Multiple Organ Dysfunction Syndrome

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KEY POINTS:

1. Multiple organ failure is the primary mechanism of death in intensive care unit patients.
2. Most organ failure is reversible.
3. Optimizing tissue perfusion is the best immediate treatment to reduce organ failure.
4. Eliminating the cause of shock and/or sepsis is the most important

overarching priority in preventing and mitigating any organ failure.

MODS can be defined as "the inability of one or more organs to support its activities spontaneously without intervention."

Initial recognition of MODS

came during World War II as advances in resuscitation strategies allowed casualties to survive the initial hemorrhagic shock insult, but rendered them vulnerable to subsequent acute renal failure

ETIOLOGY

Sepsis is the most common cause of organ failure in the ICU.
The incidence of MODS varies based on primary diagnosis and the scoring system used to determine organ dysfunction.
[7] Septic patients are more likely to have organ dysfunction and more organ failures than nonseptic patients,
And mortality is higher in MODS when sepsis is present (31% vs 21%).[8]
Patient outcomes appear to be more favorable when patients resolve or experience improvement in organ failure within the first 24 hours of admission to the ICU.

Of organ systems, hepatic failure and dysfunction in coagulation are most predictive of mortality.

Risk Factors for MODS

Infection
Peritonitis and intra-abdominal infection
Pneumonia
Necrotizing soft tissue infections
Tropical infections (eg, falciparum malaria, typhoid fever, dengue fever)
Inflammation
Pancreatitis
Ischemia
Ruptured aortic aneurysm
Hemorrhagic shock
Mesenteric ischemia

Immune reactions
Autoimmune disease
Reactive hemophagocytic syndrome
Antiphospholipid antibody syndrome
Transplant rejection
Graft-versus-host disease
Iatrogenic causes
Delayed or missed injury
Blood transfusion
Injurious mechanical ventilation
Treatment-associated increased intra-abdominal pressure
Intoxication
Drug reactions (anticonvulsants, carboplatin, antiretrovirals, colchicines, propofol, amiodarone, monoclonal antibodies)
Arsenic
Drug intoxication (ecstasy, cocaine, salicylates, acetaminophen)
Endocrine disorders (thyrotoxicosis, pheochromocytoma)
Adrenal crisis
Pheochromocytoma
Thyroid storm
Myxedema coma

For many years, death from organ failure after sepsis was considered to be bimodal.

Early deaths were the result of cardiac or pulmonary failure, perhaps exacerbated by inadequate resuscitation.

Later deaths were the result of sequential MODS.

More recently, a third peak of mortality has been identified.

This may occur 90 days or longer after initial injury and occurs in patients who develop chronic critical illness and persistent inflammation, immunosuppression, and catabolism syndrome.[14]

Risk factors for chronic critical illness include increased age, medical comorbidities, severe injury, septic shock, and malnutrition.[15]

Mitigating chronic critical illness represents the next horizon for improving care of the critically ill patient.

DIAGNOSTIC CRITERIA AND SCORING SYSTEMS

Criteria Used in Common Organ Dysfunction Scoring Systems

Organ	Variable	Denver MOF[10]	SOFA[11]	LODS[12]	MOD
Respiratory	PaO_2/FiO_2	Yes	Yes	Yes	Yes
	MV		Yes		
Hematology	Platelets	Yes	Yes	Yes	
	WBC			Yes	
Hepatic	Bilirubin	Yes	Yes	Yes	Yes
	Prothrombin time			Yes	
Cardiovascular	MAP		Yes		
	SBP			Yes	
	Heart rate			Yes	
	PAR [(HR × CVP)/MAP]				Yes
	Dopamine			Yes	
	Dobutamine			Yes	
	Epinephrine			Yes	
	Norepinephrine			Yes	
	Any inotrope	Yes			
CNS	GCS		Yes	Yes	Yes
Renal	Creatinine	Yes	Yes	Yes	Yes
	BUN			Yes	
	Urine output		Yes	Yes	

MECHANISMS OF MULTIPLE ORGAN DYSFUNCTION SYNDROME

The systemic inflammatory response syndrome (SIRS) is frequently viewed as a predecessor and lies on a continuum of dysfunction with MODS.

Components of the SIRS response are seen in virtually all patients following an operation, febrile illness, or injury.
SIRS frequently resolves without progression to MODS.

MODS may be viewed as a result of an ongoing, dysregulated, or treatment refractory SIRS response with progressive organ system derangement.

Several mechanisms for the onset and propagation of MODS have been proposed, including an initial insult in which ischemia,
oxidative stress,
mitochondrial dysfunction, and
activation of apoptotic pathways lead immediately to organ failure, release of toxic intestinal derived mediators into mesenteric lymph, a "two hit" model, where an initial stimulus primes the immune system to respond to a subsequent insult or stimulus with an exuberant reaction, and the concept that dysregulated immune responses lead to MODS.

A common theme in the onset and propagation of MODS is the presence of a disordered immune response.

Ongoing tissue hypoperfusion likely leads to activation of the acute inflammatory response, oxidative imbalance, structural rearrangement of cellular proteins, dysregulation of the immune system, activation of apoptotic pathways, cell death, and organ dysfunction.[28]

Although inflammation is a normal process during recovery from tissue injury and infection, organ failure may result from persistent pro-inflammatory immune system activation.

This process leads to alterations in **the microcirculation**, with resultant **endothelial cell dysfunction**, loss of the endothelial cell glycocalyx, impaired red blood cell deformity, increased leukocyte and platelet adhesion, and formation of microvascular thrombi, with resultant cellular hypoxia and organ mdysfunction.

PICS

(persistent inflammation, immunosuppression, and catabolism syndrome), this syndrome consists of loss of lean body mass, recurrent infection, and increased debility.

PICS

is associated with severe bone marrow dysfunction, alterations in innate immunity, persistent elevation of inflammatory biomarkers, prolonged intensive care unit stays, and increased mortality.

CURRENT MANAGEMENT CONSIDERATIONS

Ranging from 0 to 24, an increase in SOFA score by 2 points is associated with a 10% increase in mortality.

SOFA can be used to allocate clinical resources, predict outcome, and provide context for decision-making and for enrolling and monitoring research subjects in clinical trials.[34]

In patients admitted to the ICU, a change in SOFA score during the first 4 days is associated with worsening mortality

The major strategy to reduce progression from sepsis to MODS is to restore adequate oxygen delivery and normalization of physiology.

Optimal initial resuscitation begins with a balanced crystalloid solution, followed by restoration of mean arterial blood pressure support with the use of vasopressors.

In adults with ongoing requirements for vasopressor support, intravenous corticosteroids should then be added.

Source control

If the patient is suspected to have sepsis or septic shock, broadspectrum antibiotic therapy should be rapidly initiated, with the addition of antifungal therapy if deemed at high risk for fungal infection[36].

On the basis of the possible role of the gut and enteric bacteria as a “motor” for MODS, several groups have proposed cleansing the bowel of bacteria to disrupt this relationship, but studies have yielded conflicting results and this practice remains controversial.

Transfusion is a risk factor for MODS, suggesting that a conservative approach to blood transfusion is appropriate

Respiratory failure

common and may arise from local or distant lung infection but also noninfectious etiologies including trauma, burns, cardiopulmonary bypass, and other causes of shock.[5]

In severe cases, increased capillary permeability leads to alveolar fluid accumulation and loss of surfactant, with diminished lung compliance and impaired gas exchange and progression to

ARDS

avoidance of high inspiratory pressures (peak inspiratory pressures below 35 cm H_2O and plateau pressures below 30 cm H_2O), elevating mean airway pressure through prolonged inspiratory times or alternative modes of ventilation such as airway pressure release ventilation, prone positioning, and inhaled vasodilators such as epoprostenol or nitric oxide.**ECMO**

Cardiovascular failure during sepsis and MODS begins with overproduction of nitric oxide in vascular smooth muscle and endothelium as a result of a potent pro-inflammatory cascade.

Myocardial dysfunction follows the initial vasodilation response and consists of systolic and diastolic dysfunction mediated by multiple factors, including altered calcium channels, increased oxidative stress, and direct effects of pro-inflammatory cytokines

Use of echocardiography or a pulmonary artery catheter may aid with diagnosis. Therapy consists of resuscitation in order to restore adequate intravascular volume and oxygen delivery as well as support with inotropes and vasopressors.

Renal failure

up to 20% of all patients admitted to the ICU suffering acute kidney injury. This finding is associated with mortality up to 70%, with increased mortality occurring with increasing age, severity of illness, need for mechanical ventilation, and requirements for vasopressor support

Acute kidney injury may result from sepsis, heart failure, major operations, or hypovolemia. For many patients, acute kidney injury appears to be the result of hypoperfusion plus pro-inflammatory mediators but may occur without renal hypoperfusion

Strategies to prevent acute kidney injury include adequate resuscitation with intravenous fluids, vasopressors to maintain adequate organ perfusion, and avoidance of nephrotoxic agents

but volume administration in excess increases interstitial fluid, contributes to the low oncotic pressures seen in acute kidney injury, and can worsen renal function.

Ideally, patients receive intravenous fluids in amounts adequate to restore euvolemia, with consideration of “deresuscitation” with judicious use of diuretics as the patient enters the recovery phase.

Recombinant human alkaline phosphatase[47] and the anti-CD28 antibody reltecimod[48] have each undergone clinical efficacy trials and show promise as a potential therapy to decrease acute kidney injury.

Dysfunction of the gastrointestinal tract

The gastrointestinal tract may be both an inciting party and a victim in MODS and appears to release pro-inflammatory mediators that play a key role in this process.[2]

[7] The gut includes the largest single-organ mass of lymphoid tissue in the body, and these cells, along with the intestinal mucosa, appear to be particularly sensitive to tissue ischemia.[49]

Loss of intestinal mucosal barrier integrity may lead to bacterial translocation and infection.

The role of the gut microbiome in health and disease is not fully understood and is the subject of ongoing investigation.

Malnutrition may result from gastrointestinal dysfunction in combination with elevated metabolic needs after injury or infection.

Maintenance of adequate nutritional status is associated with improved outcome for patients with severe trauma, surgery, sepsis, and MODS.

The American Society for Parenteral and Enteral Nutrition (ASPEN) recommends starting enteral nutrition within 24 to 48 hours for critically ill patients who cannot take nutrition orally and in patients with preserved hemodynamics, with advancement of nutrition to the nutritional goal within 5 days.

Neurological dysfunction, termed sepsis-associated encephalopathy,

This is a diagnosis of exclusion and is difficult to evaluate as part of a cognitive exam due to sedation.

The presence of sepsis-associated encephalopathy is supported by absence of focal neurological deficits and the presence global cognitive impairment that exceeds that expected by the amount of sedation present.[54]

The etiology is complex and includes endothelial activation, breakdown of the blood-brain barrier, cerebral inflammation, and apoptosis.[55]

Sepsis-associated encephalopathy is rarely fatal by itself but may lead to significant morbidity among survivors

hematologic system dysfunction

alterations in erythrocytes, coagulation, and platelet functions. Anemia of critical illness occurs secondary to bone marrow suppression as well as impaired erythropoietin and iron metabolism.

This is exacerbated by chronic illness
anemias that precede acute critical illness and are further worsened by blood loss
to procedures and phlebotomy.

Dysregulation of the coagulation system occurs
due to multiple factors, including activation of coagulation mechanisms and inhibition of normal physiological anticoagulation mechanisms,

Thrombin formation due to altered tissue factor expression on monocytes and endothelial cells, impairment of protein C by cytokines, and upregulation of plasminogen

activator inhibitor 1, which impairs fibrin removal.

Each of these processes leads to formation of microvascular thrombi, with subsequent tissue ischemia and organ damage.[57]

Platelet disorders include thrombocytopenia and consumption by formation of microthrombi.

PROGNOSIS AND ICU LENGTH OF STAY

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Up to 20% of patients admitted to an ICU develop aspects of MODS, with significantly increased morbidity and mortality.[59]

MODS severity is decreasing but ICU mortality remains stable, perhaps because overall acuity is increasing.[60]
In an epidemiologic study of sepsis in 2001, Angus et al[61] determined that dysfunction of one, two, or three organ systems conveys 1%, 4.7%, and 20.7% mortality, respectively.

Four-organ dysfunction was associated with 65% to 74% mortality.[8,61]

A more recent study examining the outcomes of critically ill patients reported ICU mortality of 10% for failure of three systems or less, increasing to 25% and 50% for four- and five-organ system failure, respectively.

Mortality of seven-system failure was 100%.[62] In addition to mortality, MODS can also affect long-term functional outcomes

با تشکر از توجه شما