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Review Article

Shock: What is it?, Why N = 1 and the Essential Monitored Therapeutic Goals Interventions

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Abstract

Objective: This perspective 1) defines Shock, 2) describes its inherent transient clinical nature, 3) explains why the published literature does not help in treating individual patients in Shock and 4) reviews proven individualized monitored therapeutic goals interventions approach for Shock management.

Data Sources: Published Critical Care Literature.

Data Selection: Reported Outcomes.

Data Synthesis: Success vs Failure of Shock Interventions.

Conclusions: Shock is a commonly misunderstood clinical metacondition occurring unpredictably in a wide variety of clinical diseases and infirmities. The published Shock studies are not helpful in managing individual patients with shock because critical outcome determinant combinations are not individually evaluated. Even with the lack of reporting of critical outcome determinants, monitored therapeutic goals interventions to achieve 'supra-therapeutic' goals appear to lead to the best outcomes.

Keywords: *Shock; Cardiogenic; Hemorrhagic; Septic; Pulmonary Artery Catheter; Monitored Therapeutic Goals*

Introduction

Shock is an unstable, inconsistently occurring, life-threatening metacondition that remains poorly defined, understood and managed. It is associated with a vast spectrum of diseases and infirmities (D/I), of varying severity and unpredictably may lead to a variety of Post-Shock Syndromes (PSS).

This perspective defines Shock and discusses the causes of the wide variability of Shock studies and their uselessness in managing an individual in Shock. It also addresses a common misunderstandings on the usefulness of basic invasive monitoring and how the initial management of Shock requires an individualized, early monitored therapeutic goals interventions approach if patients are to benefit. Finally, it describes a case of Shock managed using a stepwise monitored therapeutic goal intervention protocol.

Defining Shock

A Medical Shock webpage provides the following definition: 'Shock is a life-threatening medical condition as a result of insufficient blood flow throughout the body. Shock often accompanies severe injury or illness. Medical shock is a medical emergency and can lead to other conditions such as lack of oxygen in the body's tissues (hypoxia), heart attack (cardiac arrest) or organ damage. It requires immediate treatment as symptoms can worsen rapidly' [1].

Another UpToDate definition is as follows: 'Shock is defined as a state of cellular and tissue hypoxia due to reduced oxygen delivery and/or increased oxygen consumption or inadequate oxygen utilization' [2].

These and other Shock definitions fail to fully explain hypoglycemic or 'Insulin Shock' and shock from cyanide or carbon dioxide poisonings or thiamine deficiency. In these Shock situations, cellular and tissue blood flow and oxygen levels are actually increased. Shock is more than just 'insufficient blood flow throughout the body' or tissue hypoxia even though both of these are important elements of shock.

Since cells are the basic unit of life, Shock begs to be defined at the cellular level. What all Shock metaconditions have in common is the failure of cellular metabolism which is associated with anaerobic metabolism and the production of lactic acid [3]. With the exception of red blood cells, anaerobic metabolism cannot sustain prolonged cellular life and normal cellular metabolism must be reestablished for continued cell life. If it is not reestablished cellular death will ensue and if not reestablished quickly enough severe temporary and/or permanent cellular damage may result.

From a cellular perspective, Shock is defined as the unstable metacondition of failing pathophysiologic responses to D/I that are incapable of sustaining cellular life.

This Shock definition requires distinguishing between two spectrums of pathophysiologic responses. These are:

1. Normal Pathophysiologies (NP) that are pathophysiologic responses to D/I that are capable of sustaining cellular life; and
2. Shock Pathophysiologies (SP) that are pathophysiologic responses to D/I that are incapable of sustaining cellular life.

Practically, there is a continuum of pathophysiologic responses to D/I and the 'points' where NP degenerates into SP or SP improves into NP are largely unknown. It is highly likely that these points: 1) are not identical, 2) differ from person to person, and 3) vary over time in a person depending on many extenuating clinical and pathophysiologic circumstances. In general, NP are described as 'supranormal physiologic parameters' and associated with improved outcomes [4]. In contrast, SP are frequently in the 'normal physiologic ranges' and associated with decreased outcomes [5]. As a general rule, 'normal physiologic' parameters in advanced D/I is SP.

Based on the cellular definition, Shock may vary from being: 1) microscopic limited to a small number of cells such as the microangiopathy of diabetes mellitus; 2) localized within an organ such as cerebral or myocardial ischemia and infarction; 3) regional such as limb or bowel ischemia and infarction; to 4) whole body Shock. As a practice, the term Shock has been reserved for whole body Shock. The others are usually called organ 'ischemia' or 'infarction' based on the presence or absence of cell/tissue death.

For expediency, the remaining discussion on Shock is limited to the whole body Shock metacondition. The 'localized and regional Shocks' are fairly well described by their local names such as TIA/Stroke, Angina/STEMI, Critical Limb Ischemia/Gangrene and the like.

The majority of Shock is associated with one or more of three normal physiologic conditions, i.e., the Cardiogenic, Hemorrhagic or Septic 'Syndromes' that accompany many D/I. Not infrequently, these syndromes lead to the development of their Shock metaconditions, i.e. Cardiogenic Shock [6], Hemorrhagic Shock [7] or Septic Shock [8]. Each of these conditions with or without Shock have nuances that require specific tailoring of therapeutic goal interventions.

Finally, it is vital to determine the prognosis of the underlying D/I processes causing Shock. Shock is frequently part of an imminent death syndrome and therapeutic goal interventions are not medically indicated when death is the expected natural outcome. The inclusion of these patients in Shock studies contribute to their inutility.

Post-Shock Syndromes

If the SP are not corrected, cellular death is expected. Additionally, cellular injuries may result from Shock before the SP are corrected. If the patient survives their Shock, these cellular injuries may result in single or multi-organ dysfunction syndromes, i.e. Post-Shock Syndromes (PSS). Post-Shock Syndromes include Adult Respiratory Distress Syndrome (ARDS), Shock Liver, Acute Kidney Injury (AKI), Multi-Organ Dysfunctions/Failures (MOD/MOF), blood dycrasias and the like.

In scholarly articles, 'surviving Shock' also means surviving PSS. Surviving PSS depend on: 1) the extent and severity of cellular injury caused by the Shock; 2) the patient's ability to heal their cellular injuries; 3) any additional injuries related to medical management ('medical complications') and/or 4) progression of underlying D/I.

Shock and PSS survivals are analogous to 'CPR success' and 'CPR survival to discharge.' Although CPR is 'successful' 30 - 40% [9] of the time, hospital survival to discharge after CPR is a dismal 12 - 13% [10]. Likewise, many patients survive Shock only to succumb to PSS.

Thus, Shock Outcomes are frequently two phenomena. The first is survival of the actual Shock and the second is survival of any PSS. Again, for expediency, the remaining discussion is limited to the Shock metacondition and PSS are not discussed.

Why in Shock, N = 1

Overall, Shock Outcomes are determined by combinations of: 1) the patient's general physical status (PS); 2) the underlying D/I manifestations including severity, progression and treatment effects; 3) if present, comorbid conditions (CC); 4) the severity and duration of Shock; and 5) the presence or absence of PSS (Table 1A and 1B). The problems are even more complicated when the underlying D/I develop a concurrent Cardiogenic (C), Hemorrhagic (H) or Septic (S) conditions which in turn develops Shock and subsequently PSS (Table 1C).

A. D/I without Shock Metacondition: PS (± CC) + D/I --> Outcomes
B. D/I with Shock Metacondition: PS (± CC) + D/I + Shock (± PSS) --> Outcomes
C. D/I with C/H/S Condition and Shock Metacondition: PS (± CC) + D/I + C/H/S + Shock (± PSS) --> Outcomes

Table 1: *Outcome determinants in patients.*

(PS: Physical Status; CC: Comorbid Conditions; D/I: Disease/Infirmity Manifestations; S: Shock Metacondition; C/H/S: Cardiogenic, Hemorrhagic or Septic Condition; PSS: Post-Shock Syndrome).

The voluminous variations and nuances of all the factors (Table 1) determining outcomes are too complex for any single Shock study to address. So, scholarly studies focus on outcomes of similar types of Shock, e.g. Cardiogenic, Hemorrhagic or Septic Shock with or without PSS in very dissimilar patients, i.e. different PS, D/I and CC. In addition, PSS are descriptively grouped such as Adult Respiratory Distress Syndrome (ARDS) or Multi-Organ Failure (MOF). There are generally no stratifications by severity of ARDS or matching of the organ failures and their severities.

Scholarly studies evolved in this manner because it is impossible for any given institution or small consortium of institutions to amass enough patients with matching PB, CC and D/I and similar types of Shock and PSS to study. A minimum of regional and most likely national networks are necessary for such complex studies [11]. Hence, generalizations became a necessity.

Thus, due to the above it is a N = 1 for every patient in Shock since scholarly articles provide no help in managing an individual patient in Shock with known PS, CC, D/I and if they occur, PSS.

Managing Shock

The therapeutic goals of Shock interventions are aimed at converting SP to NP before 1) the patient dies and 2) there is un-survivable cellular injury. The mainstay of Shock management is fluid resuscitation and it is the single most useful early intervention identified. Yet, how to best monitor patients (especially since cardiac dysfunction is common) during the fluid resuscitation for Shock remains misunderstood.

Many issues still surrounds fluid resuscitations [see Fluid Challenge Revisited [12], Positive Study in Sepsis [13], Negative Study in Sepsis [14]]. In spite of this, every patient in Shock should undergo a monitored fluid challenge with hemodynamic responses measured. Individualization of Shock management through protocols leads to the best outcomes [4]. Yet, since this hasn't been studied in patients with identical PS, CC, D/I and PSS, the best fluid resuscitation protocols for any particular patient remain largely undetermined for any type and severity of Shock. Thus, N = 1.

A very common feature of Shock is marked cardiovascular dysfunction. Basically, the Frank-Starling Law 'states that the stroke volume of the heart increases in response to an increase in the volume of blood filling the heart (the end diastolic volume) when all other factors remain constant' [15]. The problem in Shock is that "all other factors" do not remain constant. One or more determinants of ventricular performance, i.e. inotropy, chronotropy, preload, afterload and ventricular interdependence, are effected in NP and adversely effected in SP.

Thus, in Shock the ventricular performance for any given ventricular preload is unknown since it is unknown whether the ventricular responsiveness is depressed, control/normal or enhanced (Figure 1) [16].

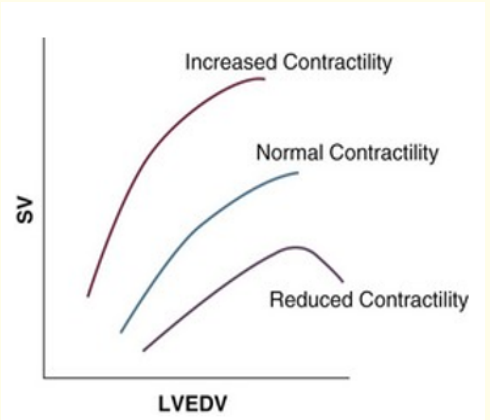

Figure 1: *Normal Physiologic Response is Increased Contractility vs Shock Physiologic Response is Reduced Contractility.*

Also, the LV performance for the same LV preload (Figure 2) [17] varies in patients with 'normal' (Group 1), 'moderate' (Group 2) and 'severe' LV dysfunction (Group3).

Clinically, the LV preload is the stretch of the LV muscle prior to contraction and is related to the left ventricular end diastolic volume (LVEDV). And the LVEDV is dependent on the left ventricular end diastolic pressure (LVEDP). This Volume-Pressure relationship defines LV Compliance and equals LVEDV/LVEDP. Like any muscle, LV Compliance will determine the effect LVEDP will have on LV performance. And, it is LV compliance that changes unpredictably in Shock and is manifested as cardiac dysfunction. Consequently, monitoring Ventricular Preload alone such as with the Pulmonary Capillary Wedge Pressure (PCWP) or Central Venous Pressure (CVP) without knowing LV compliance is clinically useless.

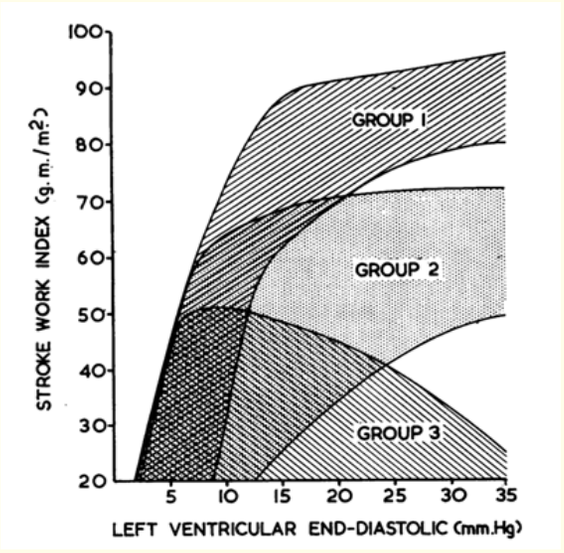

Figure 2: *Variable LV Performance (SWI) for same LV Preload (LVED).*

Other cardiovascular dysfunctions of Shock include Intravascular Volume (IVV) and/or Intravascular Volume Capacity (IVVC) derangements. Generally, primary IVV losses lead to normal physiologic and compensatory decreases in IVVC. At some point, further IVV losses exceed the IVVC to decrease, NP fails and Shock will ensue. Hemorrhagic Shock is an example.

In contrast, in Sepsis there are abnormal and marked increases in IVVC. This causes a previously 'normal' IVV to then be markedly deficient. Depending on a multitude of factors, Compensatory mechanisms, i.e. NP, may or may not, i.e. SP, be capable of sustaining cellular life.

The combinations of cardiac dysfunction and IVV and IVVC changes necessitate the invasive monitoring of Shock. The questions of how and what to monitor remain controversial due to unfortunate circumstances.

Monitored therapeutic goals interventions for shock

At best, patterns of therapeutic goals interventions associated with improved Outcomes from Shock were reported in the late 20th Century [18]. Then, a 2006 meta-analyses on Shock scholarly articles changed everything. Not surprisingly, joining studies of mixed methodologies on dissimilar patients and outcomes led to the conclusion that 'Pulmonary Artery Catheters as currently used, do not benefit patients' [19].

Paradoxically, the Pulmonary Artery Catheter (PAC) is not a therapeutic device! Like other ICU monitoring device, the PAC is only a monitoring tool and, at times, a diagnostic device. It was the lack of or inadequate therapeutic goals intervention protocols or failure to adhere to determined protocols that led to the conclusion the PAC "as currently used" was not benefiting patients. This means the failure was in the users of the PAC and not in the PAC itself.

What clinicians failed to heed were the words PACs 'as currently used' and go back and evaluate which PAC monitored therapeutic goal interventions appear to have success and which didn't. Then study and further refine those successful interventions as suggested [20].

Unfortunately, the 2006 meta-analysis did not inspired new studies refining and defining patients with Shock had and possibly describing useful specific PAC monitored therapeutic goals intervention protocols. Instead, as if the PAC itself was itself therapeutic that meta-analyses stopped the utilization of PAC in Shock management altogether.

Hence, since 2006 clinicians attempting to manage Shock are in a state of limbo, i.e. knowing that they need to use therapeutic goals intervention protocols but also unable to monitoring them because the use of the PAC does "not benefit patients".

There are demonstrated benefits of hemodynamic monitoring in similar patients for example when the Central Venous Pressure (CVP) is used in early goal directed therapy in patients with severe Sepsis and Septic Shock [21]. As noted, even though the CVP may be an indicator of IVV status, it does not assess concomitant cardiac dysfunction. Thus, a higher CVP may be due to increased IVV, worsening cardiac dysfunction, isolated right ventricular dysfunction or some degree of each. This makes the CVP minimally helpful and may explain the variation in fluid resuscitation in Sepsis outcomes noted.

Also, since the increased lactic acid in Shock reflects cellular anaerobic metabolism and a key goal of therapy is to re-establish cellular aerobic metabolism, Oxygen Delivery (DO_2) and Oxygen Consumption (VO_2) are probably key parameters to follow [13-15]. A PAC is required to measure these parameters.

In summary, when used with therapeutic goal intervention protocols, the PAC is invaluable [22] and frequently indispensable tool in monitoring protocol effects in critically ill patients with Shock. Below describes the appropriate knowledge for using the PAC for monitoring therapeutic goals interventions in one patient with Shock.

Clinical lessons from a shock case study

The best way to learn is through stories [23]. (What are Case Presentations but stories?) The following case study ('story') illustrates a basic intervention protocol for managing Shock in a patient. Even though the narrative changes for every patient in Shock the approach to Shock in this story is that shown to lead to improved outcomes.

Case

A healthy 35 y.o. woman had recently returned from a vacation during which she developed urinary symptoms. She saw her PCP who determined she had a lower urinary tract infection and started her on trimethoprim/sulfamethoxazole. Several days later she presented to the Emergency Department obtunded and unresponsive. Her PMH, SH, FH and ROS were noncontributory.

Pertinent findings included an obtunded woman with BP 88/55, HR 125, RR 28, T99.9F. The physical exam was essentially normal except for mild abdominal guarding, cool extremities and the decrease mental status.

On laboratory testing she was found to have a serum Lipase of over 35,000 U/L and arterial blood gases on a 2L NC revealed a pH of 7.30 $PaCO_2$ 28 mmHg, PaO_2 100 mmHg and SaO_2 of 95%.

She was diagnosed with drug-induced Pancreatitis and admitted to the MICU where I was the Attending. I managed her care with a Resident and taught him as we went along. The following is an approximate sequence of my teaching points.

#1 In the ICU her physical exam was unchanged and her skin was cool and dry and her great toe temperatures were both 75oF suggesting she had a low cardiac index.

Lesson #1: 'Great Toe Temperature'.

'A significant correlation was demonstrated between the cardiac output and temperature of the toe (r = 0.71). Correlations were increased to 0.73 when corrections were made for changes in ambient temperature. A stepwise regression analysis provided no significant improvement in the predictability of cardiac index when the values for temperatures of other skin sites were included. Discriminant function analysis showed that an early measurement of toe temperature correctly predicts patient outcome 67% of the time' [24].

This is valuable 'lost' information from the past. The 'normal' great toe temperature is 88°F. A great toe temperature > 90°F suggests increased CI and/or vasodilation and frequently seen in sepsis. In contrast, a low great toe temperature of < 80°F suggests a low CI and significant cardiac dysfunction.

#2 I strongly suspected she was in "Shock" due to her decreased mental status, a low cardiac index suggested by her great toe temperature and the metabolic acidosis on arterial blood gases. In order to determine the presence and severity of cardiac dysfunction suspected, I immediately inserted a PAC. Her initial PCWP of 25 mmHg was abnormal but her Cardiac Index (CI) of 3.5 L/min/m^2 and her Left Ventricular Stroke Work Index (LVSWI) of 35 gm-m/m^2/beat were both 'normal'.

Lesson #2: As noted above, in advanced D/I "Normal physiology" = SP. There was marked cardiac dysfunction because the CI and LVSWI were 'normal' (Figure 2).

Lesson #2b: Why use a LVSWI?

Cardiac Index (CI) is CO/BSA L/min/m^2; Stroke Volume Index is [(CI/Heart Rate) x 1000] ml/m^2/beat; MAP is Mean Arterial Pressure in mmHg, PCWP is Pulmonary Capillary Wedge Pressure in mmHg. The LVSWI = [SVI x MAP-PCWP x 0.0136]. The Normal range is 30 - 100 gm-m/m^2/beat.

The three major parameters of LVSWI, i.e., SVI, MAP and PCWP are individually important cardiovascular values; so when the LVSWI is abnormal one just needs to look at which one(s) of this value(s) is amiss. The SV and LVSWI are the 'most powerful hemodynamic predictors of 30-day mortality' in Cardiogenic Shock patients [25].

We then plot ted LV Performance vs. Preload using the LVSWI as the LV Performance surrogate and PCWP as Preload surrogate on a graph (Figure 3) [26].

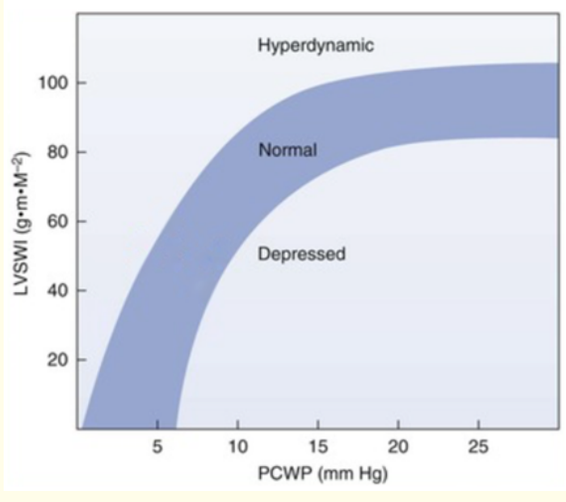

Figure 3: *Left Ventricular Stroke Work Index (LVSWI) vs. Pulmonary Artery Wedge Pressure (PACWP) Relation.*

For this patient, plotting the PCWP of 25 mmHg and LVSWI of 35 gm-m/m/beat revealed a markedly depressed cardiac performance consistent with SP. This was supported by an elevated lactic acid level of 8 mg/dl. She was diagnosed with Shock due to Pancreatitis. From arriving in the MICU to this diagnosis took less than an hour.

#3 Once determined that she was in Shock, a fluid resuscitation was started.

Lesson #3a: The Resident complained about the fluid challenges because her PCWP was 25 mmHg! He suggested a diuretic which is the common response to these parameters. This is an example of applying old Cardiogenic Shock knowledge to other types of Shock management. The left ventricular dysfunction is usually reversible with fluid administrations in Shock even in a minority of Cardiogenic Shock and should always be attempted.

The causes of severe cardiac dysfunction in systemic inflammatory response syndromes are unknown [27]. The fact that some are reversible in is known [28].

Lesson #3b: There is a monitored stepwise fluid challenge study that individualizes patient responses (Table 2 and 3) [29]. The key to this protocol is that it is stepwise and follows the patient's hemodynamic response to each fluid challenge and proceeds based on the patient's hemodynamic response. It is not generalize to a disease state but rather individualized to the patient. This protocol has been recently updated [30] but it suffers from the use of CVP only; thus LVSWI and the ability to assess SVI, MAP and PCWP effects cannot be followed.

Basically the original protocol uses a CVP or PCWP to monitor patient responses to a fluid challenge given every 10 minutes. The following tables show the protocols for CVP (Table 2) and PCWP (a.k.a., P_{PAW}) or Pulmonary Artery Diastolic Pressure (P_{PAD}) (Table 3). The PCWP methodology is the preferred since the LVSWI can be calculated and it allows the effects of the fluid challenges on SVI, MAP and PCWP.

Fluid challenge: CVP, cm Hg (5-2 rule)			
Observe CPV for 10 minutes	< 8 cm H_2O	200 ml x 10 min	Peripheral VI
	<14 cm H_2O	100 ml x 10 min	
	≥ 14 cm H_2O	50 ml x 10 min	
During infusion 0 - 9 minutes	> 5 cm	STOP	
following infusion	>2 < 5 cm	Wait 10 minutes	
	> 2 cm	Wait STOP	
	≤ 2 cm	Continue infusion	

Table 2: *Guidelines for fluid challenge utilizing central venous pressure monitoring.*

Fluid challenge: P_{pAw}, P_{pAD} mm Hg (7-3 rule)		
Observe PPAD/PPAW for 10 minutes	< 12 mm Hg	200 ml x 10 min
	< 16 mm Hg	100 ml x 10 min
	≥ 16 mm Hg	60 ml x 10 min
During infusion 0 - 9 minutes	> 7 mm Hg	STOP
Immediately following 10 minutes infusion	>3 < 7 mm Hg	Wait 10 minutes
	> 3 mm Hg	Wait STOP
	≤ 3 mm Hg	Continue infusion

Table 3: *Guidelines for fluid challenge utilizing pulmonary artery diastolic or pulmonary artery wedge pressure monitoring.*

Her fluid challenge using PCWP was started and proceeded per protocol. With the stepwise fluid challenges, her PCWP of 25 mmHg dropped stepwise to 12 mmHg and her LVSWI increased stepwise to 105 gm-m/m3/beat after a fluid challenge over about 2 hours.

Plotting her last values on the graph (Figure 3) showed a hyperdynamic, a.k.a., 'supranormal' cardiac performance consistent with NP. Her LV Compliance continuously improved with her stepwise fluid challenge. This could not have been discerned from just CVP monitoring. Her fluid challenge was stopped because her SP had been converted to NP.

In support of her improvement were improving vital signs, a great toe temperature that was increasing and in the upper-80's at the time her fluid challenge was stopped and a repeat lactate level a few hours later that was normal as expected [31].

Lesson #3c: This case demonstrated a 'textbook' response to a monitored therapeutic goals intervention protocol. She was young and otherwise healthy and thus the exception to most patients in Shock.

The vast majority of patients in Shock undergoing monitored therapeutic goal interventions were/are not young nor healthy and do not do as well. Typically, fluid resuscitation continues for hours and an inotropic agents are needed to enhance LV performance.

Importantly, comprehensive knowledge of the treatment and management of the three major types of Shock, i.e. Cardiogenic Shock Treatment and Management [6], Hemorrhagic Shock Treatment and Management [7] and Septic Shock Treatment and Management [8] is required in order to individualize monitored therapeutic goals interventions. Without monitored therapeutic goals intervention protocols, interventions are either "novel" or "cookbook" and may be a disservice to individual patients.

Conclusion

In Shock, restoration of NP survived leads to improved outcomes. Deaths when they occur are frequently from PSS or the underlying D/I. The vast majority who remain with SP (and lactic acidosis) die. Studies using monitored therapeutic goals intervention protocols that convert SP to NP in patients show improved survival [32]. Thus, monitored therapeutic goals interventions are state of the art. The questions are "which goals", "in whom" and in which D/I. Answers to these questions require further studies.

Due to the diverse and variable manifestations of Shock, individualized management is mandated. And due to the complex relationships between the cardiac dysfunction, IVV and IVVC, monitored therapeutic goals intervention protocols are essential.

Finally, the underlying PS and D/I and their natural outcomes must be taken into account in order to avoid interventions when death is the expected imminent outcome. Intervening in these circumstances is not only futile and wasteful but also unethical.

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