

Journal of Shock and Hemodynamics

Volume 1 | Issue 1

Article 16

2022

Journal of Shock and Hemodynamics, Vol 1., Iss. 1 (Print Version)

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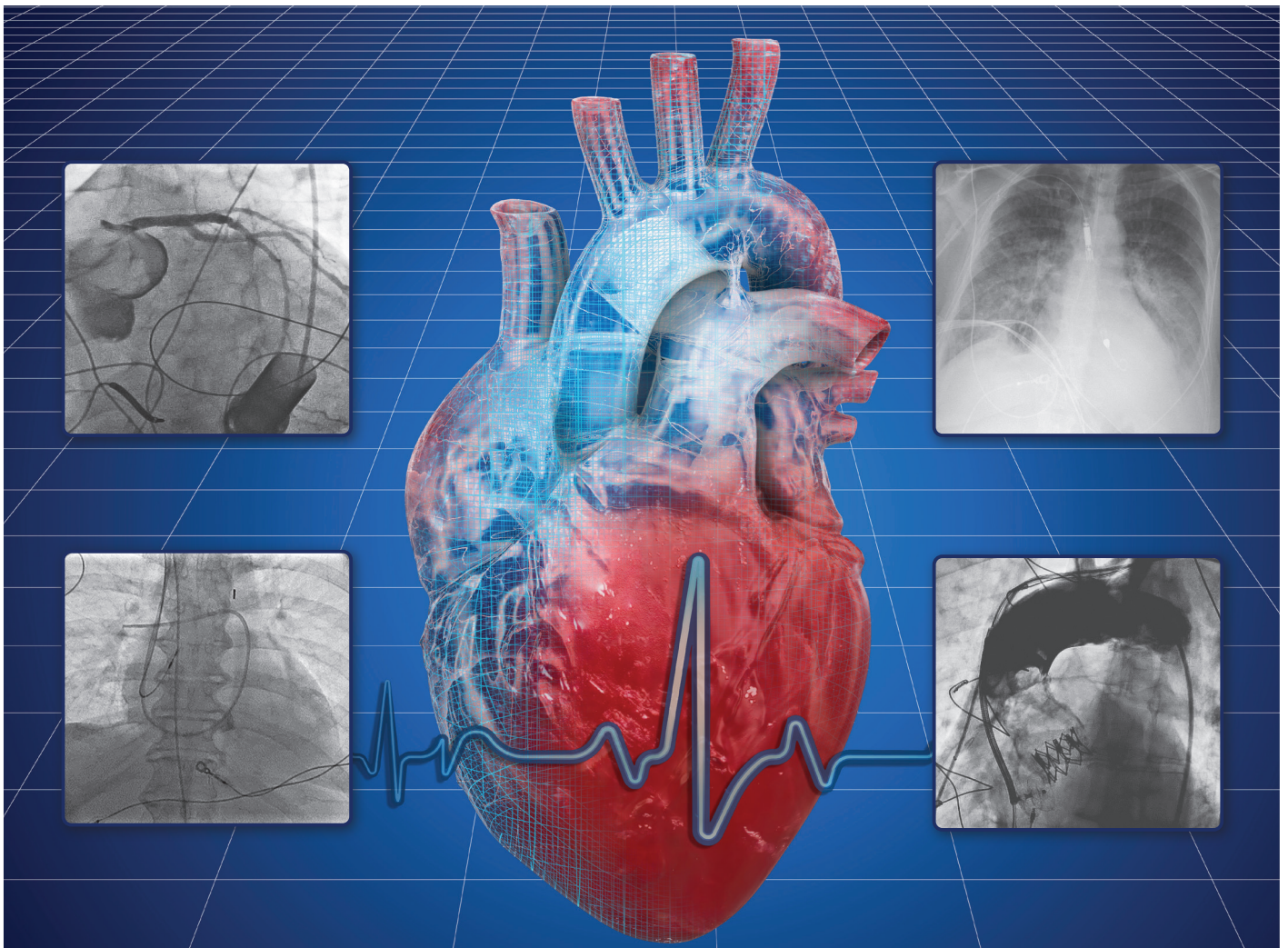


Volume 1

Issue 1

JOURNAL OF SHOCK & HEMODYNAMICS

September 2022



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Selected topics from the 2022 Houston Shock Symposium

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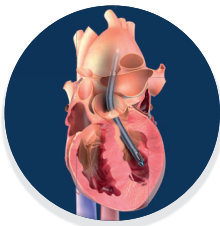
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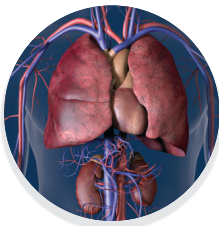


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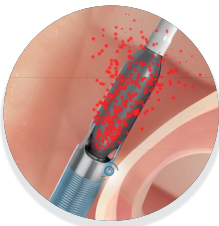
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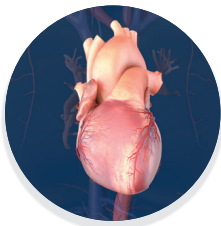
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Cardiogenic shock mortality remains unacceptably high despite advances in medical management and the widespread use of percutaneous mechanical circulatory support device therapy. Its mortality rate has been largely stagnant in the past two decades. 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.

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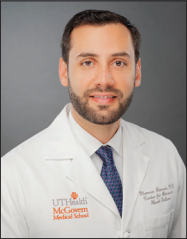
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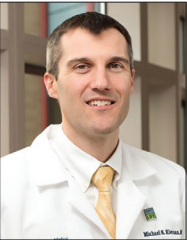
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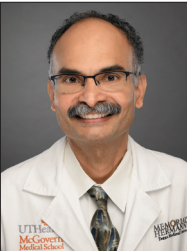
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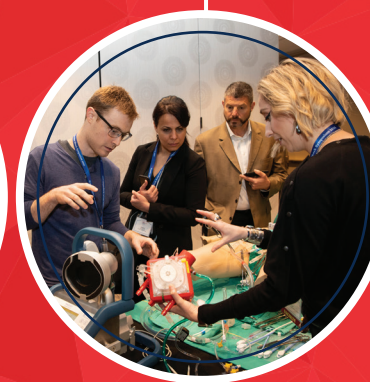
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Houston SHOCK: A Practical Scoring System Incorporating Cardiogenic Shock Dynamic Changes

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Abstract

Cardiogenic shock has an unacceptably high mortality rate and additional tools are needed to improve outcomes. The Society of Cardiovascular Angiography and Interventions (SCAI) shock severity classification has provided a unified definition of shock severity that has proven to be reproducible and predictive of survival. However, cardiogenic shock assessment goes beyond standardizing its severity, and a uniform and practical approach to comprehensive assessment that may guide therapy in a dynamic state is currently lacking.

Since cardiogenic shock is a rapidly evolving pathophysiological catastrophe, we propose a new assessment tool – the Houston SHOCK Score – which incorporates dynamic changes. The acronym SHOCK can be used to emphasize five key aspects of patients in cardiogenic shock: **S**everity, **H**emodynamics, **O**nset, **C**auses, and **K**inetics. We believe this tool provides physicians with vital information that will facilitate appropriate care by incorporating dynamic changes in the patient’s profile.

Keywords: cardiogenic shock, mechanical circulatory support device, SCAI shock

Background

Cardiogenic shock (CS) is a devastating clinical condition with an overall mortality rate ranging from 25-50%.¹⁻⁴ Mortality remains high despite advances in medical management,² the adoption of early revascularization and emergent reperfusion strategies after acute myocardial infarction (AMI),¹ and the advent and widespread utilization of percutaneous mechanical circulatory support (pMCS) device therapy.⁵ In fact, in an analysis of 56,497 patients in the CATH-PCI registry, the mortality rates from AMI-CS rose from 27.6% in 2005-2006 to 30.6% in 2011-2013 (P < .0001).⁵

In addition, the burden on healthcare systems is significant. CS has an unacceptably high 30-day readmission rate of 18.6% amongst survivors of AMI-CS.⁶

The Society for Cardiovascular Angiography and Interventions (SCAI) expert consensus statement on the classification of CS offers a standardized taxonomy for providers.⁷ It supports the early identification and triage of patients presenting with CS in a simple, readily applicable, and intuitive manner. The classification is a step closer to the standardization of a CS definition. Based on this new **severity** classification, CS is classified into five categories, from at-risk

Table 1. Profiles of shock based on invasive hemodynamic assessment.

Cardiogenic	Classic (cold and wet): reduced CI, high SVRI, elevated PCWP Mixed (warm and wet): reduced CI, reduced SVRI, elevated PCWP Euvolemic (cold and dry): reduced CI, elevated SVRI, normal PCWP
Hypovolemic	Characterized by reduced intravascular volume; typically with reduced CI, elevated SVRI, and reduced PCWP
Distributive	Characterized by severe peripheral vasodilatation; typically with increased CI, reduced SVRI, and reduced PCWP
Obstructive	Tamponade: reduced CI, elevated SVRI, and elevated PCWP Pulmonary: reduced CI, elevated SVRI, and reduced PCWP
Right Ventricular	Reduced CI, elevated SVRI, reduced PCWP, elevated RAP, elevated RA:PCWP ratio, reduced pulmonary artery pulsatility, reduced PAPi, reduced RVSWI

Abbreviations: CI, cardiac index; PAPi, pulmonary artery pulse pressure index; PCWP, pulmonary capillary wedge pressure; RAP, right atrial pressure; RVSWI, right ventricular stroke work index; SVRI, systemic vascular resistance index

(stage A) to extreme CS (Stage E); however, CS assessment goes beyond standardizing its severity. A comprehensive, uniform approach is currently lacking, especially one that considers changes in patients’ clinical or hemodynamic status, response to therapy, and trajectory. Comprehensive classification of CS is difficult due to a myriad of reasons that we will review below.

Classification Complications

First, patients with CS present with a wide spectrum of presentations. The inability to accurately recognize the different **hemodynamic phenotypes** of CS (Table 1) in a timely fashion is a major contributing factor to poor outcomes. The current definitions of CS used in clinical trials⁷⁻⁹ require a systolic blood pressure (SBP) of less than 90 mmHg despite pressor support with evidence of end-organ hypoperfusion and/or hemodynamic parameters of reduced cardiac index (CI). However, septic and hypovolemic shock also manifest with hypotension and end-organ hypoperfusion (Table 2), and assessment of hemodynamics is oftentimes not readily available. Furthermore, mixed forms of shock frequently exist simultaneously.⁹ In addition to including absolute blood pressure parameters in the definition of CS, the degree of hypotension relative to the patient’s preexisting blood pressure should be considered in any attempt to redefine the spectrum of CS. In fact, 5.2% of patients in the SHOCK trial registry were in CS but had an SBP > 90 mmHg, and 7.1%

had no evidence of organ hypoperfusion with an SBP < 90 mmHg; yet, both groups of patients have increased mortality.⁸

Second, the **onset of CS** and its impact on outcomes has not been fully studied. Traditionally, *acute* onset refers to CS cases that develop within less than 24 hours of the onset of symptoms and are typically seen in acute ischemic events or electrical storms. A *subacute* onset, defined as symptom onset of fewer than 7 days, is seen most often in mechanical complications of myocardial infarction and acute myocarditis. Finally, *chronic* onset is defined as symptom onset of greater than 7 days but is typically seen in patients with known stage D heart failure.

Third, CS is the final culmination of **multiple disease states**. The heterogeneity of CS is akin to heart failure with preserved ejection fraction (HFpEF) heterogeneity in clinical trials. An impact on long-term mortality has not been seen in most HFpEF clinical trials due to the different underlying pathophysiological mechanisms of diseases that lead to HFpEF. Outcomes of post-cardiotomy shock vary dramatically from those of acute myocarditis. A patient suffering AMI-related CS behaves differently than a stage D heart failure patient presenting with CS. The hemodynamic profiles of these two subsets of patient populations are different, with the latter having higher filling pressures, pulmonary artery pressures, and a different metabolic

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Table 2. Parameters of end-organ hypoperfusion.

Clinical Parameters	Impaired mental status, UOP < 40cc/hour, progressive pulmonary edema
Hemodynamic Parameters	High doses of pressors to maintain adequate BP is defined as: Norepinephrine dose of > 0.2mcg/kg/min Epinephrine dose of > 0.2mcg/kg/min Dopamine > 5mcg/kg/m Two vasoactive agents
Biochemical Parameters	Creatinine > 0.4mg/dL X baseline, elevated AST/ALT > 4X upper limit, lactate > 4.0 units

Abbreviations: AST/ALT, aspartate aminotransferase/alanine aminotransferase; BP, blood pressure; UOP, urinary output

profile.¹⁰ As such, one would expect the hemodynamic goals of management to differ based on the inciting event.

Lastly, there are aspects of CS that are not addressed in the current literature, especially responses to initial therapy. Many questions arise when considering the approach to CS management. For example, it is not clear if full pMCS support followed by de-escalation in CS would be superior to a strategy of tailored escalation of pMCS support, or whether an approach of maximum pMCS support be utilized routinely in stages C to E of CS. It is unclear if dynamic changes in the patient’s hemodynamic status and response to therapy play a role and whether the “*kinetics*” of either approach has an impact on mortality.

Mortality in CS is not solely related to the initial myocardial insult and the acute drop in CI. In fact, in a meta-analysis of randomized controlled trials of pMCS, Thiele et. al demonstrated the improvement in hemodynamic profiles of patients who were supported with pMCS when compared to those supported with an intra-aortic balloon pump (IABP).¹¹ Reductions in pulmonary capillary wedge pressure and improvements in CI and mean arterial pressure were observed; however, an improvement in 30-day mortality was not found.¹¹ Thus, it remains to be seen if this lack of effect on mortality was due to the limited power of the study or the true absence of an effect. Indeed, the complex pathophysiological way in which the body responds to the initial insult that leads to progressive cardiac dysfunction varies from one patient to another. The variations in the activation of systemic inflammatory response syndrome (SIRS), the extent of metabolic derangements, the impact of pMCS on SIRS activation, and the complex interplay between the different pMCS types and the CS patient (eg, the balance between the salubrious hemodynamic effects and the complications associated with these large bore devices) need to be further studied as they play a major role in the outcomes of these

patients. As such, the differentiation of CS patients based on the use of a pMCS device is inadequate. pMCS support should be tailored to different hemodynamics of shock presentation and active changes in the patient’s profile. A CS patient who **stabilizes** on an IABP may need to be classified differently than a patient who requires veno-arterial extracorporeal membrane oxygenation for hemodynamic support due to **refractory** CS. Treatment during or following stabilization should be tailored to the inciting cause of CS and the likelihood of reversibility of its cause.

Recommendation

Given that CS outcomes are highly dependent on the **severity** at the time of presentation *AND* the above-mentioned elements including the dynamic changes in the patient’s profile, which we refer to as “Kinetics,” we propose incorporating the following five elements to provide a more comprehensive assessment of the CS patient. The five variables, encapsulated by the acronym SHOCK are: (1) the Severity of CS; (2) the Hemodynamic profile of the patient, (3) the Onset of CS symptoms, (4) the Cause of CS, and (5) the Kinetics of CS (Figure 1). This approach offers healthcare providers and researchers a uniform language, a standard platform, and clinically relevant parameters that include dynamic changes and response to therapy that allow for a more accurate portrayal of the clinical picture of a CS patient. This proposed assessment will support the accurate identification of CS patients with similar pathophysiology and severity while addressing most of the aforementioned shortcomings of the current CS definitions. We believe that this comprehensive assessment will fulfill a vital need to be able to compare the effects of different therapies and aid the design of meaningful trials in specific subsets of patients with CS taking into consideration the hemodynamic profiles of patients, the kinetics of patients, and the likelihood of reversibility of causes.

The following is a description of the five parameters of the SHOCK Scoring System.

Variable		Points
Severity	SCAI A-C	0
	SCAI D, E	1
Hemodynamics	Classic	0
	Mixed & Euvolemic	1
Onset	Acute	0
	Chronic	1
Cause	Acute Treatable	0
	Other Causes	1
Kinetics	Stabilized	0
	Refractory/Worsening	2

Severity

As stated earlier, the SCAI expert consensus statement on the classification of CS simplifies the severity into one of five stages, mirroring the Interagency Registry for Mechanically Assisted Circulatory Support profiling of advanced heart failure patients.⁷ In a recent single-center retrospective study of 10,004 patients admitted to an intensive care unit, the unadjusted hospital mortality rose steadily as the severity of CS increased.¹² Mortality in stage A was 3.0%, stage B 7.1%, stage C 12.4%, stage D 40.4%, and stage E 67% (P < .001); each higher SCAI shock stage was associated with increased hospital mortality with an adjusted odds ratio of 1.53 to 6.8 (all P < .001).¹² Thus, we suggest the first assessment should include ascertaining the severity of CS via the SCAI system. The Houston SHOCK Score assigns a value of 0 to patients classified as stages A-C, and those individuals classified as stages D or E are assigned a value of 1 (Table 3).

Hemodynamics

While the classic form of CS is frequently seen, the hemodynamic profile is varied and can be classified in one of three main presentations:⁹

- 1. The classic cold and wet, the most frequently encountered form, is often seen in AMI-CS
 - 2. Mixed CS (warm and wet), and
 - 3. Euvolemic CS (cold and dry) — often seen in chronic heart failure patients who present in a decompensated state
- Since CS management is dependent on the predominant phenotype, the second step in our assessment model is to account for such variability in presentation. The SHOCK Score

encourages users to provide a more detailed classification of shock after invasive and non-invasive hemodynamic assessments are attained. Patients would be delineated by one of the following types of shock: cardiogenic, hypovolemic, distributive, obstructive, or right ventricular (Table 1). The Houston SHOCK Score assigns a value of 0 to patients classified as classic; those individuals classified as mixed or euvolemic are assigned a value of 1.

Onset

As mentioned earlier, an AMI-CS patient behaves differently than a stage D heart failure patient presenting with CS. Such differentiation is critical when looking at therapeutic modalities and mortality outcomes. CS onset after AMI occurred within 24 hours in 74% of patients in the SHOCK trial registry.¹³ However, patients in stage D heart failure often have acute episodes of decompensation. Further, the hemodynamic profiles of these two subsets of patients are different with the latter having higher filling pressures, pulmonary artery pressures, and a different metabolic profile.¹⁰ The Houston SHOCK Score assigns a value of 0 to patients with acute onset, and those classified as chronic are assigned a value of 1.

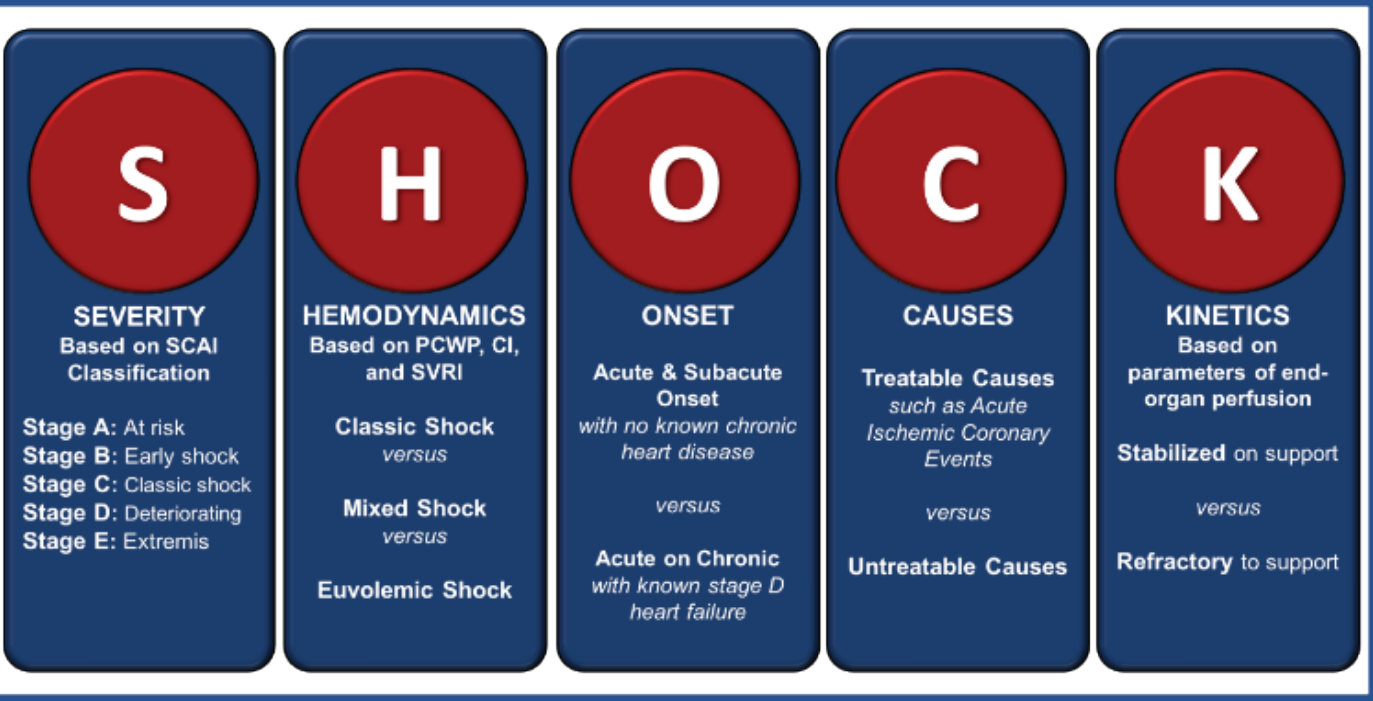
Cause

The only form of CS to have a proven therapy that can impact mortality is AMI-CS. One may argue that the diagnosis of AMI-CS is more readily available and, as such, tailored therapies have existed for decades. Discerning the etiology of CS upon presentation, however, is difficult, and trying to ascertain a diagnosis as quickly as possible can pave the wave to initiating early therapies that can potentially impact mortality. A broad assessment of CS must be made based on the cause. We propose the following etiologies: ischemic due to AMI, ischemic due to a mechanical complication, non-ischemic (such as acute myocarditis, acute on chronic stage D heart failure), right ventricular failure, and electrical storms. The Houston SHOCK Score assigns a value of 0 to patients classified as acute reversible and treatable; all other causes are assigned a value of 1.

Kinetics

Perhaps the least understood aspect of CS management is the kinetics (dynamic changes in the patient’s profile) and predicting the outcome of support on pMCS devices. While some consider pMCS support devices a therapeutic option in the armamentarium utilized in CS management, it is crucial to emphasize that in most instances adequate pMCS support is intended to stabilize (*not to treat*) a worsening CS patient. In addition, pMCS devices help determine response to therapy

Figure 1. The Houston SHOCK Score incorporates the dynamic changes seen in this rapidly evolving hemodynamic catastrophe. The acronym SHOCK emphasizes five key aspects of patients in cardiogenic shock - Severity, Hemodynamics, Onset, Causes, and Kinetics - and allows healthcare workers to capture and score the dynamic changes encountered in cardiogenic shock.



Abbreviations: CI, cardiac index; PCWP, pulmonary capillary wedge pressure; SVRI, systemic vascular resistance index

and improve the overall clinical status and the patient’s trajectory. While the optimal approach is not fully known, the ability to stabilize a patient by pMCS support represents a different group of patients than those that are unable to be stabilized. By describing the kinetics of CS, i.e. dynamic changes and responsiveness to therapy, patients can be classified as *stabilized* CS vs. *refractory shock* despite support. Assessment of the response to therapy is based on improvement in parameters of perfusion listed in Table 2. This will allow for quicker triage of worsening patients to dedicated shock centers. The Houston SHOCK Score assigns a value of 0 to patients classified as stabilized; those individuals classified as worsening/refractory are assigned a value of 2.

Applicability in Clinical Practice

In addition to offering a standardized approach to comprehensively assess patients in shock, we believe the SHOCK Score can serve important purposes that are yet to be validated. We believe dichotomizing each of the five variables of the Houston SHOCK Score into a score (Table 3) is practical. Healthcare providers can quickly triage the “sicker and refractory” patients to dedicated shock centers and offer time-sensitive therapies. In addition, admission score can be validated prospectively for outcomes including mortality. We believe the higher the score, the higher the acuity of the patient

resulting in worse inpatient and long-term outcomes. Our initial scores are arbitrarily dichotomized to 0 and 1 (except for kinetics where 0 and 2 are used, as those in refractory CS should be given a higher weighted score in our opinion); however, we believe that ongoing validation research can offer a more accurate weighted score for some variables. Lastly, similar to SCAI Severity Classification of shock, this scoring system is dynamic and can be applied and utilized in a dynamic manner incorporating new data and response to therapy as available. As the kinetic response is a key component of this score, we believe capturing the score on admission (for triage purposes), and at 72 hours of admission may serve to be of prognostic significance that further validation is necessary. Retrospective data analysis is currently underway at our institution to validate this score.

Clinical Examples

A 68-year-old male presented with two hours of chest pain and was found to have large anterior STEMI, for which he underwent percutaneous coronary intervention (PCI) of the proximal left anterior descending coronary artery. The left circumflex and right coronary arteries were chronically occluded. His blood pressure was 75/44 mmHg on arrival for which an IABP was placed following the PCI. In the ensuing hours, the patient had a low blood pressure of 80/50 mmHg,

cool extremities, S3 gallop, reduced urine output, and elevated lactic acid requiring the addition of high doses of epinephrine and norepinephrine. This patient receives a Houston Shock Score of 4 (S1H0O1C0K2). Such a high score would allow for a more urgent referral to a shock center and the allocation of the shock center’s resources to be ready for support escalation at the time of arrival, such as a percutaneous MCS device implantation.

A 23-year-old female with familial cardiomyopathy on milrinone therapy and known reduced left ventricular systolic function presented for the fourth time in 3 months with 1 week of 4 pillow orthopnea and dyspnea on minimal exertion. On presentation, the patient had an SBP of 88 mmHg, S3 gallop on examination with 3+ pedal edema, and ascites. She underwent a right heart catheterization that revealed a right atrial pressure of 19 mmHg, pulmonary artery pressure of 49/35 mmHg, pulmonary capillary wedge pressure (PCWP) of 32 mmHg, and a CI of 1.7 L/m/m². An Impella 5.5 was placed, and her repeat hemodynamics at 24 hours showed a right atrial pressure of 10 mmHg, PCWP of 19 mmHg, and CI of 2.2 L/m/m². This patient receives a Houston Shock Score of 2 (S0H0O1C1K0). While both patients are classified as “classic” CS per SCAI definition, the first patient has a higher Houston Shock Score as he needs more urgent attention, triage to a shock center, and escalation of therapy.

Conclusion

In summary, CS is a disease state with a heterogeneous pathophysiology, and its management starts with a comprehensive assessment that incorporates not only its *severity*, but also its *hemodynamic* profile, *onset*, *cause*, and *kinetic* response to therapy. The SHOCK Score offers a more comprehensive and standardized taxonomy that can help move this field forward.

Acknowledgments

The authors thank Michelle Gehring PhD, ELS and Jessica Moody, PhD for editorial services.

Funding

No funding or in-kind support was received for the preparation of this manuscript.

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2022 Symposium Presentation

Extracorporeal Membrane Oxygenation Therapy in COVID-19

Patients with Acute Respiratory Distress Syndrome

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Abstract

Patients with coronavirus disease of 2019 (COVID-19) may present with a wide range of symptoms ranging from asymptomatic to critically ill. Approximately 10-14% of patients require hospitalization. Those individuals requiring hospitalization can deteriorate rapidly with worsening hypoxemia or new-onset pneumonia, resulting in 20-30% of patients developing acute respiratory distress syndrome (ARDS).

When refractory to medical management, severe ARDS secondary to other illnesses has been successfully treated with extracorporeal membrane oxygenation (ECMO). We completed a comprehensive literature review of ECMO utilization for patients with severe COVID-19 who were unresponsive to critical care management. Of the 1419 patients with a reported diagnosis of COVID-19-related ARDS requiring ECMO therapy, 53.6% were discharged alive, 8.4% remained on ECMO in the intensive care unit, and 43.0% are deceased. These results are similar to the discharge rate of 60% for patients with non-COVID-related ARDS treated with ECMO. Data reported by the Extracorporeal Life Support Organization notes that 49% of patients with COVID-19 ARDS were discharged alive, 38% of whom were discharged home or to a long-term facility, and 11% were discharged to another hospital. In summary, using ECMO to treat patients with severe ARDS unresponsive to critical care management yields similar results in both non-COVID and COVID-related ARDS.

Keywords: coronavirus, acute respiratory distress syndrome, extracorporeal membrane oxygenation

Background

Critical care management of acute respiratory distress syndrome (ARDS), independent of the cause, relies on respiratory support ranging from a nasal cannula to full mechanical ventilation and eventually extracorporeal membrane oxygenation (ECMO) therapy if hypoxemia is refractory to medical management.¹ The coronavirus pandemic has incited alarm within communities worldwide. Many clinicians initially questioned the efficacy of utilizing ECMO as a treatment for severe coronavirus disease (COVID)-related ARDS that is unresponsive to critical care management. Factors that contributed to this uncertainty include the constantly evolving and spreading of the virus, the

wide range of symptoms that can result from infection, delay of diagnostic test availability, misinformation concerning symptoms, and the overall uncertainty of health care resources.

ECMO Considerations in Patients with ARDS Secondary to COVID-19

ECMO in ARDS for Respiratory Management

ECMO is recommended as supportive therapy for cardiac and/or respiratory failure refractory to medical management. ECMO is considered to have a positive risk/benefit when patients have persistently decreased PaO₂/ FiO₂ of less than 80

mmHg for more than 6 hours, less than 50 mmHg for greater than 3 hours, or if the pH is less than 7.25 with a PaCO₂ greater than 60 mmHg for more than 6 hours despite adequate FiO₂ and positive end expiratory pressure settings. Kassirian et al summarize the appropriate respiratory management for hypoxemic respiratory failure in figures.²

When to Start ECMO Treatment

Every day of mechanical ventilation before ECMO initiation is associated with an increased odds of mortality. In a study by Kunavarapu et al, those who survived post-ECMO support were, on average, initiated on treatment earlier (11.4 ± 4.8 days) as compared to those patients that died (14.4 ± 5.5 days) (P = .047).³ The total number of days spent on ECMO support also significantly affects mortality outcomes. The survival group spent 10.7 ± 16.6 days on ECMO while the deceased group averaged 20.9 ± 16.8 days on support (P = .001). One explanation for the difference in survival is the high incidence of ventilator-associated morbidity and mortality in patients with ARDS, which ECMO may mitigate. Alternatively, the number of days spent on ECMO support may be a marker of disease severity.³ Overall, earlier ECMO intervention increases the survival odds of ARDS that is unresponsive to critical care.

Indications vs Contraindications for ECMO

Recommended indications for the use of ECMO include refractory hypoxemia, use of mechanical ventilation for < 7 days, risk of death greater than 50%, severe air leak syndrome, and a diagnosis of severe myocarditis or cardiogenic shock.⁴

Absolute contraindications include significant comorbidities from which a patient cannot recover. These include severe immunosuppression, sepsis with bacteremia, contraindications to systemic anticoagulation, severe multiple organ failure, severe aortic dissection, acute intracerebral hemorrhage, irreversible severe brain injury, critical congenital heart defects, chronic lung disease, and lethal chromosomal anomalies.⁴ Relative contraindications also include an age of 65 years or older, a body mass index > 30 kg/m², prolonged ventilatory support, frailty, allo-sensitization with prolonged waitlist time, and limitations in vascular access.⁴ During the early phase of the COVID-19 pandemic, the Extracorporeal Life Support Organization (ELSO) recommended prioritizing young, previously healthy patients with only a single organ failure for ECMO support, as they may derive the maximum benefit.⁵ As clinical experience continued to evolve, these priorities were relaxed based on program experience and increased access to health care resources.

Type of ECMO for COVID ARDS

Veno-venous ECMO provides total gas exchange and the easiest access in patients with COVID-related ARDS. Veno-arterial ECMO is recommended for patients with COVID-

related myocarditis, and atrio-pulmonary access has an advantage in patients with pulmonary hypertension and associated right ventricular dysfunction.⁶

Complications of ECMO

Complications of ECMO therapy in patients with both COVID-related ARDS and non-COVID ARDS include hemorrhage, arterial and venous thrombosis, infection, liver failure, and acute kidney injury.^{7,8} Survivors of ECMO were significantly less likely than non-survivors to experience renal failure (P = .007), cannula site bleeding (P = .037), septic shock (P = .130), and systemic inflammatory response (P = .013).⁷ However, patients on ECMO secondary to COVID-related ARDS were significantly more likely to experience thromboembolic events (P = .031), specifically pulmonary artery embolism (P = .008), than non-COVID ECMO patients.⁸

ECMO Results in COVID-related ARDS

Based on the review of the literature, 53.6% (760/1419) of patients initiated on ECMO support secondary to COVID-related ARDS were discharged alive, but 8.4% remained on ECMO in the intensive care unit. There is an associated 38% mortality on ECMO with 539 out of 1419 patients deceased.^{3,7,8,9,10} This data was compared to the ELSO database and found to be similar. ELSO currently reports that 49% (4754/9685) of patients treated with ECMO for COVID-related ARDS were discharged alive. Of these 49%, half were discharged home or to an acute care facility, a quarter went to another hospital, and a quarter was discharged to a long-term acute care facility or unspecified location.^{10,11} Despite limited resources and personnel during the pandemic, this mortality rate is similar to the 34%–39% mortality rate reported for patients with non-COVID-related ARDS on ECMO support.⁷

Ongoing Research

An open-label, randomized, controlled trial is currently underway in patients on ECMO support with COVID-19 pneumonia and moderate-to-severe ARDS.¹²

Current Recommendations

ECMO should be used in patients with COVID-related ARDS when the severe respiratory failure is refractory to other therapies.⁵ Current indications for ECMO in patients with ARDS secondary to COVID-19 should not be different than other ARDS cases but should be based on the availability of open beds, equipment, and access to skilled personnel.

How do these concepts impact clinical practice?

To summarize, ECMO is an appropriate treatment option for patients with ARDS secondary to COVID-19, but only after standard critical care management is used. Ideally,

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ECMO should be started before an extended trial of mechanical ventilation. Complications of ECMO are consistent among all causes of ARDS with a slightly increased risk of experiencing thromboembolic events, specifically pulmonary artery embolism, in patients with COVID-19. A comprehensive review indicates that ECMO therapy increases the number of patients discharged alive and should be utilized more consistently in COVID-19 ARDS.

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2022 Symposium Presentation

Society for Improving Medical Professional Learning
Collaborative: What’s It All About?

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Abstract

The Society for Improving Medical Professional Learning (SIMPL) Collaborative is a non-profit, educational, quality improvement consortium focused on developing tools, curricula, and policies to improve physician training. The goal is to provide educators and learners with convenient, reliable, and valid evaluation tools for frequent, real-time workplace assessment and feedback. The SIMPL Operating Room application provides this platform. It was developed to provide high-quality, time-sensitive, procedural feedback. Its objective is to facilitate intra-rotation corrections.

SIMPL is available to all residency programs and has matured to include over 175 residency programs, involving 19 different specialties, 4000 trainees, 5000 attendings, and 354,800 evaluations in 3 countries. At least 52 peer-reviewed manuscripts have used the evolving database. We have performed an expert narrative review of the entire SIMPL literature (primary research studies, reviews, and websites) to discuss the unique lessons learned from this large collaborative experience. SIMPL can be the core of a competency-based operative skills assessment that is incorporated into medical training, assessment, and certification. Higher quality feedback is provided via SIMPL compared to the routine end-of-rotation evaluations with a corrective comment 60% of the time versus 15%, respectively. A high overall correlation between residents and faculty within case complexity has also been documented (r = 0.76, P < .0001), technical performance (r = 0.66, P < .0001), and autonomy (r = 0.56, P < .0001).

The goal of the SIMPL initiative is to use resident performance to drive continuous quality improvement of the individual, programs, and larger medical system.

Keywords: SIMPL, medical learning, resident training, trainee, mentor-mentee relationship

Background

Halsted’s apprentice model of surgical education was the backbone of medical education for over 100 years when the time for training was unlimited, the educator had no teaching requirements, and you finished when the master said you were done.¹ This process has since become antiquated, secondary to rising concern for patient safety, duty hour restrictions with the introduction of the 80-hour work week, and increased expectations for faculty supervision. Likewise, introductions of combined programs, pressure to perform clinical tasks in more condensed workdays, and poor methods of evaluating surgical residents have all contributed to a convergence of

educators who began to question the autonomy, safety, and practice readiness of graduating surgery residents.²⁻⁹ No single tool has captured autonomy, performance, and case complexity principles.¹⁰⁻¹¹ The ideal tool provides educators with convenient, reliable, and valid evaluation tools for frequent, real-time workplace assessment and feedback. The Society for Improving Medical Professional Learning (SIMPL) Operating Room (OR) application (App) provides this innovative assessment tool. The SIMPL OR App provides assessment criteria for an individual’s autonomy, performance, and case complexity as measured by the resident and attending physician. The goal is to provide rapid feedback and assessment of the mentor and the mentee. SIMPL is

currently available to all residency programs and has matured to include over 175 residency programs involving 19 different specialties, 4000 trainees, 5000 attendings, and 354,800 evaluations in 3 countries. At least 52 peer-reviewed and published manuscripts have used the evolving database.

An Expert Review of the Literature to Date from
the SIMPL Collaborative

Why SIMPL?

Residents need an assessment tool that allows for real-time feedback and functions as a common avenue for faculty to administer prompt feedback. Bi-annual end-of-rotation (EOR) assessments and yearly in-service exams are inadequate for most resident training. The SIMPL OR App provides an easily navigable interface that is quick to fill out, taking reviewers less than 2 minutes to complete, even as little as 14 seconds with practice. Optional dictated feedback provides reviewers additional avenues to give specific, corrective feedback with learning plans. Evaluators can assess trainees on the individual, operation-by-operation, and day-by-day scales. SIMPL incorporates all known evidence-based best practices into one operative performance assessment.

Additionally, the SIMPL App can push procedures to the Accreditation Council for Graduate Medical Education (ACGME) website (www.acgme.org), saving time for the trainee. Before an operation, the experience for a given procedure through longitudinal data and previous evaluations of a resident’s performance is viewable by the evaluator to allow focused conversations to express expectations, individualize teaching plans, and predict autonomy level. Unsurprisingly, studies reveal that immediate feedback ratings were the most accurate, stating, “ratings completed more than 3 days after observation should be discouraged and discounted, as they lack clarity and detail about the performance.”¹ Therefore, all SIMPL data is a maximum of 72 hours “old.”

Who Gets Trained on App Usage and How?

Resident and attending training is one hour and provided through a virtual platform. The program director or coordinator receives a more prolonged discussion of the SIMPL OR App. Current training sessions include six brief operative videos with an attending, resident, and student illustrating both open and laparoscopic examples of the four basic Zwisch levels (show and tell, active help, passive help, and supervision only). The level of autonomy varies throughout a case, but the overall autonomy grade is based on the level achieved during the majority of the critical portion of the case. The training session participants then review operative performance on a 5-level scale (unprepared/critical

deficiency, inexperienced with the procedure, intermediate performance, practice-ready, and exceptional) adapted from a previously validated scale.¹¹ Residents and faculty are instructed to assess performance relative to years of training, known previous exposure to similar cases, known or expected preparation, perceived engagement during the case, and expectations relative to that case. Case complexity (easiest 1/3, middle 1/3, hardest 1/3) is a judgment call by case participants relative to the specialty, caseload of the attending surgeon, co-morbidities, and difficulties encountered during the case. Figure 1 demonstrates the Zwisch autonomy scale.

How It Works

- 1. SIMPL OR App evaluation is sent to faculty or trainee counterpart.
- 2. Users complete an assessment in as few as four “taps.”
- 3. Faculty have the option to dictate feedback.

The SIMPL OR App is available on Google Play and the Apple App Store.

Case Logs do Not Equate to Competency

Operative performance ratings for 29,885 procedures performed by 1,861 surgical residents in 54 general surgery programs were analyzed.¹³ For each core general surgery procedure, the adjusted mean probability of a graduating resident being deemed “Practice-ready” ranged from 0.59 to 0.99 (mean 0.90; standard deviation 0.08).¹³ Despite general surgery residents completing minimum requirements for a number of cases, these may not adequately represent what is encountered in common practice.^{13, 14} The Zwisch model was tested to determine a targeted number of cases to achieve a score of 3 or 4. While the number of cases varied greatly for

Show and Tell Stage	Active Help Stage	Passive Help Stage
The Resident essentially observes and assists but may participate in some parts of the procedures such as opening and/or closing the incision. Attending “shows” the resident how the procedure is done, and “tells” the resident what needs to be known.	The resident begins to assume the surgeon role in some parts of the procedure with the attending providing active guidance (i.e., verbal and/or physical) including periodically swapping “surgeon” and “assistant” roles with the resident. When the resident assumes the surgeon’s role, the attending actively assists, essentially guiding the resident through the procedure.	The resident is capable of safely doing significant parts of the procedure without active guidance (i.e., verbal and/or physical) from the attending who passively assists.
Supervision Only Stage		
The resident can safely and effectively perform the procedure using operating room staff or a junior resident to assist. The attending provides no significant verbal or physical guidance/intervention to the resident but provides supervision and consultation if needed.		

Figure 1. The Zwisch scale for levels of autonomy.

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each of the five core surgical procedures, the number of observations required to achieve competency exceeded certification requirements. This was exemplified by a prospective study of 14 general surgery programs showing that fifth-year residents in the last 6 months of training achieved meaningful autonomy in only 69.3% of cases, with the maximum autonomy rating of “Supervision Only” for only a fraction of core procedures.¹⁵ While autonomy has also been shown to increase with advancing graduate year and higher frequency procedures and decrease with case complexity,^{17, 18} operative performance remains the strongest determinant of autonomy.^{15, 16}

SIMPL Provides Objective Data

Traditional forms of performance feedback are completed physically and temporally remote from the OR experience. The SIMPL OR App was developed to provide objective, high-quality, time-sensitive, procedural feedback that facilitates intra-rotation corrections. Faculty provided substantially higher quality feedback using the SIMPL assessments compared to EOR evaluations. The SIMPL. Objectivity was also noted with a high intra-observer agreement ($P < .0001$) on the autonomy Zwisch scale.¹⁹ Similarly, a general surgery study looked at SIMPL assessments completed by both faculty and residents with a high overall correlation between residents and faculty for case complexity ($r = 0.76$, $P < .0001$), technical performance ($r = 0.66$, $P < .0001$), and autonomy ($r = 0.56$, $P < .0001$).¹² Higher quality feedback is also provided via the SIMPL OR App compared to the routine EOR evaluations with a corrective comment 60% of the time versus 15%.¹² The Zwisch performance scale is based upon resident performance (Figure 2).

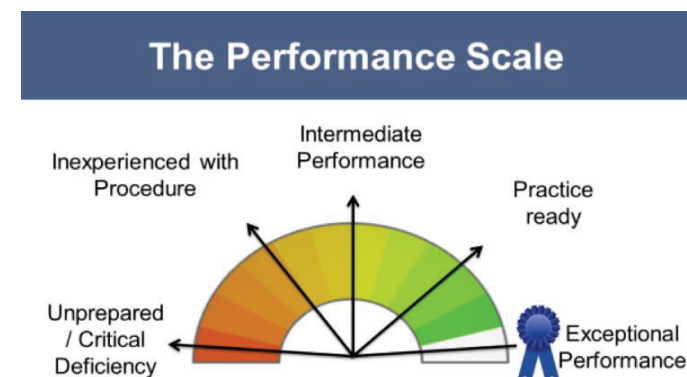


Figure 2. The Zwisch performance scale. Ratings should be based on a single operative performance, providing a snapshot of resident performance during the critical portion of the procedure. Throughout residency, these snapshots provide a movie of a resident's performance based on ratings over multiple procedures from different attendings.

The Future of SIMPL

The SIMPL mobile-based application has successfully adapted to multiple other surgical sub-specialties, including otolaryngology, oral and maxillofacial, pediatric, plastic, urology, cardiac, and neurosurgery.^{18, 20-21} Standardization of resident evaluation via SIMPL-based assessments allows data comparison across programs, enhancing generalizability and providing more robust and statistically significant conclusions. The next steps include collaborative SIMPL 2.0 to better reach other types of workplace assessment approaches with entrustable professional activities, which are also required for board certification. SIMPL is creating a Reports Dashboard, which will use machine learning to estimate the competence of surgical trainees. Four national trials, including the SIMPL Competency-Based Medical Education Pilot, are underway to understand how we can collaboratively develop, implement, and sustain change, activities which are central to educational quality improvement.

How do these concepts impact clinical practice?

Learners benefit most from real-time feedback. The SIMPL OR App creates an avenue for mentors and mentees alike to provide feedback on performance and teaching style. It is an objective, quantitative, and time-saving approach to measuring performance in an increasingly time-constrained medical professional education system. This mechanism provides immediate feedback by becoming available directly to the trainee and attending, while longitudinally tracking progress over the years. The SIMPL OR App is an excellent tool to assess trainee progress in surgical competency and autonomy while maintaining the ability to evaluate attending surgeons' teaching methods. SIMPL can drive quality improvement for individuals, programs, and larger medical systems.

Acknowledgments

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2022 Symposium Presentation

Hemodynamics of Prolonged Percutaneous Mechanical

Circulatory Support – When Vasodilatation Sets

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Abstract

Hemodynamics play an important role in cardiogenic shock assessment for prognosis estimation and for phenotyping cardiogenic shock. This is best done by pulmonary artery catheters. In general, at the beginning of cardiogenic shock, patients have vasoconstriction, which over time may lead to vasodilation. This is often triggered by percutaneous mechanical circulatory support. This review will elucidate the hemodynamics and the factors that possibly lead to vasodilation in patients with mechanical circulatory support.

Keywords: percutaneous mechanical circulatory support, cardiogenic shock, vasodilation

Background

At present, there is a dearth of published literature concerning the hemodynamics of prolonged percutaneous mechanical circulatory support (pMCS). However, the pathophysiology of vasodilation in patients with acute myocardial infarctions has been described in particular after longer persistence of cardiogenic shock.^{1,2} A similar pathophysiology is seen in patients with congestive heart failure-related cardiogenic shock. Initially, reduced cardiac output and stroke volume are noted, and the body is trying to counteract the reduced blood pressure by vasoconstriction, at least in the beginning. Over time, inflammation increases and leads to a vasodilation state because of a pro-inflammatory response which might even be triggered by pMCS.

Unfortunately, we do not know when vasodilation truly occurs. We hypothesize it occurs earlier in patients that have undergone resuscitation, received MCS, or have active bleeding. We also know that patients with cardiogenic shock can develop concomitant septic shock and vice versa. Thus, a combination of cardiogenic and septic shock can affect treatment and outcomes.

Current Knowledge

Multiple options are currently available for MCS. Each option differs regarding flow, pump speed, cannulation, placement options, and ability to unload the right or left ventricle.³ The Society for Cardiovascular Angiography and Interventions (SCAI) recently updated and published its definition of cardiogenic shock.⁴ The SCAI SHOCK II definition advises the team to use MCS to reverse severe cardiogenic shock when a patient reaches stages D or E. The goal of MCS at those stages is to stabilize the patients and revert them to the A or B classification.

In addition, data from trials and registries have identified the cardiac power index as one of the strongest hemodynamic parameters to predict outcomes.⁵ It is calculated by multiplying the cardiac index by the mean blood pressure and a factor (i.e., 0.0022). Some randomized trials have shown that MCS can improve the cardiac index and, thereby, the cardiac power index.⁶ However, in an individual patient data meta-analysis, this could not be shown for MCS versus control.⁶

Importantly, reperfusion can stop ischemia. In general, it is thought that MCS along with inotropes and vasopressors

can increase inflammation, which leads to vasodilation.^{1,2} The timing and variance of inflammation may differ based on the type of device used. The answer remains unknown, and comparative data are needed.

In the intensive care unit, patients on MCS develop inflammation and vasodilation over time. This common observation is supported by a recent review article from Krychtiuk and colleagues.⁷ Once a patient enters the severe cardiogenic shock stages of D and E, often the systemic vascular resistance goes down. At the same time, the inflammatory activation increases, and systemic inflammatory response syndrome is observed. Of note, this summary of cardiogenic shock progression remains a theory and needs more data over time.

Jentzer and colleagues studied concomitant sepsis in patients with cardiogenic shock.⁸ Since 2000, the incidence of concomitant cardiogenic shock and sepsis has increased. The incidence is higher in patients with non-ST-elevation myocardial infarction (NSTEMI) than in those with STEMI. Without question, sepsis leads to vasodilation; thus, this parameter must be considered when treating cardiogenic shock.

The search for fast, objective, biomarker-based scores for cardiogenic shock prognosis continues. The CLIP-Score was recently developed from trial data and combines measures of renal function, tissue hypoxemia, inflammation, and heart failure (cystatin C, lactate, interleukin-6, and N-terminal [NT]-pro hormone Brain natriuretic peptide, respectively).⁹ This underlines the importance of inflammation in the cardiogenic shock progress, as shown in this objective prognosis score.

Among treatments with extracorporeal membrane oxygenation (ECMO), the combination with Impella devices (ECMELLA) for venting recently emerged. In theory, the concomitant use results in better pressure-volume curves and improved outcomes compared to ECMO alone, as shown in propensity-matched studies.¹⁰ However, patients with ECMELLA had more complications, including severe and moderate bleeding and hemolysis, access-site-related ischemia, and abdominal compartment syndrome.¹⁰

In terms of medical therapy, vasodilation is generally treated with vasopressors in the ICU. Norepinephrine is likely the strongest and best vasopressor we currently have; thus, it is recommended for use in patients with Impella or ECMO support who remain in hypotensive cardiogenic shock.¹

Currently, there is a lack of randomized evidence in cardiogenic shock. Only a few adequately powered trials have provided relevant data. There is strong evidence for early revascularization for an acute myocardial infarction, as it can reduce mortality.³ Multivessel coronary artery disease is present in roughly 80% of the patients with cardiogenic shock, and the CULPRIT-SHOCK trial determined that culprit lesion-only PCI is better than immediate-multivessel PCI.¹¹

Multiple trials have confirmed norepinephrine is better than any other vasopressor.³ However, more research is needed; thus, multiple large-scale randomized trials are underway.³

Disclosures

Dr. Thiele has received research funding for his institution from the German Research Foundation, German Heart Research Foundation, German Cardiac Society, European Union, Else-Kroner-Fresenius Foundation, Schwiete Foundation, and Boston Scientific.

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2022 Symposium Presentation

Microcirculation versus Macrocirculation in Cardiogenic

Shock

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Abstract

Macro- and microcirculation are important parameters in cardiogenic shock. Microcirculation is relevant for monitoring organ function and prognosis. Serum lactate might be the best daily life parameter to assess microcirculation, and the crude 8-hour value can be used for outcome prediction. Any treatment should consider the consequences of microcirculation and macrocirculation.

Keywords: microcirculation, macrocirculation, lactate, cardiogenic shock

Background

The terms micro- and macrocirculation refer to blood flow in vessels smaller than and greater than 100 micrometers, respectively. All forms of shock involve a vicious cycle centered around impaired microcirculation.¹ Organ function, perfusion, and failure all depend on microcirculation status. In cardiogenic shock, reduced cardiac output leads to hypoxia and acidosis. Atonia of the capillaries follows and leads to relative hypovolemia, creating a cycle of microcirculatory disorders. Thus, physicians must know how to assess microcirculation. The diagnostic tools have been reviewed.² This paper focuses on the tools of serum lactate and intravital microscopy.

Serum Lactate

Lactate is the alarm marker. In a large cohort of critically ill patients, arterial lactate levels above 1.4 mmol/L were associated with an increased risk of admission to the intensive care unit and hospital mortality.³ The IABP-Shock II trial reported that serum lactate levels greater than 4.6 mmol/L were associated with a higher risk of 30-day mortality (P<.001) in the cardiogenic shock population.⁴ After investigation, we determined that the best cutoff value regarding 30-day mortality is a baseline serum lactate level of 4.6 mmol/L.

Lactate clearance can also be used to assess lactate levels. A large study of more than 7000 patients with increased lactate levels compared different strategies to assess lactate clearance.^{5,6} One measure uses the delta-24 lactate levels, where the maximum lactate level on day 1 is compared to the maximum level on day 2. A dramatic difference was found at the 19% mark, indicating that a 19% change in lactate levels over one day has a strong prognostic role regarding short- and long-term mortality (P < .001). In the IABP-Shock II trial, lactate levels from survivors and non-survivors were compared at baseline, 0-8 hour clearance, and after 8 hours.⁷ Survivors had lower lactate levels at baseline (P < .001), and a negative clearance was found in non-survivors (-0.4). The crude 8-hour values can discriminate between groups, as survivors have significantly lower lactate levels (5.1 versus 1.7, P < .001). Of note, the area under the curve calculation was highest for the crude 8-hour values, and lactate levels at that timepoint can be used in daily practice.

Intravital Microscopy

Intravital microscopy is an imaging technique that uses dynamic, real-time three-dimensional, tissue-level images in vivo. Multiple devices are now on the market. Daniel de Backer was the first to use intravital microscopy in patients with septic shock and to provide a detailed description of how

it can document impaired microcirculation.⁸ Also, in patients with cardiogenic shock, video images can be derived from the sublingual mucosa and taken at the patient’s bedside.⁹ The images show that sustained microcirculation is associated with very low mortality rates compared to impaired microcirculation, which has a much higher 30-day mortality rate (P < .001). Analysis of sublingual images can even predict future lactate levels in these patients.

Impact on Treatment

In cardiogenic shock, micro- and macrocirculation are impaired; thus, it is of crucial importance to assess how treatment strategies affect not only macrocirculation but also microcirculation. For example, of catecholamines, epinephrine is not the first choice for treatment because it also affects microcirculation.¹ Epinephrine triggers strong vasoconstriction and limits organ perfusion; thus, alternatives that are less harmful to microcirculation are preferred.

Further, a clinical study using therapeutic hypothermia in cardiogenic shock patients assessed the effects of hypothermia on microcirculation hemodynamics.¹⁰ While the results were neutral, they underscore the importance of collecting microcirculatory parameters as endpoints in clinical studies. Macrocirculation often refers to blood pressure, so vasopressors and inotropic support should be titrated to reach a mean arterial pressure of around 65 mmHg, but not higher. Regulation and monitoring of microcirculation are more complex.¹¹ Monitoring lactate levels is one strategy to identify microcirculation abnormalities, but further research is needed.

Conclusion

Macro- and microcirculation are important parameters in cardiogenic shock. Microcirculation is relevant for monitoring organ function and prognosis. Serum lactate might be the best daily life parameter to assess microcirculation, and the crude 8-hour value can be used for outcome prediction. Any treatment should consider the consequences of microcirculation and macrocirculation.

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2022 Symposium Presentation

Early Unloading in Venoarterial Extracorporeal Membrane

Oxygenation Shock: When, How, Where, and Why?

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Abstract

As extracorporeal membrane oxygenation increases the left ventricular afterload, a successful treatment plan should include strategies to address this issue. One promising approach to do so is the addition of a second device for active left ventricular unloading. However, this relatively new approach is currently only based on retrospective data. This article summarizes the current perspectives on this approach, provides recommendations for its application, and highlights the need for randomized data on this topic.

Keywords: extracorporeal membrane oxygenation, percutaneous mechanical circulatory support, cardiogenic shock, heart failure

Why?

When extracorporeal membrane oxygenation (ECMO) is used to retrogradely perfuse the aorta, the left ventricle (LV) afterload increases. Although some patients can compensate quite well, others do not. Thus, myocardial recovery can be hampered, which might lead to fatal complications, such as an LV thrombus formation. Consequently, we need to think about the increase in LV afterload in ECMO patients. Thus, clinical teams that manage ECMO-supported patients must prepare protocols to address the increase in LV afterload, deciding on when an intervention is necessary or not.

How?

Patients receiving ECMO support for cardiogenic shock experience an increase in wedge pressure, a surrogate marker for LV end-diastolic pressure. Many institutions will add an Impella device (Abiomed) to decrease and normalize LV pressures in such cases. The combined Impella and ECMO support (ECMELLA) actively unloads the LV, thereby preserving or enabling myocardial recovery. Although

prospective, randomized data are lacking, some observational studies on using ECMELLA are available. In a recent study, more than 500 propensity score-matched patients were compared, indicating lower mortality in the ECMELLA cohort.¹ However, ECMELLA was also associated with more complications in that study. The rationale for this association is that a second mechanical circulatory support device requires secondary vascular access, so there is a higher risk of bleeding and ischemia. Thus, more work on decreasing the risk of complications with ECMELLA is needed, which might improve the benefit-risk ratio of this approach. For example, using ultrasound for vascular access alongside meticulous follow-up care might reduce the risk of severe bleeding or ischemic events.

In addition to the Impella device, other options for LV unloading exist. A Canadian meta-analysis showed that an intra-aortic balloon pump for LV unloading in ECMO patients might also work, and this therapy combination may contribute to counteracting the increase in LV afterload.² The best strategy for the patient depends on the hospital setting and the health care team’s familiarity and expertise with the specific percutaneous device.

When?

While early LV unloading may improve outcomes, using ECMELLA could also be seen as a bailout strategy. In the previously mentioned propensity score-matched study, the data implied that the use of ECMELLA is better earlier than later. In this regard, a recently completed follow-up analysis reviewed ECMELLA-supported patients receiving both devices within 24 hours and indicated that those with early LV unloading had a lower mortality risk than patients with a delayed LV unloading. In fact, the later the Impella was implanted after the ECMO, the higher the risk of mortality. Thus, this supports the use of LV unloading as a primary (early) treatment strategy rather than as a bailout strategy.

Where?

The LV unloading can be done in the catheterization laboratory or the operating room. Once again, the best place depends on the individual hospital setting and team expertise. Some hospitals use different strategies to address the increase in LV afterload, eg by centrally cannulating the patient on ECMO or using left atrial venoarterial (LAVA) ECMO. Other hospitals are familiar with the Impella device and complete the procedure in a catheterization laboratory. These preferences will primarily determine the best place to perform the LV unloading. The most important takeaway is that the increase in LV afterload is recognized as a relevant problem and that there is a structured way to assess and, if needed, to address it.

Conclusion

Because ECMO support increases the LV afterload, a successful treatment plan must include strategies to address this, tailored to the local expertise and resources. An interdisciplinary approach is necessary, as multiple experts need to work together to yield favorable results. ECMELLA support should be used earlier rather than later; however, this recommendation is based on retrospective data. Therefore, inherent bias does exist. Future prospective, randomized trials are planned.

Acknowledgments

Dr. Schrage has received funding from the German Research Foundation and the Else Kroner-Fresenius-Stiftung; he has received speaking fees from AstraZenaca and Abiomed.

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2022 Symposium Presentation

A Case of Inferior Myocardial Infarction Complicated by Ventricular Septal Rupture Leading to Cardiogenic Shock: Tandem Heart to the Rescue!

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Abstract

Ventricular septal rupture (VSR) is a rare but life-threatening complication of acute myocardial infarction. We present a case of VSR-related refractory cardiogenic shock that was successfully managed with TandemHeart® followed by surgical repair.

Keywords: ventricular septal rupture, myocardial infarction, cardiogenic shock

Background

Ventricular septal rupture (VSR) is a life-threatening, albeit rare, mechanical complication of ST-segment elevation myocardial infarction (STEMI), occurring in 0.3-2% of patients.¹ If left untreated, VSR in this setting can progress to cardiogenic shock, associated with a mortality rate of 94%.² Although the definitive treatment is surgery, this can often be challenging due to friable necrotic myocardial tissue and unstable hemodynamics. Surgical repair is associated with a mortality rate of 42.9%;² therefore, a multi-disciplinary approach should be considered when managing this grave complication.

We describe a case of inferior STEMI complicated by VSR and cardiogenic shock.

Case Description

A 30-year-old Hispanic male with a past medical history notable for hypertension and hyperlipidemia presented to the emergency room with a 1-week history of substernal chest heaviness and shortness of breath. Upon evaluation, the patient was hemodynamically stable with a blood pressure of 111/80 mmHg, heart rate of 105 beats per minute, and oxygen saturation of 97% on 2 liters of oxygen. Physical examination was positive for a new soft pan-systolic murmur at the left lower sternal border in addition to cold lower extremities. Electrocardiogram revealed ST-segment elevation in leads II and III, AVF associated with Q waves, reciprocal ST-segment depression in lead I, and AVL consistent with a subacute inferior STEMI (Figure 1).

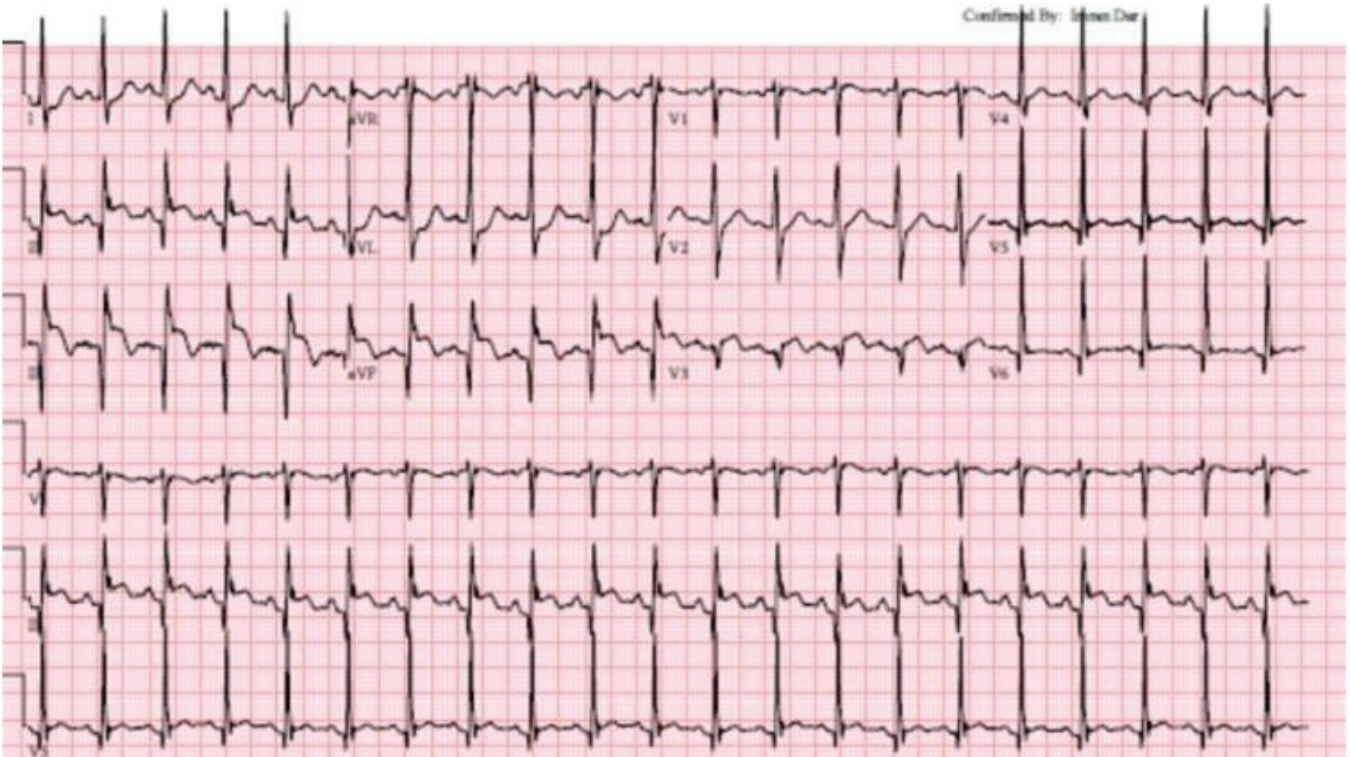


Figure 1. Electrocardiogram. ST-segment elevation in leads II and III, AVF associated with Q waves, reciprocal ST-segment depression in lead I, and AVL consistent with a subacute inferior ST-segment elevation myocardial infarction.

Pertinent laboratory work revealed a high sensitivity troponin I of 5500 ng/L (reference < 14.0 ng/L), serum creatinine of 3.2 mg/dL (0.7-1.3 mg/dL), blood urea and nitrogen of 50 mg/dL (6.0-24.0 mg/dL), aspartate transaminase of 2500 U/L (8.0-24.0 U/L), alanine transaminase of 3250 U/L (4.0-36.0 U/L), and lactic acid of 2.5 mmol/L (0.5-2.2 mmol/L), suggestive of end-organ hypoperfusion. Selective coronary angiography was performed, which showed a 100% ostial right coronary artery (RCA) thrombotic lesion, 70% stenosis in the mid and distal left anterior descending artery (LAD), diffusely diseased first obtuse marginal branch, and 70% mid left circumflex disease (Figure 2).

As a temporizing measure, balloon angioplasty of the culprit RCA ostial lesion was done, which partially restored blood flow (thrombolysis in myocardial infarction 2 flow) (Figure 3). Aspiration thrombectomy was attempted but unsuccessful due to technical difficulties. Ventriculography revealed left to right contrast shunting suggestive of a ventricular septal defect (VSD). This was confirmed with a bedside echo which illustrated a muscular VSD with evidence of left to right shunting and features of right ventricular dysfunction (Figure 4). Left ventricular function was preserved. Due to concerns for clinical and hemometabolic cardiogenic shock, an intra-aortic balloon pump was placed.

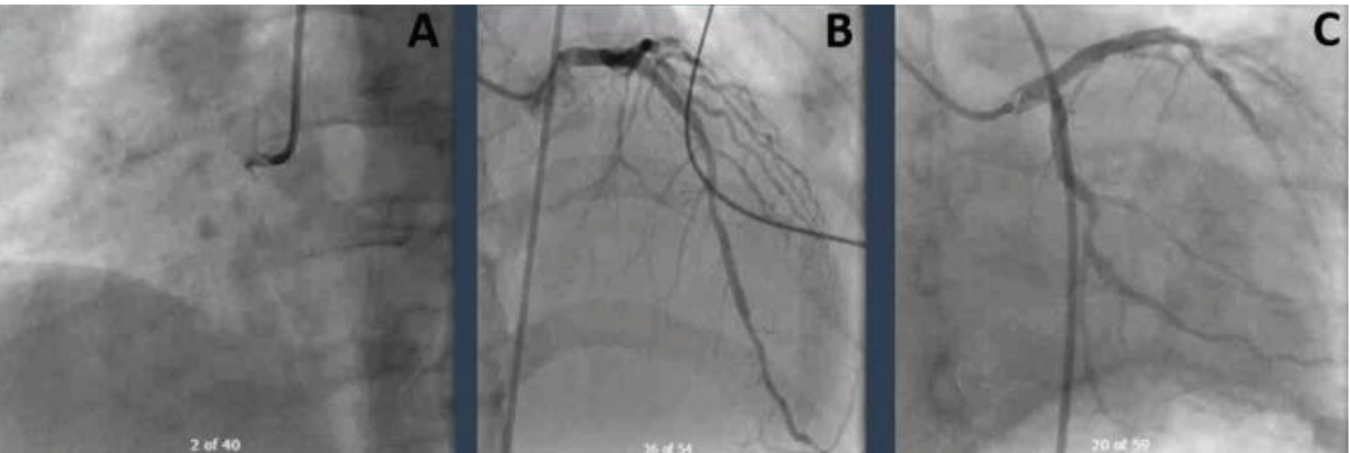


Figure 2. A) 100% thrombotic ostial right coronary artery lesion, B) significant mid and distal left anterior ascending artery disease, C) diffusely diseased obtuse marginal 1 and significant mid left circumflex disease.

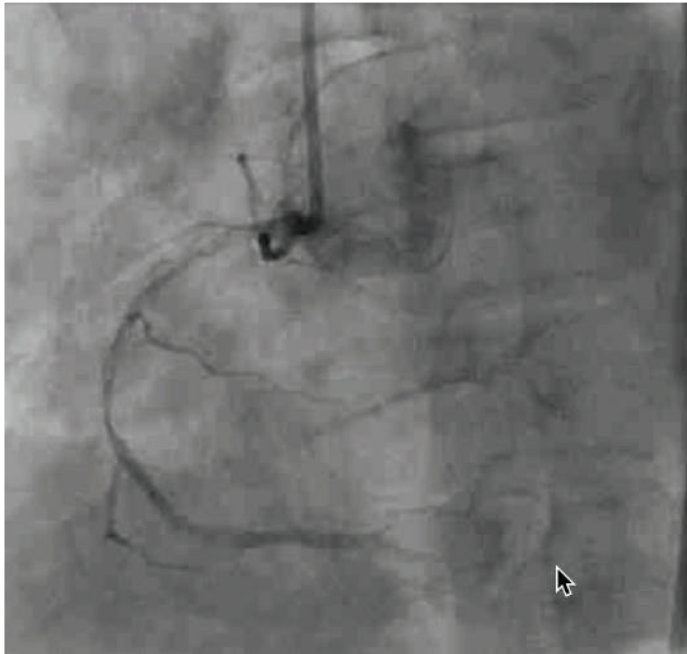


Figure 3. Patient status after balloon angioplasty of ostial right coronary artery lesion, demonstrating TIMI 2 flow.

Although the patient’s vitals remained stable 24 hours later, end-organ status continued to deteriorate with worsening lactic acidosis and liver and kidney function. The decision was made to proceed with placing a TandemHeart® to stabilize the patient. Within forty-eight hours of escalating mechanical circulatory support (MCS) to TandemHeart, the aforementioned hemometabolic parameters returned to normal.

Twelve days after initial presentation, the patient underwent two-vessel coronary artery bypass grafting with a left internal mammary artery to LAD and saphenous vein graft to RCA, patch repair of the VSD, and a switch of the TandemHeart to veno-arterial extracorporeal membrane oxygenation (V-A ECMO) intra-operatively to allow for right ventricular function recovery. The patient was eventually discharged home. Trans-esophageal echo revealed no residual shunting across the VSD.

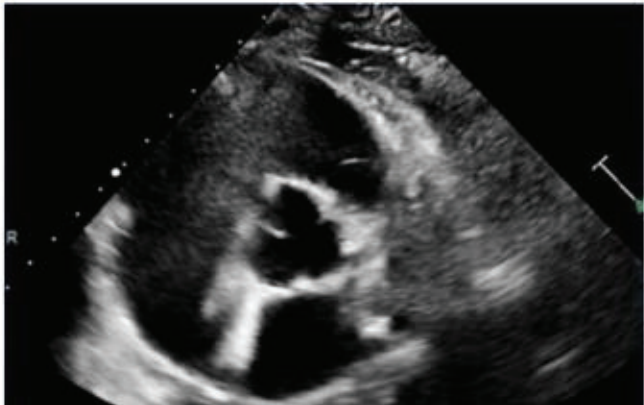
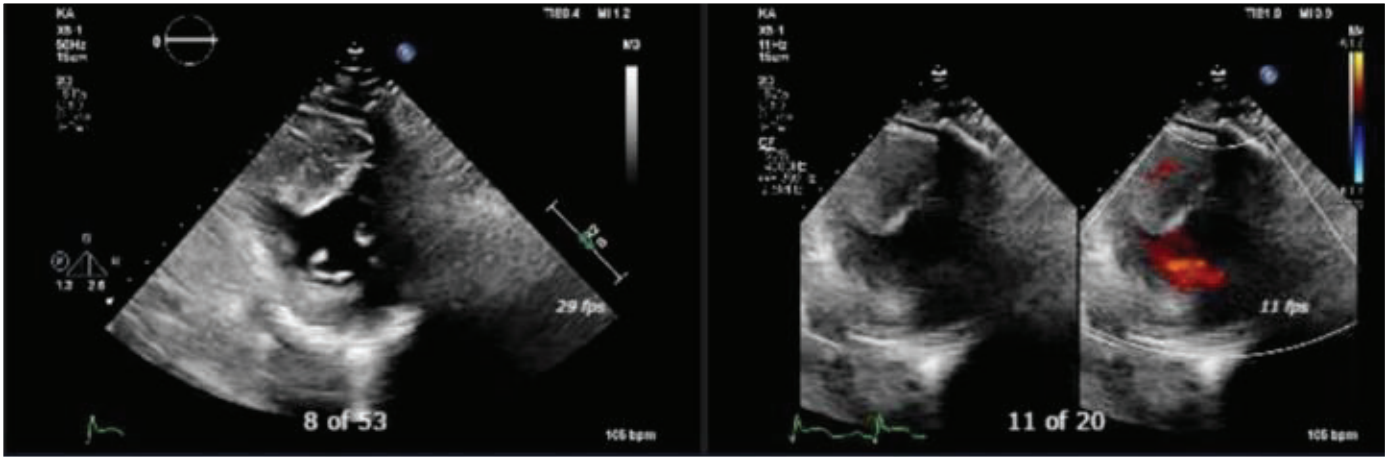


Figure 4. Echocardiographic images demonstrating ventricular septal defect with left to right shunting and an enlarged right ventricle.

Discussion

Although the incidence of post-STEMI VSR-related cardiogenic shock has decreased in the reperfusion era, it still carries a high mortality rate.² This case highlights the importance of prompt recognition and initial hemodynamic stabilization of patients experiencing this complication using contemporary MCS before surgical repair. We felt that TandemHeart was most suitable in this case as it is a left atrial to femoral artery bypass system that does not involve interacting interventricular septum. The theoretical risks of left ventricular unloading with an Impella device (Abiomed) include interacting with the friable necrotic myocardium around the VSR and inducing hypoxia by right to left shunting at the level of the ventricle. V-A ECMO can be used in STEMI complicated by VSR; however, accurately assessing right ventricular function before patch repair and its ability to recover after patch repair may be hindered, and as such, we feel the use of TandemHeart in acute VSR offers the best strategy to stabilize patients.

Conclusion

The optimal timing of definitive surgical repair of VSR remains controversial.¹ In this case, surgery was delayed to allow time for hemodynamic stabilization and healing of the myocardial tissue to increase the chances of successful surgical repair.

Acknowledgments

We would like to acknowledge and thank all of the healthcare providers involved with patient care.

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2022 Symposium Presentation

Management of Severe Aortic Stenosis in Cardiogenic Shock: Early Percutaneous Mechanical Circulatory Support or Emergent Transcatheter Aortic Valve Replacement?

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Abstract

Aortic stenosis (AS) affects an estimated 1.5 million patients in the United States, with 250,000 patients or more suffering severe, symptomatic aortic stenosis. A subset of these patients also have unrevascularized coronary artery disease and left ventricular dysfunction, representing an extreme risk population of AS patients. Cardiogenic shock (CS) complicates a small minority of AS presentations and/or patients referred for transcatheter aortic valve replacement (TAVR) but is responsible in these cases for a disproportionately high rate of morbidity and mortality. Indeed, CS results in a 4-fold increase in TAVR mortality, proportional to shock severity and largely independent of procedural complications. All patients undergoing TAVR should undergo an assessment of hemodynamics and vascular access as well as an estimation of risk for conduction system abnormalities, coronary occlusion, landing zone rupture, and stroke. In patients with pre-procedural CS or at a high risk of hemodynamic deterioration, preemptive or carefully planned, provisional use of mechanical circulatory support (MCS) helps ensure the best possible outcomes during TAVR.

Keywords: percutaneous mechanical circulatory support, cardiogenic shock, transcatheter aortic valve replacement

Introduction

It is estimated that as many as 1.5 million people in the United States suffer from aortic stenosis (AS).¹⁻³ While approximately 500,000 Americans are classified as suffering from severe AS, only half of these patients are symptomatic. Patients with severe AS, left ventricle (LV) dysfunction, and unrevascularized coronary artery disease are particularly susceptible to hemodynamic compromise due to limited myocardial reserve, propensity for ischemically-driven arrhythmias, and a further decline in LV systolic performance.¹ The timing and choice of AS treatment in the setting of these coexistent conditions may vary greatly given differences in local practice paradigms and the limited data available to guide therapy.

The interventional management of AS primarily focuses on pressure, volume, flow, and resistance. In reality, however, maladaptive remodeling processes frequently accompany AS,

introducing the deleterious effects of pulmonary hypertension, left ventricular hypertrophy, diastolic dysfunction, reduced coronary flow reserve, etc.¹ Thus, what ensues in the patient with severe AS and acute or chronic decompensation, is a complex interplay between numerous recognized and clinically silent variables. Furthermore, flow parameters in the aorta often vary in patients with severe or critical AS. Variable, asymmetric helical flow patterns have been observed in proximity to the aortic valve (AV) across the spectrum of bicuspid and tricuspid aortic valve disease.¹ While imaging and interventional cardiologists often take note of these flow disturbances, the clinical implications of these and other dynamics are infrequently acknowledged and incompletely understood.

Cardiogenic Shock and Aortic Stenosis

In patients presenting with cardiogenic shock, the incidence of AS is close to 6%.^{1,4} While AS is infrequently a

coincident finding, the mortality rate in such patients has historically been very high ($\geq 70\%$) if no durable valve intervention or surgery is performed during the index hospitalization.⁴ Medical therapy alone is almost always insufficient, and surgery is often avoided because patients are deemed a prohibitive surgical risk. Thus, the practical decision is to either perform high-risk transcatheter aortic valve replacement (TAVR) or attempt stabilization with mechanical circulatory support (MCS). It should be recognized, however, that in severe AS and worsening cardiogenic shock, it is often impossible to stabilize the shock state without valvular therapy.

A recent study linked data from the Society of Thoracic Surgeons (STS) and American College of Cardiology’s (ACC) Transcatheter Valve Therapy (TVT) Registry with claims data sourced from the Centers for Medicare and Medicaid Services (CMS) and identified patients who presented with cardiogenic shock in the setting of severe AS.⁴ Approximately 4.1% of patients who underwent TAVR in the United States suffered from cardiogenic shock prior to the procedure. The CS patients (n=2,220, median STS score=9.8%) were compared to the 12,851 high-risk patients without cardiogenic shock (median STS score=10.2%). Patients with cardiogenic shock had significantly higher 30-day mortality rates (19.1% versus 4.9%, $P < .001$) and higher rates of complications than non-CS TAVR patients. Interestingly, the gap between the cardiogenic shock cohorts did not close with time, and the mortality rate remained significantly higher at one year ($P < .001$). A subgroup of patients who met the modified Valve Academic Research Consortium-2 early safety criteria were also analyzed to evaluate the dependence of late adverse outcomes on procedural complications. The absence of 30-day major complications was not associated with a commensurate reduction in 30-day mortality in patients presenting with CS.⁴ Simply stated, cardiogenic shock conferred far worse short- and long-term clinical outcomes in TAVR, independent of any procedural complications. Observed 30-day post-TAVR mortality in the cardiogenic shock cohort was nearly 400% of the high-risk matched cohort. The mortality hazard appeared to be proportional to the degree of shock, as evidenced by inotrope usage, percutaneous MCS prior to TAVR, prior cardiac arrest, and use of cardiopulmonary bypass support.⁴

Optimal Technical Planning and Management

In all patients undergoing TAVR, an objective evaluation of preprocedural hemodynamics is a vitally important step in addition to a thorough assessment of vascular access along with an estimation of risk for conduction system abnormalities, coronary occlusion, landing zone rupture, and stroke. Scarsini, et al. compiled a pre-TAVR procedural planning checklist, integrating the aforementioned variables into an easily adaptable format.⁵ In patients already manifesting CS or at high risk for rapid hemodynamic compromise during TAVR, additional consideration is

mandatory for pre-emptive or bailout mechanical circulatory support. Villablanca, et al. proposed an algorithm using balloon aortic valvuloplasty (BAV) with Impella (Abiomed) support or backup in those patients where TAVR may be safely deferred until clinical stability is restored.⁶ Single or bilateral vascular access may be utilized, and in the setting of clinical decompensation or intercurrent oxygenation issues, MCS escalation to extracorporeal membrane oxygenation (ECMO) should be considered. If TAVR cannot safely be deferred in the setting of CS, a number of different options exist to provide left ventricular or biventricular support.⁶ One novel solution that has been proposed is a bi-atrial (left atrial (LA)/right atrial) drainage with a vented venous cannula across the interatrial septum returning oxygenated flow via an ECMO circuit through a femoral arterial cannula (LAVA ECMO).⁶ Such cannulation strategies, especially when performed under the duress of time and patient acuity, dictate the procedures to be performed at highly experienced TAVR centers.

Challenges to Operationalization: A Case Study

A 61-year-old female with morbid obesity (body mass index=47 kg/m²), numerous medical comorbidities, and a reduced ejection fraction of 40% was referred for treatment of severe AS. She had a history of multiple percutaneous coronary interventions (PCIs), including recent PCI with multiple drug-eluting stents implanted. Increasing chest pain and shortness of breath were noted prior to admission but were ascribed to her worsening AS, in the absence of any overt ischemic manifestations. Her calculated STS Score was high (12.4%), as was her estimated risk of major morbidity or mortality (46.1%), rendering surgical AVR a high risk. She was deemed suitable for TAVR based on adequate aortic valve complex and peripheral vasculature. The pre-TAVR checklist did not reveal any points of major concern. Based on CT-derived measurements, a 23-mm Sapien S3 (Edwards LifeSciences, Irvine, CA) TAVR implant was chosen. A detailed hemodynamic evaluation was not performed, as she was nominally normotensive, and hemodynamics obtained at the time of recent PCI were unremarkable.

Once in the hybrid operating room, ultrasound-guided, bifemoral arterial access was obtained, and after administration of therapeutic heparin, the patient’s activated clotting time was maintained at >300 seconds. A pigtail injection of the aortic root was performed in preparation for crossing the aortic valve. Shortly thereafter, profound hypotension was noted. After ruling out bleeding, vascular complications, and pericardial effusion, coronary angiography was performed, revealing complete thrombotic occlusion of the left main artery. It later became known that the patient had stopped antiplatelet medications one week prior in anticipation of TAVR, presumably leading to acute stent thrombosis. In the context of shock-resistant ventricular fibrillation and ongoing CPR, the patient was emergently cannulated for VA-ECMO

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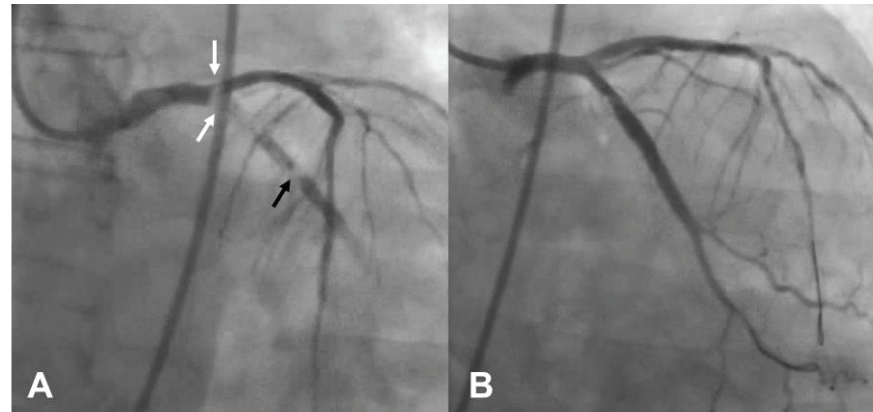


Figure 1. Thrombotic occlusion of the left main coronary artery (LMCA) bifurcation. Angiography was performed after cannulation for extracorporeal membrane oxygenation and stabilization of hemodynamics (Fig. 1A). revealed near-complete thrombotic occlusion of the LMCA bifurcation (white arrows) with resistant thrombus noted within the recently placed left circumflex stent (black arrow). After thrombectomy and PCI of the LMCA bifurcation TIMI III flow was successfully restored (Fig. 1B).

via the same femoral vessels intended for the performance of TAVR. Mean arterial pressure increased to 100 mm Hg, organized electrical activity returned, and PCI of the left main, left anterior descending, and left circumflex arteries were performed with adequate technical results (Figure 1). After discussion, TAVR was aborted in favor of hemodynamic stabilization on ECMO.

Two days later, the patient was still unable to be weaned off ECMO; thus, the decision was made to proceed with TAVR on VA-ECMO after confirmation of intact neurologic

function. A second large-bore femoral arterial sheath was placed contralateral to the ECMO sheath cannulation site. BAV was performed, during which time it was noted that the force of retrograde ECMO flow (4-5 L/min) rapidly moved the BAV balloon into the ventricle during inflation across the aortic valve. We, therefore, elected to deploy the TAVR valve with ECMO flows reduced to 1 L/min and rapid (190-200 bpm) pacing, resulting in a mean arterial pressure of ~20 to 30 mm Hg and zero arterial pulsatility, effectively ensuring that the TAVR valve remained precisely where it was intended to be deployed (Figure 2).

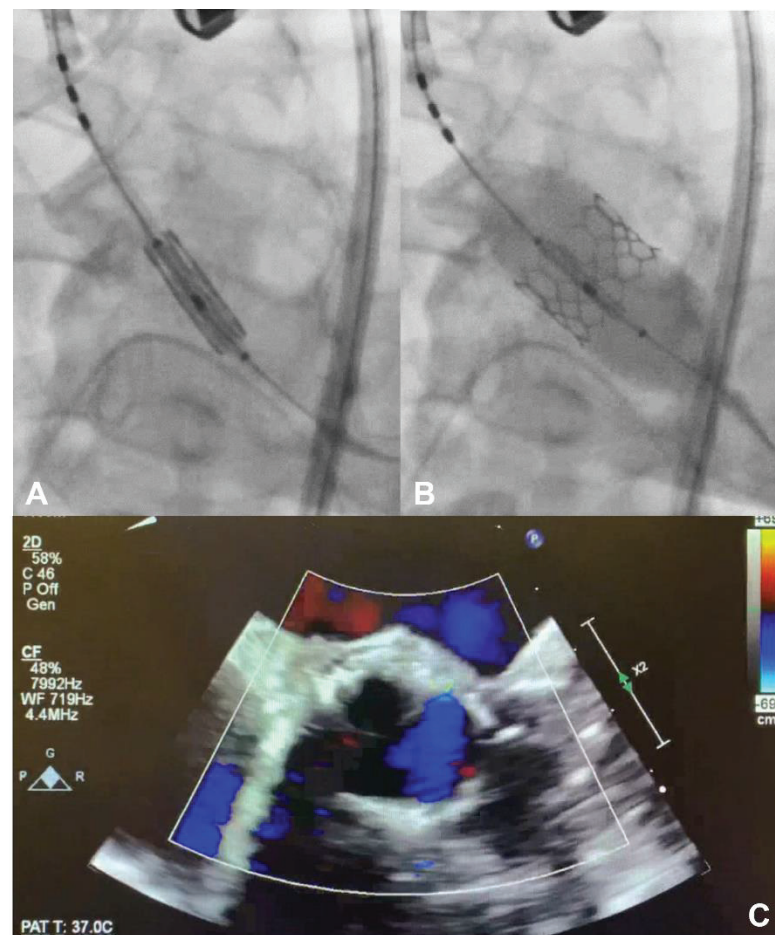


Figure 2. A 23 mm Edwards Sapien S3 transcatheter heart valve was deployed with rapid ventricular pacing at 200 beats per minute, and extracorporeal membrane oxygenation flows decreased to 1 L/min (Figs. 2A, B). Transesophageal echocardiography confirmed a well-seated valve with a trace paravalvular leak (Fig. 2C).

Immediately after valve deployment, pacing was discontinued, and ECMO flow rapidly increased to 4-4.5 L/min. The patient was successfully liberated from ECMO 2 days later, made a complete functional recovery, and she is alive and well over one year later.

Conclusion

In patients with severe AS and cardiogenic shock, management begins with gathering objective data. Other explanations for the shock state should be explored using invasive hemodynamics whenever possible. Immediate valve replacement may potentially be deferred if BAV with MCS is performed. A plan to proceed with TAVR during the index CS admission should mandatorily take primary and provisional hemodynamic support strategies into account.

Disclosures

Dr. Nathan has previously served as a consultant or received honoraria from Abiomed, Biotronik, Cardiovascular Systems, Inc., Getinge, Janssen, Medtronic, Merit Medical, Terumo Interventional Systems and Zoll.

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Role of Hypothermia in Cardiogenic Shock

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Abstract

While patient management in the intensive care unit has undoubtedly improved over the last 20 years, many questions remain. Neurological prognostication has become very important and aided in improving survival outcomes over time. The limited number of randomized control trials and limitations from currently completed studies leave the field with little certainty regarding targeted temperature management. In addition, implementing hypothermia can use multiple methods and protocols that impact the interpretation and comparison of results.

Keywords: hypothermia, cardiogenic shock, target temperature management

Introduction

To improve survival after sudden cardiac arrest, the American Heart Association published the concept of “the chain of survival” as early as 1991.¹ Peter Safar first used this phrase to describe the coordinated effort to gain spontaneous circulation by paramedics, emergency physicians, and intensivists.² As field care improved, the number of critically ill patients requiring care in the intensive care unit (ICU) grew. Currently, early mortality after resuscitation arises from the underlying cardiogenic shock state and the precipitating cause of cardiac arrest. Later mortality is largely caused by neurological injury and end-organ damage as a sequela of cardiac arrest.

36.0°C. Cooling actively prevents pyrexia, which decreases damage to the brain and other organs by lowering tissue metabolism, reminiscent of limiting the infarct size in the heart, post-myocardial infarction by attenuating ischemia/reperfusion injury. The evidence to support this recommendation stems from data indicating that fevers greater than 37.7°C are associated with a poor outcome. The worst outcomes are associated with temperatures greater than 39.0°C. Initial clinical trials with mild hyperthermia within 12 to 24 hours of care showed improved survival and neurological outcomes after out-of-hospital cardiac arrest in patients with shockable rhythms compared to usual care.³

Literature Review

Written guidelines strongly recommend the use of TTM despite evidence with low certainty. In 2019, the results of an open-label trial of 584 patients from 25 ICUs were published.⁴ Subjects experienced out-of-hospital cardiac arrest and were randomized to TTM or usual care regardless of shockable rhythm; the study failed to show the superiority of the use of TTM.

Target Temperature Management

Early data from the Hypothermia After Cardiac Arrest Study Group demonstrated a benefit from target temperature management (TTM),³ which is a strategy of deliberate temperature management with active cooling, rewarming, and extended fever control. The recommendation for all adult comatose patients with Glasgow Coma Scales less than 8 is to undergo TTM to achieve temperatures between 32.0 and

A more recent study from 2021 enrolled 1900 adults without a hospital cardiac arrest who were randomized to hypothermia with temperatures targeting 33°C or normothermia.⁵ The results of this randomized controlled trial (RCT) showed that both the hypothermia and the normothermia groups had a 50% mortality rate, and there was no difference concerning functional outcomes at six months for survival or neurological outcomes. Interestingly, arrhythmias were more common in the hypothermia group (24 vs. 17%), but there was no difference in other prespecified adverse events.⁵

A lot has changed in the last two decades regarding ICU care; thus, it is not surprising that this study directly contradicts the study published 20 years ago where the benefit of hypothermia was reported. Further, the more recent trial has several limitations, including the lack of a true control group.⁵ The intervention could not be blinded, which may have influenced the outcomes. In addition, about 20% of subjects were co-enrolled in another trial.⁵ A letter to the editor commented on several concerns that mainly related to the generalizability of the study.⁶ They noted that 75% of patients had a shockable rhythm, and only 80% of patients had received bystander cardiopulmonary resuscitation (CPR).⁶

With so much debate, a recent systematic review provides key takeaways.⁷ Over 3400 articles from 2001 to 2020 were screened, and 32 related trials were identified. Of note, only 9 trials compared normothermia and hypothermia (32 - 34°C). Most of the trials were small feasibility or pilot studies, with only 3 trials having more than 100 patients enrolled. The overall summary of this systematic review and meta-analysis was that TTM does not clearly provide a benefit when compared to normothermia, although the certainty of the evidence was low.⁷

Veno-arterial extracorporeal membrane oxygenation (V-A ECMO) has emerged as a viable therapy for cardiac arrest, particularly in the setting of extracorporeal CPR (ECPR). Studies are currently being conducted in France, the Czech Republic, and Taiwan to assess outcomes of ECPR in out-of-hospital cardiac arrest. More importantly, there have also been studies that considered V-A ECMO in an acute setting with hypothermia.⁸ The 2022 Extracorporeal Life Saving Organization Registry Report confirmed the survival to hospital discharge in adults with ECPR is as low as 30%. There is no further granularity concerning TTM in these patients. In considering ECPR with hypothermia, one of the first reports was from the CHEER Trial in 2015.⁸ This was a single-center, feasibility trial that compared only 26 patients. The authors concluded that hypothermia was associated with higher survival than ECPR alone.⁸

Duan and colleagues completed a meta-analysis of articles that evaluated CPR strategies for patients with cardiac arrest. They analyzed 21 full-text articles from 2000 to 2020.⁹ Many of the studies enrolled patients who had out-of-hospital

cardiac arrest, with most of these arrests being witnessed. There was inconsistent use of bystander CPR, and surprisingly, the time of initiation of cannulation ranged from 34 minutes to 185 minutes. More importantly, most of these studies were retrospective in nature, and only five studies were prospectively designed or included randomization and controls. Sample sizes ranged from 600 to 231 patients. There was a favorable rate of survival to hospital discharge over 28 days (odds ratio [OR] = 2.27) and better neurological outcomes in the group that received hypothermia (OR > 2.0). The benefit holds for survival outcomes at 3 months for both survival and neurological outcomes.⁹

This year, Levy and colleagues from the ECMO Net published the results of an RCT of early initiation of hypothermia versus normothermia for 24 hours in patients with cardiogenic shock supported with V-A ECMO.¹⁰ The multi-site study in France collected data from 20 centers between 2016 and 2019. They hypothesized that early hypothermia improves survival rates of patients with cardiogenic shock supported by V-A ECMO. A total of 374 patients were randomized, and they found that the hypothermia group had a lower mortality rate when compared to the normothermia group (42% versus 51%). However, this was not statistically significant, with a P-value of only .07.¹⁰ Likewise, a single-center experience with patients on V-A ECMO demonstrated improved neurological recovery with TTM, but there was no association with improved mortality with hypothermia.¹¹

Conclusion

While patient management in the ICU has undoubtedly improved over the last 20 years, many questions remain. Neurological prognostication has become very important and aided in improving survival outcomes over time. The limited number of randomized control trials and limitations from currently completed studies leave the field with little certainty regarding temperature management. In addition, implementing hypothermia can use multiple methods and protocols that impact the interpretation and comparison of results.

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2022 Symposium Presentation

Should All Shock Centers Offer ECPR? Balancing Futility, Cost Effectiveness, and Hope

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Abstract

There are over 400,000 out-of-hospital cardiac arrests (OHCA) in the United States annually. Of those, 50% are refractory cardiac arrest, defined as the lack of return of spontaneous circulation (ROSC) after 30 minutes of appropriate cardiopulmonary resuscitation (CPR) in the absence of hypothermia. Extracorporeal cardiopulmonary resuscitation (ECPR) has been increasingly used given its potential to improve survival and offer improved neurological outcomes.

Keywords: ECPR; extracorporeal cardiopulmonary resuscitation; cardiac arrest; out-of-hospital cardiac arrest, OHCA

Background

Out-of-hospital cardiac arrest (OHCA) carries a significant socioeconomic burden to society. Following OHCA, outcomes are favorable in patients younger than 75 years, with shockable rhythms (ventricular tachycardia or fibrillation), and adequate cardiopulmonary resuscitation (CPR) of less than 30 minutes. As the duration of CPR increases, the survival and likelihood of a favorable neurological outcome decreases dramatically, with very poor outcomes after 30 minutes of CPR. In light of retrospective data on OHCA and survival, extracorporeal cardiopulmonary resuscitation (ECPR) has been recently recognized as a potential approach to modulate this outcome and extend favorable outcomes to 45 minutes for those in refractory cardiac arrest [1].

For successful implementation of ECPR in OHCA, the connection between emergency medical service and extracorporeal membrane oxygenation (ECMO) teams, the different disciplines, proper training, and operator familiarity with performing ECPR are all critical elements. Japan, Korea and, to a lesser extent, Taiwan have the highest rate of ECPR

use worldwide. Currently, ECPR is only offered in select, pocketed locations in the United States.

Based out of Minneapolis, Minnesota, the ARREST trail was led by Dr Yannopoulos et al.² ARREST was the first US-based, randomized trial of ECPR. The study included adults aged 18 to 75 years presenting to the University of Minnesota Medical Center (MN, USA) with OHCA and refractory ventricular fibrillation, no ROSC after three shocks, automated CPR with a Lund University Cardiac Arrest System (LUCAS), and an estimated transfer time shorter than 30 minutes. Patients were randomized on arrival to the emergency room into one of two treatment arms: standard advanced cardiovascular life support (ACLS) or early ECMO-facilitated CPR.² A treatment algorithm for triage and management after arrival to the emergency department was used.

Survival to hospital discharge was observed in 1 (7%) of 15 patients (95% credible interval 1·6–30·2) in the standard ACLS treatment group versus 6 (43%) of 14 patients (21·3–67·7) in the early ECMO-facilitated resuscitation group. One of the primary concerns of offering ECPR up front in OHCA

is poor neurological outcomes with cerebral performance category (CPC) scores of over 4. However, the ARREST trial revealed that the neurological function was mainly preserved, and functional status scores were significantly improved after physical therapy and rehabilitation.²

It is important to consider complications of ECPR. ECPR should not be viewed as a *nothing to lose* solution because there are adverse events. Over time, ultrasound and fluoroscopy have led to less complications: about 36% if not used, compared to 8% when used.³ Limb ischemia was between 3% to 15%, infection 8% to 20%, and bleeding at the CPR site, insertion site, and abdominal bleeding were 28%, 49%, and 14%, respectively.

Based on the ARREST trial, the Minnesota Mobile Resuscitation Consortium (MMRC) brought the ECPR to the community. ECMO teams were deployed from an ECMO center to regional facilities to perform ECPR quickly. Their outcomes were surprisingly good, with 27 of 58 patients (47%) surviving to hospital discharge and 25 of 58 with favorable neurological outcome with a CPC score of 1 or 2. The data further validates the ARREST trial results.

Belohlavek et al. randomized 256 patients in a single center clinical trial in Prague, the Czech Republic, of adults with witnessed OHCA of presumed cardiac origin without ROSC to either an invasive strategy group of 124 patients (mechanical compression, followed by intra-arrest transport to a cardiac center for ECPR and immediate invasive assessment and treatment) vs regular ACLS in the standard strategy group.⁶ Thirty-nine patients (31.5%) in the invasive strategy group and 29 (22.0%) in the standard strategy group survived to 180 days with good neurologic outcomes (odds ratio [OR], 1.63 [95% CI, 0.93-2.85]; difference, 9.5% [95% CI, -1.3 to 20.1; *P* = .09). At 30 days, neurologic recovery had occurred in 38 patients (30.6%) in the invasive strategy group and in 24 (18.2%) in the standard strategy group (OR, 1.99 [95% CI, 1.11-3.57]; difference, 12.4% [95% CI, 1.9-22.7]; *P* = .02), and cardiac recovery had occurred in 54 (43.5%) and 45 (34.1%) patients, respectively (OR, 1.49 [95% CI, 0.91-2.47]; difference, 9.4% [95% CI, -2.5% to 21%]; *P* = .12). Bleeding occurred more frequently in the invasive strategy vs standard strategy group (31% vs 15%, respectively). Unlike the ARREST trial, the bundle of early intra-arrest transport, ECPR, and invasive assessment and treatment did not significantly improve survival with neurologically favorable outcome at 180 days compared with standard resuscitation.⁶ However, this study included shockable and nonshockable rhythms; 64% of patients had an arrest of over 45 minutes; LUCAS system was not used uniformly.

When combining data from the two clinical trials, especially OHCA with shockable rhythms, there is a clear mortality benefit from ECPR in OHCA.

Ongoing Clinical Trials of ECPR

There are currently several ongoing ECPR trials including EROCA, APACAR2, ECPB4OHCA, and INCEPTION. The INCEPTION study is being done in the Netherlands, where emergency medicine physicians follow a different approach and are cannulating patients on ECMO.⁷

A recent meta-analysis of ECPR with hypothermia favors therapeutic hypothermia with an odds ratio of survival of 2.27 (1.60, 3.23).⁵ Among 374 patients in the HYPO-ECMO randomized clinical trial, which is a clinical trial of patients who were eligible if they had been endotracheally intubated and were receiving venoarterial ECMO for cardiogenic shock for <6 hours. It was conducted in the intensive care units at 20 cardiac shock care centers in France between October 2016 and July 2019. Patients were randomized to either early moderate hypothermia (33-34 °C; n=168) for 24 hours or strict normothermia (36-37 °C; n=166). At 30 days, 71 patients (42%) in the moderate hypothermia group had died vs 84 patients (51%) in the normothermia group (adjusted odds ratio, 0.71 [95% CI, 0.45-1.13], *P* = .15; risk difference, -8.3% [95% CI, -16.3% to -0.3%]).⁸

Conclusion

All shock centers should consider implementing an ECPR program and therapeutic hypothermia. ECPR improves outcomes, and development of these programs is valuable in managing refractory cardiac arrest, while also benefiting patients in the timely implementation of ECMO, particularly those with potentially reversible causes.

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2022 Symposium Presentation

Systemic Inflammatory Response Syndrome and Mechanical Circulatory Support Devices

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Abstract

Systemic inflammatory response syndrome is an increased inflammatory state affecting the whole body. Mechanical circulatory support (MCS) is a temporary or permanent form of extracorporeal support that may have an associated complication of an exacerbated inflammatory response to the extracorporeal circuit. This brief review will focus on understanding the complex pathophysiology of inflammatory response to MCS, factors that influence the extent of the inflammatory response, the inflammatory response and outcomes as well as potential therapeutic strategies.

Keywords: mechanical circulatory support, extracorporeal life support, systemic inflammatory response syndrome

Introduction

Systemic inflammatory response syndrome (SIRS) is an exacerbated response of the human body to harmful stressors like infections, pancreatitis, burns, surgery, trauma, ischemia, reperfusion, or the presence of mechanical circulatory support devices (MCS) as well as others.¹ The current SIRS criteria are based on changes in body temperature, heart rate, respiratory rate, and white blood cell count.² MCS devices can provide circulatory support for patients with acute hemodynamic compromise as well as chronic end-stage heart failure, acute respiratory failure, or chronic respiratory failure as a bridge to lung transplantation.³ These devices include veno-arterial (V-A) and veno-venous (V-V) extracorporeal membrane oxygenation (ECMO), percutaneous right ventricular assist device (pRVAD) as well as percutaneous temporary left ventricular assist devices (pLVAD), intra-aortic balloon pump (IABP), left ventricular assist devices (LVAD) and total artificial heart (TAH).

Pathophysiology of the Inflammatory Response to Mechanical Circulatory Support Devices

Extracorporeal Membrane Oxygenation

The pathophysiology of inflammation during ECMO is extremely complex and not fully understood. The commencement of extracorporeal life support is associated with an instantaneous inflammatory response similar to systemic inflammatory response syndrome secondary to contact between a patient’s blood and the foreign surfaces of the ECMO circuit. The levels of proinflammatory cytokines and complement levels increase rapidly, which results in leukocyte activation.⁴ If the inflammatory response is severe and persistent without any compensatory anti-inflammatory response,⁵ it may lead to endothelial injury and end-organ failure.

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The factors implicated in the complex immune and inflammatory response to ECMO include:

- The contact system—factor XII, factor XI, prekallikrein and high-molecular-weight kininogen. The activation of these factors leads to formation of kallikrein and bradykinin, which in turn will promote coagulation and inflammation.⁴
- Intrinsic coagulation is triggered by the contact system, and extrinsic coagulation is activated as well to a lesser degree, promoting subsequent clot formation.⁴
- Platelet activation—has two critically important roles, the first one in hemostasis and the second one in triggering inflammation through the release of their granular content.⁴
- The complement system plays a critical role in the innate immune response. While its response to cardiopulmonary bypass has been described earlier in the literature,⁶ the interaction between complement activation and ECMO requires additional investigations.
- Endothelial cell activation is another key element in the inflammatory response during ECMO. The inflammatory mediators triggered in response to ECMO, lead to activation of the endothelial cells, which further exacerbates the inflammatory response by producing proinflammatory cytokines and increases the expression of adhesion molecules, leading to the increased migration of leukocytes.⁴
- Furthermore, neutrophils are also activated by the extracorporeal circuit. Upon neutrophil activation, the cells degranulate, releasing cytotoxic enzymes, which further exacerbate the inflammation leading to end-organ damage.⁷
- Cytokines play an important role in the innate immune response. Upon ECMO initiation, proinflammatory, as well as anti-inflammatory cytokines, are produced. The most studied cytokines in relationship to ECMO are TNF- α , IL-6, IL-8, and IL-10.⁴ Their precise roles require further investigations.

Indications versus Contraindications for ECMO

Recommended indications for the use of ECMO include refractory hypoxemia, use of mechanical ventilation for <7 days, risk of death greater than 50%, severe air leak syndrome, and a diagnosis of severe myocarditis or cardiogenic shock.⁴

Absolute contraindications include significant comorbidities from which a patient cannot recover. These include severe immunosuppression, sepsis with bacteremia, contraindications to systemic anticoagulation, severe multiple organ failure, severe aortic dissection, acute intracerebral hemorrhage, irreversible severe brain injury, critical congenital heart defects, chronic lung disease, and lethal chromosomal anomalies.⁴ Relative contraindications also include an age of 65 years or older, a body mass index greater than 30, prolonged ventilatory support, frailty, allosensitization with prolonged waitlist time, and limitations in vascular access.⁴ During the early phase of the COVID-19 pandemic, the Extracorporeal Life Support Organization recommended prioritizing young, previously healthy patients with only a single organ failure for ECMO support, as they may derive the maximum benefit.⁵ As clinical experience continued to evolve, these priorities were relaxed based on program experience and increased access to health care resources.

The Inflammatory Response to Ventricular Assist Devices

Heart failure patients with reduced ejection fraction have a baseline proinflammatory state secondary to myocardial infarction, cardiogenic shock, or acute or chronic systolic heart failure.

The mechanism through which VAD impacts inflammation remains to be fully understood. The two key elements involved in the body’s immune response are high levels of shear stress and the contact of blood with foreign materials.⁸ Leukocytes and platelets are continuously exposed to high shear stress resulting in their activation.⁹ Published data shows that neutrophils exposed to wall shear stress greater than 25 dyne/cm², lead to structural disruption.¹⁰ Moreover, the contact of leukocytes with foreign bodies leads to protein absorption, creating either an inert surface or a highly dynamic matrix, which can further promote cellular activation and adhesion.¹¹

Factors that Influence the Inflammatory Response

The factors that influence the extent of the inflammatory response include the etiology of shock, the patient’s clinical status (the degree of shock), the hemocompatibility as well as the performance of the mechanical circulatory device applied (ECMO, percutaneous LVAD or RVAD, surgically implanted VAD). Another critical factor that can influence the inflammatory response includes the trauma and potential complications associated with the device insertion.

The Inflammatory Response and Outcomes

Diakos et al. retrospectively analyzed the neutrophil-to-lymphocyte ratio (NRL) among 111 patients with cardiogenic

shock supported by V-A ECMO or pLVAD/pRVAD and found that compared to nonsurvivors, the survivors had a lower NLR (7.4±0.9 vs 14.4±11; *P*<.001). Setiadi et al. investigated Oncostatin M (OSM), a member of the IL-6 family of cytokines, as a potential biomarker to predict outcomes in 30 patients with ARDS requiring V-V ECMO support (manuscript in progress). Preliminary data showed that the percentage of pre-ECMO decannulation plasma OSM levels as compared to pre-ECMO cannulation levels was significantly lower in the recovered patients compared to expired patients.

Furthermore, OSM was also used as a potential biomarker to predict infections in patients with LVADs. A study that included 41 patients showed that elevated plasma OSM pre-LVAD implantation was associated with an increased risk of developing infections postimplantation as compared to the control.¹²

Potential Therapeutic Strategies

At this point, there is no proven therapy to mitigate an exacerbated inflammatory response. Most strategies are currently experimental and primarily target cardiopulmonary bypass. Therapies that were or are under investigation include steroids, statins, protease inhibitors, milrinone, monoclonal antibodies, mesenchymal stromal cells (animal model only), and extracorporeal cytokine absorber therapy. An interesting method is the potential removal of inflammatory factors by extracorporeal methods. In a study by Gruda et al., hemoadsorption through porous polymer bead devices reduced the levels of a broad spectrum of cytokines, pathogen-associated molecular patterns, damage-associated molecular patterns, and mycotoxins by more than 50%.¹³

Summary

The pathophysiology of the inflammatory response to MCS is extremely complex and requires further studies to better understand the interaction between the two key components: the host and the extracorporeal support. Using MCS in patients with a certain degree of inflammation or systemic inflammatory response syndrome adds to the complexity and requires additional research to better understand the patient and device interaction and to help advance the technology as well as potential therapeutics.

How do These Concepts Impact Clinical Practice?

By better understanding the complex pathophysiology of the inflammatory response to MCS, we can help to develop therapeutics, improve the current forms of extracorporeal circulatory support to minimize an exacerbated immune inflammatory response to the foreign circuits and pumps, discover inflammatory markers to help predict outcomes, and eventually provide better and safer patient care.

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SCAI SHOCK Stage Classification: What is Missing from the Latest Update?

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Abstract

The revised Society for Cardiovascular Angiography and Interventions classifications reflect graduation of severity within each stage and pathway by which patients progress or recover. However, they are limited regarding the following: their predictive role to guide therapy; escalation of therapy or referral; variability in diagnostic criteria and interpretation; presence of other disease modifiers and confounders; variability of etiology and reversibility of cause; response to therapy and trajectory to be taken into risk stratification; magnitude and phenotypes of end-organ damage. Thus, we need a modified risk score to predict the necessity to escalate therapy and consider advanced therapies, such as mechanical circulatory support. Future research on validation studies and reclassification analyses is needed.

Keywords: cardiogenic shock, classification

Background

In December 2021, the latest statement of the Society for Cardiovascular Angiography and Interventions (SCAI) shock stage classification for adult patients was endorsed by the American College of Cardiology (ACC), American College of Emergency Physicians (ACEP), American Heart Association (AHA), European Society of Cardiology (ESC) Association for Acute Cardiovascular Care (ACVC), International Society for Heart and Lung Transplantation (ISHLT), Society of Critical Care Medicine (SCCM), and Society of Thoracic Surgeons (STS).¹ Despite its recent publication, the consensus in the field is that this latest strategy needs refinement.

The original 2019 SCAI Shock Stages rank the severity of cardiogenic shock using the A, B, C, D, E scale.² The initial goal was to standardize the terminology used in the field. However, the practical utility of this system to guide management in a clinical setting has been challenging. While the extremes of the scale (A, D, and E) are now relatively agreed upon and recognized, the middle of the spectrum (B and C) can be more difficult to identify and use. Importantly,

the current stages identify severity, but they lack actionable terminology. To move classification systems forward, six current limitations need to be addressed (Figure). Each limitation includes a practical and simple solution that could be used in a future scoring system.

Ideally, future scoring systems should not measure and classify what *was* done but identify what *needs to be* done. The ideal scoring system can guide physicians on when and what type of care escalation is needed. Further, diagnostic and prognostic accuracy and management targets could be improved with additional standardization of variables and expansion of criteria to include important factors, such as etiology.

Conclusion

If these challenges in the current staging approach are addressed and incorporated in future iterations of cardiogenic shock classifications, the management of cardiogenic shock will certainly move forward.

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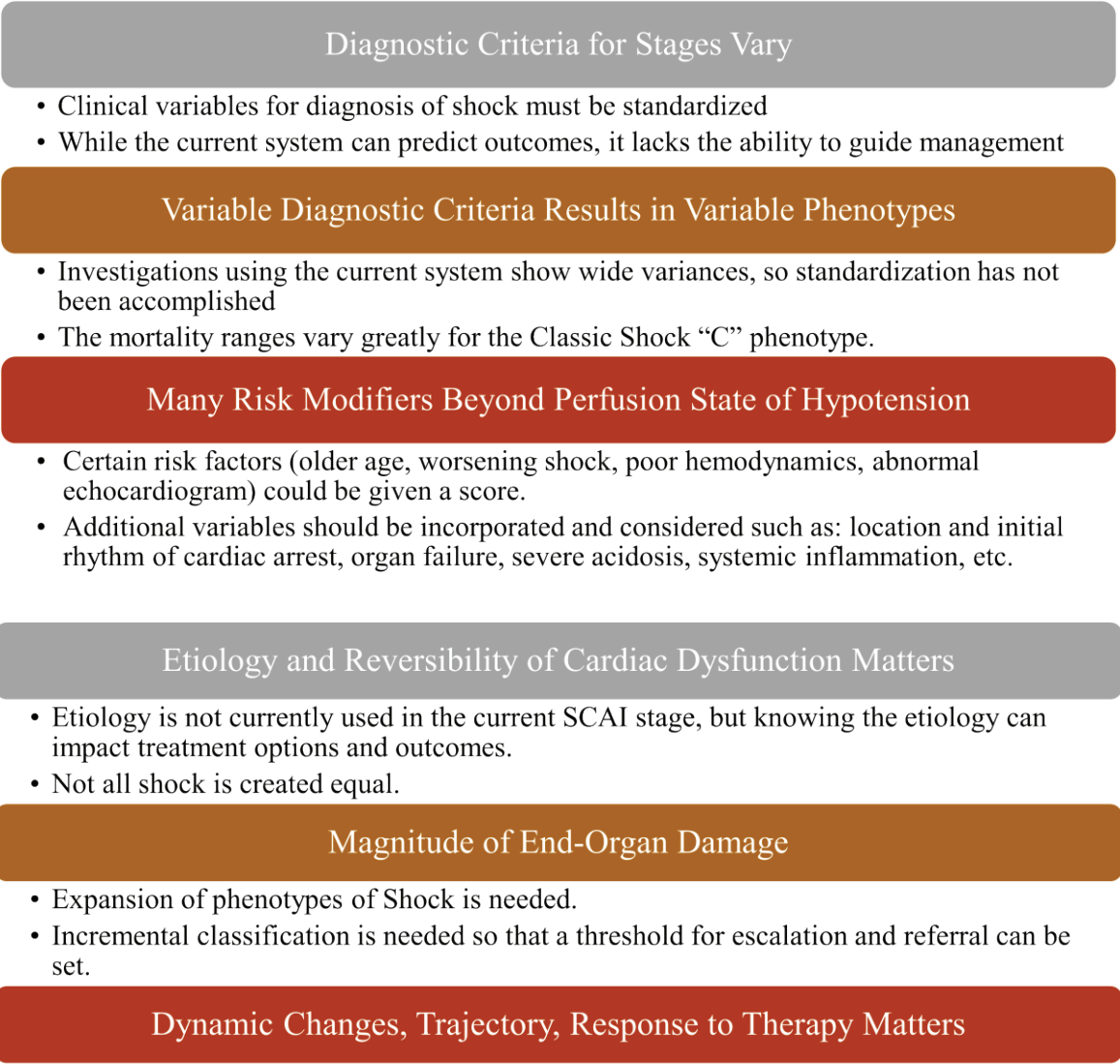


Figure. Summary of the challenges to the current cardiogenic shock classification scheme.

Disclosures

Dr. Bozkurt serves on clinical event committees for the GUIDE-HF Trial (Abbott Laboratories). She is a consultant for scPharmaceuticals, Amgen, Vifor, Relypsa, and Respicardia. Dr. Bozkurt also serves on the data safety and monitoring committee for the ANTHEM trial (LivaNova).

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2022 Symposium Presentation

Hemodynamic Variations in Cardiogenic Shock Phenotypes

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Abstract

Patients with cardiogenic shock are not all the same. They present with a variety of hemodynamic profiles and other features that may allow us to create specific phenotypes. It is possible that phenotyping these patients at presentation may then help us to identify the optimal and earliest therapies that will improve outcomes and, at the same time, help us to overcome some of the heterogeneity currently undermining clinical trials.

Keywords: phenotype, hemodynamics, heart failure, cardiogenic shock

Background

The guidelines for and definitions of cardiogenic shock are slowly evolving. Put simply, cardiogenic shock is a low cardiac output state that leads to end-organ hypoperfusion, tissue hypoxemia, and its sequelae. Ten years ago, a specific phenotype for hemodynamic shock was investigated, and separate phenotypes for cardiogenic hypovolemic shock were presented. However, we know now that not all cardiogenic shock is created equal. Patients in the cardiac intensive care unit with cardiogenic shock may have very different baseline characteristics, illness severity, shock presentations, and hemodynamic profiles.

Cardiogenic Shock Phenotypes

In 2017, the American Heart Association published a scientific statement that emphasized and reintroduced the concepts involved in understanding and managing cardiogenic shock.¹ There are multiple phenotypic and hemodynamic presentations for cardiogenic shock that include combinations of wet and dry volume status with warm and cold peripheral circulation. The classifications presented were extrapolated largely from the acute heart failure literature, but they were limited by the lack of research available at the time. Indeed, patients can present with classic cardiogenic shock in which their cardiac filling pressures and systemic vascular resistance

are elevated; this presentation is the classic cold and wet phenomenon. Other patients may present in vasodilatory cardiogenic shock and are relatively euvolemic with normal cardiac filling pressures. In fact, the seminal SHOCK Trial and Registry found that a quarter of patients presented with cardiogenic shock and a low systemic vascular resistance—an allusion to a sepsis-like phenotype for patients who are actually in cardiogenic shock.²

Thus, without question, cardiogenic shock has multiple phenotypes. The term *phenotype* means a set of observable characteristics of an individual brought about by the genotype interacting with an environment. Many clinicians in the field of heart failure have observed that patients with different phenotypes of cardiogenic shock may respond differently to the pharmacologic and mechanical support strategies that are available. Individual patient groups could be classified by phenotypic presentations and may have variable risk-benefit profiles, particularly when applying different therapeutic strategies. Further, completed clinical trials in the field have identified a marked heterogeneity in the cardiogenic shock population, which confounds the results. Thus, there is a high likelihood that the failure of the clinical trials to show demonstrable improvement in outcomes for certain therapeutic modalities, particularly mechanical circulatory support modalities, may be due to a lack of understanding of hemodynamic variations and phenotypes.

To complicate matters, the definition of cardiogenic shock has also varied between trials and guidelines.¹ Most definitions have minimal hemodynamic data and qualifiers as inclusion or exclusion criteria, which makes comparing results across studies difficult, if not impossible. As a proof of concept, Seymour and colleagues looked at a noncardiac population and were able to ascertain sepsis phenotypes through cluster and multidimensional cluster techniques.³ Each phenotype had different immune responses and outcomes. More recently, the Cardiogenic Shock Working Group used a cluster demonstration to identify hemodynamic phenotypes.⁴ However, the question now is, how do we use phenotype knowledge in practice?

Treatment

When treating patients in the cardiac intensive care unit, pathophysiology should be used to guide therapy, especially for patients receiving mechanical circulatory support services. By understanding and leveraging the knowledge of physiology, one can begin to see the different hemodynamic effects of our pharmacologic agents. Invasive hemodynamic information can identify what the appropriate pharmacologic therapy should be. If the patient is in classic cardiogenic shock with high systemic vascular resistance, an agent that increases contractility but also vasodilates would be ideal. However, if the patient has a low systemic vascular resistance or a mixed shock picture, adding a vasodilator may not be appropriate. Instead, an agent that increases systemic vascular resistance with or without increasing contractility might be better.

Historically, the pulmonary artery (PA) catheter has not been recommended for this patient population. In heterogeneous critical care populations, using a PA catheter did not demonstrably change outcomes.⁵ The ESCAPE trial confirmed the meta-analysis in an acute heart failure population and did not show a demonstrable benefit in the use of PA catheters for routine therapy. Thus, the PA catheter was “put to rest” in the mid-2000s, but there has been a resurgence in recent times. Today, cardiogenic shock and the use of temporary mechanical circulatory support strategies may benefit from an understanding of the hemodynamic and metabolic profiles of these patients; thus, the American College of Cardiology/American Heart Association Guidelines now support the use of PA catheters in patients with cardiogenic shock.

Conclusion

Invasive hemodynamic assessment is important for cardiogenic shock management. To understand how to more precisely leverage invasive hemodynamic information, however, more data is needed. For any patient profile, complexity should be balanced with practicality. Etiology, cardiomyopathy characteristics, and hemodynamics are factors that can contribute to developing an optimal and informative phenotype. A better understanding of the utility of patient phenotyping in cardiogenic shock should help to advance the field and optimize patient outcomes.

Disclosures

Dr. Katz has received research support from Abbott Laboratories.

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Case Report

Role of Veno-arterial Extracorporeal Membrane Oxygenation in Left Ventricular Conditioning after Lung Transplantation

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Abstract

End-stage pulmonary hypertension alters intracardiac pressures, leading to distention and failure of the right ventricle, leftward shifting of the intraventricular septum, and, thus, underfilling of the left ventricle (LV). Following the resolution of severely elevated pulmonary vascular resistance with bilateral lung transplantation, the LV is exposed to relatively high filling pressures from a potentially hypertrophic right ventricle pushing blood through normalized pulmonary vascular resistance. Veno-arterial extracorporeal membrane oxygenation (V-A ECMO) may be a valuable tool to provide a more gradual exposure of the LV to the newly available preload in the immediate postoperative phase of transplantation, thereby reducing the likelihood of primary graft dysfunction developing from the LV diastolic dysfunction. This paper presents a case in which V-A ECMO was initiated during cardiac arrest in a patient with advanced pulmonary hypertension and right ventricular failure and maintained for two days for postoperative patient stability and cardiac conditioning. The discussion includes data from transplant programs using this method to reduce the need for dual organ transplantation and postoperative primary graft dysfunction in the allograft.

Keywords: lung transplantation, diastolic dysfunction, right ventricular failure, veno-arterial extracorporeal membrane oxygenation, pulmonary hypertension, left ventricle remodeling

Background

Idiopathic pulmonary artery hypertension lung transplant patients have the highest 1-year mortality (about 25%). Still, they also have the second-best long-term survival rate compared to transplant recipients with other pulmonary diseases.¹ One factor contributing to this statistic is primary graft dysfunction (PGD) caused by a small and unconditioned left ventricle (LV) prone to developing diastolic dysfunction when exposed to a normal or relatively high pre-load after transplantation. These patients may benefit from veno-arterial extracorporeal membrane oxygenation (V-A ECMO) bridging peri-operatively to allow the LV time to condition to new filling pressures, thereby reducing the incidence of PGD in this population of transplant recipients.

Case Report

Patient History and Presentation

The patient, in this case, is a 46-year-old female who presents to the emergency department with four days of

worsening productive cough, shortness of breath, and abdominal pain. She has a past medical history significant for idiopathic pulmonary artery hypertension diagnosed in 2019, hypothyroidism, and type 2 diabetes. She complied with her home medication regimen of dual pulmonary artery hypertension therapy (bosentan and sildenafil) and optimized heart failure guideline-directed medical therapy (metoprolol succinate, spironolactone, and empagliflozin).

In the emergency department, she developed acute hypoxia with perioral cyanosis and cool extremities. Her arterial blood gas showed a compensated metabolic acidosis with a partial pressure of oxygen of 166 mm Hg and a lactate of 6.6 mmol/L, mild transaminitis, as well as elevated brain natriuretic peptide and troponin T levels. Her chest x-ray revealed an enlarged cardiac silhouette and right lower lobe consolidation.

Diagnosis and Intervention

Her initial transthoracic echocardiogram (Figure 1) showed a severely enlarged right ventricle causing a small LV internal diameter, moderate pericardial effusion without tamponade,

and abnormal septal wall motion. The parasternal short view showed a D-sign during diastole and systole. Per the report, there was no LV hypertrophy, and the diastolic function of the LV was difficult to determine. Her right atrium was severely dilated, and her tricuspid valve was reported as severely regurgitant with a dilated inferior vena cava and mild pulmonic valve regurgitation. Her initial right heart catheterization measured a pulmonary artery mean pressure of 59 mm Hg, pulmonary artery occlusive pressure of 9 mm Hg, right atrial pressure of 19 mm Hg, a Fick cardiac index of 2.17 L/min, and a pulmonary artery saturation of 55%. Following the procedure, she was initiated on intravenous (IV) treprostinil and dopamine with aggressive diuresis.

After titrating up to 21 ng/kg/min of IV treprostinil and 2 mcg/kg/min of dopamine, she underwent a second right heart catheterization, which showed refractory disease with a pulmonary artery mean pressure of 63 mmHg, pulmonary artery occlusive pressure of 10 mmHg, a right atrial pressure of 21 mmHg, and a Fick cardiac index of 2.39 L/min. At this time, the lung transplant team was consulted for evaluation, and five days later, she arrested and required intubation, V-A ECMO cannulation, and high-dose vasopressors. Her transthoracic echocardiogram following this event showed decreased LV function with an ejection fraction of 52%, and the right ventricle was decompressed by V-A ECMO, revealing some right ventricular hypertrophy.

Outcome

About a month after the arrest, she received a bilateral lung transplant and a tricuspid valve repair. She came out of the operating room on V-A ECMO. She required a massive transfusion for hemorrhagic shock postoperatively, leading to persistently elevated LV filling pressures despite diuresis. To

preserve her pulmonary artery anastomoses, her pulmonary artery diastolic pressure was used as a surrogate for a pulmonary artery occlusive pressure. It ranged from 10 mm Hg immediately postoperatively to 30 mm Hg after her transfusions. She developed grade 3 PGD, which slowly resolved with aggressive diuresis and intermittent, pharmacologic afterload reduction. Two days following her transplant, she was transitioned from V-A to veno-venous (V-V) ECMO with only minimal vasopressor support. After changing cannulation from V-A to V-V, her transthoracic echocardiogram (Figure 2) reported a hyperdynamic LV with an ejection fraction of 79%, indeterminate LV diastolic function, and an enlarged, hypertrophic right ventricle which was no longer compressing the LV.

Comment

The concept of right ventricular failure in the setting of pulmonary artery hypertension contributing to an unconditioned LV is not new.²⁻³ However, treatment approaches to this problem vary from peri-operative V-A ECMO to inotropes with aggressive diuresis. Primary pulmonary artery hypertension comprises 5-6% of lung transplantation nationally, and postoperative ECMO data is not tracked.¹ However, in the center where this case occurred, postoperative ECMO is rarely utilized in pulmonary hypertension lung transplant cases. This patient was particularly vulnerable to PGD because of her peri-operative mechanical ventilation and the large volume of blood administration due to coagulopathies related to IV prostacyclin analogue administration. She remained on V-A ECMO postoperatively, with the understanding that she was at high risk for developing PGD and requiring cardiac support in the immediate postoperative period that may not have been adequately supported with IV inotropes alone.

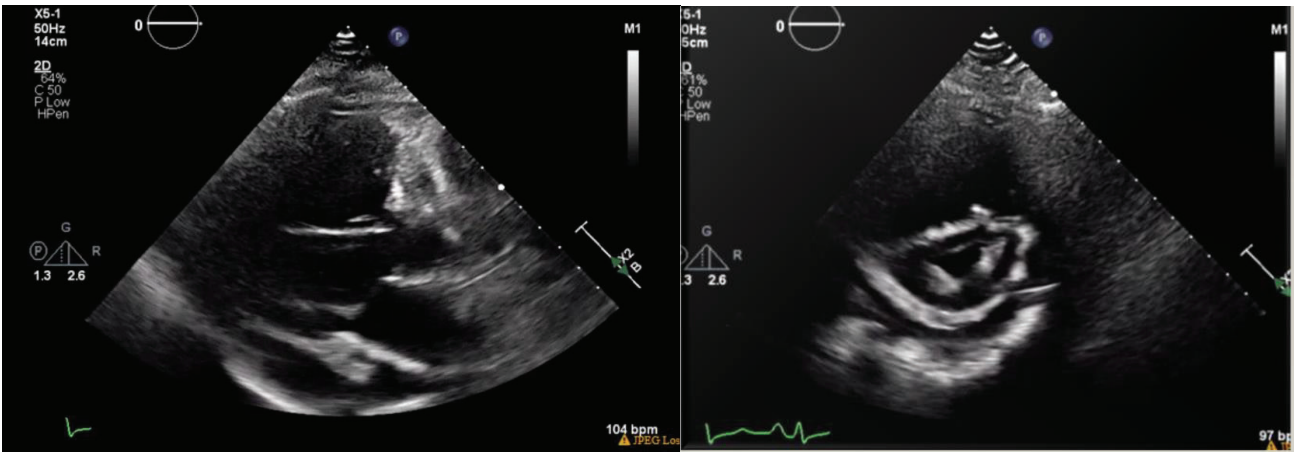


Figure 1. Pre-transplant transthoracic echocardiogram. Pre-transplant parasternal long axis and short axis views show a distended right ventricle and D-sign. Reported values: left ventricle ejection fraction 73%, left ventricle internal diameter during diastole 2.74 cm.

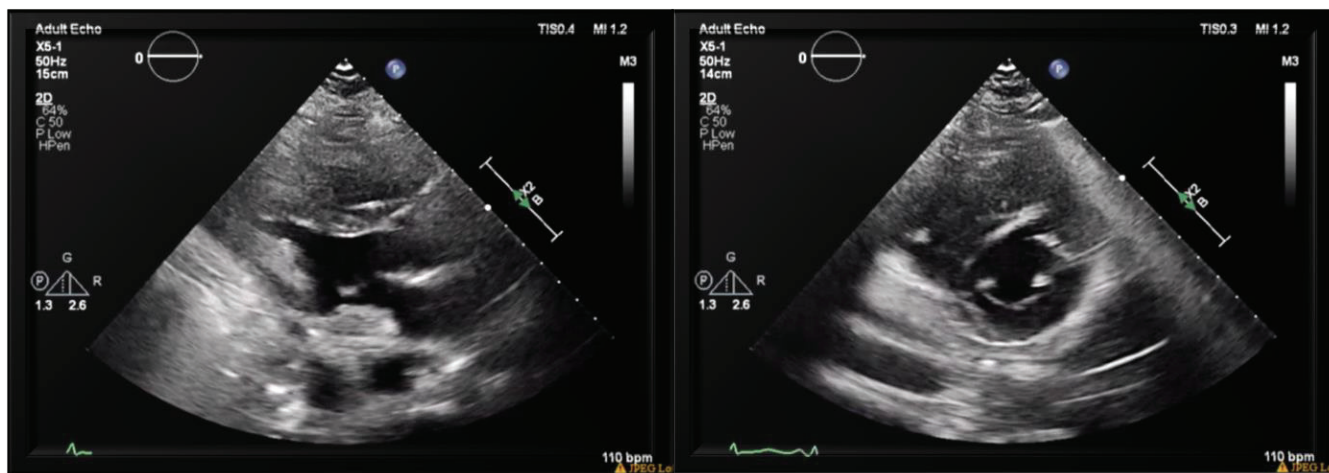


Figure 2. Post-transplant transthoracic echocardiogram. Post-transplant parasternal long axis and short axis views show a decompressed right ventricle and larger left ventricle internal diameter. Reported values: left ventricle ejection fraction 79%, left ventricle internal diameter during diastole 3.11 cm.

In 2002, a team in Austria published a prospective study (n=17) in which they found that peri-operative V-A ECMO, instead of cardiopulmonary bypass, reduces postoperative reperfusion injury by reducing forceful blood flow through the graft initially.⁴ Their study resulted in more controlled reperfusion, less aggressive ventilation strategies, and improved postoperative hemodynamics.⁴ Another prospective study of 23 bilateral lung transplants for patients with severe pulmonary hypertension in Germany looked at V-A ECMO as a bridge for LV conditioning while monitoring left atrial pressures, invasive hemodynamics, and LV diameter for weaning.⁵ They reported decreased total ventilator, intensive care unit, and inpatient days with increased 90-day and 1-year survival rates (94%) in their transplant-ECMO group as compared to their other groups.⁵

The physiology of a poorly conditioned LV also exists among the chronic thromboembolic pulmonary hypertension population, as evidenced by a study conducted in the Netherlands, which revealed a reversible reduction in LV free wall mass likely related to atrophic remodeling in the setting of right ventricular failure among patients with chronic thromboembolic pulmonary hypertension (CTEPH).⁶ Though the application of V-A ECMO is not without risk of complications, this is an exciting topic and deserves the focus of future research because of its potential to reduce the need for dual heart-lung transplantation and improve the one-year survival of pulmonary hypertension patients undergoing transplantation. The concept also may have application among CTEPH patients undergoing pulmonary thromboendarterectomy.

Acknowledgments

The author would like to acknowledge Dr. Eugene M. Golts for his mentorship during the preparation of this case presentation.

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Perspectives

Pulmonary Hypertension with “Normal” Pulmonary Vascular Resistance

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It is widely known and accepted that as heart failure progresses, the hemodynamic changes of increasing mean pulmonary arterial pressure (mPAP) and pulmonary vascular resistance (PVR) are compensated by concentric remodeling of the right ventricle (RV), thus maintaining a normal cardiac index (CI) and a normal right atrial pressure (RAP). As the disease progresses and the RV fails, a different hemodynamic profile is noted: an elevated RAP, a relative reduction in mPAP, a narrower pulmonary artery (PA) pulse pressure, and a drop in CI (Figure). Clinically, this manifests with early satiety, persistent volume overload, worsening liver congestion, and renal failure. If this is not corrected rapidly, further reduction in CI, protein-losing enteropathy, hypoalbuminemia, and anasarca ensue.

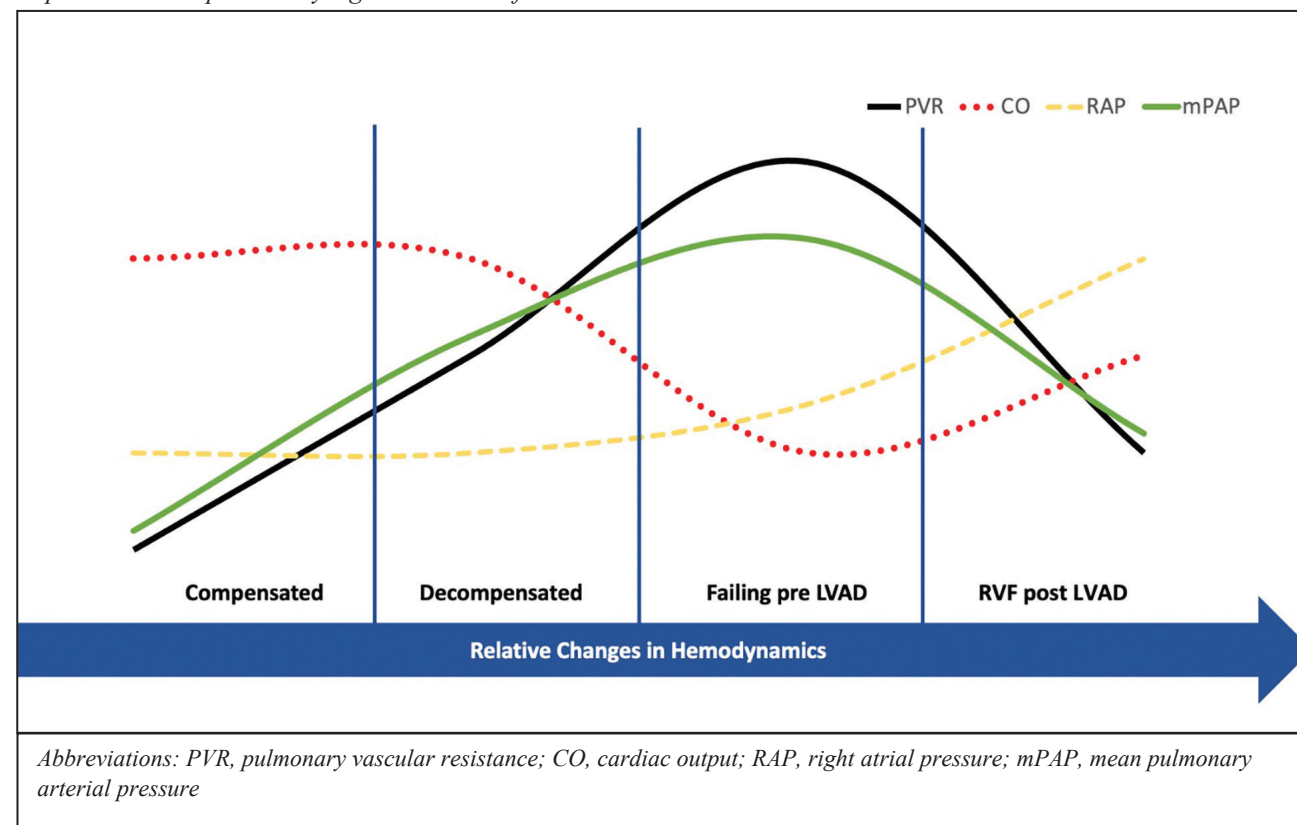
Orthotopic heart transplantation (OHT) is contraindicated in patients with high PVR (greater than 3 woods Unit) as it is associated with early graft dysfunction and increased mortality.¹ In longstanding stage D heart failure patients with elevated PVR, chronic unloading of the failed left ventricle with left ventricular assist device (LVAD) therapy allows for reverse remodeling of the pulmonary circulation and a reduction in PVR in most patients within six to twelve months.² This allows a previously high or prohibitive risk patient to become an acceptable risk with lower PVR and undergo successful OHT. However, some studies have also demonstrated that patients with a history of severe pulmonary hypertension pre-LVAD have a higher risk for in-hospital mortality after OHT, suggesting that reversal of pulmonary vascular remodeling may be incomplete and that PVR calculation is affected mainly by improvement in cardiac output (CO) rather than real changes in trans-pulmonary gradient (TPG). This underrecognized pulmonary vascular remodeling could be the substrate for pulmonary hypertensive crisis immediately after a heart transplant that would be

associated with primary graft dysfunction due to severe RV failure.³

In addition, a different clinical and hemodynamic profile is noted in a subset of patients with LVADs with severe refractory RV failure (Figure). Those patients suffer chronic sequelae of persistently elevated right-sided filling pressures with liver congestion, renal failure often necessitating renal replacement therapy, and a persistently vasodilated state. While they may appear stable with LVAD therapy, the hemodynamics of this state consist of a persistently elevated RAP > 15mmHg, equalization of chamber pressures in diastole, and normal to high CI. As such, PVR, calculated as TPG divided by CO, will not be elevated. CO calculations by thermodilution and Fick methods in this setting are often inaccurate due to severe tricuspid regurgitation and presumed fixed oxygen consumption, respectively. The reduction in mPAP is driven by RV failure, not by chronic LV unloading. Additionally, the obliteration of the diastolic gradient between pulmonary capillary wedge pressure and PA diastolic pressure is driven by RV failure.

As such, the commonly used parameters and calculations by which we assess RV afterload are often inaccurate in patients with LVADs with severe RV failure. PVR is often underestimated. We believe that this state of pulmonary hypertension with seemingly “normal” PVR (PHnPVR) is associated with a very high mortality rate, and exercising caution before listing these patients for heart transplantation is paramount. Perhaps using parameters of resistive and pulsatile afterload of the RV, such as pulmonary artery compliance and elastance, may better risk stratify this subset of patients. In light of the increasing utilization of LVAD therapy in heart failure patients, further research in understanding the incidence, implications, and prognosis of PHnPVR is critical.

Figure 1. Relative changes in hemodynamics as heart failure progresses and following left ventricular assist device implantation complicated by right ventricular failure.



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