Med Intensiva. 2014;38(7):455–462

medicina intensiva

www.elsevier.es/medintensiva

UPDATE IN INTENSIVE CARE

# Multiorgan failure in the serious trauma patient☆

**J.A. Llompart-Pou[a,*], M. Talayero[b], J. Homar[a], C. Royo[a], Trauma and Neurointensive Care work group of the SEMICYUC**

[a] *Servei de Medicina Intensiva, Hospital Universitari Son Espases, Palma de Mallorca, Spain*
[b] *Unidad de Cuidados Intensivos de Trauma y Emergencias, Servicio de Medicina Intensiva, Hospital Universitario 12 de Octubre, Madrid, Spain*

Received 7 April 2014; accepted 7 May 2014

**KEYWORDS**
Severe trauma;
Multiorgan failure;
Clinical scales

**Abstract** Multiorgan failure remains one of the leading causes of late morbidity and mortality after severe trauma. In the early phase, it is related with an uncontrolled hyper-inflammation state, whereas in the late phase (>72 h), septic complications play a major role. We review the underlying pathophysiology, the evaluation with different scales and the clinical factors associated with multiorgan failure, as well as potential treatment options.


**PALABRAS CLAVE**
Trauma grave;
Fallo multiorgánico;
Escalas clínicas

**Fallo multiorgánico en el paciente con trauma grave**

**Resumen** El fallo multiorgánico tras el trauma grave constituye una de las principales causas de morbimortalidad tardía en este grupo de pacientes. En su fase precoz, es consecuencia de un estado de hiperinflamación no controlado, mientras que en su presentación tardía (>72 h) se relaciona principalmente con las complicaciones infecciosas. Se resumen los mecanismos fisiopatológicos implicados en su desarrollo, la valoración mediante diferentes escalas y los factores clínicos asociados, además de las potenciales opciones de tratamiento.


## Introduction

The development of multiorgan failure (MOF) after severe trauma is one of the leading causes of late mortality in such patients.[1,2] The incidence of MOF varies between 7% and 66%, and despite recent advances in the pre- and in-hospital management of these patients, the disorder is associated to important mortality and prolonged hospital stay.[1–5] Although MOF is recognized to be a dynamic process, agreement

☆ Please cite this article as: Llompart-Pou JA, Talayero M, Homar J, Royo C, grupo de trabajo de Trauma y Neurointensivismo de SEMICYUC. Fallo multiorgánico en el paciente con trauma grave. Med Intensiva. 2014;38:455–462.

* Corresponding author.
*E-mail addresses:* juanantonio.llompart@ssib.es, ja_llompart@hotmail.com (J.A. Llompart-Pou).

is lacking regarding its definition.[6] The underlying physiopathology is moreover subject to debate, and involves the participation of different components of the immune and inflammatory systems.[7,8]

The present article reviews the current knowledge on the epidemiology and physiopathology of MOF, the scales used to evaluate the disorder, the clinical factors associated to the development of MOF, and the possible treatment options.

## Definition

While no uniform definition of post-trauma MOF has been established to date,[6] a number of scales have been developed for evaluating patient respiratory, cardiovascular, hepatic, renal, neurological and coagulation function–including particularly the Denver, Marshall and Sequential-related Organ Failure Assessment (SOFA) scales. These instruments will be examined further below.

Despite the limitations imposed by the lack of a clear definition of MOF, there is agreement in regarding early MOF as multiorgan failure occurring in the first 72 h after trauma (this representing approximately 40% of all cases), while late MOF is taken to be multiorgan failure occurring beyond day three post-trauma (60% of all cases).[6]

## Epidemiological aspects

Post-trauma MOF is the leading cause of late mortality in severe trauma, accounting for 50–60% of all deaths in such patients.[1–6] Those individuals that develop post-trauma MOF have a longer stay in the Intensive Care Unit (ICU). The associated mortality rate varies between 27% and 100%, and increases with the number of affected organs.[6,8,9] As early as 1980, Fry et al.[8] showed mortality to increase from 30% in the presence of single-organ dysfunction to 100% in the case of dysfunction affecting four organs. A study conducted in a single reference center for severe trauma in the United States, involving data prospectively collected over a period of 12 years, has found the incidence, duration and mortality of MOF to have decreased in recent years–this being related to advances and new treatment modalities in application to severe trauma patients, and to a decrease in the number of transfusions.[1] A recent multicenter study including 1643 trauma patients reported a decrease in incidence of almost 50%–though the related mortality remains very high.[2]

The incidence of MOF is greater in closed trauma patients, and in these cases are associated to greater mortality than in penetrating trauma.[1,6]

## Physiopathology

Although the physiopathology of MOF in severe trauma is not fully clear and has evolved over the last 30 years, it is currently accepted that the disorder is a bimodal phenomenon with two peaks of presentation, due to an alteration in the balance of the systemic inflammatory response followed by ischemia-reperfusion after hemorrhagic shock. This is in contrast to the early theories which pointed to generalized infection as the sole cause of MOF.[6,9]

In this regard, respiratory failure appears to play a key role in early MOF, manifesting in 99% of all cases and usually preceding heart dysfunction by a few hours, and liver and kidney dysfunction by about 5 days.[10] In contrast, late MOF occurring beyond 72 h after trauma requires a second ''hit'',[6] usually in the form of infection (mostly of pulmonary origin).[10]

A number of mediators and effectors can potentially intervene in the physiopathology and development of post-trauma MOF (Fig. 1):

### Mediators

- Cytokines: The balance between proinflammatory and antiinflammatory cytokines plays a key role in the maintenance of homeostasis. Following severe trauma there is an overproduction of proinflammatory cytokines such as tumor necrosis factor-alpha (TNF-$\alpha$), interleukin (IL)-1$\beta$, IL-6 and IL-8 on the part of monocytes and macrophages. This constitutes part of the acute phase response, contributing to initiation and perpetuation of the local and systemic inflammatory response.[7,11] TNF-$\alpha$ increases the production of nitric oxide (NO) and activates cyclooxygenase, resulting in an increased production and release of thromboxanes, prostaglandins and platelet activating factor (PAF)–with a consequent increase in procoagulant activity.[7,12] In turn, IL-6, produced by different cells such as activated monocytes, macrophages, neutrophils and endothelial cells, plays an important role in the acute response, intervening in the production of C-reactive protein, procalcitonin, fibrinogen, $\alpha$-1-antitrypsin and complement factors.[6] In addition, IL-6 regulates the growth and differentiation of lymphocytes and activates natural killer (NK) cells and neutrophils. It is widely agreed that the measurement of IL-6 is a good indicator of trauma severity and outcome.[13] Interleukin-8 participates in leukocyte recruitment, and facilitates the activation of these cells at the damage site. The levels of IL-8 are correlated to the development of acute respiratory distress syndrome (ARDS) following severe trauma.[7] Of the different antiinflammatory cytokines, mention must be made of IL-10, which is synthesized by lymphocytes and monocytes. This cytokine fundamentally inhibits the production of TNF-$\alpha$, IL-6 and IL-8.[7]
- Complement system: Activation of the complement system can occur after severe trauma via any of the known pathways (alternative, classical, lectin), generating biologically active peptides that play a key role through different mechanisms[7,14]: the elimination of invasive pathogens via opsonization and phagocytosis (C3b, C4b), leukocyte chemotaxis (C3a, C5a), and pathogen destruction through the membrane attack complex (C5b-9). In addition, the anaphylotoxins C3a, C4a and C5a attract phagocytes and polymorphonuclear cells (PMNs) toward the damage site[15,16] and induce the degranulation of mast cells, basophils and eosinophils.[7,14] Experimental and clinical studies have demonstrated that complement activation takes place both locally at the damage site and systemically after trauma.[14] The plasma C3 levels are