of RV dysfunction in COVID will improve outcome remains uncertain.

References

[1] Balanos GM, Talbot NP, Dorrington KL, Robbins PA. Human pulmonary vascular response to 4 h of hypercapnia and hypocapnia measured using Doppler echocardiography. *J Appl Physiol*. 2003;94(4):1543-51. doi: 10.1152/japplphysiol.00890.2002.

[2] Duggan M, McCaul CL, McNamara PJ, Engelberts D, Ackerley C, Kavanagh BP. Atelectasis causes vascular leak and lethal right ventricular failure in uninjured rat lungs. *Am J Respir Crit Care Med*. 2003;167(12):1633-40. doi: 10.1164/rccm.200210-1215OC.

[3] Scharf SM, Caldini P, Ingram RH Jr. Cardiovascular effects of increasing airway pressure in the dog. *Am J Physiol*. 1977;232(1):H35-43. doi: 10.1152/ajpheart.1977.232.1.H35.

2022 Symposium Presentation

COVID-19 Induced Right Ventricular Failure and Right Ventricular Assist Device Support

Marvin J. Slepian, MD
Department of Medicine and Biomedical Engineering, Sarver Heart Center, University of Arizona, Tucson, AZ

Email: Slepian@arizona.edu

Abstract

COVID-19, while primarily recognized for its pulmonary and systemic manifestations, afflicts the cardiovascular system through various abnormalities. Notably, right ventricular (RV) involvement leading to dysfunction and failure is a manifestation seen in up to 20% of severe COVID patients. RV severity correlates with overall COVID severity, serving as a prognostic marker. Data review reveals that RV failure was largely underdiagnosed, particularly early on in the pandemic. The therapy approach for RV failure in patients with COVID should focus on supporting overall RV perfusion pressure, maintaining sinus rhythm, optimizing RV loading conditions and contractility, and addressing anticoagulation and thrombus-related conditions. Beyond medical therapy, cardiac and pulmonary support should be utilized and introduced in a graded, stair-step approach of aggressiveness based on clinical need. This approach is best managed with a care team and defined protocols. Effective devices include right ventricular assistance devices (RVAD), Oxy-RVAD, veno-venous extracorporeal membrane oxygenation, and Impella (Abiomed) devices.

Keywords: RV failure, cytokines, thrombosis, coronavirus, mechanical circulatory support, ECMO

Background

Right ventricular (RV) involvement in COVID-19 was described early in the pandemic. The involvement was mainly attributed to pulmonary embolism and lung disease.[1] Myopericarditis was also described, but these early reports indicated that RV dilation was underdiagnosed.[2] Additional data showed that RV dilatation could be a mortality marker.[3]

Mechanism and Pathophysiology

Approximately 20% of patients that went to the hospital were admitted to the intensive care unit. Of those, 10% were supported with extracorporeal membrane oxygenation (ECMO); of the patients on ECMO, ~10% needed RV support. Around 1-2% of hospitalized patients had direct RV failure. Newer data suggests an even higher degree of RV involvement in severely ill COVID patients, reported in up to 20% of cases. The causes of COVID-19-mediated RV failure include pulmonary parenchymal disease, pulmonary arterial disease, pulmonary arterial thrombosis, pulmonary emboli, RV myocardial disease, and load.

Considering the pathophysiology of RV failure, additional contributors to the disease process included infection, inflammation due to pulmonary infiltration, interstitial congestion/edema leading to pulmonary congestion, vasoconstriction, hypoxia, and pulmonary hypertension and RV afterload. RV failure could also be due to cytokine involvement, pulmonary emboli, or thrombosis. Vascular thickening was seen in pulmonary arteries, and thrombosis was documented in large, medium, and small vessels.[4,5] Data out of New York showed that platelet thrombi also play an important role in RV failure.[6] Cytokines drive thrombosis, leading to increased fibrinogen and related platelet and white cell activation. COVID-19 infection results in a cytokine storm, an exuberant release of cytokines due to hyperactivation of the immune system.[7] Within this setting, D-dimer is involved as both a driver of thrombosis and a novel marker of thrombosis and disease severity.[8,9]

As to other cardiac manifestations involving the right heart, a septal shift was described, seen accompanying pulmonary hypertension in patients with COVID-19. Myocarditis was observed, with evident direct myocardial SARS-CoV-2 infiltration noted in several cases. Of note, direct significant myocardial viral infiltration was not the prototypic dominant feature of COVID-19.[10]

Clinical Strategies

The clinical presentation of RV failure in patients with COVID-19 consisted of general symptoms and signs consistent with RV failure. Patients presented with elevated central venous pressure, tricuspid regurgitation, pulmonic insufficiency, abdominal distention associated with ascites, peripheral edema, and, if increasingly severe hypotension, syncope, shock, and cardiac arrest. There were several interesting diagnostic indicators related to RV dilation on echocardiography, such as RV/LV ED area > 0.6; RV diameter > 42 mm (base); TAPSE < 17mm: RV FAC < 35%: RV EF < 45%; however, radial dysfunction was primarily unique to COVID patients.

Treatment

The treatment approach focused on 1) supporting overall RV perfusion pressure, 2) maintaining sinus rhythm, 3) optimizing RV loading conditions and contractility, and 4) addressing anticoagulation and thrombus-related conditions.[11]

The initial recommendation for mechanical circulatory support was a staged approach using a single cannula right ventricular assistance device (RVAD), specifically Protek Duo (LivaNova), paired with a gas exchanger. The next step was support using veno-venous ECMO and an Impella (Abiomed) device.[12-14] A surgical approach was recommended for special cases only. The downside to using ECMO is the increased risk of inflammation driven by foreign material. Using data from the Specialty Care database of 500 patients, the survival rate on ECMO was 40-45%.

The access point and insertion site are the next issues to consider in the staged approach.[15] In selected cases, support can be added on the left side. Data kindly provided by Dr. A. El Banyosy from Integris Medical Center in Oklahoma showed that in 87 patients with severe COVID who were on ECMO support, almost 10% (9/87) had severe RV dysfunction requiring support with an Oxy-RVAD. Half of these patients were successfully discharged. The Food and Drug Administration provided emergency use authorization for Impella RP to treat right heart failure in COVID-19 patients and Impella CP in tandem with ECMO for critically ill patients. Field data from Abiomed demonstrated increased use of Impella in patients with COVID-19; 10% (70/700) of patients were supported with ECMO and Impella.

Conclusion

Overall, COVID-19 RV failure was underdiagnosed. The mechanisms behind RV failure are multifactorial, involving thrombotic, embolic, proliferative, inflammatory, and loading pathogenic mechanisms. The initial treatment approach involved maintaining overall pressure, rhythm, optimized RV pre- and afterload, anticoagulation, and inotropes. A graded approach was recommended to avoid increased inflammation, hemolysis, and other complications if mechanical support was considered. Oxy-RVAD with Protek Duo was preferred in 95% of cases reviewed, followed by support with Impella. Understanding mechanisms and addressing all pathophysiologic components will improve our approach to RV failure in COVID. At this point, defining and systematizing an overall approach and optimal treatment strategies, all implemented in a tiered and team fashion, is the best approach for preventing and treating RV dysfunction and failure in COVID.

Acknowledgment

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Disclosures

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References

[1] Creel-Bulos C, Hockstein M, Amin N, Melhem S, Truong A, Sharifpour M. Acute Cor Pulmonale in Critically Ill Patients with Covid-19. N Engl J Med. 2020;382(21):e70. doi: 10.1056/NEJMc2010459.

[2] Rauch S, Regli IB, Clara A, et al. Right ventricular myopericarditis in COVID-19: a call for regular echocardiography. *Minerva Anestesiol*. 2020;86(11):1253-4.
[3] Ferrante G, Fazzari F, Cozzi O, et al. Risk factors for myocardial injury and death in patients with COVID-19: insights from a cohort study with chest computed tomography. *Cardiovasc Res*. 2020;116(14):2239-2246. doi: 10.1093/cvr/cvaa193.
[4] Suzuki YJ, Nikolaienko SI, Dibrova VA, et al. SARS-CoV-2 spike protein-mediated cell signaling in lung vascular cells. *Vascul Pharmacol*. 2021;137:106823. doi: 10.1016/j.vph.2020.106823.
[5] Lax SF, Skok K, Zechner P, et al. Pulmonary Arterial Thrombosis in COVID-19 With Fatal Outcome : Results From a Prospective, Single-Center, Clinicopathologic Case Series. *Ann Intern Med*. 2020;173(5):350-361. doi: 10.7326/M20-2566.
[6] Borczuk AC, Salvatore SP, Seshan SV, et al. COVID-19 pulmonary pathology: a multi-institutional autopsy cohort from Italy and New York City. *Mod Pathol*. 2020;33(11):2156-2168. doi: 10.1038/s41379-020-00661-1.
[7] Vaninov N. In the eye of the COVID-19 cytokine storm. *Nat Rev Immunol*. 2020;20(5):277. doi: 10.1038/s41577-020-0305-6.
[8] Lippi G, Favaloro EJ. D-dimer is Associated with Severity of Coronavirus Disease 2019: A Pooled Analysis. *Thromb Haemost*. 2020;120(5):876-878. doi: 10.1055/s-0040-1709650.
[9] Induruwa I, Moroi M, Bonna A, et al. Platelet collagen receptor Glycoprotein VI-dimer recognizes fibrinogen and fibrin through their D-domains, contributing to platelet adhesion and activation during thrombus formation. *J Thromb Haemost*. 2018;16(2):389-404. doi: 10.1111/jth.13919.
[10] Tavazzi G, Pellegrini C, Maurelli M, et al. Myocardial localization of coronavirus in COVID-19 cardiogenic shock. *Eur J Heart Fail*. 2020;22(5):911-915. doi: 10.1002/ejhf.1828.
[11] Bonnemain J, Ltaief Z, Liaudet L. The Right Ventricle in COVID-19. *J Clin Med*. 2021;10(12):2535. doi: 10.3390/jcm10122535.
[12] Rajagopal K, Keller SP, Akkanti B, et al. Advanced Pulmonary and Cardiac Support of COVID-19 Patients: Emerging Recommendations From ASAIO-a Living Working Document. *Circ Heart Fail*. 2020;13(5):e007175. doi: 10.1161/CIRCHEARTFAILURE.120.007175.
[13] Rajagopal K, Keller SP, Akkanti B, et al. Advanced Pulmonary and Cardiac Support of COVID-19 Patients: Emerging Recommendations From ASAIO-A "Living Working Document". *ASAIO J*. 2020;66(6):588-598. doi: 10.1097/MAT.0000000000001180.
[14] Kapur NK, Esposito ML, Bader Y, et al. Mechanical Circulatory Support Devices for Acute Right Ventricular Failure. *Circulation*. 2017;136(3):314-326. doi: 10.1161/CIRCULATIONAHA.116.025290.
[15] Hall CA, Jacobs JP, Stammers AH, et al. Multi-institutional Analysis of 505 Patients With Coronavirus Disease-2019 Supported With Extracorporeal Membrane Oxygenation: Predictors of Survival. Ann Thorac Surg. 2022;114(1):61-68. doi: 10.1016/j.athoracsur.2022.01.043.

2022 Symposium Presentation

Revascularization in Cardiogenic Shock: Residual Syntax Score and Chronic Total Occlusions

Venugopal Menon, MD, FACC, FAHA
Department of Cardiovascular Medicine, Cleveland Clinic, Cleveland, OH

Email: Menonv@ccf.org

Abstract

The residual syntax score (rSS) is strongly associated with outcomes in patients with stable coronary artery disease. In patients with acute myocardial infarction-associated cardiogenic shock (AMI-CS), the correlation or association of the rSS, mortality risk, and revascularization strategy has not yet been elucidated and needs more investigation. The SHOCK trial demonstrated that patients with left main and severe triple-vessel disease, who underwent coronary artery bypass grafts, had improved outcomes and higher 1-year survival rates than those with initial medical stabilization. However, it is unclear which is the superior technique for achieving complete revascularization. In contrast to the SHOCK trial's results, the CULPRIT-MI trial indicated that multivessel intervention had no impact on patient outcomes. Patients with AMI-CS usually have high rSSs due to their complex multivessel disease. Thus, the rSS may be more of a surrogate for the kind of disease than the strategy employed. We, therefore, hypothesize that lowering the rSS might lead to better outcomes. In addition, as there is currently no data confirming an effective targeted strategy, reintroduction of the bypass surgery should be considered.

Keywords: multivessel coronary artery disease, coronary artery bypass graft, percutaneous coronary intervention, myocardial infarction

Background

Findings from a randomized trial showed that the mortality in patients having acute myocardial infarction-associated cardiogenic shock (AMI-CS) was consistently high (40% to 50%), and early revascularization appeared to be the only beneficial therapy.[1] Of note, multivessel coronary artery disease (CAD) is observed in 75% of AMI-CS cases.[2] Physicians rely on risk assessment scores to curb this devastating disease and determine treatment plans. The SYNTAX score (SS) assesses the extent of CAD by quantifying the disease based on lesion number, location, and complexity.[3] The residual syntax score (rSS), which is derived from the SS score, quantifies the residual CAD after percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) and acts as an independent predictor for clinical adverse events.[4-6] Although the rSS is strongly associated with outcomes in patients having CAD and acute coronary syndrome, its importance in patients with cardiogenic shock remains uninvestigated.

Clinical Trials

SHOCK Trial

The relevance of the rSS in the setting of cardiogenic shock started with the SHOCK trial in the mid-1990s. At the

time of the SHOCK trial, the application of balloon angioplasty was ubiquitous in early revascularization, while stents were minimally used.[7] Specifically, the SHOCK trial was designed to compare the survival advantage of initial medical stabilization versus emergency revascularization in patients with AMI-CS.[8] Most patients enrolled in the trial had double- or triple-vessel disease; very few had single-vessel disease. All the patients with left main and triple-vessel disease opted for coronary artery bypass graft (CABG), and most had good outcomes. This trial demonstrated that emergency revascularization was associated with higher 1-year survival rates compared with initial medical stabilization. Indeed, patients with CABG had good outcomes despite being sicker from more extensive coronary disease. The subsequent questions are: (1) Is it important to achieve complete revascularization as CABG can in this setting? and (2) Is this benefit due to more complete revascularization with a CABG strategy?

CULPRIT Trial

In contrast to the findings of the SHOCK trial, the CULPRIT-MI study demonstrated that multivessel intervention had no impact on outcomes in the AMI-CS population.[9] In fact, multi-vessel intervention resulted in worse outcomes. The CULPRIT-MI study included an assessment of the rSS and its impact. Patients with cardiogenic shock had very high rSSs because they had complex multivessel disease. After PCI, whether in a multivessel approach or deferred approach, the amount of residual ischemia was still high.

Comparing the rSS with the baseline SS, it was apparent that the rSS increased when the baseline SS increased. Although the rSS was anticipated to be lower in the multivessel group, it was not impacted by the initial revascularization strategy. The rSS appeared to be a surrogate for the kind of disease rather than a reflection of the employed strategy. Indeed, the rSS was strongly associated with poorer outcomes; i.e., patients had higher 30-day mortality when their rSS increased. This finding raises the question: Should mechanical devices and other supportive devices be used to do more complex remote revascularization in the setting of cardiogenic shock? Although it is logical to hypothesize that patient outcomes would be improved when the rSS is lower, this hypothesis has yet to be proven.

Case Study

Consider the following situation:

A 60-year-old male patient was admitted with chest pain caused by an AMI. He had a right bundle branch block and a left anterior hemiblock. His electrocardiogram showed that he had sinus tachycardia and an acute ST elevation in the anterior precordial leads, along with PR prolongation. The patient's coronary angiography revealed a diffuse disease in the right coronary artery, but there was no flow-limiting lesion. There was poor flow on the left side due to a blocked circumflex vessel and a compromised left anterior descending (LAD) artery. The LAD was opened, but should the circumflex vessel be opened?

The non-infarct zone was not studied in the CULPRIT nor the SHOCK trial. Therefore, we would like to assess the condition of the non-infarct zone to know whether it was ischemic, normal, or scarred. In the case of a wafer-thin inferior wall, the right coronary artery would not be opened despite the severe disease and circumflex distribution.

The LAD was opened up in an acute setting, but mitral regurgitation was not observed. Using extra time and dye to open the circumflex is not advisable in this scenario, but if this person had severe hypokinesis in that wall, opening the circumflex would have been considered.

This kind of practical judgment should be further considered in future clinical trials. The LAD was wired, ballooned, and subsequently stented in this specific case. The electrocardiogram revealed a second-degree AV block in the setting of an LAD infarction. The PR prolongation led to the suspicion of an impaired conduction system. In the case of anterior wall AMI, a wire should be very quickly placed in the patient, which was done. Eventually, the patient's condition improved and became stable after the LAD intervention.

Conclusion

The rSS appears to be related to baseline findings rather than the intended revascularization strategy. The rSS is associated with 30-day and 60-day mortality in patients with AMI-CS; however, no data confirm that a targeted strategy to achieve complete revascularization in patients with cardiogenic shock would improve outcomes. Thus, we advise that the role of bypass surgery in AMI-CS should be reconsidered.

References

[1] Hochman JS, Lynn SA, 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(9):625-34. doi: 10.1056/NEJM199908263410901.

[2] Thiele H, Desch S, Piek JJ, et al. Multivessel versus culprit lesion only percutaneous revascularization plus potential staged revascularization in patients with acute myocardial infarction complicated by cardiogenic shock: Design and rationale of CULPRIT-SHOCK trial. *Am Heart J*. 2016;172:160-9. doi: 10.1016/j.ahj.2015.11.006

[3] Sianos G, Morel M-A, Kappetein AP, et al. The SYNTAX score: an angiographic tool grading the complexity of coronary artery disease. *EuroIntervention.* 2005;1(12):219-27.

[4] Genereux P, Palmerini T, Caixeta A, et al. Quantification and impact of untreated coronary artery disease after percutaneous coronary intervention: the residual SYNTAX (Synergy Between PCI with Taxus and Cardiac Surgery) score. *J Am Coll Cardiol*. 2012;59(24):2165-74. doi: 10.1016/j.jacc.2012.03.010.

[5] Farooq V, Serruys PW, Bourantas CV, et al. Quantification of incomplete revascularization and its association with five-year mortality in the synergy between percutaneous coronary intervention with taxus and cardiac surgery (SYNTAX) trial validation of the residual SYNTAX score. *Circulation*. 2013;128(2):141–51. doi: 10.1161/CIRCULATIONAHA.113.001803.

[6] Qiu M, Li Y, Li J, et al. Impact of six versus 12 months of dual antiplatelet therapy in patients with drug-eluting stent implantation after risk stratification with the residual SYNTAX score: Results from a secondary analysis of the I-LOVE-IT 2 trial. *Catheter Cardiovasc Interv*. 2017;89(S1):565–573. doi: 10.1002/ccd.26948.

[7] White HD, Assmann SF, Sanborn TA, Jacobs AK, Webb JG, Sleeper LA, Wong CK, Stewart JT, Aylward PE, Wong SC, Hochman JS. Comparison of percutaneous coronary intervention and coronary artery bypass grafting after acute myocardial infarction complicated by cardiogenic shock: results from the Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock (SHOCK) trial. *Circulation*. 2005;112(13):1992-2001. doi: 10.1161/CIRCULATIONAHA.105.540948.

[8] Sanborn TA, Sleeper LA, Webb JG, et al. Correlates of one-year survival inpatients with cardiogenic shock complicating acute myocardial infarction: Angiographic findings from the SHOCK trial. *J Am Coll Cardiol*. 2003;42(8):1373-9. doi: 10.1016/s0735-1097(03)01051-9.

[9] Barthélémy O, Rouanet S, Brugier D et al.. Predictive Value of the Residual SYNTAX Score in Patients With Cardiogenic Shock. *J Am Coll Cardiol*. 2021; 77(2):144-155. doi: 10.1016/j.jacc.2020.11.025.

Peer-reviewed Case Series

Management of Patients with Refractory Cardiogenic Shock and Cardiointestinal Syndrome with Impella 5.5 as Bridge to Decision: Case Series

Ismael A. Salas De Armas, MD;[1] Bindu Akkanti, MD;[2] Amanda Bergeron, MSN, APRN, AGACNP-BC;[3] Anju Bhardwaj, MD;[1] Ali Shirafkan, MD;[1] Kha Dinh, MD;[2] Mehmet H. Akay, MD;[1] Jayeshkumar Patel, MD;[1] Manish K. Patel, MD;[1] Igor D. Gregoric, MD;[1] Biswajit Kar, MD[1]

[1]Department of Advanced Cardiopulmonary Therapies and Transplantation, The University of Texas Health Science Center at Houston, Houston, TX 77030.
[2]Divisions of Pulmonary, Critical Care, and Sleep, The University of Texas Health Science Center at Houston, Houston, TX 77030.
[3]Memorial Hermann Hospital-Texas Medical Center, Houston, TX 77030.

Email: Biswajit.Kar@uth.tmc.edu

Abstract

Patients with advanced heart failure require multi-system management as most succumb to end-organ dysfunction, including gastrointestinal sequelae. Temporizing measures, such as early mechanical circulatory support, can assist in the recovery of patients with acute cardiogenic shock. The temporary support can improve patient characteristics to enable future definitive heart failure therapies such as durable left ventricular assist devices and orthotopic heart transplantation. We present two cases of cardiogenic shock that were successfully bridged with an Impella 5.5 (Abiomed). The management enabled the patients to recover from **reversible** cardiointestinal syndrome and undergo successful definitive therapies.

Keywords: Cardiointestinal syndrome, Impella

Background

Patients in "hemometabolic" cardiogenic shock are characterized by severe lactic acidosis and acidemia; they are at high risk for severe shock, multi-organ dysfunction, and reduced survival.[1] In cases of such decreased perfusion, there is reduced blood flow to vital organs, including the mesenteric bed. Furthermore, these patients have significant post-operative complications despite the treatment of heart failure with durable assist devices or heart transplantation.[2]

Different strategies have been successfully used to temporize advanced heart failure, including inotropic support, optimization of pre-load, management of multiorgan dysfunction, and timely mechanical circulatory support

through the femoral vessel. However, these options have the potential for gastrointestinal consequences based on the splanchnic vasomotor response.[3] Inotropic and vasoconstrictor agents may further reduce the blood supply to the gastrointestinal system by increasing splanchnic vascular tone and potentiating gut ischemia. The combination of fluid restriction and diuretic use can cause enterocyte dysfunction.[4] Thus, hypokalemia, as a result of loop diuretics, can further reduce intestinal peristalsis. Cardiointestinal syndrome can also occur in heart failure patients and is characterized by portal venous congestion and splanchnic hypoperfusion with intestinal dysfunction. This ultimately results in severe intestinal dysmotility, edema, inflammation, ischemia with bacterial translocation, and additional myocardial depression.[5]

In addition, mechanical circulatory support utilizing femoral artery insertion precludes patient mobilization, affecting the intestine and colon motility. As a result, constipation, abdominal distention, anorexia, paralytic ileus, bowel edema and distention, malabsorption, constipation, and even bowel perforation could be the spectrum of gastrointestinal manifestations. There is evidence that inadequate splanchnic perfusion in critically ill patients increases morbidity and mortality.[6]

Currently, definitive advanced heart failure therapies include orthotropic heart transplantation and a durable left ventricular assist device (LVAD) implantation. Unlike individuals undergoing elective cardiac surgery, patients with cardiogenic shock who are approved for LVAD implantation represent a special subgroup that may benefit from optimization. Since the implantation of an LVAD requires cardiopulmonary bypass (CPB) support, it is important to consider the associated gastrointestinal complication risk.[7-10] In addition, the postoperative period for patients undergoing durable LVAD surgery requires opioids for pain control, which leads to reduced peristalsis and worsening gastrointestinal distension and exacerbates these conditions in this high-risk group.

There are no specific guidelines for patients in cardiogenic shock experiencing severe gastrointestinal dysfunction and undergoing implantation of a durable LVAD. We present our experience with two chronic heart failure patients diagnosed with refractory cardiogenic shock on both inotropic support and subsequent transfemoral mechanical support that developed significant gastrointestinal dysfunction due to early cardiointestinal syndrome.

Case Descriptions

Patient 1

We present the case of a 33-year-old female with a history of peripartum cardiomyopathy. She has two children, and the last delivery was an uncomplicated caesarian section approximately a year before the current presentation. She has had four prior hospitalizations for advanced heart failure. There is a known family history of non-ischemic cardiomyopathy. The patient was treated medically. She was recently seen during a clinic visit where she presented with New York Heart Association Class IV symptoms. She complained of worsening dyspnea, for which she was admitted to the hospital. The patient suffered from fatigue, dyspnea, and recent constipation that responded to an at-home bowel regimen. Upon physical exam, she was alert and oriented and had signs of jugular vein distension. The abdomen was soft, non-tender, and non-distended, and there was no lower extremity edema. The echocardiogram was significant for depressed left ventricular ejection fraction (< 20%). She had a left ventricular internal dimension in diastole of 6 cm, normal right ventricle (RV), mild mitral regurgitation, and mild tricuspid regurgitation. Pre-hospital abdominal imaging showed moderate to severe narrowing of the celiac axis of uncertain etiology. Results from a right heart catheterization (RHC) done on arrival at the hospital are reported in Table 1. RHC on presentation showed significantly elevated filling pressures with a severely depressed cardiac index (CI) of 0.8 L/min/m^2 in the setting of significantly elevated systemic vascular resistance (> 3000 dynes/sec/cm). Our multidisciplinary team decided the patient was too sick to remain on the transplant list. To escalate her temporary support to ambulatory mechanical circulatory support, an axillary Impella 5.5 (Abiomed) was placed. An aggressive ambulation regimen was initiated with subsequent improvement of ileus and stabilization of debility. She underwent implantation of a HeartMate 3 (Abbott) twenty days after the Impella 5.5 placement (Figure 1). Her postoperative course was complicated by acute, severe right heart failure that required the implantation of a temporary right ventricular assist device (Protek-Duo; LivaNova). The internal jugular approach with a 26 French veno-venous cannulae was used to implant the Protek-Duo. The device was decannulated five days after placement. The patient was discharged to a rehabilitation facility and then home 90 days after presentation. During the recovery period, she had no further episodes of severe intestinal ileus. She continues to manage her heart failure with an LVAD and is regularly seen in the clinic for follow-up care.

Patient 2

A 42-year-old male with a recent diagnosis of non-ischemic cardiomyopathy secondary to extensive cocaine and alcohol use was transferred to our facility from an outside hospital for advanced therapies. He was in stage D cardiogenic shock, as classified by the Society for Cardiovascular Angiography and Interventions. On arrival, the patient noted that he quit alcohol and cocaine within the last year and was hospitalized four times for heart failure. The patient had worsening shortness of

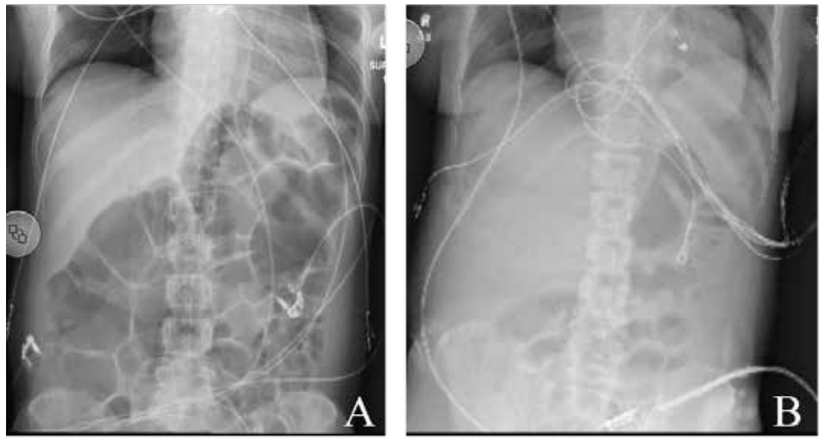

Figure 1. Case 1 Abdominal X-rays A) X-ray taken on the morning of the Impella 5.5 insertion B) X-ray taken on the morning of the left ventricular assist device placement.

breath, fatigue, orthopnea, and paroxysmal nocturnal dyspnea despite adhering to guideline-based medical therapy. He reported no family history of heart failure and was committed to advanced heart failure therapies. Upon physical examination, he was alert and oriented with signs of jugular vein distention, significant pitting edema, and abdominal distension. He had coarse rales and was supported on non-invasive positive pressure with supplemental oxygen therapy. His hemodynamics upon arrival are listed in Table 1.

A left heart catheterization did not reveal any obstructive coronary artery disease. He was initiated on bumetanide infusion and milrinone therapy at 0.375mcg/kg/min. He continued to have signs of low cardiac output; dopamine (2 mcg/kg/min) was added to his medical management. A repeat RHC was done 18 days after admission while the patient received dual inotrope support (Table 1). Given a persistent low cardiac output, a femoral IABP was placed. After social support was established, the patient was presented to the

Table 1. Data collected from right heart catheterizations. For Case 1, no inotrope support was provided on arrival and the repeat data was attained 39 days after admission while the patient was on intra-aortic balloon pump support. For Case 2, the patient was on milrinone (0.25 mcg/kg/min) on admission, and the repeat data was attained 18 days after admission while the patient was on milrinone (0.375 mcg/kg/min) and dopamine (2 mcg/kg/min).

	Case 1		Case 2	
	Arrival	**Repeat**	**Arrival**	**Repeat**
Mean right atrial pressure (mmHg)	26	6	22	13
Right ventricular mean pressure (mmHg)	54/22	40/11	51/24	39/14
Pulmonary artery pressure (mmHg)	46/33	38/19	50/30	40/22
Mean pulmonary artery pressure (mmHg)	44	26	37	30
Pulmonary capillary wedge pressure (mmHg)	33	14	33	24
Pulmonary artery saturation (%)	27	70	41	48
Hemoglobin (g/dL)	11.0	12.8	14.2	11.7
Estimated Fick cardiac output (L/min)	1.3	3.8	2.0	2.6
Estimated Fick cardiac index (L/min/m^2)	0.8	2.4	1.3	1.7
Thermodilution cardiac output (L/min)	1.3	NA	NA	NA
Thermodilution cardiac index (L/min/m^2)	0.8	NA	NA	NA

medical review board and deemed to be a reasonable candidate for implantation of a durable LVAD as destination therapy due to substance abuse. A month into the hospitalization, the patient continued to deteriorate despite aggressive diuresis, inotropic support, and multidisciplinary management of cardiac cachexia. He developed intestinal pseudo-obstruction (Figure 2A), and the decision was made to further rehabilitate and stabilize the patient with an Impella 5.5 before implantation of a durable device.

The patient began aggressive physical therapy and ambulation, as well as increased caloric intake. With the continued bowel regimen and mobility, the ileus was resolved on hospital day 38 (Figure 2B). On hospital day 40 (8 days after insertion of the Impella 5.5), the patient underwent placement of a durable LVAD. The postoperative course was unremarkable, and the patient was discharged home on hospital day 58. The patient continues to do well and maintains his follow-up appointments at the outpatient clinic.

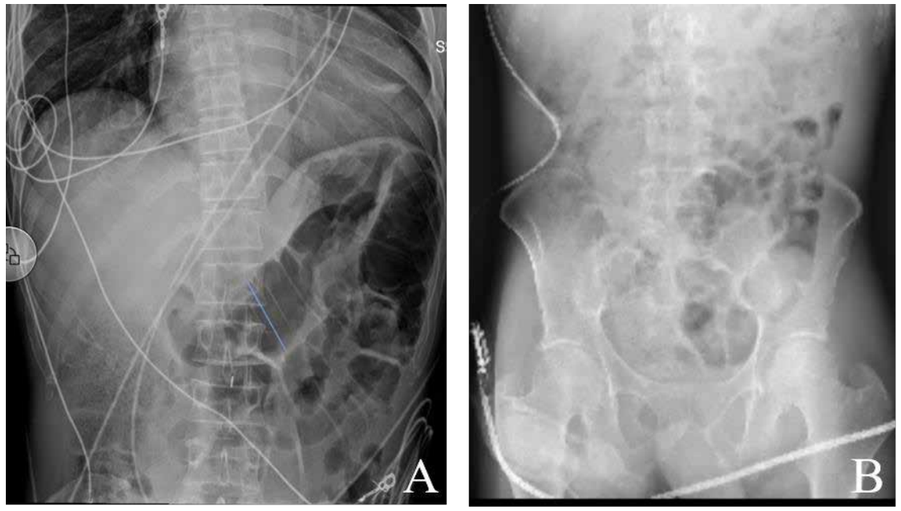

Figure 2. Case 2 Abdominal X-rays A) X-ray taken on the morning of the Impella 5.5 insertion B) X-ray taken on the morning of the left ventricular assist device placement.

Discussion

The current FDA indications to upgrade patients with advanced heart failure to temporary mechanical circulatory support utilizing the Impella 5.5 system include inadequate support to achieve end-organ perfusion.[11] This manuscript describes how to support patients with cardiogenic shock and gastrointestinal dysfunction, likely secondary to reversible cardiointestinal syndrome, via the Impella 5.5 before implantation of a durable LVAD. Gastrointestinal dysmotility, like ileus and pseudo-obstruction, in patients with cardiogenic shock is often viewed as a concomitant gastrointestinal symptom rather than a component of an early and reversible stage of cardiointestinal syndrome. Thus, due to a low cardiac output state, our patients likely had decreased end-organ perfusion with markedly reduced gastrointestinal perfusion and worsening splanchnic vasoconstriction (Figure 3). The trans-axillary Impella 5.5 served as a bridge to the implantation of a durable LVAD with the objective of improving splanchnic circulation, decreasing the amount of inotropic and vasopressors use, and promoting ambulation to improve the gastrointestinal condition.

The cardiogenic shock state is characterized by increased filling pressures with portal and splanchnic venous congestion with subsequent bowel edema, malabsorption, and decreased peristalsis. In addition, the high filling pressures can only be ameliorated with aggressive diuresis therapy, which leads to electrolyte abnormalities that can worsen peristalsis. This combination further exaggerates these complications by decreasing appetite and intestinal absorption and predisposing the patient to a vicious deterioration that eventually leads to an ischemic gut. Finally, the inability to perform ambulation due to trans-femoral mechanical circulatory support further reduces gastrointestinal peristalsis.[12,13] Irreversible consequences include bacterial translocation, bowel

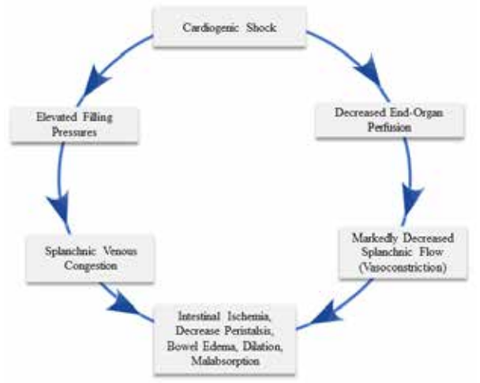

Figure 3. The compounded flow of complications resulting from cardiogenic shock.

perforation, sepsis, and metabolic acidosis leading to further myocardial dysfunction and, eventually, death.

Durable LVADs augment cardiac output, thereby improving end-organ perfusion to all vital organs, including the mesenteric bed;[14] however, patients with pre-existing dysfunction in the gastrointestinal tract may not tolerate CPB support during definitive LVAD surgery. Furthermore, the addition of intraoperative inotropic support and postoperative inotropic and vasopressor support further exacerbate gastrointestinal complications.[15] In addition, patients may need a considerable amount of postoperative narcotic medication for pain control, which can further impair bowel motility.

There are several advantages to using the trans-axillary Impella 5.5 before implantation of an LVAD to improve gastrointestinal dysfunction in patients suffering from cardiogenic shock and cardiointestinal syndrome, as demonstrated in our cases. The ability of the device to provide up to 5.5 L/min of flow is enough to reverse the low-output state resolving the splanchnic vasoconstriction and to improve the forward flow relieving the right-sided elevated pressures. The implantation procedure is a relatively minor surgery without the need for significant narcotic use. Finally, the Impella 5.5 allows for ambulation, which improves peristalsis and optimizes the patient for future definitive durable therapies.

We believe that cardiointestinal syndrome is underdiagnosed in this population until later irreversible stages and want to provide awareness and emphasize that early intervention and resolution of the primary organ dysfunction will likely improve the secondary organ involved. In conclusion, patients with advanced heart failure and multiorgan dysfunction who present with gastrointestinal dysmotility due to a low-flow splanchnic state in the form of cardiointestinal syndrome can be optimized with the Impella 5.5 device. Using this bridge therapy can lead to successfully implanting a durable LVAD or other definitive therapies such as orthotopic heart transplantation.

"Prehab" patients can improve cardiointestinal syndrome, nutritional status, and physical deconditioning to make them suitable candidates for durable LVAD or heart transplant with improved outcomes in an otherwise sick group of patients with very high-risk mortality.

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References

[1] Jentzer JC, Schrage B, Patel PC, et al. Association between the acidemia, lactic acidosis, and shock severity with outcomes in patients with cardiogenic shock. *J Am Heart Assoc*. 2022;11(9): e024932. doi: 10.1161/JAHA.121.024932.

[2] Kirklin JK, Naftel DC, Pagani FD, et al. Seventh INTERMACS annual report: 15,000 patients and counting. *J Heart Lung Transplant*. 2015;34(12):1495-504. doi: 10.1016/j.healun.2015.10.003.

[3] D'Ancona G, Baillot R, Poirier B, et al. Determinants of gastrointestinal complications in cardiac surgery. *Tex Heart Inst J*. 2003;30(4):280-5.

[4] Ratnaike, Ranjit N, Milton, et al. Drug-associated diarrhoea and constipation in older people; Constipation. *Aust J Hosp Pharm*. 2000;30(5):210-213. https://doi.org/10.1002/jppr2000305210

[5] Jarry S, Calderone A, Dion D, Bouchard D, Couture ÉJ, Denault A. Acute cardiointestinal syndrome resulting from postoperative acute biventricular heart failure. *J Cardiothorac Vasc Anesth*. 2022;36(7):2220-2227. doi: 10.1053/j.jvca.2022.02.011.

[6] Jakob SM. Clinical review: splanchnic ischaemia. *Crit Care*. 2002;6(4):306-12. doi: 10.1186/cc1515.

[7] Zacharias A, Schwann TA, Parenteau GL, et al. Predictors of gastrointestinal complications in cardiac surgery. *Tex Heart Inst J*. 2000;27(2):93-9.

[8] Mishra V, Hewage S, Islam S, Harky A. The correlation between bowel complications and cardiac surgery. *Scand J Surg*. 2021;110(2):187-192. doi: 10.1177/1457496920983618.

[9] Rodriguez R, Robich MP, Plate JF, Trooskin SZ, Sellke FW. Gastrointestinal complications following cardiac surgery: a comprehensive review. *J Card Surg*. 2010;25(2):188-97. doi: 10.1111/j.1540-8191.2009.00985.x.

[10] Huddy SP, Joyce WP, Pepper JR. Gastrointestinal complications in 4473 patients who underwent cardiopulmonary bypass surgery. *Br J Surg*. 1991;78:293-6.Thiele H, Jobs A, Ouweneel DM, et al. Percutaneous short-term active mechanical support devices in cardiogenic shock: a systematic review and collaborative meta-analysis of randomized trials. *Eur Heart J*. 2017;38(47):3523-3531. doi: 10.1093/eurheartj/ehx363.

[11] Salas de Armas I, Bergeron A, Bhardwaj A, et al. Surgically Implanted Impella Device for Patients on Impella CP Support Experiencing Refractory Hemolysis. *ASAIO J*. 2022;68(12):e251-e255. doi: 10.1097/MAT.0000000000001712
[12] Stethen TW, Ghazi YA, Heidel RE, et al. Walking to recovery: the effects of missed ambulation events on postsurgical recovery after bowel resection. *J Gastrointest Oncol*. 2018;9(5): 953-961. doi: 10.21037/jgo.2017.11.05.
[13] Story SK, Chamberlain RS. A comprehensive review of evidence-based strategies to prevent and treat postoperative ileus. *Dig Surg*. 2009;26(4):265-75. doi: 10.1159/000227765.
[14] Badami A, Fehrenbach Prell EA, Murray MA, et al. A novel approach to prevent post-operative ileus after continuous-flow left ventricular assist device implantation: A retrospective cohort study. *Int J Surg*. 2015;20:135-9. doi: 10.1016/j.ijsu.2015.06.054.
[15] Spotnitz WD, Sanders RP, Hanks JB, et al. General surgical complications can be predicted after cardiopulmonary bypass. *Ann Surg*. 1995;221(5):489-96. doi: 10.1097/00000658-199505000-00006.

Editorial

Future Perspectives in Acute Myocarditis Complicated by Cardiogenic Shock

Giovanni Amedeo Tavecchia, MD[1,2]; Iside Cartella, MD[1,2]; Enrico Ammirati, MD, PhD[1]
[1]De Gasperis Cardio Center, and Transplant Center, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy
[2]University of Milano Bicocca, Milan, Italy

Email: Enrico.ammirati@ospedaleniguarda.it

Abstract

Acute myocarditis is an inflammatory disease of the myocardium with a highly variable clinical course. Fulminant myocarditis (FM) represents the most threatening scenario with hemodynamic compromise and cardiogenic shock at presentation. Despite medical advances and the availability of promising mechanical circulatory support (MCS), FM is burdened by a dismal prognosis. Early referral to tertiary hospitals with MCS facilities and prompt diagnosis with endomyocardial biopsy are critical steps toward optimal management. Moreover, beyond supportive care, the prevention of irreversible myocardial damage with immunomodulating therapies must be proven in clinical trials. In this editorial, we briefly describe current evidence and future perspectives regarding the management of myocarditis complicated by cardiogenic shock.

Keywords: cardiogenic shock, fulminant myocarditis, immunosuppression, endomyocardial biopsy

Background

Acute myocarditis (AM) is an inflammatory disease of the myocardium of recent onset, which could be triggered by infections, drugs, toxic substances, and abnormal immunoreactivity.[1-3] Its clinical presentation is highly variable, ranging from a mild self-limiting syndrome to a severe life-threatening condition.[4] Similarly, the course of patients with myocarditis is heterogeneous, varying from partial or full recovery to advanced heart failure (HF) requiring a durable left ventricular (LV) assist device (LVAD) or heart transplantation (HTx).[5] Clinically aggressive forms of myocarditis are labeled as fulminant myocarditis (FM) and are characterized by an acute-onset clinical presentation with hemodynamic compromise, cardiogenic shock, and/or fatal arrhythmia.[2,6]

Diagnosis

During the last decade, the measurement of high-sensitivity cardiac troponin and the use of cardiac magnetic resonance imaging (CMRI) has allowed the diagnosis of non-complicated forms of AM non-invasively with high accuracy.[7] However, endomyocardial biopsy (EMB) is the reference standard for diagnosing myocarditis and should be performed in selected clinical scenarios.[8,9] EMB is an invasive procedure and carries a considerable risk of cardiac complications if performed in low-volume centers (up to 9%), whereas the risk is relatively low (1-2%) if performed in experienced centers.[8,10] To date, EMB is essential in discriminating between specific histology, such as giant cell myocarditis (GCM), eosinophilic myocarditis, and lymphocytic myocarditis. The use of EMB is highly recommended in

patients with FM or AM with rapidly progressing HF, in whom information derived from histology is essential for optimal management (eg, immunosuppressive treatment in GCM or eosinophilic myocarditis).[1,9]

Cardiogenic Shock

Cardiogenic shock is a low-cardiac-output state resulting in life-threatening end-organ hypoperfusion and hypoxia.[11] According to the Lombardy registry, the incidence of cardiogenic shock in a cohort of 443 patients with definite AM demonstrated by CMRI or histology is 8-9%.[5] Meanwhile, cardiogenic shock can occur in 38.9% of COVID-19-associated AM cases.[12] Patients with FM have a high rate of events,[13] with a 60-day rate of death or HTx as high as 28% based on a large international cohort.[5] These data are consistent with the United States administrative data, which documented a significant increase in the incidence of cardiogenic shock over time (from 7% in 2005 to 12% in 2014) and a strong relationship between hemodynamic compromise at presentation and long-term prognosis.[14] In patients presenting with FM and cardiogenic shock, supportive measures play a key role in ensuring adequate tissue perfusion and oxygenation. Initial treatment often requires mechanical ventilation, inotropic agents, and vasopressors, as recommended by consensus documents on the management of cardiogenic shock.[11] Of note, it should be kept in mind that high doses of vasoactive agents could be detrimental by increasing myocardial oxygen consumption and reducing the probability of myocardial recovery.[4,15] Use of a pulmonary artery catheter can be useful to guide treatment escalation and/or wean patients with AM and cardiogenic shock.

Temporary Mechanical Circulatory Support

In patients unresponsive to maximal pharmacological therapy, temporary mechanical circulatory supports (t-MCS) should be considered. The United States administrative data has shown a growth in the use of t-MCS among AM patients between 2005 and 2014, from 4.5% to 8.6%.[14] This trend was significant for all devices except for the intra-aortic balloon pump (IABP), the most frequently used support. Veno-arterial extracorporeal membrane oxygenation (V-A ECMO) is still the most extensively used advanced t-MCS in patients with profound cardiogenic shock (SCAI class D-E) and guarantees full cardiorespiratory assistance with survival rates in FM ranging from 56% to 87%.[10,11] Nevertheless, it is well known that V-A ECMO increases LV afterload, and venting strategies, such as vasodilators and/or IABP implantation, may be required to prevent LV distension and pulmonary edema.

In this setting, the role of the Impella® system (Abiomed) has emerged over time. It has been postulated that the presence of LV overload could worsen myocardial inflammatory reaction and that the axial flow pump, by directly unloading the LV, could exert anti-inflammatory disease-modifying effects.[16,17] Before using the Impella® system, three conditions should be fulfilled: 1) right ventricular function should be preserved, 2) LV thrombosis should be excluded to avoid systemic embolism, and 3) the LV cavity should have adequate size to avoid the suction phenomenon. Nevertheless, the multicenter cVAD registry on microaxial flow catheter (Impella®) used for FM (34 patients from 2009 to 2016) showed an in-hospital survival of 62%, similar to other registries on t-MCS;[18,19] furthermore, 29% of patients required the transition to another MCS.[20]

Heart Transplantation and Left Ventricular Assist Devices

If a patient cannot be weaned from t-MCS after 2 or 3 weeks, HTx or a durable LVAD may be considered. HTx survival is similar to that of patients with other types of HF (5-year survival rate of 78% for patients with myocarditis versus 77% for those with nonischemic cardiomyopathy and 74% for those with ischemic cardiomyopathy). Nevertheless, higher rates of early cellular rejection (16% versus 5%) and relapses of GCM in transplanted hearts have been reported.[21]

Immunosuppressive Treatment

The role of immunosuppressive therapy is well-established for treating GCM, eosinophilic myocarditis, cardiac sarcoidosis, and FM associated with systemic autoimmune diseases.[2] Regarding lymphocytic post-viral FM, the role of immunosuppressive therapies remains controversial.[22] Current evidence, mainly derived from patients with chronic inflammatory cardiomyopathy, suggests that immunosuppressive treatment should be administered in patients with high inflammatory markers and without a viral genome on myocardial samples.[23] However, the role of the viral genome in guiding the treatment is not well-established, and the majority of evidence suggests that virus-triggered immune-mediated reactions are the principal cause of cardiomyocyte injury rather than direct virus-mediated cell injury.[3] Molecular mimicry between cardiac and viral antigens could be a possible mechanism of myocardial injury in virus-triggered AM. Moreover, a growing body of evidence indicates that viruses such as PVB-19 and HHV6 may be found in the EMB of patients without myocarditis.[24] These findings indicate that the presence of viruses in the setting of AM may not represent an absolute contraindication to immunosuppressive treatments. Though not supported by evidence from clinical trials, current recommendations in our center consider intravenous gamma globulin administration in pediatric patients (single-infusion regimen of 0.5–2 g/kg) and steroids in adults (eg, methylprednisolone 1 g daily for 3 days, followed by oral prednisone 1 mg/kg daily with gradual tapering) if high suspicion of immune-mediated FM exists.[22] To elucidate the role of immunosuppression in FM and complicated AM, randomized controlled trials are needed. The MYocarditis THerapy With Steroids (MYTHS) trial (ClinicalTrials.gov identifier: NCT05150704), is an ongoing international randomized, single-blind pragmatic trial, that is randomizing 288 patients with FM or AM complicated by HF and impaired LV ejection fraction (< 41%) to pulse corticosteroid therapy (methylprednisolone 1g IV daily for 3 days) on top of standard therapy and maximal supportive care versus placebo. The trial will evaluate a combined primary endpoint defined as the time from randomization to the first event occurring within six months, including (1) all-cause death, (2) HTx, (3) LVAD implantation, or (4) the need for an upgrade of the t-MCS, or (5) a ventricular tachycardia/fibrillation treated with direct current shock, or (6) first rehospitalization due to HF or ventricular arrhythmias or advanced atrioventricular block. The trial started enrollment in October 2021 with an estimated duration of 3–4 years.[22]

Future Directions

A pivotal goal for the future is to reduce mortality rates of FM. In contrast with a previous report,[25] it is now well established that FM has poor in-hospital outcomes.[5,13] To reduce in-hospital mortality, prompt referral of patients with FM to hub centers and EMB performance is crucial. Histologic confirmation of specific FM etiologies (GCM and eosinophilic myocarditis) is of utmost importance for the timely start of immunosuppressive treatments and, thus, prevention of irreversible myocardial injury. The role of immunosuppressive treatment in lymphocytic FM needs to be clarified since there is a lack of standardized management. For this reason, we believe that the MYTHS trial could provide further insights regarding the potential beneficial effects of corticosteroids in lymphocytic FM. Eventually, regarding t-MCS, the role of axial flow pumps such as the Impella® system is growing, and the potential anti-inflammatory effects of direct LV unloading deserve consideration. An international network of tertiary centers experienced in cardiogenic shock and AM can help solve these unsolved questions.

Disclosures

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References

[1] Tschope C, Ammirati E, Bozkurt B, et al. Myocarditis and inflammatory cardiomyopathy: current evidence and future directions. *Nat Rev Cardiol*. 2021;18(3):169-193. DOI: 10.1038/s41569-020-00435-x.

[2] Ammirati E, Frigerio M, Adler ED, et al. Management of acute myocarditis and chronic inflammatory cardiomyopathy: An expert consensus document. *Circ Heart Fail*. 2020;13(11):e007405. DOI:10.1161/CIRCHEARTFAILURE.120.007405.

[3] Veronese G, Ammirati E, Chen C, et al. Management perspectives from the 2019 Wuhan international workshop on fulminant myocarditis. *Int J Cardiol*. 2021;324:131-138. DOI: 10.1016/j.ijcard.2020.10.063.

[4] Ammirati E, Veronese G, Bottiroli M, et al. Update on acute myocarditis. *Trends Cardiovasc Med*. 2021;31(6):370-379. DOI: 10.1016/j.tcm.2020.05.008.

[5] Ammirati E, Veronese G, Brambatti M, et al. Fulminant versus acute nonfulminant myocarditis in patients with left ventricular systolic dysfunction. *J Am Coll Cardiol*. 2019;74(3):299-311. DOI: 10.1016/j.jacc.2019.04.063.

[6] Kociol RD, Cooper LT, Fang JC, et al. Recognition and initial management of fulminant myocarditis: A scientific statement from the American Heart Association. *Circulation*. 2020:CIR0000000000000745. DOI:10.1161/CIR.0000000000000745.

[7] Ferreira VM, Schulz-Menger J, Holmvang G, et al. Cardiovascular magnetic resonance in nonischemic myocardial inflammation: Expert recommendations. *J Am Coll Cardiol*. 2018;72(24):3158-3176. DOI:10.1016/j.jacc.2018.09.072.

[8] Ammirati E, Buono A, Moroni F, et al. State-of-the-art of endomyocardial biopsy on acute myocarditis and chronic inflammatory cardiomyopathy. *Curr Cardiol Rep*. 2022;24(5):597-609. DOI: 10.1007/s11886-022-01680-x.

[9] Cooper LT, Baughman KL, Feldman AM, et al. The role of endomyocardial biopsy in the management of cardiovascular disease: a scientific statement from the American Heart Association, the American College of Cardiology, and the European Society of Cardiology. *Circulation*. 2007;116(19):2216-33. DOI:10.1161/CIRCULATIONAHA.107.186093.

[10] Bennett MK, Gilotra NA, Harrington C, et al. Evaluation of the role of endomyocardial biopsy in 851 patients with unexplained heart failure from 2000-2009. *Circ Heart Fail*. 2013;6(4):676-84. DOI: 10.1161/CIRCHEARTFAILURE.112.000087.

[11] van Diepen S, Katz JN, Albert NM, et al. Contemporary management of cardiogenic shock: A scientific statement from the American Heart Association. *Circulation*. 2017;136(16):e232-e268. DOI:10.1161/CIR.0000000000000525.

[12] Ammirati E, Lupi L, Palazzini M, et al. Prevalence, characteristics, and outcomes of COVID-19-associated acute myocarditis. *Circulation*. 2022;145(15):1123-1139. DOI: 10.1161/CIRCULATIONAHA.121.056817.

[13] Ammirati E, Cipriani M, Lilliu M, et al. Survival and left ventricular function changes in fulminant versus nonfulminant acute myocarditis. *Circulation*. 2017;136(6):529-545. DOI: 10.1161/CIRCULATIONAHA.117.026386.

[14] Pahuja M, Adegbala O, Mishra T, et al. Trends in the incidence of in-hospital mortality, cardiogenic shock, and utilization of mechanical circulatory support devices in myocarditis (Analysis of National Inpatient Sample Data, 2005-2014). *J Card Fail*. 2019;25(6):457-467. DOI: 10.1016/j.cardfail.2019.04.012

[15] Tarvasmaki T, Lassus J, Varpula M, et al. Current real-life use of vasopressors and inotropes in cardiogenic shock - adrenaline use is associated with excess organ injury and mortality. *Crit Care*. 2016;20(1):208. DOI: 10.1186/s13054-016-1387-1.

[16] Spillmann F, Van Linthout S, Schmidt G, et al. Mode-of-action of the PROPELLA concept in fulminant myocarditis. *Eur Heart J*. 2019;40(26):2164-2169. DOI: 10.1093/eurheartj/ehz124.

[17] Tschope C, Van Linthout S, Klein O, et al. Mechanical unloading by fulminant myocarditis: LV-IMPELLA, ECMELLA, BI-PELLA, and PROPELLA concepts. *J Cardiovasc Transl Res*. 2019;12(2):116-123. DOI: 10.1007/s12265-018-9820-2.

[18] Kondo T, Okumura T, Shibata N, et al. Differences in prognosis and cardiac function according to required percutaneous mechanical circulatory support and histological findings in patients with fulminant myocarditis: Insights from the CHANGE PUMP 2 study. *J Am Heart Assoc*. 2022;11(4):e023719. DOI: 10.1161/jaha.121.023719.

[19] Lorusso R, Centofanti P, Gelsomino S, et al. Venoarterial extracorporeal membrane oxygenation for acute fulminant myocarditis in adult patients: A 5-Year multi-institutional experience. *Ann Thorac Surg*. 2016;101(3):919-26. DOI: 10.1016/j.athoracsur.2015.08.014.

[20] Annamalai SK, Esposito ML, Jorde L, et al. The Impella microaxial flow catheter is safe and effective for treatment of myocarditis complicated by cardiogenic shock: An analysis from the Global cVAD Registry. *J Card Fail*. 2018;24(10):706-710. DOI: 10.1016/j.cardfail.2018.09.007.

[21] Elamm CA, Al-Kindi SG, Bianco CM, Dhakal BP, Oliveira GH. Heart transplantation in giant cell myocarditis: Analysis of the United Network for Organ Sharing Registry. *J Card Fail*. 2017;23(7):566-569. DOI: 10.1016/j.cardfail.2017.04.015.

[22] Ammirati E, Bizzi E, Veronese G, et al. Immunomodulating therapies in acute myocarditis and recurrent/acute pericarditis. *Front Med (Lausanne)*. 2022;9:838564. DOI:10.3389/fmed.2022.838564.

[23] Frustaci A, Russo MA, Chimenti C. Randomized study on the efficacy of immunosuppressive therapy in patients with virus-negative inflammatory cardiomyopathy: the TIMIC study. *Eur Heart J*. 2009;30(16):1995-2002. DOI:10.1093/eurheartj/ehp249.

[24] Verdonschot J, Hazebroek M, Merken J, et al. Relevance of cardiac parvovirus B19 in myocarditis and dilated cardiomyopathy: review of the literature. *Eur J Heart Fail*. 2016;18(12):1430-1441. DOI:10.1002/ejhf.665.

[25] McCarthy RE, 3rd, Boehmer JP, Hruban RH, et al. Long-term outcome of fulminant myocarditis as compared with acute (nonfulminant) myocarditis. *N Engl J Med*. 2000;342(10):690-5. DOI:10.1056/NEJM200003093421003.

Editorial

SCAI SHOCK: Does the Stage Help with Management Decisions?

Jacob C. Jentzer, MD[1] and David A. Baran, MD[2]
[1]Department of Cardiovascular Medicine, Mayo Clinic, Rochester, Minnesota
[2]Cleveland Clinic Heart Vascular and Thoracic Institute, Weston, Florida

Email: Barand@ccf.org

The original Society for Cardiovascular Angiography and Intervention (SCAI) SHOCK Classification statement was presented at the Houston Shock Symposium in 2019, shortly before its official publication.[1] This generated substantial discussion among the conference attendees, and it was immediately apparent that validation studies were needed to demonstrate the utility of this new staging system for defining the severity and prognosis of cardiogenic shock (CS). Together with several other attendees who were coauthors on the SCAI SHOCK Classification statement, we started planning a retrospective analysis to explore how to assign the SCAI SHOCK Classification using clinical data objectively. To achieve this, we met as a group to develop a consensus definition for each SCAI Shock stage using clinical, laboratory, and vital sign data available in the Mayo Clinic cardiac intensive care unit (CICU) database. The SCAI Shock Classification provided surprisingly robust mortality risk stratification in this population of 10,000 CICU patients with or at risk for CS, even after adjusting for established markers of illness severity and other prognostic variables.[2] The results held true in patients with acute coronary syndromes or heart failure, and cardiac arrest conferred incremental risk at each SCAI SHOCK stage consistent with the proposed "A" modifier from the SCAI SHOCK Classification statement.[3]

The manuscript was published later that year, quickly followed by several additional publications confirming and expanding upon these findings. These studies uniformly demonstrated that the SCAI SHOCK Classification provided incremental mortality risk stratification for patients across the spectrum of shock severity, regardless of the population studied.[4-7] Furthermore, additional potential risk modifiers emerged that could provide a graded prognostic assessment at each SCAI SHOCK stage.[8] This led to the development and publication of a revised SCAI SHOCK Classification earlier this year, which we were both fortunate to participate in writing.[9] This new statement highlighted the validity of the original SCAI SHOCK Classification and provided subtle modifications and clarifications while, by and large, maintaining the same structure. Based on studies published since the original SCAI SHOCK Classification statement, age was added as an established risk modifier, and the arrest modifier was changed to reflect only those post-arrest patients with possible neurologic compromise (i.e., coma).[8-11]

The revised SCAI SHOCK Classification statement underscores the practical application of the SCAI SHOCK Classification for mortality risk stratification, yet several unanswered questions remain. Chief among these is the need to leverage the SCAI SHOCK Classification to provide risk-tailored treatment strategies for individual patients with CS. To date, no randomized clinical trial has demonstrated clear evidence of heterogeneity of response to treatment in CS patients according to baseline mortality risk. To some extent, this may result from the inclusion of both shock-related and non-modifiable risk factors in established mortality prediction scores.[12, 13] However, the SCAI SHOCK Classification could provide a unique opportunity to provide individualized management of CS patients by matching the degree of support to the severity of CS. While this approach remains speculative, it seems logical to evaluate this strategy objectively.

Our first attempt to address this question utilized the Mayo Clinic CICU database. It examined the propensity-adjusted association between intra-aortic balloon pump (IABP) use and mortality across the SCAI SHOCK stages in patients with CS

from diverse etiologies.[14] This analysis suggested an association between the use of the IABP and lower mortality, an effect that may have been more prominent at lower shock severity. This finding was conceptually appealing considering the modest hemodynamic support provided by the IABP, particularly when compared to the high severity of CS observed in randomized clinical trials evaluating this therapy. These findings are speculative based on the observational nature of this analysis but stress the potential to utilize the SCAI SHOCK Classification to tailor hemodynamic support. We have proposed an incremental approach to hemodynamic support according to the SCAI SHOCK Classification, recognizing that prior studies have not demonstrated improvements in outcomes when temporary mechanical circulatory support (MCS) devices are used uniformly.[15, 16] The impetus to use the SCAI SHOCK Classification to guide therapy is supported by the surprisingly minimal differences in most standard hemodynamic measurements across the SCAI SHOCK stages despite dramatic differences in the severity of shock and critical illness.[4, 7] CS is too heterogeneous a disease to realistically create a formulaic one-size-fits-all care strategy that applies to all patients with CS, but a structured approach to evaluation and management tailored to shock severity is feasible.[16]

An ideal opportunity to utilize the SCAI SHOCK Classification to facilitate clinical care comes in the context of the shock team. Despite different approaches utilized at various institutions, establishing a shock team has improved outcomes for patients with CS.[17-19] In addition to providing a standardized multidisciplinary evaluation for patients with CS, the shock team can facilitate consistent care tailored to each patient's needs. By assigning the SCAI SHOCK stage in an agreed-upon manner, the shock team members can communicate clearly and provide a structured approach to initiating and escalating temporary MCS that is more likely to yield benefits than use without a formal approach. Each institution can develop a consensus approach to assigning the SCAI SHOCK Classification to help specify which patients will be selected for specific temporary MCS devices, enabling streamlined care congruent with institutional best practices. While the shock team can come to these same conclusions *ad hoc* for each patient, having an established algorithm ensures that the team's composition does not impact the quality of care. This strategy allows each institution to define the preferred approach to CS management in a manner that can be used to expand beyond a single facility to build a hub-and-spoke CS care network.[20] Unfortunately, examining the effects of such an approach in a classic randomized clinical trial may not be feasible. However, an implementation science approach (eg, stepped-wedge pragmatic trial) could be effective. Nonetheless, determining which aspects of shock team management are associated with improved outcomes can be evaluated objectively to develop a set of core best practices for shock team performance.

Implementation of the SCAI SHOCK Classification can take many incarnations. Simplified approaches to the SCAI SHOCK Classification can be taught quickly and easily to providers of all training and experience, and clinician assignment of the SCAI SHOCK stage performs as well as a more complex data-driven algorithm for risk stratification.[4] Alternatively, the electronic medical record can be utilized to determine the SCAI SHOCK stage automatically using laboratory and vital sign data. The former approach in the prehospital and emergency department setting might enable better triage decisions and early management for patients with CS. The latter approach can identify hospitalized patients with established or impending CS to facilitate rapid recognition and stabilization; we are currently exploring this approach at the Mayo Clinic. Either of these assessments can be performed serially over time to assess patient trajectory, with important prognostic and treatment implications. A persistently high or rising SCAI SHOCK stage portends a poor outcome and should prompt consideration of escalation in terms of medical therapy and MCS.[4, 5]

It is essential to recognize that decision-making for patients with CS is substantially more complicated than matching the flow provided by a temporary MCS device to the hemodynamics or even the SCAI SHOCK stage. This was delineated in the revised SCAI SHOCK Classification statement, which identified three core constructs involved in prognostication and decision-making for patients with CS: shock severity, phenotype, and risk modifiers.[9] The premise is that at each level of shock severity, patients may display different patterns of cardiac, hemodynamic, and other clinical features that portend different levels of risk and necessitate different approaches to hemodynamic support, including temporary MCS. Additionally, a host of non-modifiable risk factors for mortality (including brain injury from cardiac arrest and age, among others) that are not directly related to shock severity can further impact prognosis and determine candidacy for different potential therapies. Integrating all these components is necessary for risk stratification and, more importantly, developing a management strategy for each CS patient in a manner analogous to the TNM staging system used for malignancy or the MOGE(S) or HLM classification systems proposed for heart failure.[21-23] In this way, a patient with mild shock may have a poor outcome due to ineligibility for temporary MCS in the setting of advanced age, extensive comorbidities, and severe anoxic brain injury after cardiac arrest. A different patient with severe shock may have a more favorable prognosis in the absence of these complicating factors, allowing the patient to be a candidate for advanced temporary MCS and cardiac replacement therapy if needed. These complex and nuanced decisions are difficult to operationalize, but this paradigm can be used to guide shock team discussions. The essential component to recognize is that many of the prognostically important variables in CS patients are not related to shock severity per se and may not be improved using temporary MCS, resulting in poor outcomes.

Despite the ongoing trials, there will continue to be unanswered questions.[24, 25] There is a significant role for multicenter registries such as the Cardiogenic Shock Working Group and VANQUISH registries, as well as the planned American Heart Association Cardiogenic Shock Registry.[7, 26] The VANQUISH registry will record the team-assessed SCAI SHOCK Stage at baseline and two days, as well as collect quality of life data and biomarkers serially throughout the course of the patient with cardiogenic shock.[26] Additionally, this registry includes all cases seen by the local shock teams, whether the patient received MCS or not, to reduce selection bias. Prospective enrollment of patients in these multicenter registries with mature shock teams will enable greater insights to be gleaned, ideally including linking underlying biomarker patterns and clinical phenotypes with outcomes and treatment responses.[16]

Beyond the potential utility of the SCAI SHOCK Classification for improving patient care, our story should be particularly instructive to early career researchers. The relationships with other interested experts that are developed at small but focused meetings, such as the Houston Shock Symposium, are invaluable, and the experience is hard to replicate at larger and less intimate meetings. The impact of the research collaboration and career mentorship that grows from these chance meetings cannot be overstated. We are both grateful to have met at the Houston Shock Symposium in 2019. Due to this chance meeting, we have published a dozen (and counting) collaborative manuscripts together. Even more importantly, we believe that together, we are moving the science of CS research forward and hope that lives will be saved by a better understanding of this disease that will translate to improved care strategies.

References

[1] Baran DA, Grines CL, Bailey S, et al. SCAI clinical expert consensus statement on the classification of cardiogenic shock: This document was endorsed by the American College of Cardiology (ACC), the American Heart Association (AHA), the Society of Critical Care Medicine (SCCM), and the Society of Thoracic Surgeons (STS) in April 2019. *Catheter Cardiovasc Interv*. 2019;94(1):29-37. doi: 10.1002/ccd.28329.

[2] Jentzer JC, van Diepen S, Barsness GW, et al. Cardiogenic Shock Classification to Predict Mortality in the Cardiac Intensive Care Unit. *J Am Coll Cardiol*. 2019;74(17):2117-2128. doi: 10.1016/j.jacc.2019.07.077.

[3] Jentzer JC, Henry TD, Barsness GW, Menon V, Baran DA and Van Diepen S. Influence of cardiac arrest and SCAI shock stage on cardiac intensive care unit mortality. *Catheter Cardiovasc Interv*. 2020;96(7):1350-1359. doi: 10.1002/ccd.28854.

[4] Baran DA, Long A, Badiye AP and Stelling K. Prospective validation of the SCAI shock classification: Single center analysis. *Catheter Cardiovasc Interv*. 2020;96(7):1339-1347. doi: 10.1002/ccd.29319.

[5] Hanson ID, Tagami T, Mando R, et al. SCAI shock classification in acute myocardial infarction: Insights from the National Cardiogenic Shock Initiative. *Catheter Cardiovasc Interv*. 2020;96(6):1137-1142. doi: 10.1002/ccd.29139.

[6] Schrage B, Dabboura S, Yan I, et al. Application of the SCAI classification in a cohort of patients with cardiogenic shock. *Catheter Cardiovasc Interv*. 2020;96(3):E213-E219. doi: 10.1002/ccd.28707.

[7] Thayer KL, Zweck E, Ayouty M, et al. Invasive Hemodynamic Assessment and Classification of In-Hospital Mortality Risk Among Patients With Cardiogenic Shock. *Circ Heart Fail*. 2020;13(9):e007099. doi:10.1161/CIRCHEARTFAILURE.120.007099.

[8] Jentzer JC, Schrage B, Holmes DR, et al. Influence of age and shock severity on short-term survival in patients with cardiogenic shock. *Eur Heart J Acute Cardiovasc Care*. 2021;10(6):604-612. doi: 10.1093/ehjacc/zuaa035.

[9] Naidu SS, Baran DA, Jentzer JC, et al. SCAI SHOCK Stage Classification Expert Consensus Update: A Review and Incorporation of Validation Studies: This statement was endorsed by the American College of Cardiology (ACC), American College of Emergency Physicians (ACEP), American Heart Association (AHA), European Society of Cardiology (ESC) Association for Acute Cardiovascular Care (ACVC), International Society for Heart and Lung Transplantation (ISHLT), Society of Critical Care Medicine (SCCM), and Society of Thoracic Surgeons (STS) in December 2021. *J Am Coll Cardiol*. 2022;79(9):933-946. doi: 10.1016/j.jacc.2022.01.018.

[10] Kanwar M, Thayer KL, Garan AR, et al. Impact of Age on Outcomes in Patients With Cardiogenic Shock. *Front Cardiovasc Med*. 2021;8:688098. doi: 10.3389/fcvm.2021.688098.

[11] Padkins M, Breen T, Anavekar N, et al. Age and shock severity predict mortality in cardiac intensive care unit patients with and without heart failure. *ESC Heart Fail*. 2020;7(6):3971–82. doi: 10.1002/ehf2.12995.

[12] Harjola VP, Lassus J, Sionis A, et al. Clinical picture and risk prediction of short-term mortality in cardiogenic shock. *Eur J Heart Fail*. 2015;17(5):501-9. doi: 10.1002/ejhf.26

[13] Poss J, Koster J, Fuernau G, et al. Risk Stratification for Patients in Cardiogenic Shock After Acute Myocardial Infarction. *J Am Coll Cardiol*. 2017;69(5):1913-1920. doi: 10.1016/j.jacc.2017.02.027.

[14] Jentzer JC, van Diepen S, Henry TD, Baran DA, Barsness GW and Holmes DR, Jr. Influence of intra-aortic balloon pump on mortality as a function of cardiogenic shock severity. *Catheter Cardiovasc Interv*. 2022;99(2):293-304. doi: 10.1002/ccd.29800.

[15] Wiley BM, Eckman PM and Jentzer JC. Vasopressor Load: Sounding the Alarm in Management of Cardiogenic Shock Associated With Acute Myocardial Infarction. *Crit Care Med*. 2021;49(5):865-869. doi: 10.1097/CCM.0000000000004906.

[16] Jentzer JC, Rayfield C, Soussi S, et al. Advances in the Staging and Phenotyping of Cardiogenic Shock Part 1: Clinical Context *JACC: Advances*. 2022.

[17] Papolos AI, Kenigsberg BB, Berg DD, et al. Management and Outcomes of Cardiogenic Shock in Cardiac ICUs With Versus Without Shock Teams. *J Am Coll Cardiol*. 2021;78(13):1309-1317. doi: 10.1016/j.jacc.2021.07.044.

[18] Basir MB, Kapur NK, Patel K, et al. Improved Outcomes Associated with the use of Shock Protocols: Updates from the National Cardiogenic Shock Initiative. *Catheter Cardiovasc Interv*. 2019;93(7):1173-1183. doi: 10.1002/ccd.28307.

[19] Tehrani BN, Truesdell AG, Sherwood MW, et al. Standardized Team-Based Care for Cardiogenic Shock. *J Am Coll Cardiol*. 2019;73(13):1659-1669. doi: 10.1016/j.jacc.2018.12.084.
[20] Tehrani BN, Sherwood MW, Rosner C, et al. Abstract 12839: A Standardized and Regionalized System of Care Network for Cardiogenic Shock: Insights From the Inova-Shock Registry. *Circulation*. 2021;144.
[21] Arbustini E, Narula N, Dec GW, et al. The MOGE(S) classification for a phenotype-genotype nomenclature of cardiomyopathy: endorsed by the World Heart Federation. *J Am Coll Cardiol*. 2013;62(22):2046-72. doi: 10.1016/j.jacc.2013.08.1644.
[22] Fedele F, Severino P, Calcagno S and Mancone M. Heart failure: TNM-like classification. *J Am Coll Cardiol*. 2014;63(19):1959-60. doi: 10.1016/j.jacc.2014.02.552.
[23] Westphal JG, Rigopoulos AG, Bakogiannis C, et al. The MOGE(S) classification for cardiomyopathies: current status and future outlook. *Heart Fail Rev*. 2017;22(6):743-752. doi: 10.1007/s10741-017-9641-4.
[24] Udesen NJ, Moller JE, Lindholm MG, et al. Rationale and design of DanGer shock: Danish-German cardiogenic shock trial. *Am Heart J*. 2019;214:60-68. doi: 10.1016/j.ahj.2019.04.019.
[25] Banning AS, Adriaenssens T, Berry C, et al. Veno-arterial extracorporeal membrane oxygenation (ECMO) in patients with cardiogenic shock: rationale and design of the randomised, multicentre, open-label EURO SHOCK trial. *EuroIntervention*. 2021;16(15):e1227-e1236. doi: 10.4244/EIJ-D-20-01076.
[26] Tehrani BN, Drakos SG, Billia F, et al. The Multicenter Collaborative to Enhance Biologic Understanding, Quality, and Outcomes in Cardiogenic Shock (VANQUISH Shock): Rationale and Design. *Can J Cardiol*. 2022;38(8):1286-1295. doi: 10.1016/j.cjca.2022.03.005.

Editorial

Hemodynamics and Kinetics of Heart Failure with Preserved Ejection Fraction Shock

Yevgeniy Brailovsky, DO[1]; Eduardo J Rame, MD[1], Thierry Le Jemtel, MD[2], Indranee Rajapreyar, MD[1]
[1]Division of Cardiology, Jefferson Heart Institute, Sidney Kimmel College of Medicine, Thomas Jefferson University, Philadelphia, PA
[2]Section of Cardiology, John W. Deming Department of Medicine, Tulane University School of Medicine, New Orleans, LA

Email: Indranee.rajapreyar@jefferson.edu

Abstract

The classical paradigm of cardiogenic shock is severe impairment of left ventricular, right ventricular, or biventricular contractility resulting in decreased cardiac output and end-organ failure. In patients with preserved ejection fraction, cardiogenic shock results from impaired left ventricular filling leading to decreased cardiac output and end-organ hypoperfusion. Heart failure with preserved ejection fraction (HFpEF) comprises a heterogenous group of myocardial and systemic metabolic derangements. Cardiogenic shock with preserved left ventricular ejection is thought to be less common than with reduced left ventricular ejection fraction, and therapeutic approaches are not well standardized. We aim to review the pathophysiology of cardiogenic shock in HFpEF, define various etiologies that culminate in the HFpEF shock state, and present our algorithmic approach to managing these complex patients.

Keywords: cardiogenic shock, heart failure with preserved ejection fraction, HFpEF, hemodynamics, restrictive, hypertrophic, amyloidosis

Background

The classical paradigm of cardiogenic shock is severe impairment of left ventricular, right ventricular, or biventricular contractility resulting in decreased cardiac output and end-organ failure. Large acute myocardial infarction, acutely decompensated heart failure, and acute myocarditis are common causes of cardiogenic shock.[1]

In restrictive and hypertrophic cardiomyopathies, cardiogenic shock results from impaired left ventricular filling and not from impaired ventricular contractility. In turn, impaired left ventricular filling leads to decreased cardiac output and end-organ hypoperfusion.[2]

Heart failure with preserved ejection fraction (HFpEF) comprises a heterogenous group of myocardial and systemic metabolic derangements. HFpEF includes patients with typical risk factors for diastolic dysfunction such as aging, systemic hypertension, obesity, type 2 diabetes, or coronary artery disease, but also includes patients with restrictive and infiltrative cardiomyopathies, constrictive pericarditis, hypertrophic (obstructive and non-obstructive) cardiomyopathy, valvular heart disease, myocarditis, and complications of heart transplantation (rejection and cardiac allograft vasculopathy) (Figure 1). Differences in etiopathogenesis, natural history, and prognosis present challenges in epidemiologic surveillance and prognostication.[3] Cardiogenic shock with preserved left

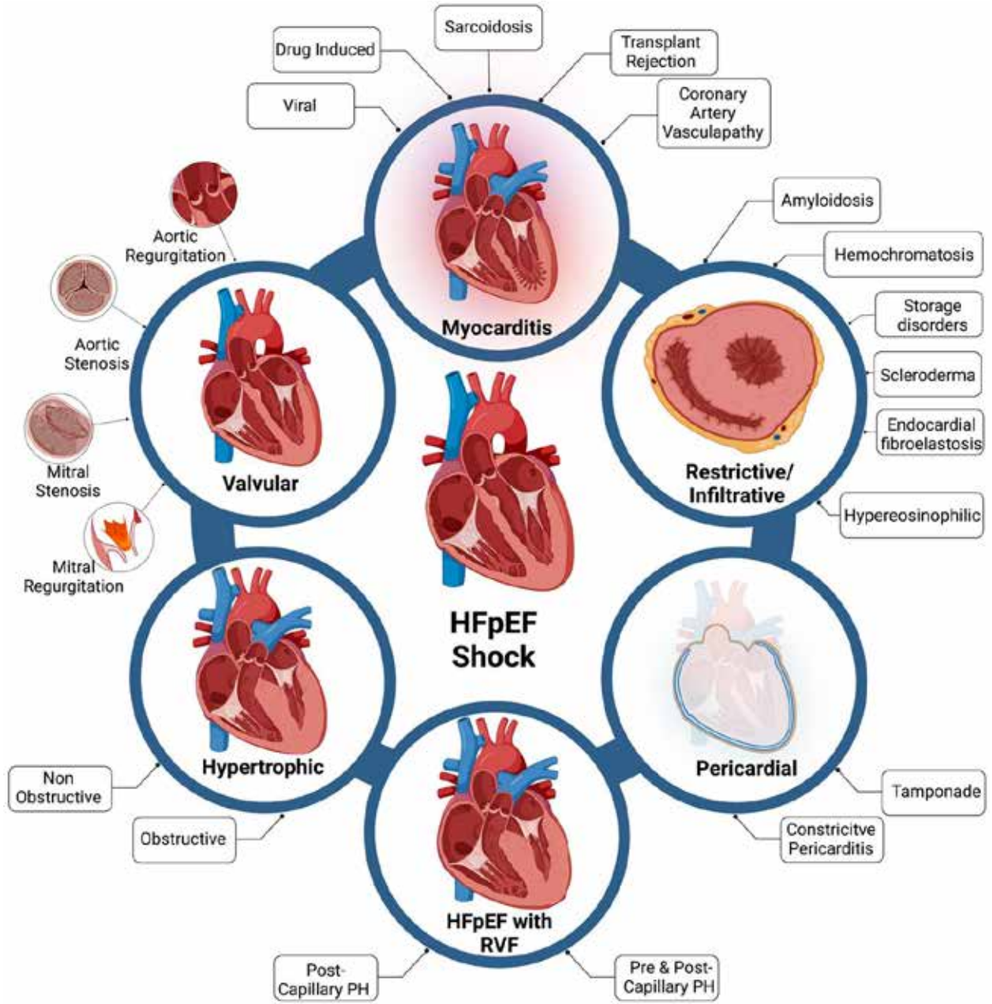

Figure 1. Various etiologies of cardiogenic shock in patients with preserved left ventricular ejection fraction.

ventricular ejection is thought to be less common than with reduced left ventricular ejection fraction, and therapeutic approaches are not well standardized. We aim to review the pathophysiology of cardiogenic shock in HFpEF, define various etiologies that culminate in the HFpEF shock state, and present our algorithmic approach to managing these complex patients.

Pathophysiology

Recognition of the clinical phenotypes of cardiogenic shock with preserved left ventricular ejection fraction has important clinical implications (Figure 1). The management and prognosis of primary myocardial pathology, like restrictive or hypertrophic cardiomyopathy, differs from that of cardiogenic shock due to the pleiotropic manifestations of advanced heart failure with preserved ejection fraction.

Restrictive and Hypertrophic Cardiomyopathies

Restrictive left ventricular or biventricular filling with reduced stroke volume may result in a low cardiac output state and end-organ hypoperfusion. Atrial arrhythmias resulting from atrial dilation and dysfunction can impair left ventricular filling and further decrease stroke volume.[4] Excessive cardiac preload reduction due to aggressive diuresis or bradyarrhythmia may cause systemic hypoperfusion, end-organ dysfunction, and cardiogenic shock.[5] At times, various pathologies that lead to different types of HFpEF coexist and often accelerate the progression to shock. For example, 15% of patients with severe aortic stenosis and approximately 30% of patients with low-flow, low-gradient aortic stenosis have transthyretin cardiac amyloidosis.[6] Severe aortic stenosis promotes left ventricular hypertrophy that impairs left ventricular filling and, together with a fixed outflow obstruction, leads to a low cardiac output state and, thereby, cardiogenic shock. Hypertrophic cardiomyopathy with a dynamic left ventricular outflow tract obstruction and systolic anterior motion of the mitral valve may precipitously lower cardiac output and trigger cardiogenic shock presentation.[7]

Cardiomyopathy Due to Comorbidities

Aging, obesity, hypertensive heart disease, type 2 diabetes, and coronary artery disease promote left ventricular remodeling and atrial dilation. Left atrial non-compliance due to chronically elevated left ventricular filling pressure decreases pulmonary vascular compliance and causes pulmonary venous hypertension. At the same time, in other patients, this leads to an increase in pulmonary vascular resistance with the development of pre- and post-capillary pulmonary hypertension. In some instances, this results in right ventricle-pulmonary artery uncoupling, and right ventricular failure (RVF) ensues. Atrial arrhythmias due to left atrial dilation and atrial functional mitral regurgitation due to left atrial annular dilation can perpetuate the vicious cycle from pulmonary hypertension (PH) to RVF. Progression of RVF in patients with severe PH due to left-sided heart disease results in a clinical syndrome that manifests as cardiogenic shock in severe states. Furthermore, worsening renal dysfunction due to systemic venous congestion may exacerbate RVF.[8-10]

Constrictive pericarditis is a result of loss of pericardial compliance, which leads to a decoupling of the intrapericardial and intrathoracic pressure and interventricular interdependence. While this is an entirely separate entity from a classic HFpEF, the presentation is often similar to elevated filling pressures, heart failure syndrome, and the appearance of preserved ejection fraction on transthoracic echocardiogram; therefore, we thought it deserved mention in this manuscript.[2]

Similarly, acute myocarditis is distinct from typical HFpEF syndromes; however, patients can present with heart failure syndrome and overt cardiogenic shock. Acute myocarditis, acute viral infection, or other etiologies lead to an acute inflammatory response within the myocardium, increased LV wall thickness, impaired filling, and impaired contractility. Myocarditis is also often manifested by atrial and ventricular arrhythmias, which further worsen myocardial oxygen demand and ventricular filling and contractility, leading to a low cardiac output state.[11]

Various valvular pathologies may lead to cardiogenic shock, but myocardial dysfunction is often not the primary etiology of shock in these cases. Since the ejection fraction is preserved in most of these cases and clinical presentation may be similar, we mention these etiologies here but will not discuss them in detail.

Clinical Presentation

The clinical manifestations of cardiogenic shock with reduced and preserved left ventricular ejection fraction are indistinguishable. They include hypotension, decreased urine output, altered mental status, and respiratory compromise. Renal and hepatic dysfunction and lactic acidosis are laboratory evidence of hypoperfusion.[2] While most of the etiologies of HFpEF have an insidious onset of symptoms, myocarditis often presents as more of an acute presentation, differentiating it from other pathologies.

Echocardiogram and Hemodynamics

Patients with restrictive and hypertrophic cardiomyopathy have increased left ventricular thickness, small cavity size, and bi-atrial enlargement. Left ventricular outflow tract obstruction may be present at rest in patients with hypertrophic cardiomyopathy or with exacerbating maneuvers such as Valsalva, exercise, hypotension, or hypovolemia.

The hemodynamic parameters of cardiogenic shock due to restrictive or constrictive cardiomyopathy include depressed cardiac index and equalization of elevated left atrial and right atrial pressures (RAP) and elevated pulmonary artery pressures (PAP).[12] Hemodynamic parameters of cardiogenic shock due to hypertrophic cardiomyopathy are often mildly elevated RAP but with severely elevated PAP and PAWP and depressed cardiac index. Hemodynamic parameters of cardiogenic shock due to predominant right ventricular failure are elevated RAP out of proportion to left atrial pressure, elevated PAP and pulmonary vascular resistance (PVR), and depressed cardiac index.[13]

Diagnosis and Management

A bedside echocardiogram provides an initial non-invasive assessment of cardiac performance, including diastolic and systolic ventricular function, valvular heart disease, and pericardial alterations. Insertion of a balloon tip pulmonary artery catheter allows serial measurements of right and left

filling pressures and cardiac output and thereby helps guide fluid resuscitation, diuretic therapy, and initiation/titration of inotropes, pressors, or mechanical circulatory support. Right heart catheterization (RHC) is a crucial part of investigating patients with undifferentiated HFpEF shock, as it allows phenotyping of patients regarding univentricular versus biventricular shock and degree of pulmonary vascular involvement. RHC also allows real-time monitoring of response to therapy and helps guide volume management, inotropes, pressor use, pulmonary vasodilator therapy, and mechanical circulatory support.[2] When RHC cannot be rapidly performed, a central venous catheter may be used as a rudimentary tool to guide fluid management based on central venous pressure and inopressor therapy based on central venous oxygen saturation. Central venous pressure and calculated cardiac index based on central venous oxygen saturation help differentiate cardiogenic shock from distributive shock due to sepsis or hypovolemic shock.[14] However, relying solely on central venous catheters, compared to RHC, may lead to false assumptions and inadequate or frankly incorrect tailoring of therapy. Early institution of invasive mechanical ventilation can improve hypoxemia, coronary perfusion, and end-organ hypoperfusion by lowering the metabolic cost of breathing in patients with limited oxygen delivery.[15] Cardioversion for atrial arrhythmias in the setting of hemodynamic instability and atrial pacing in the setting of intact AV node or ventricular pacing in patients with complete AV block improves cardiac output by restoring atrial contribution to left ventricular filling and improves chronotropic response. Renal replacement therapy to correct acidosis and volume overload improves end-organ function and prevents pulmonary injury.[16]

Institution of temporary mechanical circulatory support in refractory cardiogenic shock hinges on the reversibility of the shock state, a life expectancy > 1 year, or a possible exit strategy such as candidacy for heart transplantation or chance for myocardial recovery. The type of mechanical circulatory support for restrictive and hypertrophic cardiomyopathies depends on several factors: local interventional or surgical expertise, vascular access site availability, and extent of left, right, or bi-ventricular contribution to the shock state. Left atrial unloading with tandem heart versus veno-arterial extracorporeal oxygenation (V-A ECMO) or bi-atrial unloading using multistage cannula left atrial V-A ECMO can provide temporary support as a bridge to recovery or heart transplantation (HT). Durable mechanical circulatory support with left ventricular assist devices is challenging in restrictive cardiomyopathies due to a small left ventricular cavity leading to suction events and right ventricular failure. Total artificial heart as a bridge to HT is an option in highly selected individuals.[17]

Right ventricular failure is a therapeutic challenge in heart failure with preserved ejection fraction. Management includes inotropic support and, in select cases, V-A ECMO as a bridge to recovery when reversible causes are identified. Pulmonary vasodilators or isolated right ventricular assist device support may worsen pulmonary edema or cause pulmonary hemorrhage due to high PAP, PAWP, and impaired left ventricular diastolic function.

Conclusions

The first step in managing cardiogenic shock with preserved ejection fraction is to recognize the underlying disorder: hypertrophic or infiltrative cardiomyopathy, valvular or pericardial disease or end-stage heart failure with preserved ejection fraction, right ventricular failure and pulmonary hypertension, or acute myocarditis. Echocardiographic and invasive hemodynamic assessment should guide the management of patients in cardiogenic shock with preserved ejection fraction. A multidisciplinary team-based approach for cardiogenic shock management allows rapid triage and a timely escalation of support for appropriate candidates.

Disclosures

The authors report no relevant disclosures.

References

[1] van Diepen S, Katz JN, Albert NM, et al. Contemporary Management of Cardiogenic Shock: A Scientific Statement From the American Heart Association. *Circulation*. 2017;136(16):e232-e68.

[2] Chatterjee K, McGlothlin D, Michaels A. Analytic reviews: cardiogenic shock with preserved systolic function: a reminder. *J Intensive Care Med*. 2008;23(6):355-66.

[3] Burkhoff D, Maurer MS, Joseph SM, et al. Left atrial decompression pump for severe heart failure with preserved ejection fraction: theoretical and clinical considerations. *JACC Heart Fail*. 2015;3(4):275-82.

[4] Schneider SM, Kochar K, Ruge M, et al. Cardiogenic Shock Due to Atrial Arrhythmia as the Initial Presentation of Transthyretin Cardiac Amyloidosis Clinical Case Series. *J Am Coll Cardiol Case Rep*. 2022;4(22):1490–1495.

[5] Cheung CC, Roston TM, Andrade JG, Bennett MT, Davis MK. Arrhythmias in Cardiac Amyloidosis: Challenges in Risk Stratification and Treatment. *Can J Cardiol*. 2020;36(3):416-23.

[6] Ternacle J, Krapf L, Mohty D, et al. Aortic Stenosis and Cardiac Amyloidosis: JACC Review Topic of the Week. *J Am Coll Cardiol*. 2019;74(21):2638-51.

[7] Sherrid MV, Swistel DG, Olivotto I, et al. Syndrome of Reversible Cardiogenic Shock and Left Ventricular Ballooning in Obstructive Hypertrophic Cardiomyopathy. *J Am Heart Assoc*. 2021;10(20):e021141.

[8] Vaduganathan M, Patel RB, Michel A, et al. Mode of Death in Heart Failure With Preserved Ejection Fraction. *J Am Coll Cardiol*. 2017;69(5):556-69.

[9] Gevaert AB, Boen JRA, Segers VF, Van Craenenbroeck EM. Heart Failure With Preserved Ejection Fraction: A Review of Cardiac and Noncardiac Pathophysiology. *Front Physiol*. 2019;10:638.

[10] Gorter TM, van Veldhuisen DJ, Bauersachs J, et al. Right heart dysfunction and failure in heart failure with preserved ejection fraction: mechanisms and management. Position statement on behalf of the Heart Failure Association of the European Society of Cardiology. Eur J Heart Fail. 2018;20(1):16-37.

[11] Tschope C, Cooper LT, Torre-Amione G, Van Linthout S. Management of Myocarditis-Related Cardiomyopathy in Adults. Circ Res. 2019;124(11):1568-83.

[12] Geske JB, Anavekar NS, Nishimura RA, Oh JK, Gersh BJ. Differentiation of Constriction and Restriction: Complex Cardiovascular Hemodynamics. J Am Coll Cardiol. 2016;68(21):2329-47.

[13] Melenovsky V, Hwang SJ, Lin G, Redfield MM, Borlaug BA. Right heart dysfunction in heart failure with preserved ejection fraction. Eur Heart J. 2014;35(48):3452-62.

[14] Simmons J, Ventetuolo CE. Cardiopulmonary monitoring of shock. Curr Opin Crit Care. 2017;23(3):223-31.

[15] Tavazzi G. Mechanical ventilation in cardiogenic shock. Curr Opin Crit Care. 2021;27(4):447-53.

[16] Singh S, Kanwar A, Sundaragiri PR, et al. Acute Kidney Injury in Cardiogenic Shock: An Updated Narrative Review. J Cardiovasc Dev Dis. 2021;8(8).

[17] Lanmueller P, Eulert-Grehn JJ, Schoenrath F, et al. Durable mechanical circulatory support in patients with heart failure with preserved ejection fraction. Interact Cardiovasc Thorac Surg. 2021;33(4):628-30.

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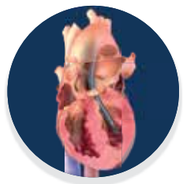

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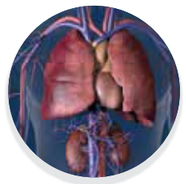

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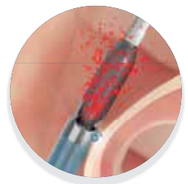

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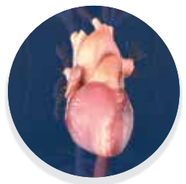

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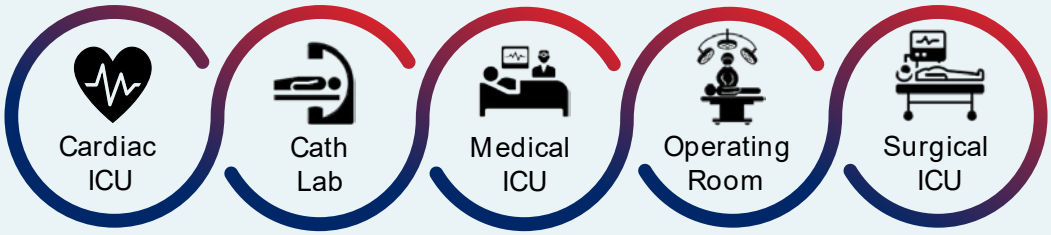

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