Med Intensiva. 2017;xxx(xx):xxx–xxx

medicina intensiva

www.elsevier.es/medintensiva

POINT OF VIEW

Management of myocardial dysfunction in septic shock. Potential role of extracorporeal membrane oxygenation

Manejo de la disfunción miocárdica en el shock séptico. Potencial papel de la oxigenación por membrana extracorpórea

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Received 29 August 2017; accepted 12 October 2017

Introduction

Septic cardiomyopathy (SC) is an increasingly recognized condition in patients with sepsis. First described by Parker et al. in 1984, is defined as an acute onset, reversible intrinsic myocardial impairment that could cause heart failure and aggravate the whole picture.[1]

The incidence of myocardial dysfunction in sepsis can vary from 18 to 29% in the first 6 h and could be as high as 60% later on, during the course of the syndrome.[2] Mortality is high but with important variability within the studies mainly depending on their case-mix and the different diagnostic methods. In very severe cases, extracorporeal membrane oxygenation (ECMO) has been proposed as a potential cardiorespiratory support for maintaining an adequate oxygen delivery.

The aim of this ''point of view'' is to make a short review of its clinical features and the management strategy, including the potential role of ECMO.

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Pathophysiology

Several mechanisms have been proposed for SC,[3] shown in Fig. 1.

Cardio toxic factors

By exposing myocytes to plasma of septic shocked patients, many investigators reported the presence of ''myocardium-depressing factors'' as some of the responsible of SC. Several substances have been proposed, including TNF-α, IL-1, IL-6, complement (C5a) and endotoxin.[4] Also high-circulating histone levels may be associated with left ventricular (LV) dysfunction in patients with sepsis.

Catecholamine toxicity

β-Adrenergic receptors dysfunction has been proposed as an intrinsic mechanism of SC. While β3-adrenoceptors (negative inotropic response to agonists) are upregulated by catecholamine use during sepsis, β1-receptors (positive inotropic to agonist) even when they are stimulated, they are downregulated in the next few hours after septic shock.

https://doi.org/10.1016/j.medin.2017.10.004

Please cite this article in press as: Riera J, et al. Management of myocardial dysfunction in septic shock. Potential role of extracorporeal membrane oxygenation. Med Intensiva. 2017. https://doi.org/10.1016/j.medin.2017.10.004

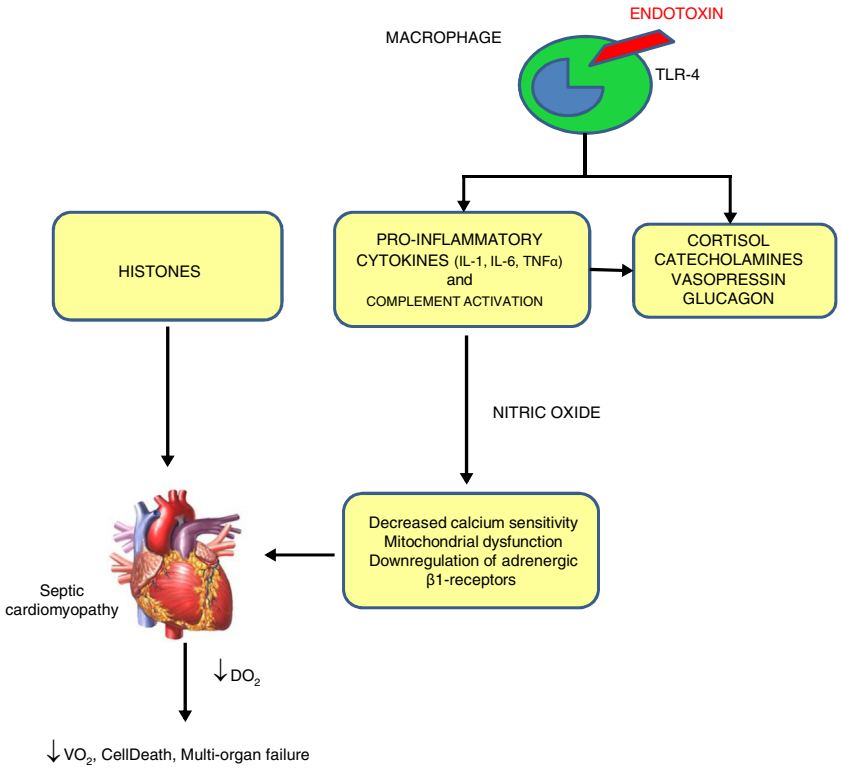

Figure 1 Mechanisms of sepsis-induced cardiomyopathy. Endotoxins cause depressed cardiac contractility, which is mediated by enhanced nitric oxide (NO) production. Tumor necrosis factor and interleukin-1β also contribute to NO overproduction. NO is believed to act in the heart by decreasing myofibril response to calcium, inducing mitochondrial dysfunction, and downregulating β-adrenergic receptors. These reactions lead to sepsis-induced cardiomyopathy. Histones occur inside the nucleus and can be released into circulation because of extensive inflammation and cellular death during sepsis and are also implicated in the pathophysiology of sepsis-induced cardiomyopathy.

Decreased calcium sensitivity

Beta stimulation leads to the formation of Cyclic Adenosine Monophosphate (cAMP), which in turn triggers the release of calcium ions from the sarcoplasmic reticulum so contraction of myofibrils begins. During sepsis, phosphorylation of troponin complex decreases its calcium sensitivity and reduces myocardial contraction.

Nitric oxide (NO)

This ubiquitous and multifunctional compound can be produced by constitutive and/or inducible NO synthases. Inducible NO synthases specially NOS-2 are increased in septic humans leading to increased levels of NO which in turn can cause indirect oxidative injury made by free oxygen radicals and its nitrous derivatives and decreased mitochondrial activity and glutathione depletion.

Clinical characteristics and diagnosis

The main features of SC are the absence of coronary occlusion and is transience. SC usually appears within the first few hours of septic shock, then there is a progressive return toward a normal or previous Ejection Fraction (EF) in 7–10 days after the onset of sepsis.[5] In this setting, systolic dysfunction may be evaluated by two-dimensional speckle tracking echocardiography (STE), due to its higher sensitivity than conventional echocardiography.

Clinical features and echocardiography:

- Clinical signs of heart failure: Tachycardia, persistent hypotension after norepinephrine, elevated lactate levels and low SvO_2 or $ScvO_2$.
- Slight LV dilatation with normal or low filling pressure due to increased LV compliance and end-diastolic volume, associated with a reversible hypocontractility, as described in the seminal publication by Parker.[1]
- Despite of global ventricular dysfunction and low EF, stroke volume remains preserved in the early phase.
- Catecholamines may unmask SC by increasing systemic vascular resistance, causing decreased Cardiac Index (CI).
- Takotsubo cardiomyopathy is very infrequent.
- Right ventricular (RV) dysfunction could be present in 30% of the patients. Severe RV dysfunction (free wall strain) assessed by STE may be associated with a worse prognosis.

Biomarkers

Troponin elevation is very specific and reflects myocardial injury. Troponins are elevated in 31% to 85% of patients with severe sepsis probably by reversible damage to intracellular organelles. Troponin elevation is associated with a higher

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