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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).

The Annual Houston Shock Symposium launched in 2018 and offers a unique platform to challenge the current concepts and ideas in cardiogenic shock. Participants exchange new ideas via a multidisciplinary approach that challenges the status quo and pushes the field forward. The Houston Shock Skills Lab is a state-of-the-art experience run by our multidisciplinary Skills Faculty to provide hands-on training on percutaneous approaches to managing cardiogenic shock.

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

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Role of Invasive Hemodynamics in Shock Management:

Is a Pulmonary Artery Catheter Always Necessary?

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Keywords: pulmonary artery catheter, cardiogenic shock, hemodynamics

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.

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, saturation) 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 (e.g., 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 (e.g., 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 in place to be able to then manage the patient. Using Medicare data, Ikatia and colleagues showed that, overall, the use of PA catheter is declining over time.1 However, for patients with heart failure, there is 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.3,4 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, check.”1,5,6 One must be aware on how patients are doing.6 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.7

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.8 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 and volume optimization.9 Similarly, both sides of the heart must be assessed to determine the best treatment, as a significant proportion of patients have biventricular congestion.10 Emerging data has shown how PA catheter measurements can be used to identify RV dysfunction.11 Ultimately, PA catheter assessments have been useful in determining device weaning protocols.12 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 2019.13 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, 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 ventricle 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 the catheterization lab in a coronary care unit. Unfortunately, once the catheter was placed, the patient had a horrific run of ventricular tachycardia that was induced by the catheter tip failing 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.

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Disclosures

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References


Intra-aortic balloon pump (IABP) therapy, as a first-line mechanical circulatory support (MCS) option, is associated with a low risk of complications compared to large bore devices including:

- Lower bleeding rates and vascular injury
- Lower stroke rates and limb ischaemia
- Lower hospitalization costs due to decreased length of stay resulting from complications

IABP Therapy — the safe, first-line MCS option.
Surviving Sepsis Campaign: Strategies to Implement in Cardiogenic Shock Management

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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 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.

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 crystallloid (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 several 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

Hemodynamic Goals in Shock Management: Is There One

Target for All?

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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.

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 state similar goals:

- Central venous pressure (CVP) of 8-12 mmHg
- Mean arterial pressure (MAP) greater than 65 mmHg
- Mixed venous saturation (SvO2) greater than 65%
- Urine output greater than 0.5 mL kg⁻¹ 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. The in-hospital mortality for goal-directed therapy was 30.5% versus 46.5% with standard therapy. A post hoc analysis of a multicenter trial investigated the association of MAP and vasopressor load in septic shock patients. 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. 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. 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 organ hypoperfusion, tissue hypoperfusion, and cardiac index are all commonly seen after the immediate 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. 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 organ hypoperfusion, tissue hypoperfusion, and cardiac index are all commonly seen after the immediate cardiogenic shock setting. This is especially important since not all cardiogenic shock cases are created equal.

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

Racial Variations in Shock Presentation and Outcome

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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. Most individuals undergoing TAVR are Medicare-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 White patients and non-White patients present and their assessment. In terms of outcomes, some questions to consider are:

• How precise is our assessment of shock among patients?
• 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.

The Data

There are three programs with variable interpretations and assessments of the SCAI stages of shock. 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 Caveat

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 Black men at 21.6%. 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.

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.

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

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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 foremost in the patient's care. Fibrillation and arrest always indicates that cardiomyocyte death has occurred as a result of oxygen deprivation, and a great deal of research is directed at reducing infarct size. The management of patients with AMI shock 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.

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. 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.

Another study in a pig model investigated MSC efficacy after 90 minutes of LAD occlusion with a balloon. 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.

This same study also investigated different molecules related to the reperfusion process. 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. The results challenge the understanding that “time is muscle,” as a strong indication that delaying reperfusion by 30 minutes with circulatory unloading onboarding was associated with improved outcomes.

A similar study using a pig model contested these results. 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.

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. 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.

The DTU STEMI pilot trial included 50 patients untreated with an Impella CP and tested the hypothesis that delaying reperfusion by 30 minutes after starting unloading with an...
Impella CP was feasible. 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. The DU STEM 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**


**2022 Symposium Presentation**

**Profound Vasoplegia after Coronary Artery Bypass Grafting**

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**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-vein 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-cardiomyotomy 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.

**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. A large meta-analysis demonstrated that a combination of norepinephrine and vasopressin was generally more beneficial than norepinephrine alone. Vasopressin may be the preferred agent in right ventricular dysfunction due to avoiding increased pulmonary vascular resistance. Moreover, when treating patients with vasopressin, one should consider that about 45% of individuals were characterized as responders while 55% were not.
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. 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.

Acknowledgments
We acknowledge the other clinicians and multidisciplinary team involved in the care of our patients.

Disclosures
Dr. Chatterjee has served on advisory boards for Edwards Lifesciences, Eagle Pharmaceuticals, La Jolla Pharmaceutical Company, and Baxter Pharmaceuticals.
From an 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. Consequently, most studies have avoided the use of epinephrine in the treatment of shock.

**2022 Symposium Presentation**

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

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**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. 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. Consequently, most studies have avoided the use of epinephrine in the treatment of shock. 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
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. In addition, the epinephrine groups had higher lactate, a higher incidence of tachycardia, 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


2022 Symposium Presentation

The Challenges of Conducting Clinical Trials for Patients with Cardiogenic Shock

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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. 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.

In addition, the prognosis for patients with cardiogenic shock remains unchanged. In-hospital mortality and 30-day mortality have stayed around 30% to 50%. 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.

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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 another occluded artery and support end-organ perfusion. There are chain of events guides the clinical priorities when treating and reduced cardiac output, which is supporting the patient before opening the artery improves the patient outcome versa?

The hemodynamics of AMI shock, which are hypotension, increased left ventricular end-diastolic pressure, and reduced cardiac output, 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 a tremendous amount of data is collected during the course of clinical care. It has long been the promise of EHR systems that a tremendous amount of data is collected during the course of clinical care. It has long been the promise of EHR systems that a tremendous amount of data is collected during the course of clinical care. It has long been the promise of EHR systems that a tremendous amount of data is collected during the course of clinical care.

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 Cardiac Shock Working Group CHF cohort (CSWG-CHF), and the Danish Retroscreen Registry (DRR)—to cluster potential phenotypes.

The results of this analysis identified three clusters of phenotypes: noncongested shock, cardiogenic 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 cardiogenic 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 noncongestive cardiogenic shock, the 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. Elucidation 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 does consideration for mechanical options (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 Emergent Revascularize Occluded Coronaries for Cardiogenic Shock (SHOCK) Trial**

Some randomized trials have been conducted. Perhaps the most noteworthy study—the SHOCK trial—randomized 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.

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. 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 = 609). 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). 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.1 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 DeBakey Acute Myocardial Infarction (DOMERI) Trial compared mirabegron 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 shock to receive one of these vasopressor agents. For the 280 patients with cardiogenic shock, norepinephrine was associated with a better outcome than dopamine. 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 Intracoronal Balloon Pump (IABP) SHOCK II trial randomly assigned patients with cardiogenic shock to either IABP intervention or control.13 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 awaits more randomized data, these guidelines will serve to inform clinical practice.

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2022 Symposium Presentation

Coronary Flow and Unloading in Acute Myocardial Infarction

Shock

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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. In contrast, for patients with AMI and cardiogenic shock, culprit lesion PCI was a better treatment option than multivessel PCI. 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 vasoconstriction, 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 flow.
pressure and flow but does not improve clinical outcomes.1,2

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.2 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 microspheres 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 mycardium, allowing quantification of the tissue flow by counting the spheres in retrieved tissues.3

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.4 Univariate analysis in data from 15 pigs identified cardiac contractility, high diastolic pressure, or AMI shock benefit the individuals treated with ECMO alone.5 This data further demonstrates this concept, porcine models underwent the previously described procedure and were monitored for pressure and volume during LV unloading.6 Theses 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.6 This data further supports the importance of LV unloading as a key factor in recovery from cardiogenic shock.

References


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.

CentriMag Acute Circulatory Support System

Abbott

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References

2022 Symposium Presentation

Right Ventricular Hemodynamics in COVID-19 Patients

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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 Overdistension of alveoli also increases 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 venous return in a normal heart, but this decrease is generally responsive to fluid administration. In left ventricular failure, PEEP decreases venous return to 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/m²).

The mean right ventricular systolic pressure (RVSP) was 38.8 ± 12.2 mm Hg, and the mean PEEP was 11.0 ± 3.7 cm H₂O. 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 H₂O versus 10.2 ± 0.3 cm H₂O, 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

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

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Abstract

COVID-19, while primarily recognized for its pulmonary and systemic manifestations, affects 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. Myopericarditis was also described, but these early reports indicated that RV dilation was underdiagnosed. Additional data showed that RV dilatation could be a mortality marker. 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 embolism, or thrombosis.

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.

Vascular thickening was seen in pulmonary arteries, and thrombosis was documented in larger, medium, and small vessels. Data out of New York showed that platelet thrombi also play an important role in RV failure. 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. Within this setting, D-dimer is involved as both a driver of thrombosis and a novel marker of thrombosis and disease severity.

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.

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, pulmonary 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 dyskinesis 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.

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.3 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 severe COVID 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.3 In selected cases, support can be added on the left side. Data kindly provided by Dr. A. El Banayosy from Integris Medical Center in Oklahoma City showed that in 87 patients with severe COVID who were on ECMO support, almost 10% (8/87) 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 involving maintained overall pressure, rhythm, optimized RV pre- and afterload, anticoagulation, and inotropes. A graded approach is 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

The author expressly thanks Dr. A. El Banayosy for sharing data from Integris in support of this work.

Disclosures

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References

Revascularization in Cardiogenic Shock: Residual Syntax

Score and Chronic Total Occlusions

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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. Of note, multivessel coronary artery disease (CAD) is observed in 75% of AMI-CS cases. The residual syntax score (rSS) is strongly associated with outcomes in patients having CAD and acute myocardial infarction (AMI). The SYNTAX score (SS) assesses the extent of CAD by quantifying the disease based on lesion number, location, and complexity. 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. 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 2022 Symposium Presentation

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time of the SHOCK trial, the application of balloon angioplasty was ubiquitous in early revascularization, while stents were minimally used. Specifically, the SHOCK trial was designed to compare the survival advantage of initial medical stabilization versus emergency revascularization in patients with AMI-CS. 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. 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 open, but should the circumflex vessel be open?

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 waffer-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 circumflex would have been considered.

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


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

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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 postoperative 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 multorgan dysfunction, and timely mechanical circulatory support.3

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through the femoral vessel. However, these options have the potential for gastrointestinal consequences based on the splanchic vasomotor response. Inotropic and vasodilator agents may further reduce the blood supply to the gastrointestinal system by increasing splanchic vascular tone and potentiating gut ischemia. The combination of fluid restriction and diuretic use can cause enterocyte dysfunction. 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 splanchic hypoperfusion with intestinal dysfunction. This ultimately results in severe intestinal dysmotility, edema, inflammation, ischemia with bacterial translocation, and additional myocardial depression. Hypokalemia, as a result of loop diuretics, can further reduce intestinal peristalsis. 

In addition, mechanical circulatory support utilizing femoral artery insertion precludes patient mobilization, affecting the intestine and colon motility. As a result, abdominal distension, 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 splanchic perfusion in critically ill patients increases morbidity and mortality. Currently, definitive advanced heart failure therapies include orthotopic 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. 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 caesarean 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/m² 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 auxiliary 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 cannula 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 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 distension, significant pitting edema, and abdominal distension. He had course rules and was supported on non-invasive positive pressure with supplemental oxygen therapy. His hemodynamics upon arrival are listed in Table 1.

Table 1. Data collected from right heart catheterizations. For Case 1, no inotrope support was provided on arrival and the repeat data was attained 18 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

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Arrival</th>
<th>Repeat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean right atrial pressure (mmHg)</td>
<td>26</td>
<td>22</td>
</tr>
<tr>
<td>Right ventricle mean pressure (mmHg)</td>
<td>54/22</td>
<td>40/11</td>
</tr>
<tr>
<td>Pulmonary artery pressure (mmHg)</td>
<td>46/33</td>
<td>38/19</td>
</tr>
<tr>
<td>Mean pulmonary artery pressure (mmHg)</td>
<td>33</td>
<td>33</td>
</tr>
<tr>
<td>Pulmonary capillary wedge pressure (mmHg)</td>
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<td>44</td>
</tr>
<tr>
<td>Pulmonary artery saturation (%)</td>
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<td>12.8</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>3.6</td>
<td>3.8</td>
</tr>
<tr>
<td>Estimated Fick cardiac output (L/min)</td>
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<td>2.0</td>
</tr>
<tr>
<td>Estimated Fick cardiac index (L/min/m²)</td>
<td>0.8</td>
<td>1.3</td>
</tr>
<tr>
<td>Thermolodiation cardiac output (L/min)</td>
<td>0.8</td>
<td>NA</td>
</tr>
<tr>
<td>Thermolodiation cardiac index (L/min/m²)</td>
<td>0.8</td>
<td>NA</td>
</tr>
</tbody>
</table>

A left heart catheterization did not reveal any obstructive coronary artery disease. He was initiated on bumetanide infusion and milrinone therapy at 0.375 mcg/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 

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.
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.

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. 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 to improve 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. Irreversible consequences include bacterial translocation, bowel 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; however, patients with pre-existing dysfunction in the gastrointestinal tract may not tolerate CVP support during definitive LVAD surgery. Furthermore, the addition of intraoperative inotropic support and postoperative inotropic and vasopressor support further exacerbate gastrointestinal complications. 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 vasocostriction 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 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 cardiointestinal syndrome, via the Impella 5.5 before implantation of a durable LVAD with the objective of improving splanchnic circulation, decreasing the amount of inotropic and vasopressor use, and promoting ambulation to improve the gastrointestinal condition.

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References


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

Future Perspectives in Acute Myocarditis Complicated by Cardiogenic Shock

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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. In its clinical presentation is highly variable, ranging from a mild self-limiting syndrome to a severe life-threatening condition. 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). 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.

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. However, endomyocardial biopsy (EMB) is the reference standard for diagnosing myocarditis and should be performed in selected clinical scenarios. 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. 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 the optimal multi-organ support (MOS) treatment in GCM or eosinophilic myocarditis.\textsuperscript{1,9}

Cardiogenic Shock

Cardiogenic shock is a low-cardiac-output state resulting in life-threatening end-organ hypoperfusion and hypoxia.\textsuperscript{27} According to the American Heart Association, the incidence of cardiogenic shock in a cohort of 443 patients with definite AM demonstrated by CMRI or histology is 8-9%.\textsuperscript{7} Meanwhile cardiogenic shock can occur in 38.9% of COVID-19-associated AM cases.\textsuperscript{13} Patients with FM have a high rate of events,\textsuperscript{17} with a 60-day rate of death or HTx as high as 28% based on a large international cohort.\textsuperscript{3} These data are consistent with the United States administrative data, which demonstrate a 6-fold 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.\textsuperscript{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.\textsuperscript{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 hyperemic cardiac recovery.\textsuperscript{4,5} 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 support (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%.\textsuperscript{14} This trend was detrimental by increasing myocardial oxygen consumption, and thus high doses of vasoactive agents should be considered. The United States administrative data has shown a growth in the use of t-MCS among AM patients (from 2009 to 2016) showed an in-hospital survival of 62%, similar to other registries on t-MCS;\textsuperscript{16,17} furthermore, 29% of patients required the transition to another MCS.\textsuperscript{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 HT types (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.\textsuperscript{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.\textsuperscript{2} Regarding lymphocytic post-FM, the role of immunosuppressive therapies remains controversial.\textsuperscript{22} Current evidence, mainly derived from patients with chronic inflammatory cardiomyopathy, suggests that immunosuppressive therapy should be administered in patients with high inflammatory markers and without a viral pathogen on testing samples.\textsuperscript{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 cardiac inflammatory injury rather than direct virus-mediated cell injury.\textsuperscript{24} 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 PVIII-19 and H1N16 may be found in the EMB of patients without myocarditis.\textsuperscript{25} These findings indicate that the presence of viruses in the setting of AM may not represent an absolute contraindication to immunosuppressive therapy, although 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.\textsuperscript{26} To elucidate the role of immunosuppression in FM and complicated AM, randomized controlled trials are needed. The MYocarditis 1H4erapy With Steroids (MYHIS) trial (ClinicalTrials.gov identifier: NCT01517004) is an ongoing international randomized, single-blinded 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 1 g IV daily for 5 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 6 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) death due to HF life-threatening arrhythmias or advanced atrioventricular block. The trial started enrollment in October 2021 with an estimated duration of 3-4 years.

Future Directions

A pivotal goal for the future is to reduce mortality rates of FM. In contrast with a previous report,\textsuperscript{37} it is now well established that FM has poor in-hospital outcomes.\textsuperscript{1,13} To reduce in-hospital mortality, prompt referral of patients with FM to hub centers and EMR 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 immunosuppression due to HF in viral and post-viral cardiomyopathies, and the potential anti-inflammatory effects of direct LV unloading deserve consideration. An international network of tertiary centers experienced in the management of cardiomyopathy in patients with left ventricular systolic dysfunction. J Am Coll Cardiol. 2019;74(3):299-311. DOI: 10.1016/j.jacc.2019.04.063.


SCAI SHOCK: Does the Stage Help with Management

Decisions?

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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.7 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 cardiogenic shock, and cardiac arrest conferred incremental risk 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.5 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.10,11 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 mortality of each SCAI SHOCK stage in patients with possible neurologic compromise (i.e., coma).8,11

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.5,7 Furthermore, additional potential risk modifiers emerged that could provide a graded prognostic assessment at each SCAI SHOCK stage.3 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.5 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

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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. This analysis suggested an association between circulatory support (APB and MCS) 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 APB, 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 categorization: the SCAI SHOCK Classification. Recognizing that prior studies have not demonstrated improvements in outcomes when temporary mechanical circulatory support (MCS) devices are used uniformly, but a structured approach to evaluation and management of MCS patients is associated with improved outcomes can be taken quickly and easily to provide an evaluation of shock management. The assignment of the SCAI SHOCK stage performs as well as or better than a more complex data-driven algorithm for risk stratification. Additionally, 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 earlier triage and early management for patients with CS. The latter approach can identify hospitalized patients with established or impending CS to facilitate rapid recognition and support, including hemodynamic stabilization; we have tested this concept at Mayo Clinic. Either of these assessments can be performed serially over time to assess patient trajectory, with important prognostic and treatment implications. Persistently high or rising SCAI SHOCK stage portends a poor outcome and should prompt consideration of escalation in terms of medical therapy and MCS.

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.
- The premise is that at each level of shock severity, patients may display different disease patterns, and the clinical features that portend different levels of risk and necessitate different approaches to hemodynamic support, including hemodynamic monitoring, other clinical risk factors, and modifiable risk factors for mortality (including brain injury from cardiac arrest and age, among others) that are not directly related to shock severity.

Integrating all of 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 many cancers. The impetus to use the SCAI SHOCK Classification to guide the potential utility of the SCAI SHOCK Classification for improving patient care, our study should be particularly instructive to early career researchers. The relationships with other important factors that are developed are of particular interest to future researchers; the impact of the transesophageal echocardiography SHOCK Classification, 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 better understanding of this disease that will translate into improved care strategies.

References

Editorial

Hemodynamics and Kinetics of Heart Failure

with Preserved Ejection Fraction Shock

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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 heterogeneous 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.1

Heart failure with preserved ejection fraction (HFpEF) comprises a heterogeneous 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.1 Cardiogenic shock with preserved left

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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 approaches are not well standardized. We aim to review the pathophysiology of cardiogenic shock in HFpEF, 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 pleotropic 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. Excessive cardiac preload reduction due to aggressive diuretics or bradyarrhythmias may cause systemic hypoperfusion, end-organ dysfunction, and cardiogenic shock. 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. 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.

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 dilatation 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 syndrome that manifests as cardiogenic shock in severe states. Furthermore, worsening renal dysfunction due to systemic venous congestion may exacerbate RVF.

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.

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. 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. 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). 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.

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
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

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