THE UNIVERISTY OF TEXAS SOUTHWESTERN INTERNAL MEDICINE GRAND ROUNDS

Cardiogenic Shock Today

Will better cardiac rest be the difference?

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12/6/2013

This is to acknowledge that Tayo A. Addo, M.D. has disclosed that he does not have any financial interests or other relationships with commercial concerns related directly or indirectly to this program. Dr. Addo will be discussing off-label uses in his presentation.

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Clinical and Research Interests:

Percutaneous revascularization of vascular diseases including coronary and lower extremity vascular atherosclerotic disease

Anti-platelet and anti-thrombotic therapy in vascular diseases

Purpose an Overview:

The in-hospital and short-term outcomes of patients suffering acute myocardial infarction (AMI) have improved substantially in the last several decades with mortality rates now falling below 5%. For patients who develop cardiogenic shock after myocardial infarction however (~50,000 patients), mortality still exceeds 40% today. This review examines this subset of patients and introduces new treatment modalities to improve outcomes.

Objectives:

1. Describe the characteristics and natural history of patients with AMI developing cardiogenic shock
2. Describe the pathophysiology of shock and the effects of initial treatments including the IABP
3. Describe the role of rapid reperfusion and revascularization by primary angioplasty
4. Describe the mechanisms of percutaneous cardiac assist devices in combating cardiogenic shock

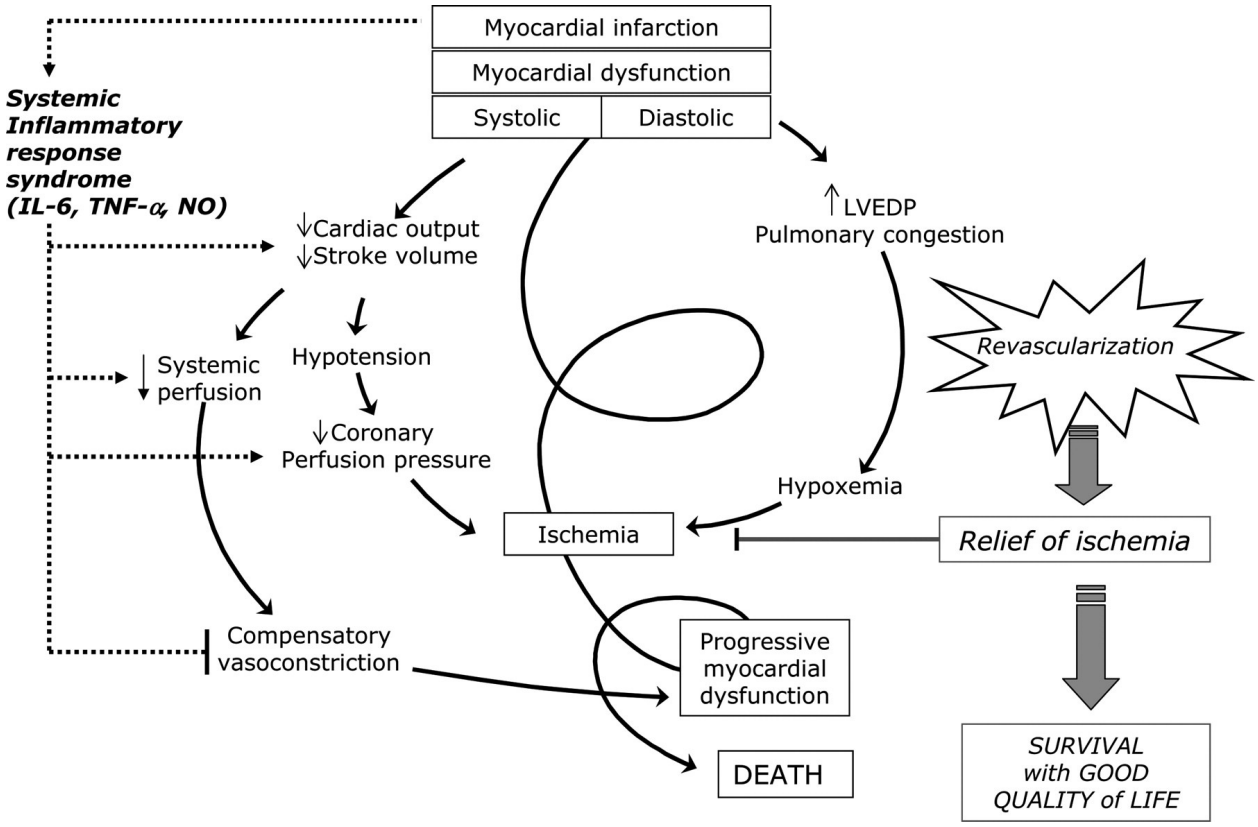
Cardiogenic Shock refers to the inability of the heart to further support circulation. It is the terminal form of all heart disease short of unexpected cardiac arrest. Its causes are diverse and can include ischemic heart disease, arrhythmia, valvular heart disease, cardiomyopathies, pulmonary arterial hypertension and cardiac tamponade. This review focuses on acute cardiogenic shock developing as a result of acute ischemia and/or infarction of the left ventricle and efforts to treat this event. The scenario typically develops rapidly, is virulent and often fatal, and has proved very difficult to manage despite tremendous advances in modern cardiovascular medicine (1).

Natural History

Cardiogenic shock occurred in 15-20 percent of cases of acute myocardial infarction and carried a fatality rate exceeding 80% before the modern era of reperfusion therapy for acute myocardial infarction. With the advent of advanced critical care, anti-platelet, and reperfusion therapies for myocardial infarction, incidence rates fell to under 10% and mortality to 50% (2, 3). Unfortunately these rates remained largely unchanged through the last decade and currently accounts for the vast majority of the mortality among patients with myocardial infarction who make it to the hospital (4). The classical patient developing shock has sustained a large myocardial infarction with the most frequent site been the anterior wall, reperfusion was delayed, unavailable or unsuccessful, and there is multiple vessel coronary disease or poor myocardial reserve due to prior infarction (5, 6). Approximately 20% of shock patients will arrive with signs of shock at presentation, many of whom may have suffered myocardial infarction for several hours, or have been resuscitated from cardiac arrest prior to arrival. The majority of the remaining patients will develop symptoms within 24 hours of arrival but a few may take a few days for shock to become manifest particularly when ST segment elevation is not present at admission. Hospital mortality is high regardless of the form of presentation and typically exceeds 40% due to multiple organ failure and circulatory collapse (7, 8).

Pathophysiology

The pathophysiology of cardiogenic shock has been well described and is beyond the scope of this review (9). Briefly once a critical mass of myocardial dysfunction develops as a result of ischemia and or infarction, the cardiac stroke volume and thus systemic blood pressure becomes markedly reduced. A compensatory tachycardia ensues but this is insufficient to preserve cardiac output. The falling cardiac output initially triggers systemic vasoconstriction but tissue hypoperfusion soon results in tissue ischemia, acidosis, capillary leak and vasodilation. A systemic inflammatory response syndrome is triggered (10, 11). This causes a further fall in systemic pressure and soon coronary perfusion pressure drops further exacerbating ischemia and left ventricular failure. Cardiac filling pressures rise, progressively increasing myocardial work and oxygen demands in the failing heart. This further exacerbates ischemia and infarction resulting in a viscous cycle that if left unchecked is fatal.



Diagnosis

The diagnosis is easily made in patients with acute cardiac injury (myocardial infarction) who are becoming hypotensive and show evidence of end-organ dysfunction or hypoperfusion. Common signs of hypoperfusion or end-organ dysfunction include renal hypoperfusion resulting in oliguria, cerebral hypoperfusion resulting in reduced mental function, and hypoperfusion of the extremities resulting in cool, mottled skin, weak pulses or limb ischemia. Given the different shock syndromes and urgency of definitive diagnosis, invasive right heart cardiac catheterization is frequently employed to provide clarity. Generally the cardiac index is less than 2.0 L/min/m2 and the mixed oxygen saturation is low <60% due to high tissue level extraction. The left heart filling pressure (wedge) pressure may or may not be markedly elevated but is typically > 12 mmHg, and the systemic vascular resistance is often normal or low due to systemic vasodilation, typically < 1400 dynes(s)/cm5. The cardiac power output, an index derived from the product of the cardiac index and mean arterial pressure is a particularly useful tool for determining shock severity and it correlates with short-term outcomes (12). A value less than 1 is highly indicative of severe cardiogenic shock and lower values predict mortality.

Initial Treatments

Treatment usually begins with efforts to support blood pressure and improve cardiac output. A variety of pressors can be employed but titrated infusions of dopamine and norepinephrine have been the most successful due to dual effects on cardiac augmentation and systemic vasoconstriction. In a recent study testing different pressors for a variety of shock syndromes, norepineprine proved most beneficial in cardiogenic shock (13). These agents however do not address the underlying problem of ischemia and may often exacerbate ischemia by increasing myocardial work and oxygen consumption through tachycardia and enhanced contractility. They should therefore be applied sparingly and more definitive treatments should not be delayed on account of these agents. Given the presence of abnormal vasodilation in cardiogenic shock, the use of vasodilators such as nitroglycerin or nitroprusside is often intolerable and drugs such as dobutamine result in exacerbation of tachycardia. Unfortunately, trials designed to inhibit nitric oxide, a primary mediator of vasodilation so far have been unsuccessful (14).

The Intraaortic balloon counterpulsation pump was the first specific advance for shock management (15). This simple device places a large inflatable balloon catheter within most of the descending aorta and inflation/deflation is matched to the cardiac cycle. During diastole, there is rapid inflation of the IABP displacing a significant amount of blood from the descending aorta. The result is a rise in the ascending aortic pressure and volume which augments coronary and cerebral blood flow. Cardiac ischemia is therefore reduced. During systole rapid deflation results in a drop in aortic impedance which reduces the work of the heart during ejection. Cardiac output is measurably increased albeit quite modestly at 0.5L/min, and coronary ischemia is improved by the IABP in a variety of studies. The IABP when employed in the early experience of treating shock contributed to better survival however reperfusion and revscularization of ischemic myocardium soon became the definitive therapeutic goal (16). The IABP was widely used alongside reperfusion therapy but in recent years it has been called into question given ischemia is now quickly eliminated in most patients presenting with myocardial infarction. A meta-analysis showed favorable benefits when it was applied alongside thrombolytic therapy but no benefit when applied alongside primary PCI with definitive coronary revascularization (17). This is intuitive as thrombolytic therapy establishes patency but does not revascularize the infarct artery. Moreover when thrombolytics are administered, there is failure to establish patency in up 15% of patients and 20% of patients experience reocclusion of the infarct artery. These rates are even worse in patients who are presenting in cardiogenic shock.

Reperfusion therapy and aggressive revascularization

Primary PCI has become the preferred method of reperfusion in STEMI for several reasons. It allows definitive evaluation and treatment of the infarct artery eliminating ischemia in >95% compared to about 50% with thrombolytics. Normal coronary flow (TIMI 3 flow) a surrogate of tissue level perfusion is achieved in >90% of patients compared to about 60% with thrombolytics and is correlated with enhanced survival. Additional benefits include large reductions in recurrent ischemia or infarction, less risk of stroke, and immediate access to a critical care team for additional supportive measures if needed.

Thrombolytic therapy is less effective in patients with cardiogenic shock generally and so primary PCI has long been considered the preferred treatment (18). This recommendation was solidified after the SHOCK trial and registry conducted in the 1990s became available (19). In this trial 302 patients with cardiogenic shock due to myocardial infarction were randomized to receive standard care which included thrombolytics and IABP at the time or a rapid invasive management with the intent to revascularize the infarct related artery and other critical stenosis with PCI or CABG. A survival advantage was noted in the invasively treated group that became apparent at 6 months and continued for many years (20). It confirmed the importance of eliminating ischemia early in shock and this was done more effectively through invasive revascularization compared to thrombolytics. As mentioned previously it remained unclear if the IABP provided added benefits in patients with shock once the infarct artery was revascularized with primary PCI and significant ongoing ischemia eliminated. The IABP shock II trial looked at this question specifically (21, 22). Briefly, 600 patients with shock who underwent successful primary PCI were randomized to receive an IABP for continued support or conservative therapy. The primary endpoint of cardiovascular mortality was not different at 30 days and through 12 months of follow up despite a high mortality in both groups. There were also no differences in hospital stay, reinfarction or the subsequent development of heart failure. In the current era therefore, routine support with an IABP after successful primary PCI for cardiogenic shock offers little or no benefit.

Mechanical Support beyond the IABP

Cardiac hemodynamics remains poor even after revascularization in most patients with cardiogenic shock and this may explain the persistent high mortality even today. The IABP provides very little support for the acutely failing heart given its modest effects on hemodynamics (23). The demands on the left ventricle remain very high from increasing left ventricular volume, pressure and wall stress. This is further exacerbated by poor coronary perfusion pressure related to systemic hypotension. To interrupt this cycle the left ventricle must be aggressively unloaded of volume and circulation assisted by an alternative pump. This must also be accomplished rapidly and safely on such a critically ill patients. Three devices now available in the cardiac lab are discussed for consideration.

Extracorporeal membrane oxygenation ECMO

This may be considered a miniature form of cardiopulmonary bypass and has been available in some form for decades (24). It previously required significant surgery to establish but in the past several years it is now possible to establish this treatment percutaneously and expeditiously in the cath lab. Briefly a large 18-21 Fr cannula is advanced from the femoral vein and positioned in the IVC or right atrium to extract venous return and therefore unload the heart. A 15-17 Fr cannula is placed in the iliac artery or distal aorta via the common femoral artery to return circulation, mediated by a centrifugal pump. Since blood extracted has not made it to the lungs, it must be oxygenated by a membrane oxygenator before returning to circulation. In experienced centers, this device can be established in as short as 30 min at an acceptable risk and can remain place for days to allow for myocardial rest and recovery. There are several draw backs however (25). The large catheters and ongoing systemic anticoagulation result in frequent ongoing access site bleeding that may result in early termination. Without systemic anticoagulation, thrombosis of the circuit is almost certain and may be fatal. The large arterial catheter

also not infrequently, results in ischemia and or thrombosis of the limb vesels. The efficacy of support from ECMO is also of question. Pressure volume loop recordings show that the mechanical work of the heart is only slightly reduced. To date there have no trials to show overall benefits other than anecdotal reports. In the largest meta-analyses to date which involve about 1800 patients, mortality remained approximately 50% and major complications included major bleeding in a 3rd of patients and major limb ischemia in 15% (26).

Tandem Heart

The Tandem Heart Device (Cardiac Assist, Inc, Pittsburgh, Pa) places a large outflow cannula 21 Fr in the left atrium via a trans-septal atrial puncture and extracts oxygenated blood from the left atrium therefore effectively unloading the left ventricle. The blood is then returned to the arterial circulation via an adjustable pump through a 15-17 Fr cannula again placed in the iliac artery or descending aorta. Bleeding, thrombosis and ischemia are of similar concerns and magnitude with this device. The trans-septal puncture also requires high technical skills and can results in cardiac perforation and tamponade. Hemodynamic effects however are robust as evident from pressure volume loops indicating significant myocardial rest is achieved (27). The device can provide up to 4 L/min of output, be left in place for several days and be weaned gradually as the shock syndrome wanes. The device can also run with the patient awake and without ventilator support.

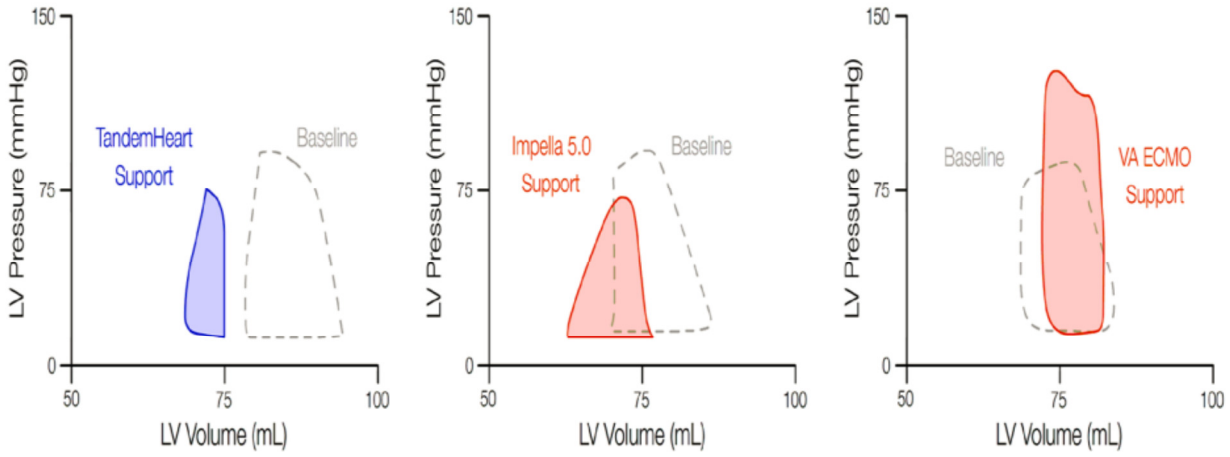
Impella

This device (Abiomed, Inc, Danvers, Mass) avoids a venous outflow catheter by a placing a 14 Fr catheter with a built in axial flow pump directly in the left ventricle. Blood is extracted from the left ventricle and delivered to the aorta effectively unloading the left ventricle and similarly assisting circulation (28, 29). The single arterial catheter is a major advance in rapidly establishing support and complications appear lower although the catheter positioned in the left ventricle can trigger arrhythmia and cardioembolic stroke. It often requires frequent manipulation to ensure optimal positioning but if uncomplicated, can be left in place for days. It does have an added benefit of increasing coronary and cerebral flow in these critically ill patients as the outflow is in the ascending aorta. Current models can provide up to 3.5 L/min of cardiac output almost totally obviating need for left ventricular contribution.

These newer mechanical devices substantially reduce left ventricular work improve allow myocardial rest and recovery. Hemodynamics are notable better compared to IABP and dramatic case of myocardial restoration have been described following acute ischemic injury and other forms of acute injury such as acute myocarditis. It remains to be seen if these devices with the higher risk profile will prove more successful in shock. The only comparative trials thus far have been small involving <60 patients and so are not definitive (30).

Percutaneous Cardiac Mechanical Assist Devices

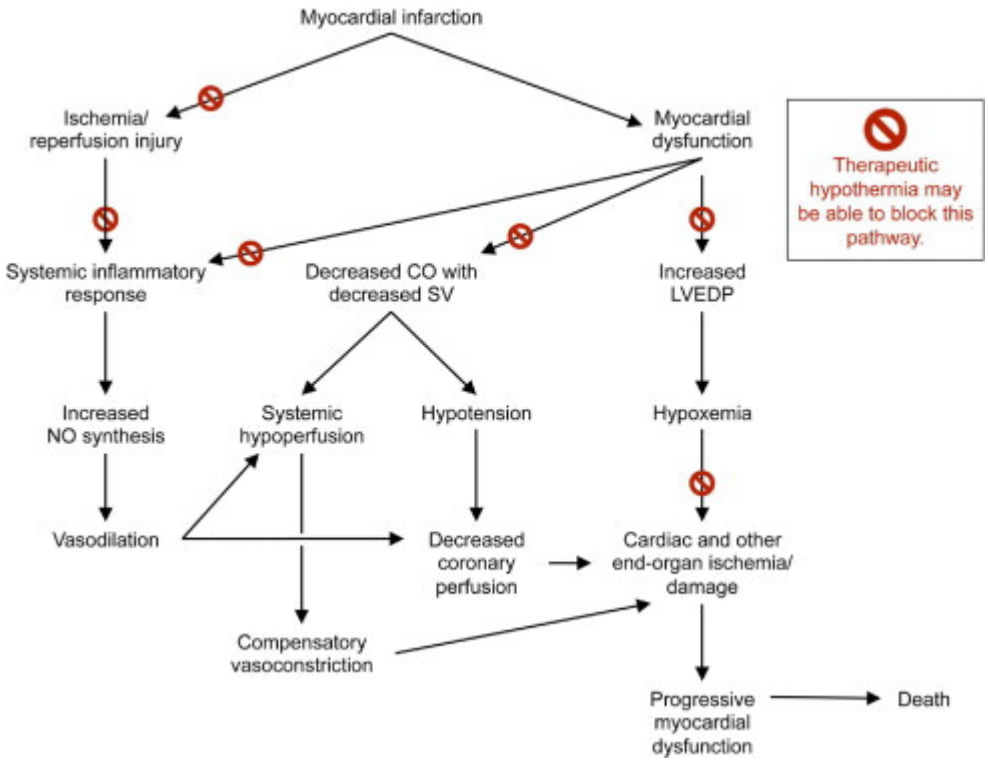
	ECMO	Tandem Heart	Impella LP 2.5/CP
Cannula or Catheter size	18-22 Fr Venous 15-17 Arterial	21 Fr Venous 15-17 Fr Arterial	13-14 Fr Arterial
Flow/Support(L/min)	3-6	~4	2.5-3.5
Pump type	Centrifugal	Centrifugal	Axial
Insertion sites	FV to VC + FA	LA + FA	FA to LV
Complexity	++	+++++	+++
Anticoagulation	Yes	Yes	+/-
Bleeding/Ischemia	++++	++++	+++
LV unloading	++	++++	+++
Insertion costs	~$10,000	~$25,000	~25,000



Pressure volume loops of percutaneous cardiac assist devices

Hypothermia

Finally, another management strategy for shock under investigation is reducing myocardial work along with reducing systemic demand and consumption (31, 32). This may be achieved by inducing moderate systemic hypothermia. The systemic inflammatory response syndrome and vascular derangements may be tempered by hypothermia. Cooling catheters placed in the vena cava are now available and can be rapidly employed to reduce core body temperature to as low as 33-35 degrees rapidly. This appears well tolerable in these ill patients and can be used alongside cardiac assist devices.



Conclusion

Cardiogenic shock is the most feared complication today after acute myocardial infarction as it accounts for most of the residual mortality today in this disease. Despite rapid revascularization, shock remains very difficult to manage and reverse once it develops. Devices that can be rapidly deployed to unload and rest the heart as well as reduce metabolic demands for a few days are now available for selective use. Definitive trials however are needed to prove clinical efficacy in light of costs and safety concerns.

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