University of CINCINNATI Emergency Medicine

ANNALS OF B POD

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ANNALS OF **B POD**
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IMPELLA SUPPORT

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History of Present Illness

The patient is a male in his 60s with a past medical history of hypertension, hyperlipidemia, ischemic cardiomyopathy, and heart failure with reduced ejection fraction (HFrEF, EF 20-25%) who presented to an outside hospital with chest pain. The patient endorsed substernal chest pain with worsening shortness of breath with no other associated symptoms. At the outside hospital, the patient was found to have dynamic EKG changes and subsequently received 325 mg of aspirin and sublingual nitroglycerin. The patient's initial troponin and brain natriuretic peptide (BNP) were elevated. He was started on a heparin drip, loaded with ticagrelor and was taken to the cardiac catherization lab. A left heart catheterization showed a 95% stenosis of the proximal left anterior descending (LAD) artery and 70% stenosis of the mid-LAD, and subsequently underwent percutaneous coronary intervention (PCI). His right heart catheterization showed elevated a pulmonary artery pressure of 64/30 mm Hg, an elevated pulmonary artery wedge pressure of 40 mm Hg, and a low cardiac output of 2.4 L/min by Fick method. As such, an Impella percutaneous left ventricular assist device was placed and a helicopter based critical care transport medicine team was called for transport to the nearest tertiary care center with a cardiovascular intensive care unit (CVICU).

$EtCO_2$
29

HR
114

BP
142/76

RR
22

SpO2
97% on RA

Past Medical History

Hypertension
Hyperlipidemia
Heart failure with reduced ejection fraction
Ischemic cardiomyopathy

Past Surgical History

None

Medications

Aspirin 81 mg daily
Atorvastatin 80 mg daily
Torsemide 20 mg daily
Metoprolol XL 12.5 mg daily

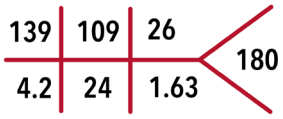
Allergies

None

Physical Exam

The patient was tachypneic but in no acute distress. The patient was tachycardic with decreased breath sounds at the bases bilaterally and coarse breath sounds. The patient had an Impella catheter in the right groin with good hemostasis at the insertion site, and a Swan-Ganz catheter in the right internal jugular vein. The patient had 3+ pitting edema in the bilateral lower extremities with strong pulses in all four extremities.

Diagnostic Tests



Troponin: 0.51
BNP: 3408
CXR: bilateral pulmonary edema and an enlarged cardiac silhouette

Hospital Course

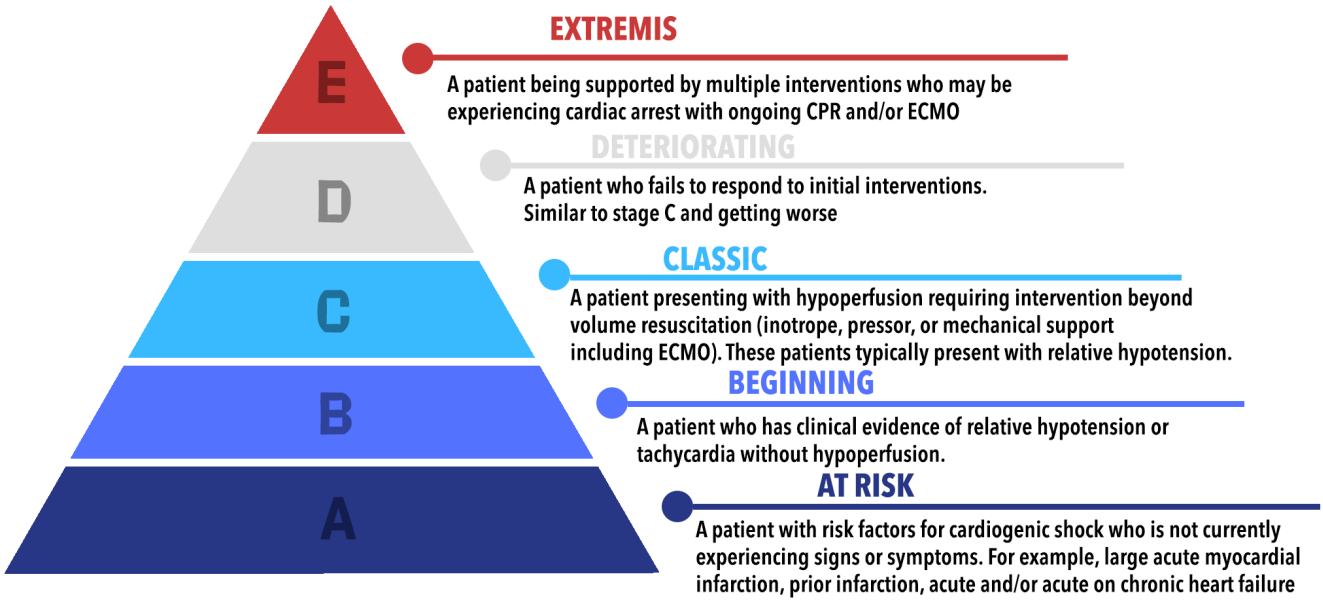
The patient had an uneventful transport to the CVICU at the tertiary care center. The patient underwent diuresis and was weaned from the Impella on hospital day two without complication. The patient was continued on 81 mg aspirin, and 80 mg atorvastatin. The patient's diuresis regimen was increased to Torsemide 40 mg daily and the patient was started on 90 mg ticagrelor daily for his stent, 25 mg metoprolol XL and 25 mg losartan daily for his congestive heart failure. It was recommended that the patient be discharged with a LifeVest; however, the patient declined.

Discussion

Cardiogenic Shock, the Pressure-Volume loop and the physiologic consequence of the Impella

Cardiogenic shock (CS) represents a spectrum of hemodynamic deficits in which the cardiac output is insufficient to provide adequate tissue perfusion. A commonly used definition for CS, adopted by the SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) and IABP-SHOCK II (Intra-aortic Balloon Pump in Cardiogenic Shock II) trials (Table 1), uses the presence of three objective factors: systolic blood pressure of less than 90 mmHg for more than 30 minutes or need for infusion of catecholamines, clinical signs of pulmonary congestion, and impaired end-organ perfusion.[1,3] While a technical definition is necessary for research, this definition of CS does not capture the continuum of disease observed in a clinical setting. To this end, the Society of Coronary Angiography and Intervention (SCAI) released a definition and classification schema in 2019, which attempts to better classify this continuum and may bridge the gap from bench to bedside (Table 2).[4] The SCAI classification schema acknowledges that patients present at different clinical stages and may benefit from different treatments along the CS continuum. The four classic phenotypes of CS are categorized based on volume status and cardiac output as described in Table 1.

SCAI Stages of Cardiogenic Shock



SCAI SHOCK STAGE	PHYSICAL EXAM	BIOCHEMICAL MARKERS	HEMODYNAMICS
A	Normal JVP Lung souds clear Strong distal pulses Normal mentation	Normal renal function Normal lactic acid	Normotensive (SBP ≥ 100 or normal for pt). If hemodynamics done: Cardiac index ≥ 2.5 CVP < 10 PA Sat ≥ 65%
B	Elevated JVP Rales in lung fields Strong distal pulses Normal mentation	Normal lactate Minimal renal function impairment Elevated BNP	SBP < 90 OR MAP < 60 OR > 30 mmHg drop Pulse ≥ 100 If hemodynamics done: Cardiac index ≥ 2.2 PA Sat ≥ 65%
C	Ashen, mottled, dusky Volume overload Extensive Rlaes Killip class 3 or 4 BiPap or mechanical ventilation Acute alteration in mental status	Lactate ≥ 2 Creatinine doubling OR >50% drop in GFR Increased LFTs Elevated BNP Urine Output <30ml/h	Drugs/device used to maintain BP above stage B values. Cardiac index < 2.2 PCWP > 15 RAP/PCWP ≥ 0.8 PAPI < 1.85 Cardiac Power Output ≤ 0.6
D	Any of Stage C	Any of stage C AND deteriorating	Any of stage C AND Requiring multiple pressors OR addition of mechanical circulatory support devices to maintain perfusion
E	Near pulselessness Cardiac collapse Mechanical ventilation Defibrillator used	Lactate ≥ 5 pH ≤ 7.2	No SBP without resuscitation PEA or Refractory VT/VF Hypotension despite maximal support

Table 1: SCAI Stages of cardiogenic shock[30]

Pressure Volume Loop:

The fundamentals of cardiogenic shock can be understood through perturbations of a classic concept in cardiovascular physiology: the pressure-volume (PV) loop (Figure 1). The PV loop is a graphical depiction of the cardiac cycle comprised of four distinct phases creating a closed loop.

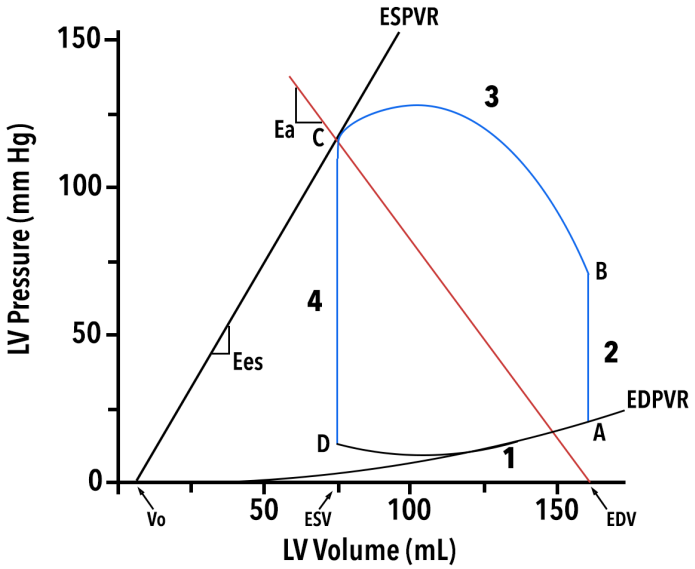


Figure 1: Pressure-Volume Loop
The four distinct phases of the PV loop are: ventricular filling, isovolumetric contraction, ejection, and isovolumetric relaxation. The transition between each phase is displayed as a point on the PV loop. Point A represents the pressure and volume in the ventricle at the end of diastolic filling, i.e., end diastolic pressure (EDP) and volume (EDV). After isovolumetric contraction (phase 2), point B corresponds to aortic valve opening, when the intraventricular pressure overcomes aortic diastolic pressure. Point C occurs after ejection when the aortic valve closes, representing the end systolic pressure and end systolic volume. Phase four represents isovolumetric relaxation of the left ventricle between point C (aortic valve closure) and point D (mitral valve opening). After mitral valve opening occurs at point D, ventricular filling (phase 1) commences, restarting the cycle.

The PV loop is bound by the end-systolic pressure-volume relationship (ESPVR) and the end-diastolic pressure-volume relationship (EDPVR). The ESPVR describes the connection between the end systolic pressure and the end systolic volume under the direct influence of ventricular contractility. The ESPVR models the linear (slope EES) relationship between the end systolic pressure (PES) and the end systolic volume (ESV) where the X-axis intercept (V0) represents the blood required to fill the ventricle before an increase in pressure is observed. The ESPVR will shift leftwards and upwards with increases in ventricular contractility and rightward and downward with decreases in ventricular contractility with little changes in V0. EES is a load-independent variable of ventricular contractility and changes proportionally with contractility.[5,6]

The EDPVR is a nonlinear PV relationship which characterizes the passive ventricular properties observed in the relaxation of the ventricle. This is described in the below equation, where constants α and β relate to mechanical properties of the extracellular matrix of the ventricle (where P = pressure; V = volume). Changes to these constants and the EDPVR can be observed in pathological states that change the myocardial matrix. Leftward shifts are observed with a thickened or more resistant myocardium (hypertrophic cardiomyopathy, sarcoidosis, and other infiltrative diseases) while rightward shifts are observed during dilated cardiomyopathy.

$$P = \beta V\alpha$$

Ventricular-vascular coupling is a concept that connects the ventricle to the vasculature ultimately describing how cardiac parameters (stroke volume, mean arterial pressure, etc.) are determined by systemic hemodynamics (preload, afterload, etc.). A line connecting the end diastolic volume (EDV) on the X-axis (volume) to the end-systolic pressure point on the PV loop creates the Ea line. The term Ea is used to describe the slope of this line and is related to the total peripheral resistance (TPR) and heart rate (HR).[6]

Ea = TPR x HR

Myocardial Oxygen Consumption (MVO_2):

PV loops can aid in characterizing the determinants of myocardial oxygen consumption. The area within the PV loop is referred to as the stroke work (SW). SW can be used to determine the cardiac power output (CPO) which is used as an index of severity in CS, and often trended to assess responses to therapies. CPO is inversely correlated with mortality in the setting of CS, with values < 0.6 watts (W) associated with hemodynamic compromise and increased mortality.[27]

CPO = SW x HR

Where SW = stroke volume x mean arterial pressure (MAP)
Clinically, it is more feasible to calculate CPO using cardiac output (CO) and the below equation.

CPO = (CO x MAP) / 451

Myocardial oxygen consumption (MVO2) is linearly related to the pressure volume area (PVA). The PVA is the sum of the SW and the potential energy (PE). PE is the determined by calculating the area bound by ESPVR and the EDPVR at LV volumes below the PV loop (Figure 2A). PE represents the residual energy stored in cardiac myofilaments at the end of systole. To practically estimate the PVA, Saurent et al. employ simple expressions of the PVA to characterize

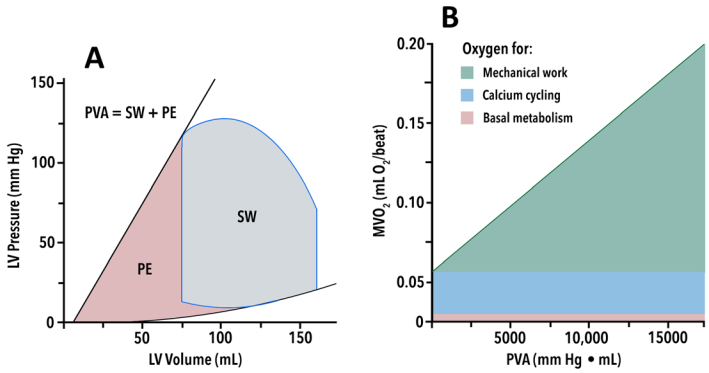


Figure 2: Pressure Volume Area and Myocardial Oxygen Consumption[31]

the total MVO2 based on hemodynamic points on the PV loop.

PVA = SW + PE
MW = (ESV-EDV) x (Ppeak – EDP)
PE = 0.5 x ESV x (Ppeak – EDP)

The components of MVO2 are displayed in Figure 2B: basal metabolism, calcium cycling, and mechanical work. It should be noted that as contractility increases, the slope of the PVA line does not

steepen. However, the Y-intercept will climb as increased contractility is largely the result of augmentation of calcium cycling. While HR does not have a significant effect on MVO2 per cardiac cycle, it does have a significant effect on MVO2 per minute as small differences between cycles are amplified.[8,9]

Hemodynamics of Cardiogenic Shock (CS):

The PV loop can aid in characterizing the hemodynamic effects of acutely decreased ventricular contractility in CS (Figure 3). In the initial stages of decompensated CS, most commonly due to acute myocardial infarction (AMI), the ESPVR shifts rightward and downward, while a small elevation is observed in the EDPVR. These changes produce a drop in SW and, subsequently, CPO. Clinically this leads to hypotension, represented by the shrinking height of the PV loop, and cardiac output declines as well.

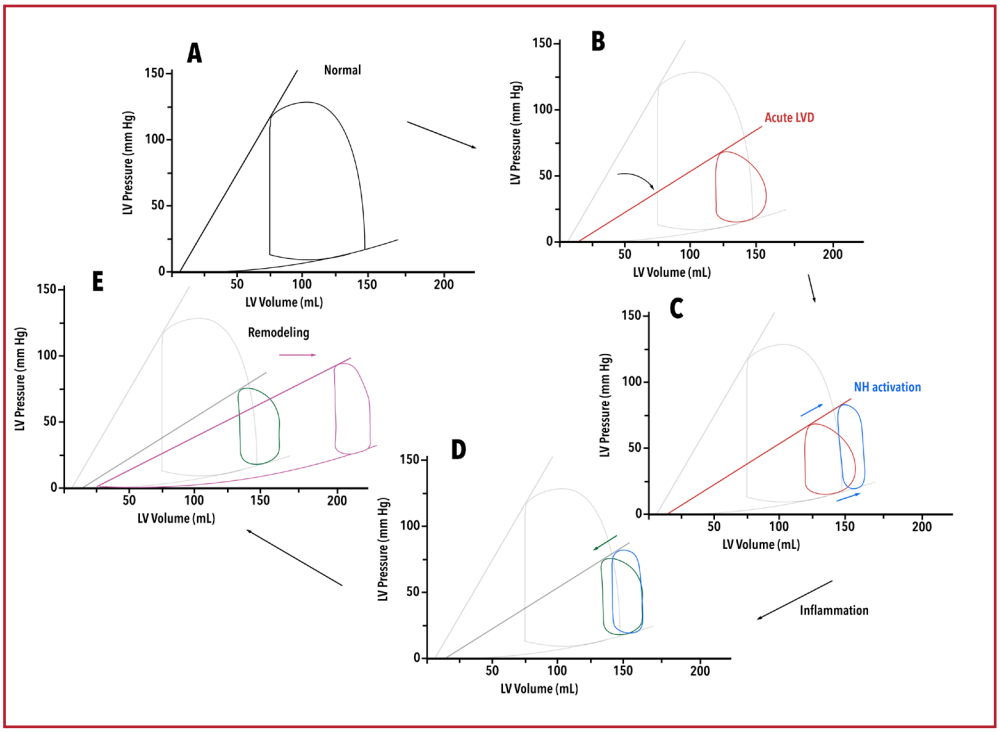


Figure 3: Pressure Volume Loop of Cardiogenic Shock[32]

Compensatory response to CS can also be characterized by the PV loop (Figure 3 C). Neurohormonal activation, the release of catecholamines from the adrenal gland, is the first compensatory response to an acute decrease in ventricular contractility. Total peripheral resistance, HR and contractility increase in response to catecholamines. In addition to the vasoconstriction, venoconstriction also occurs, shifting intravascular volume from high-capacity reservoirs (splanchnic circulation) to low-capacity reservoirs (vena cava and large veins), ultimately increasing central venous circulation (Funk). Collectively, the neurohormonal compensatory effects increase blood pressure but cause a rightward shift of the PV loop through an increase in the end diastolic pressure and volume. It should be noted that the neurohormonal effects on the PV loop can be counteracted by inflammatory changes that occur in shock states (Figure 3D).

Chronically, these compensatory responses lead to ventricular remodeling, producing larger ventricular volumes, characterized by a rightward shift of both the EDPVR and ESPVR, and worsening of LV function. This process persists until it is interrupted by pharmacological or mechanical intervention.

Cardiac Assist Devices:

While the treatment of CS is quite broad, depending on the severity and underlying etiology, the focus of this article is cardiac assist devices – specifically percutaneous ventricular support. Percutaneous ventricular support is most often indicated for classic, deteriorating, and extremis SCAI Stages of CS – CS that is not responsive to optimal medical management and conventional treatment measures. Percutaneous ventricular support devices are an evolving field of mechanical support used in high-risk elective cases and the emergent setting of AMI complicated by CS. The Impella is a contemporary micro-axial flow percutaneous ventricular assist device, which extracts blood from the left ventricle ,through the inlet cage, into the cannula portion of the pump and ejects it into the ascending aorta.[18-20] The Impella is often used in the emergent setting of AMI to increase coronary and systemic perfusion, reducing end organ failure and breaking the continuum of cardiogenic shock[1,20-21] while unloading the left ventricle, reducing myocardial oxygen demand and minimizing the infarct size[20,22,26]. The device has a quick deployment process, truncating the duration of CS.[2] Potential contraindications to Impella placement are listed in Table 4.

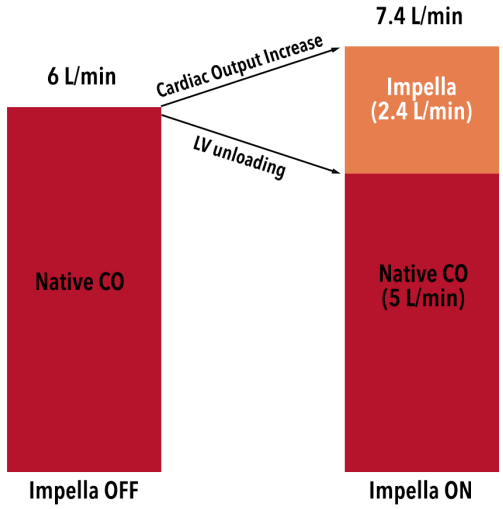


Figure 4: Impella's effect on Cardiac Output

Impella's Hemodynamic Support:

The hemodynamic support offered by the Impella device is the result of augmented forward flow through the impeller, and pressure augmentation (an increase in aortic and coronary pressure) leading to an increased cardiac power output. The Impella is an active forward flow pump that provides 2.5 to 6.0 L/minute of support. The active forward flow generated by the Impella is dependent on the specific model (2.5, CP, 5.0, LD, RP, 5.5), support level settings (termed "P" level), and the aortic-ventricular pressure gradient

(forward flow is increased with a decreased aortic ventricular gradient). The Impella 2.5, at its maximal rotation speed of 51,000 rpm, provides up to 2.5 L/minute of flow, while the Impella CP can provide mean flows of 3-4 L/minute, and the Impella 5.5 provides 6.0 L/min. Valgimigli et al. reported a total net cardiac output increase of 23% associated with Impella 2.5 support while multiple others have reported increased active forward flow.[11-12,20] It should be noted that the increased cardiac output is a net increase, accounting for both the Impella forward flow and native cardiac output (Figure 4). Remmelink et al. report augmentation of the aortic blood pressure in addition to the forward flow reported.

Myocardial protection:

Coronary blood flow is dependent on the pressure gradient within the coronary vessels and the resistance of the vasculature. If the distal (venous) pressure is assumed to be fixed, the coronary blood flow is proportional to the ratio of the aortic pressure and the microvascular resistance. In addition to increasing the aortic pressure, the Impella offloads the left ventricle, reducing the left ventricular volume, left ventricle pressure – specifically the end diastolic volume (EDV) and end diastolic pressure (EDP) – and ultimately the ventricular wall tension. The decrease in ventricular wall tension, estimated using the Law of LaPlace, decreases the microvascular resistance in the coronary circulation, leading to the desired increase in blood flow. Remmelink demonstrated this decrease in microvascular resistance in patients undergoing increasing levels of Impella support. The expected increase in coronary blood flow, as a result of increased aortic pressure and decreased microvascular resistance, has been demonstrated in many different models including through Technetium-99m sestamibi myocardial perfusion imaging by Aqel et al.[13-15]

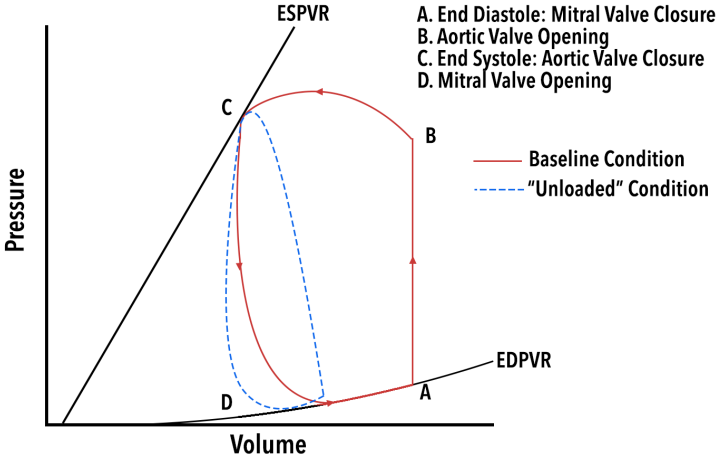


Figure 5: The Impella's impact on the Pressure-Volume loop[33]

Ventricular off-loading is a crucial role of the Impella, as the resulting reduction of the MVO2 protects at risk myocardium from ischemic insults. The ventricular off-loading accomplished by the Impella can be characterized by the PV loop (Figure 5). After active off-loading by the Impella, the area of the PV loop, and thus the amount of work performed by the myocardium, decreases. In addition to the decrease in SW, the Impella may reduce the potential energy (PE) within the myocardium, thus further diminishing MVO2. The PE within the myocardium is directly related to the ventricular wall tension. As previously discussed, the ventricular wall tension is directly related to the EDV and EDP (point A on the PV loop, Figure 4) and PE is the area bound by ESPVR and the EDPVR at LV volumes below the PV loop. The reduction in PE and SW allows the Impella to decrease both determinants of PVA.

A reduction in EDV and EDP increases coronary blood flow and decreases myocardial oxygen demand – impacting both sides of the supply-demand equation.

Safety Profile:

While the Impella provides significant hemodynamic benefit, it is not without complication. The IMPRESS trial demonstrated that both bleeding (33.3%) and hemolysis (8.3%) are frequent complications.[16] A recent systemic review by Hill et al. showed that pooled analysis of prospective CS studies utilizing the Impella had rates of hemolysis of 7.8% (95% CI: 2.3% - 16.2%) and a pooled rate of limb ischemia of 5.9% (95% CI: 0.5% - 16.7%). A pooled analysis of retrospective studies found that complications were relatively infrequent except for bleeding. The pooled analysis of the retrospective studies showed additional risks of: device malfunction 2.5% (1.1%-4.5%); in-hospital stroke 3.7% (95% CI: 1.8% - 6.2%); limb ischemia 3.6% (95% CI:1.7% - 6.3%); hematoma 4.9% (95% CI:2.3% - 8.3%); hemolysis 8.1% (95% CI: 5.6% - 11.1%); and bleeding 21.4% (95% CI: 15.9% - 27.6%) [29].

IMPRESS RCT

The IMPRESS trial was a randomized, prospective, open-label, multicenter trial, in which 48 patients with severe CS complicating AMI were assigned to percutaneous mechanical support (n = 24) or intra-aortic balloon bump (IABP) (n = 24). Mortality in patients treated with either IABP or percutaneous mechanical support was similar at 30 days (50% and 46%, respectively; hazard ratio: 0.96; 95% confidence interval: 0.42 to 2.18; p = 0.92) and 6 months (50% and 50% hazard ratio: 1.04; 95% confidence interval: 0.47 to 2.32; p = 0.923).[25]

ISAR-SHOCK

The ISAR-SHOCK trial was a prospective, two-center, randomized, open-label study which evaluated whether the Impella 2.5 provides superior hemodynamic improvement compared to IABP for patients suffering CS from an AMI. The Impella 2.5 was found to have a significantly greater increase in cardiac index compared to the IABP at 30 minutes (Impella: $\Delta CI = 0.49 \pm 0.46$ L/min/m2; IABP: $\Delta CI = 0.11 \pm 0.31$ L/min/m2; P=.02) with unchanged 30-day mortality between the two groups (Seyfarth)[26].

Summary:

Cardiogenic shock represents a spectrum of hemodynamic deficits in which the cardiac output is insufficient to provide adequate tissue perfusion. The Impella device offers increased cardiac power output, increasing coronary and systemic perfusion, reducing end organ failure and breaking the cycle of cardiogenic shock. Given the favorable safety profile, the Impella's role in cardiogenic shock is increasing. Critical care transport medicine providers should be familiar with the Impella and comfortable transporting patients supported by this device.

References

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Continued on page 16

PIOID-ASSOCIATED HEARING LOSS

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CASE 1

History of Present Illness

The patient is a female in her 40s presenting after an unintentional opioid overdose. Patient was at a hotel with a friend and found to be unresponsive. She received 2 mg intranasal Narcan from paramedics with improvement in respiratory status, but in the emergency department (ED) she remains somnolent and is unable to provide further history.

T	97.5 F
HR	112
BP	112/68
RR	23
SpO2	93% on RA

Past Medical History
Chronic Hepatitis C
Polysubstance Abuse

Past Surgical History
None

Medications
None

Allergies
None

Physical exam

Patient is shivering and somnolent but becomes agitated with physical stimulus. She has pinpoint pupils bilaterally. Her tympanic membranes are clear bilaterally and her mucous membranes are moist. She is tachycardic with regular rate and rhythm. She has normal respiratory effort with scattered wheezes. Her abdomen is soft. Her skin is warm and dry. She is moving all 4 extremities.

Diagnostics

	12.7	
27		259
	39	

137	98	36	116
6.6	22	2.49	

VBG: pH 7.19 pCO2: 59 HCO3: 23 BE: -6.1
Lactate: 5.3
CK: 496
High sensitivity troponin: 38
CXR: widespread bilateral airspace opacities, concerning for multifocal pneumonia, to include aspiration and viral etiologies.
EKG: NSR with peaked T waves in V4, V5
UDS positive for fentanyl

Hospital Course

After initial evaluation in the ED, the patient's respiratory rate dropped to 6-8 breaths per minute and she developed a new oxygen requirement. She was given an additional dose of Narcan 0.4 mg IV, with improvement in her mental status and respiratory effort, but she continued to require 4L oxygen via nasal cannula and had wheezing throughout all lung fields. The patient then reported inability to hear questions, which she stated had also occurred with previous opioid overdoses. Patient was able to respond to questions appropriately via writing.

Given the patient's persistent oxygen requirement, chest X-ray was performed and showed bilateral airspace opacities. She was also found to have an acute kidney injury and hyperkalemia with EKG changes, for which she was treated with calcium gluconate, albuterol, insulin, and dextrose. She was started on a naloxone drip, placed on supplemental oxygen via nasal cannula, and admitted to the medical step-down unit.

During admission, the patient was treated for community acquired pneumonia by the medicine team. Her oxygen requirement decreased throughout her hospitalization. Her acute kidney injury improved with hydration. There is no further mention of her hearing loss in the inpatient team notes. She was discharged to follow up with substance abuse resources and primary care.

CASE 2

History of Present Illness

The patient is a male in his 20s presenting after presumed unintentional opioid overdose. He was found down by his family. Per paramedics, the patient was responsive to 4 mg Narcan. He was found to have oxygen saturation in the low 80s by squad, with improvement to the 90s on nonrebreather mask. Patient is refusing to talk to staff and appears to have altered mental status, repeatedly stating "I can't hear."

Past Medical History
Polysubstance abuse including intravenous drug use
Hepatitis C
Hypertension
Hypothyroidism
Schizoaffective Disorder
Depression

Social History
Smokes ¼ pack per day. Denies alcohol use. Admits to methamphetamine and heroin abuse.

Medications
Clonidine
Ferrous sulfate
Fluoxetine
Invega Sustenna
Levothyroxine
Quetiapine
Risperidone

Allergies
Ceftriaxone
Hydroxyzine

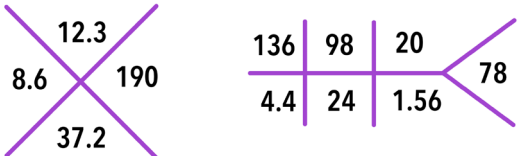
T	HR	BP	RR	
97.4 F	92	87/58	16	100% on NRB

Physical exam

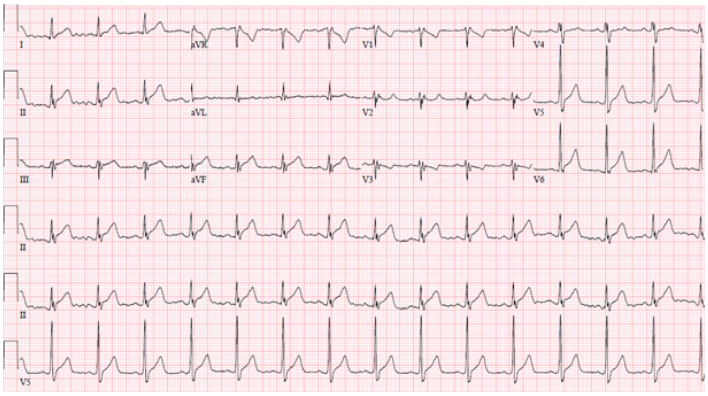
Patient is slightly ill-appearing but in no acute distress. He has reactive pupils. His oropharynx is clear and his tympanic membranes appear normal bilaterally. His breathing appears

non-labored and his breath sounds are clear bilaterally. Cardiac exam with regular rate and rhythm. He has a soft abdomen. There are needle track marks on his bilateral upper extremities. There is no skin rash noted. He is alert but unable to answer orientation questions and repeatedly tells provider "I can't hear." He does move all four extremities to command.

Diagnostics



CK: 1900
Alk Phos: 87 AST: 104 ALT: 90 Total bilirubin: 0.6
Acetaminophen: <10 Salicylate: <3
Troponin: 0.10
TSH: 18.04 T4: 0.95
UDS presumptive positive for amphetamines, benzodiazepines, fentanyl, THC
CT head: no hemorrhage, mass, edema or hypodensity.
EKG: Normal sinus rhythm, incomplete right bundle branch block, normal axis, normal intervals. J-point elevation in leads I, II, III, aVF, V5, V6.



Hospital Course

The patient was initially found to be hypotensive in the Emergency Department with a blood pressure of 87/58 mmHg. He was given an intravenous fluid bolus with minimal improvement in his blood pressure, but remained alert. Lab workup was remarkable for a troponin of 0.10 without signs of ischemia on EKG, an elevated CK of 1900, and a mild acute kidney injury with a creatinine of 1.56. His troponins remained slightly elevated during serial checks in the ED, peaking at 0.12. The cardiovascular ICU team was consulted and performed a bedside echocardiogram that demonstrated a dilated right ventricle. A CTPA was performed which was negative for pulmonary embolism, but did suggest pulmonary hypertension and left lower lobe opacities concerning for viral pneumonia or aspiration pneumonitis. Patient remained hypotensive after fluid resuscitation and was admitted to the CVICU for management.

During his admission, the patient's blood pressure improved with correction of hypovolemia with crystalloid fluid resuscitation, and his CK and troponin trended downward. He had a complete echocardiogram, which demonstrated mildly dilated left and right ventricles, thought to be secondary to cardiomyopathy as a result of heavy drug use. He was treated for community acquired pneumonia with ceftriaxone and Azithromycin and discharged to follow up with cardiology in 3-6 months. There is no further mention of the patient's hearing loss in the inpatient notes.

Discussion

Epidemiology

Opioid-associated hearing loss (OAHL) was first reported in 1979 associated with hydrocodone abuse.[1] Since then, this phenomenon has been reported with a variety of opioids including methadone, hydrocodone, hydromorphone, oxymorphone, propoxyphene, heroin, morphine, oxycodone, codeine, dextropropoxyphene, fentanyl, and tramadol.[1-7] The incidence of OAHL is unknown due to underreporting, but it is believed to be a rare side effect.[1] OAHL has been reported after various dosages, administration routes, and lengths of opioid use.[5] There are reports of OAHL occurring after oral, intranasal, intravenous, and transdermal administration, as well as one case of intra-arterial administration.[5,7,8] Cases are most frequently reported after a single opioid overdose or after chronic use at high doses.[7,9]

Pathophysiology

As OAHL typically presents as sensorineural hearing loss, the etiology is believed to be secondary to damage to the cochlea.[2,6,7] The exact mechanism is poorly understood, but there are a few theories that are commonly cited. These include hypoxia to the cochlea or vestibulocochlear system, altered pharmacokinetics due to genetic polymorphisms of metabolic enzymes, and direct ototoxic effect to the cochlea.[1,2,5,7,9]

The cochlea is known to be sensitive to ischemia due to its high metabolic activity and intense energy requirements.[7,8] It is postulated that OAHL may be in part be due to hypotensive or hypoventilatory events that frequently occur due to respiratory depression from opioid overdose, leading to hypoxia and vasospasm of the spiral modiolar artery.[1,5,7,9] However, this theory has come into question, as some reports of OAHL involve no clear hypoxic event.[7] Another hypothesis suggests that toxic substances are generated during the metabolism of opioids, with genetic differences in oxidative enzymes of the P450 system leading to the formation of more or less of these ototoxic products.[2] However, since not all opioids generate the same metabolic products, this is considered to be less likely.[7,9] The theory that is currently the most widely accepted is direct opioid effect on receptors present in the cochlea. All three subtypes of opioid receptors (μ, δ, and κ receptors) have been found to be present on the cochlea, and overstimulation of cochlear opioid receptors is thought to lead to decreased activity of cochlear hair cells, perhaps via altered signal transduction and downregulation of adenylate cyclase.[1,7,9]

Clinical Presentation

OAHL typically presents as bilateral hearing loss that is sudden in onset, although there are rare cases of unilateral hearing loss.[1,7,9] OAHL has been demonstrated to be sensorineural whenever audiometric testing has been performed on affected patients.[2,9] Severity can range from complete deafness to tinnitus to mild hypoacusis.[7] Though most have normal vestibular function on audiometric testing, there have been some cases that also have associated

Continued on page 15

SARCOIDOSIS OPTIC NEUROPATHY

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History of Present Illness

A female in her 60s with a past medical history of hypothyroidism and celiac disease presents with progressive vision loss in her left eye. She was initially evaluated by an ophthalmologist for no light perception in the left eye and referred to the emergency department for further testing and imaging. The patient noticed that her left eye was more swollen compared to the right. She went to bed and woke up in the middle of the night with significant pain in her left eye, floaters in her vision, and "kaleidoscope vision." Upon waking up, she was unable to see light or hand waving. She has had similar episodes of eye pain in the past with swelling around her eye, but these episodes resolved spontaneously. She denies any trauma to her eye, chemical injury, or drainage. She does not have any pain or vision loss in her right eye.

Eight months prior the patient had a CT scan of the neck to evaluate a vocal cord polyp, which revealed bilateral diffuse extraocular muscle enlargement with effacement of fat planes at the bilateral orbital apices, consistent with thyroid eye disease or IgG4 related ophthalmic disease. She was seen by ophthalmology at that time, had a normal eye exam, and no intervention other than periodic monitoring was recommended.

Past Medical History

Allergic Rhinitis
Celiac Disease
Hypothyroidism - diagnosed in 2012
Osteoporosis

Past Surgical History

Tonsillectomy
Vocal cord polyp removal
LASIK eye surgery

Medications

Diazepam 5mg PO q6h PRN
Loratadine 10 mg PO daily
Pseudoephedrine 30 mg q6h PRN
Levothyroxine 75 mcg PO daily

Allergies

Penicillin
Sulfonamide Antibiotics

Social History

Former Smoker - quit in 2005

T 97.7 F	HR 76	BP 120/94	RR 18	99% on RA

Physical Exam

The patient is in no acute distress. Examination of the left eye reveals proptosis. Upon direct light exposure, there is no left pupillary constriction. There is left pupillary construction upon indirect light exposure, and there is normal right pupillary constriction upon direct and indirect light exposure. Upon testing of extraocular movements, the patient is able to look medially with the left eye but is unable to move her left eye laterally or upward. Extraocular movements are intact in the right eye. Visual acuity testing reveals no light perception in the left eye, and 20/50 vision in the right eye. Intraocular pressures are 17 in the left eye and 13 in the right eye. The remainder of the patient's physical exam is unremarkable.

Notable Diagnostics

ESR 6 mm/hr (0-30 mm/hr)
CRP 6.8 mg/L (1.0-10.0 mg/L)
T4 1.04 ng/dL (0.61-1.76 ng/dL)
TSH 1.78 uIU/mL (0.45-4.12 uIU/mL)
CT orbits with contrast: Diffuse, bilateral enlargement of extraocular muscles with effacement of the fat planes at the orbital apices that is concerning for optic nerve compression. Bony remodeling of orbital walls related to chronic pressure erosion. Bilateral mild exophthalmos increased on left compared to previous CT imaging study from 8 months prior.

Hospital Course

Ophthalmology evaluated the patient in the emergency department and performed a dilated slit lamp exam, finding left optic disc edema. She was admitted to the Medicine service with a diagnosis of compressive optic neuropathy of the left eye and bilateral thyroid eye disease. Otolaryngology was consulted for surgical decompression of the bilateral orbits, which occurred without complication. Serial ophthalmologic examinations revealed that the patient had no improvement in light perception in her left eye and developed visual hallucinations in the left eye. She also started to see gray spots in her right eye and had worsening tunnel vision in her right eye. Further lab workup including anti-TPO antibodies were negative, inconsistent with the diagnosis of thyroid eye disease.

Biopsies obtained during surgery showed granulomas of the left nasal contents, left medial rectus muscle, and right periorbital area. None of the cultures of the tissue grew any organisms. The rheumatology team was consulted at this time and thought that the patient's presentation was more consistent with a diagnosis of ocular sarcoidosis given her biopsy results and negative anti-TPO antibodies. They recommended that the patient be started on an aggressive sarcoidosis regimen including infliximab, methotrexate, and continued steroids to preserve vision in her right eye. Further sarcoidosis workup including imaging indicated that the patient's disease was limited to ocular sarcoidosis. At discharge, the patient still had no light perception in her left eye, but normal vision in her right eye.

Discussion

Pathophysiology

Sarcoidosis is a granulomatous disease that can affect virtually every organ system in the body but is found commonly in the lungs and lymph nodes. In sarcoidosis, non-caseating granulomas

accumulate in body tissues, often resulting in chronic systemic inflammation and fibrosis. Granulomas are composed of macrophages, epithelioid cells, and lymphocytes and form in order to contain a pathogen and protect surrounding tissue. As they mature, granulomas may become surrounded by collagen and fibroblasts, leading to sclerosis. The inciting factor causing granuloma formation in sarcoidosis is unknown, but many studies have found associations with environmental exposures such as woodburning stoves, tree pollen, inorganic particles, insecticides, and mold. In addition, bacterial DNA and RNA has been found in the granulomatous tissue of sarcoidosis. There have also been occupational studies that have shown association with the US Navy, metalworking, firefighting, and the handling of building supplies. Genetic studies have found an increased incidence in the disease among those who have a family member with sarcoidosis, and there are several genes proposed to convey susceptibility to sarcoidosis.[1]

Epidemiology

The prevalence of sarcoidosis is variable depending on the demographic of the population. In the United States, an annual incidence of 35.5 per 100,000 black patients and 10.9 per 100,000 white patients is estimated, with black females as the most commonly affected population. Patients are usually under the age of 50 when diagnosed, but can be seen very rarely seen in children.[2,3] The prognosis and clinical course of sarcoidosis is highly variable, with spontaneous remission in about two-thirds of cases and 10-30% of cases becoming chronic or progressive.[4]

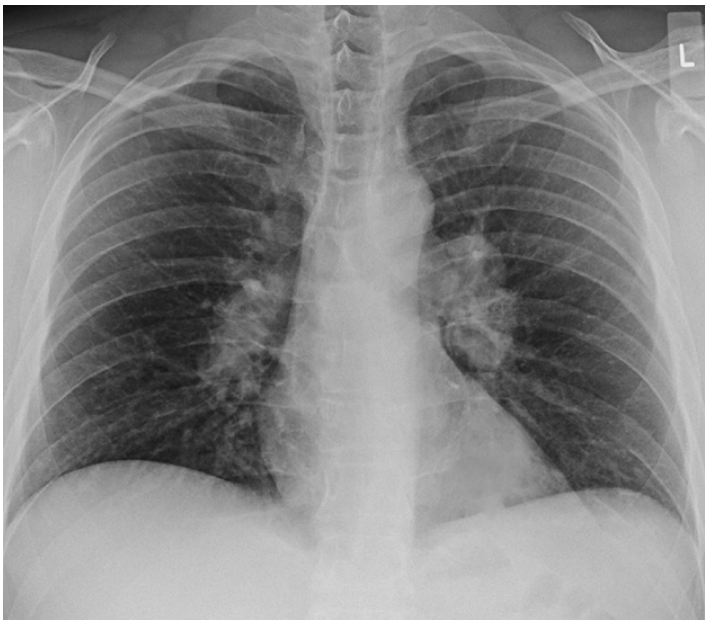

Figure 1: Chest x-ray showing hilar lymphadenopathy, which is characteristic of pulmonary sarcoidosis.

Clinical Presentation

Sarcoidosis has a wide variety of presentations in the emergency department. Patients may even be asymptomatic and present with incidental findings characteristic of the disease, such as chest radiography with bilateral hilar lymphadenopathy (figure 1).[1] Patients may have non-specific constitutional symptoms, such as fever, malaise, fatigue, and weight loss.[5] The most common organ system involved is the lungs, which are involved in about 90% of cases, and thus respiratory symptoms are the most common presentation of the disease.[5] Of particular note to the emergency physician, 11% of sarcoidosis patients have hypercalcemia, which is thought to be due to calcitriol secreted by the granulomas, leading to increased absorption of calcium in the intestines.[2,5] Various clinical presentations of sarcoidosis are summarized in table 1.

Clinical Presentation of Sarcoidosis	
Systemic	Fever, fatigue, malaise, weight loss, diffuse lymphadenopathy
Respiratory	Shortness of breath, dry cough, pleuritic chest pain, hemoptysis
Skin	Lupus pernio (pathognomonic), erythema nodosum, alopecia, maculopapular rash
Ocular	Uveitis, optic neuritis, vision loss, eye pain
Endocrine	Diabetes insipidus, hypercalcemia
Cardiac	Complete heart block, ventricular tachycardia, myocarditis, sudden cardiac death
Musculoskeletal	Arthralgias, myalgias
Neurologic	Cranial neuropathy (especially facial nerve), ataxia, seizures, dementia, aseptic meningitis, encephalopathy

Table 1: Various clinical presentations of sarcoidosis[5]

Ocular involvement has been reported in 15-25% of cases of sarcoidosis and can be isolated or may be the initial presenting symptom. Most commonly it affects both eyes, and it can involve all parts of the eye and surrounding tissues.[5] The most common presentation of ocular sarcoidosis is granulomatous uveitis, whereas optic neuropathy secondary to sarcoidosis, as was seen in this patient, is much less common. Granulomatous lesions of the surrounding tissues, leading to compression of the optic nerve, or granulomatous infiltration of the optic nerve itself, can cause optic neuropathy leading to painless or painful vision loss or changes in color perception.[6,7]

Diagnosis and Workup

While we may suspect the disease in the emergency department, we will not make the final diagnosis of sarcoidosis, and consultation of rheumatology is of paramount importance. The diagnosis of sarcoidosis is made when there is a compatible clinical picture and a biopsy showing non-caseating epithelioid granulomas, as well as exclusion of other possible causes of granulomas, such as infection and foreign bodies.[8] Testing in the emergency department is usually directed by the presenting symptoms and organ system involved, but a calcium should always be checked if the diagnosis of sarcoidosis is suspected.[5]

Treatment

Treatment of sarcoidosis is not always necessary since most patients are not disabled by the illness. If organ function is threatened, treatment is initiated. Absolute indications for treatment include neurologic, cardiac, or ocular involvement, and hypercalcemia. Corticosteroids are the mainstay of treatment, but immunomodulating drugs such as hydroxychloroquine, methotrexate, azathioprine, and cyclophosphamide have been used as well.[2,3]

Sarcoidosis Optic Neuropathy
Continued on page 16

NECROTIZING FASCIITIS

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History of Present Illness

The patient is a female in her 50s who presents following an injury to her right ankle approximately one week prior. The patient was fishing for catfish, and the barb from one of the catfish caused a puncture wound in her right lower extremity. She reports worsening erythema, edema, and pain in this area since the injury. She initially presented to an outside hospital three days prior and was sent home on oral clindamycin. She returned to the outside hospital again on the day of presentation due to worsening pain and malaise, and was found to be hypotensive, tachycardic, and hypoxic. She received intravenous (IV) fluids and cefepime and was transferred to our tertiary care medical center. On arrival, the patient remains alert and oriented but is tachycardic and hypotensive, so she is triaged to the shock resuscitation unit for further management.

T
97.5 F

HR
104

BP
82/70

RR
22

SpO2
91%
on 4L NC

Past Medical History

Chronic obstructive pulmonary disease
Coronary artery disease
Congestive heart failure
Hypertension

Past Surgical History

Left pleurodesis for spontaneous pneumothorax

Medications

Nitroglycerin, atorvastatin, carvedilol, aspirin, ticagrelor, albuterol, doxepin

Allergies

None

Physical exam

The patient is a female in no acute distress. She is alert and oriented. Pupils are equal, round, and reactive to light. Neck is supple and without meningismus. Auscultation of the heart and lungs is unremarkable. Her abdomen is soft and non-tender. The right lower extremity has a deep puncture wound above the lateral ankle with purulent drainage and surrounding bullae, erythema, and tenderness extending to the mid-thigh.

Diagnostics

	11.6	
0.9		207
	33.8	

135	105	60	99
5.3	19	3.13	

Bedside soft tissue ultrasound: fluid along fascial planes and cellulitis
X-ray right femur, knee, tibia and fibula: soft tissue ulceration and swelling, subtle hyperdensities likely to represent foreign debris

Hospital Course

Given concern for necrotizing fasciitis and sepsis, the patient was started on broad spectrum antibiotics including vancomycin, metronidazole, and clindamycin in addition to the cefepime she received at the outside hospital. Her systolic blood pressure dropped into the 70s, so IV fluids were administered and she was started on a norepinephrine infusion to maintain mean arterial pressure >65 mmHg. Acute care surgery was consulted to evaluate her right lower extremity for necrotizing fasciitis. The patient was emergently taken to the operating room (OR) with acute care surgery and podiatry for extensive debridement of the infected tissue from the lateral ankle wound up into the right thigh. Following the surgery, she remained intubated and was transferred to the surgical intensive care unit with a high vasopressor requirement including norepinephrine, epinephrine, and vasopressin. Antibiotic coverage was changed to meropenem and clindamycin to cover freshwater pathogens. She received filgrastim for her neutropenia, thought to be due to underlying sepsis.

On post-operative day one, the patient developed oliguria, worsening acidosis, and elevation of her lactate to 14. Nephrology was consulted for renal failure, and the patient was started on continuous renal replacement therapy and a bicarbonate infusion. Blood cultures returned positive with growth of gram-negative rods, which later speciated as Edwardsiella tarda. She returned to the OR for further debridement and washout given concern for remaining infected tissue. During this operation, she was found to have non-contractile muscle in bilateral lower extremities, which was thought to be secondary to sepsis and multisystem organ failure, rather than infection. Unfortunately, her clinical condition continued to deteriorate, and her family elected to pursue comfort care.

Discussion

Epidemiology and Pathophysiology

Necrotizing Fasciitis

Necrotizing soft tissue infection (NSTI) is a rare, life-threatening, and therapeutically challenging disease affecting about 1000 patients annually in the United States.[1] While diagnosis remains uncommon, the incidence of NSTIs has increased over recent decades, possibly due to emerging strains of resistant bacteria, increased bacterial virulence, and better reporting systems.[1,2] Necrotizing fasciitis (NF) is a type of NSTI that extends below the epidermis and dermis to infect fascia, adipose tissue, muscle, and tendons. Precipitating events typically include recent surgery or penetrating injury, however, there are also cases of NF after minor insult such as superficial abrasion. The clinical course of NF may be classified as subacute, with symptoms remaining localized for several weeks, or acute, with symptoms worsening within several days and involving large areas of tissue.[3] Patients with fulminant NF rapidly deteriorate and develop septic shock over the course of hours. The mortality rate associated with NF is up to 70%, primar-

ily due to delay in diagnosis.4 NF is classified into four subtypes based on microbial etiology (table 1).[4] Notable virulence factors for these microorganisms include the generation of α-toxin and θ-toxin by clostridium species, which facilitate tissue ischemia and inhibit neutrophil migration, and expression of M protein by streptococcus species, which bind T-cell receptors to induce massive inflammatory cascade.[1]

Type	Frequency	Microbiology
I	70-80%	Polymicrobial, aerobic and anaerobic E.g., Non-group A streptococci, enterobacteria, clostridium
II	20-30%	Monomicrobial E.g., Staph aureus, group A beta-hemolytic streptococci
III	<1%	Gram negative and often marine related E.g., Vibrio spp., Edwardsiella tarda
IV	<1%	Fungal E.g., Candida spp., Mucor

Table 1: Classification of necrotizing fasciitis according to microbial etiology

Risk factors for the development of NF include diabetes, obesity, advanced age, immunodeficiency, significant alcohol use, liver disease, intravenous substance use, and recent trauma.[1] Common locations of NSTIs include the extremities, perineum, and genitalia (known as Fournier's gangrene when the perineum and genitalia are involved). Pathogens enter the subcutaneous tissue either via direct injury to the integument or hematogenous seeding from another site.[1] The associated inflammation and infection lead to cell death and tissue necrosis, which creates a nidus for microbial proliferation.

Catfish Injuries

Figure 1: Man with catfish caught by noodling.

Catfish injuries, like the one sustained by the patient in this case, are fairly common both in the catfishing industry and in recreational activities. A particularly interesting recreational practice, common in the southern United States, is known as "noodling" and involves catching catfish with one's bare hands (figure 1). Participants reach blindly into a hole or crevice where the catfish reside and grab hold of the fish by its mouth, pulling it to the surface. Catfish can exert a fair amount of force during this activity, putting the "noodler" at risk of blunt force trauma. In addition, catfish have dorsal and pectoral fins with spines that become erect and swordlike when they are disturbed, and some species even have venom that is released from the spines. The spines can cause puncture wounds and lacerations, and envenomation causes local reactions including pain, erythema, edema, local hemorrhage, tissue necrosis, and muscle contractions, thus predisposing the victim to infection from water-borne bacteria.[5]

Multiple case reports have been written on severe infections after catfish injuries, with numerous bacterial species implicated. The most common gram-negative bacteria seen in catfish-related infections is Edwardsiella tarda.[5] E. tarda is a motile anaerobic gram-negative rod and the causative organism of emphysematous putrefactive disease of catfish – also known as fish gangrene. Prior testing has isolated E. tarda from 75% of pond water samples in the US and almost 90% of channel catfish fillets.[6] Despite the extensive presence of this bacterium in the environment, the majority of catfish do not become ill. Catfish that do become infected by Edwardsiella develop abscesses and necrotizing cellulitis. While an unusual human pathogen, E. tarda can cause similar tissue infection in humans, with the dreaded complication of gram-negative bacteremia and sepsis.[7] E. tarda is typically pan-sensitive to the antibiotics used in gram negative infections, but unfortunately even with adequate antimicrobial regimens, mortality has been reported in up to 44% of cases of E. tarda bacteremia. There are no guidelines regarding antibiotic regimens for catfish-associated infections, but proper antibiotic selection should include coverage for waterborne bacteria.[5]

Clinical Presentation

NF most commonly occurs on the extremities. The earliest symptoms of NF are nonspecific and include erythema and edema that often appears similar to cellulitis or abscess formation.[3] Severe pain out of proportion to clinical appearance can be an important indicator of infection deeper in the fascial planes, and early diagnosis is crucial to improve mortality.[3] As NF infection progresses, the wound appearance may develop a grayish or purple discoloration with poorly demarcated borders.[8] (Figure 2) More specific signs of NSTIs include formation of bullae or blisters and palpable crepitus underlying the wound.[9] In late stages of disseminated infection, patients present with symptoms of sepsis, including tachycardia, hypotension, fever, and encephalopathy.[8] Symptoms that should alert the clinician to the possible presence of NSTIs are summarized in table 2.

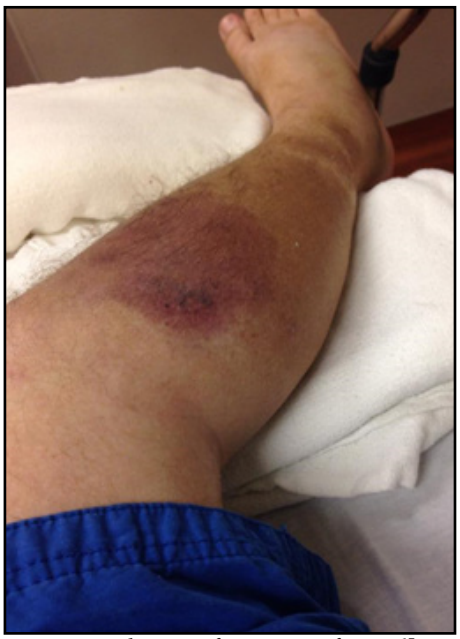

Figure 2: Early stage of necrotizing fasciitis[17] (figure via creative common license)

Clinical Features of Necrotizing Soft Tissue Infections		
Skin	**Pain**	**General**
Erythema with ill-defined margins	Pain that extends past margin of apparent infection	Fever with toxic appearance
Tense edema with grayish or brown discharge	Severe pain that appears disproportionate to physical findings	Altered mental state
Lack of lymphangitis or	Decreased pain or anesthesia at apparent site of infection	Tachycardia
Vesiles or bullae, hemorrhagic bullae		Tachypnea
Necrosis		Presentation with diabetic ketoacidosis or hyperosmolar hyperglycemic state
Crepitus		

Table 2: Clinical features of NSTIs[8]

Diagnosis

Early diagnosis is challenging due to overlapping symptoms with superficial cellulitis. Initially, many patients with NF are incorrectly diagnosed with cellulitis and discharged on oral antibiotics. The gold standard for diagnosis is surgical exploration based on clinical concern for NF.[9] Laboratory and imaging studies can provide further supporting evidence, although with limitations. The Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score attempts to stratify patients with soft tissue infection into low, moderate, and high-risk groups (Table 3).[10] However, no prospective trials have been performed utilizing this tool, and validation studies have produced inconsistent results.[11] A meta-analysis comparison of clinical signs, LRINEC score, x-ray, and computed tomography (CT) found that only CT imaging has robust sensitivity for NSTI, nearly 95%.[12] (Table 4) Magnetic resonance imaging (MRI), which was not included in this meta-analysis due to lack of data, has variable sensitivity and specificity according to the criteria used (for example, the presence of gas has 100% specificity for NSTI but poor sensitivity, and abnormalities of the intermuscular fascia has 100% sensitivity for NSTI but poor specificity).[13]

Point of care ultrasound, which is quick to perform and readily available in the emergency department, may have a role in assisting the clinical diagnosis of NSTI. Ultrasonographic signs of NSTI include a "cobblestone" appearance of the soft tissue, irregularity and thickening of the fascia, abnormal fluid collection along the fascia, and hyperechogenic foci representing subcutaneous air. However, ultrasound evaluation of the deeper tissues can be quite difficult and differentiating cellulitis from NSTI is not always possible.[14] One small study estimated ultrasound to have a sensitivity of 88.2% and specificity of 93.3% in the diagnosis of NSTI in patients who were already suspected to have NSTI on clinical exam.[15] In practice, CT, MRI, or ultrasound imaging may aid the clinician in cases of diagnostic uncertainty if it is readily available, but should never delay prompt surgical evaluation.

Laboratory Risk Indicator for Necrotizing Fasciitis		
Lab	**Value**	**Score**
CRP	<15	0
	>15	4
WBC	<15	0
	15-25	1
	>25	2
Hemoglobin	>13.5	0
	11-13.5	1
	<11	2
Sodium	>135	0
	<135	2
Creatinine	<1.6	0
	>1.6	2
Glucose	<180	0
	>180	1
Composite		<6 = low risk 6-7 = moderate risk >8 = high risk

Table 3: Components of LRINEC score

Diagnostic Value of Physical Exam, Imaging and LRINEC Score for the Identification of Necrotizing Soft Tissue Infection		
	Sensitivity (%)	**Specificity (%)**
Physical		
Fever	46.0	77.0
Hemorrhagic Bullae	25.2	95.8
Hypotension	21.0	97.7
Imaging		
Plain Radiography	48.9	94.0
CT (fascial gas only)	88.5	93.3
CT (fascial edema or enhancement or gas)	94.3	76.6
LRINEC Score		
≥ 6	68.2	84.8
≥ 8	40.8	94.9

Table 4: Sensitivity and specificty of various diagnostic modalities in NSTI.[11]

Treatment

Unfortunately, the aggressive nature of the infection and resultant tissue hypoxia mean that IV antibiotics alone are rarely sufficient for treating NSTIs. Mortality without surgical intervention is greater than 90%.[7] Emergent surgical consultation for debridement and excision of infected tissue is the most important step following diagnosis, and it may be appropriate to consult surgery prior to any available test results if there is high clinical suspicion. Obtaining

intraoperative tissue cultures is key for tailoring antibiotic therapy, which becomes more effective following surgery. Pending culture results, broad-spectrum antibiotics should include coverage for gram-positive (e.g. vancomycin), gram-negative (e.g. cefepime), and anaerobic microorganisms (e.g. clindamycin).[16] Clindamycin is frequently used since it has been shown to decreased clostridial toxin production, streptococcal M-protein expression, and lipopolysaccharide-induced tumor necrosis factor production by monocytes.[1] If fungal infection is suspected, treatment usually includes amphotericin or fluoroconazoles.[16] Patients also typically require intensive care including fluid resuscitation, vasoactive medications, and ventilator support. Limited evidence is available for other proposed interventions, including hyperbaric oxygen and intravenous immunoglobulin.[7]

Summary

Necrotizing soft tissue infection is a rare, aggressive, and life-threatening disease with high mortality unless extensive surgical intervention is performed. Diagnosis can be challenging in the emergency department due to similarity to more innocuous infections such as cellulitis, but NSTI should be suspected in the case of pain out of proportion to exam, crepitus, bullae, or signs of systemic illness. Diagnosis in the ED is primarily clinical, but diagnostic imaging such as CT scan and ultrasound can be helpful, and the final diagnosis is made after surgical debridement. The mainstays of NSTI treatment in the ED are early surgical consultation and empiric antibiotic therapy for gram positive, gram negative, and anaerobic bacteria. Catfish-associated infections, including NSTI, have been reported in the literature and can be life-threatening.

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17. Photograph by Joe Doestch, distributed under a CC 4.0 International license

Opioid-associated Hearing Loss

Continued from page 9

vertigo, suggesting possible extension of injury to the labyrinth.[2,5,7] In patients presenting after overdose, OAHL typically develops rapidly after the event and resolves spontaneously. In patients with chronic opioid use, hearing loss is usually slower in onset, but then becomes rapidly progressive and is often irreversible.[9]

Differential Diagnosis

Hearing loss can be categorized as conductive, sensorineural, or a combination of both (see figure 1). Conductive hearing loss occurs due to damage or obstruction of the mechanical components of the ear. The most common causes of conductive hearing loss in-

due to pathology with the pathway from the cochlea to the auditory cortex.[6] Other common causes of sensorineural hearing loss include cochlear injuries, cochlear ischemia, viral infections, autoimmune disorders, and ototoxic drug exposure (see table 1).[9,10] In suspected cases of OAHL, it is important to keep these other etiologies in mind and examine the patient's medication list for possible concomitant ototoxic drug use.

Causes of Acute Sensorineural Hearing Loss	
Category	**Examples**
Infection	Viral cochleitis, bacterial meningitis, mycoplasma pneumonia, Lyme disease, tuberculosis, syphilis, fungal infection
Ototoxic Drugs	Aminoglycosides, vancomycin, erythromycin, antimalarials, loop diuretics, cisplatin, sildenafil, cocaine, opioids
Neoplasm	Lymphoma, leukemia, plasma cell dyscrasia, meningeal carcinomatosis, acoustic neuroma
Trauma	Noise exposure, barotrauma, head injury
Autoimmune	Cogan's syndrome, Susac syndrome, lupus, antiphospholipid antibody syndrome, rheumatoid arthritis, Sjögren's syndrome, relapsing polychondritis, vasculitis
Vascular	Vertebrobasilar stroke, cerebellar infarct, inner ear hemorrhage
Other	Meniere's disease, otosclerosis, Paget disease, multiple sclerosis, sarcoidosis, hypothyroidism, idiopathic

Table 1: Differential diagnosis of acute sensorineural hearing loss

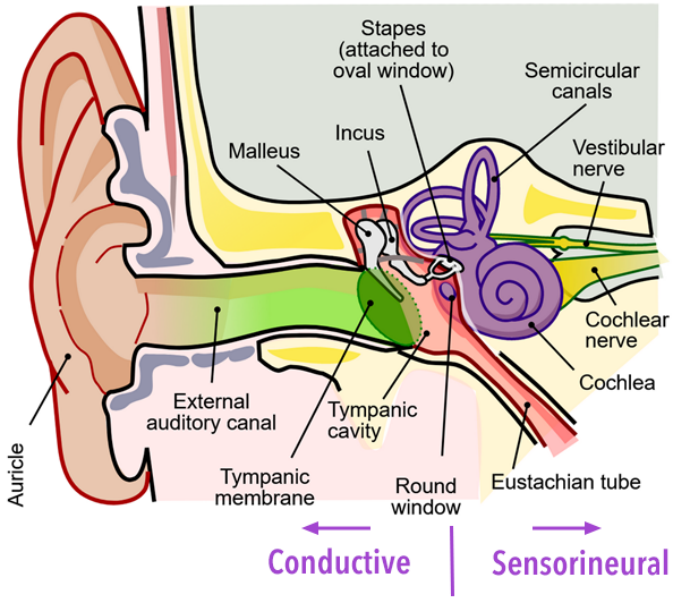

Figure 1: Diagram of the inner ear and the difference between conductive and sensorineural hearing loss[11] (figure via creative common license)

Prognosis and Treatment

Prognosis of OAHL appears to be variable, with some patients recovering hearing after only a brief time and others with permanent hearing loss.[7] Most patients do appear to recover spontaneously. However, case reports seem to indicate that hearing loss associated with acute overdose is more likely to be reversible,

usually within days to weeks, and that loss associated with heavy chronic use is much more likely irreversible.[4,7,9]

Treatment has been attempted with various interventions including naloxone, corticosteroids, and pentoxifylline.[4,5,7] However, there is little evidence of benefit from any of these interventions. In patients whose hearing loss persists at long-term follow-up, cochlear implants have been successful in restoring hearing.[5,7,9]

Summary

Sensorineural hearing loss is a known side effect of opioid class drugs in both acute overdoses and chronic high dose opioid use. The exact mechanism is unknown, but it is thought to be secondary to damage to the cochlea. Prognosis varies from rapid spontaneous resolution to long term hearing loss requiring cochlear implants. There is no evidence supporting any specific treatment to mitigate or treat OAHL.

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Impella Support

Continued from page 7

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Sarcodiosis Optic Neuropathy

Continued from page 11

Summary

Sarcoidosis is a disease characterized by the accumulation of granulomas in any body tissue, but most commonly the lungs. Sarcoidosis patients can present with a wide variety of complaints, including vision loss due to optic neuropathy, as was seen in this patient. Ultimately the diagnosis is made by biopsy of granulomatous tissue, and while treatment may not always be necessary, the mainstay of treatment is corticosteroids.

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Submitted B Pod Cases

Case	Providers
Impella Support	Stewart/Gottula
Opioid-associated Hearing Loss	Irankunda/Pulvino/Benoit/Kein
Sarcoidosis Optic Neuropathy	Rice/Minges
Necrotizing Fasciitis	Pulvino/Stolz