CHEST Special Features

Sepsis-Associated Myocardial Dysfunction*

Diagnostic and Prognostic Impact of Cardiac Troponins and Natriuretic Peptides

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Myocardial dysfunction, which is characterized by transient biventricular impairment of intrinsic myocardial contractility, is a common complication in patients with sepsis. Left ventricular systolic dysfunction is reflected by a reduced left ventricular stroke work index or, less accurately, by an impaired left ventricular ejection fraction (LVEF). Early recognition of myocardial dysfunction is crucial for the administration of the most appropriate therapy. Cardiac troponins and natriuretic peptides are biomarkers that were previously introduced for diagnosis and risk stratification in patients with acute coronary syndrome and congestive heart failure, respectively. However, their prognostic and diagnostic impact in critically ill patients warrants definition. The elevation of cardiac troponin levels in patients with sepsis, severe sepsis, or septic shock has been shown to indicate left ventricular dysfunction and a poor prognosis. Troponin release in this population occurs in the absence of flow-limiting coronary artery disease, suggesting the presence of mechanisms other than thrombotic coronary artery occlusion, probably a transient loss in membrane integrity with subsequent troponin leakage or microvascular thrombotic injury. In contrast to the rather uniform results of studies dealing with cardiac troponins, the impact of raised B-type natriuretic peptide (BNP) levels in patients with sepsis is less clear. The relationship between BNP and both LVEF and left-sided filling pressures is weak, and data on the prognostic impact of high BNP levels in patients with sepsis are conflicting. Mechanisms other than left ventricular wall stress may contribute to BNP release, including right ventricular overload, catecholamine therapy, renal failure, diseases of the CNS, and cytokine up-regulation. Whereas cardiac troponins may be integrated into the monitoring of myocardial dysfunction in patients with severe sepsis or septic shock to identify those patients requiring early and aggressive supportive therapy, the routine use of BNP and other natriuretic peptides in this setting is discouraged at the moment. ***(CHEST 2006; 129:1349–1366)***

Key words: cardiac troponins; myocardial dysfunction; natriuretic peptides; sepsis; septic shock

Abbreviations: ACS = acute coronary syndrome; ANP = A-type natriuretic peptide; APACHE = acute physiology and chronic health evaluation; BNP = B-type natriuretic peptide; CAD = coronary artery disease; CHF = congestive heart failure; cTnI = cardiac troponin I; cTnT = cardiac troponin T; E/A = ratio of early peak flow velocity to atrial peak flow velocity; LVEF = left ventricular ejection fraction; LVFAC = left ventricular fractional area contraction; LVSWI = left ventricular stroke work index; NT-proANP = N-terminal-pro-A-type natriuretic peptide; NT-proBNP = N-terminal pro-B-type natriuretic peptide; PAC = pulmonary artery catheter; PCWP = pulmonary capillary wedge pressure; S/D = ratio of systolic to diastolic pulmonary vein flow velocity; SIRS = systemic inflammatory response syndrome

Learning Objectives: 1. Assess myocardial dysfunction in sepsis and early recognition for administration of optimal therapy. 2. Analyze the elevation of cardiac troponins in patients with sepsis, severe sepsis or septic shock. 3. Evaluate the relationship between BNP (B-type natriuretic peptide) and both left ventricular ejection fraction and left-sided filling pressures.

Despite advances in therapy, sepsis causes > 200,000 deaths per year in the United States, thus equaling the number of patients dying from myocardial infarction.[1] Myocardial dysfunction is a common complication in patients with severe sepsis, and early recognition and aggressive supportive ther-

apy are mandatory as mortality in patients with septic shock is still high.[2] The value of the use of pulmonary artery catheters (PACs) has come under scrutiny after studies[3] have failed to prove a survival benefit for patients treated with PAC-guided therapy compared to those in whom PACs were not used. Nevertheless, information about cardiac performance is needed for the selection of the most appropriate catecholamine regimen after adequate fluid resuscitation.[4] In the past few years, the following two groups of biomarkers have emerged as potential candidates for the evaluation and quantification of cardiac dysfunction in patients with sepsis:

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cardiac troponins; and natriuretic peptides.[5–15] These biomarkers were initially introduced for use in diagnosis and risk stratification in patients with acute coronary syndrome (ACS)[16] and congestive heart failure (CHF) respectively,[17,18] but their spectrum of application is widening. The aim of the present review is to provide clinicians with a summary of the current evidence about the prognostic and diagnostic impact of cardiac troponins and natriuretic peptides in patients with sepsis-associated myocardial dysfunction. The available data on cardiac troponins and natriuretic peptides and the possible underlying pathophysiologic mechanisms are discussed in the light of studies on these biomarkers in patients without sepsis.

Definitions

Sepsis has been defined as the presence of the systemic inflammatory response syndrome (SIRS) in response to a culture-proven infection.[19] However, SIRS can result not only from infection, but also from a variety of conditions such as autoimmune disorders, vasculitis, thromboembolism, and burns, or after surgery. The severity of sepsis is graded according to the associated organ dysfunction and hemodynamic compromise. The original definitions have been revisited by a group of experts,[20] but, apart from expanding the list of signs and symptoms of sepsis, no relevant changes have been made. In a recently published review, Annane and coworkers[2] propose a very practical modification of the definitions including exact hemodynamic definitions of septic shock. It is important to recognize that the original definitions relied only on the degree of vasodilatation, whereas in the modification by both the International Sepsis Definition Conference[20] and Annane et al[2] myocardial depression defined as low cardiac index or echocardiographic evidence of cardiac dysfunction has been included in the definition of severe sepsis (Table 1).[2,20]

Myocardial Dysfunction and Hemodynamic Assessment

Prevalence

Abnormalities of cardiac function are quite common in patients with sepsis. The prevalence of this transient phenomenon critically depends on the population studied, the definition applied, and the time point during the course of the disease. Approximately 50% of patients with severe sepsis and septic shock seem to have any form of impairment of left ventricular systolic function.[4,9]

Pathomechanisms

The phenomenon of myocardial depression is mediated by circulating depressant substances,[21–24] which until now have been incompletely characterized. Among those on a list of possible candidates, tumor necrosis factor-α and interleukin-1β play a central role.[21,22] In addition, interleukin-6 has been shown[24] to be a key mediator of myocardial dysfunction in children with meningococcal septic shock. A comprehensive discussion of the numerous pathways involved in the complex pathogenesis of sepsis is beyond the aim of the present clinically oriented review, but can be found elsewhere.[23]

Clinical Presentation and Hemodynamics

The hemodynamic pattern in human septic shock is generally characterized by a hypercirculatory state including decreased systemic vascular resistance and a markedly increased cardiac index after adequate fluid resuscitation. Nevertheless, several studies have revealed clear evidence of intrinsic depressed left ventricular performance in patients with septic shock. The

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