

COMMENTARY

# Evaluation of left ventricular systolic function revisited in septic shock

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See related research by Huang *et al.*, <http://ccforum.com/content/17/3/R96>

## Abstract

The meta-analysis of Huang and coworkers failed to find any evidence for a protective effect of a decreased left ventricular (LV) ejection fraction (EF). These results have to be interpreted with caution since in most studies included in the meta-analysis patients with LV systolic dysfunction received inotropic drugs. We have some arguments suggesting that such a treatment may improve macrocirculation and microcirculation and finally prognosis. This paper allows us to clarify the meaning of LV function in septic shock patients. In all experimental models of septic shock using the load-independent parameter of LV systolic function, LV contractility impairment, called septic cardiomyopathy, has been reported to be constant. However, LVEF reflects the coupling between LV contractility and LV afterload. A normal LVEF may be observed when the arterial tone is severely depressed, as in septic shock, despite seriously impaired intrinsic LV contractility. LV systolic function, evaluated using an echocardiograph or another device, is then more a reflection of arterial tone (and its correction) than of intrinsic LV contractility. As a consequence, the incidence of LV systolic dysfunction greatly depends on the time of the evaluation, reflecting the fact that, during resuscitation and treatment, vasoplegia and then LV afterload are corrected, thus unmasking septic cardiomyopathy. With these points in mind, we can revisit the results of Margaret Parker's original study: it is not that the patients with a low EF survived better, but rather that the other patients had an increased mortality due to persistent profound vasoplegia.

In the previous issue of *Critical Care*, Huang and colleagues try to answer the unresolved question of the prognostic value of sepsis-related cardiomyopathy [1]. Since Margaret Parker and colleagues originally reported in 1984 that 65% of patients had significant left ventricular (LV) systolic dysfunction in the early phase of sepsis associated with acute LV dilatation (>100% increase in size!) and that such patients had a better prognosis [2], various groups have failed to replicate these results, leading to confusion and controversy.

The article by Huang and colleagues is interesting because it reports a large meta-analysis including more than 700 septic patients available for LV analysis. The meta-analysis failed to find any evidence for a protective effect of a decreased LV ejection fraction (EF) [1]. Nevertheless, the nonindexed LV dimension was moderately higher among survivors than nonsurvivors [1]. These results have to be interpreted with caution since in most studies included in the meta-analysis patients with LV systolic dysfunction received inotropic drugs. In the study by Cariou and colleagues in 10 patients, most patients were infused with epinephrine or dobutamine [3]. In the study performed by our group in 68 patients, most patients received dobutamine [4]. We have some arguments suggesting that such a treatment may improve prognosis. Bouferrache and colleagues reported recently that dobutamine significantly improves the macrocirculation in patients with a low flow state who show a 40% increase in cardiac output despite normal venous oxygen saturation [5]. This improvement was sustained by a 50% increase in LVEF. Interestingly, such improvement leads to microcirculatory amelioration. De Backer and colleagues demonstrated that the proportion of functional capillaries was decreased in septic patients compared with volunteers [6] and that dobutamine, by inducing a 21% increase in cardiac output, led to a nearly complete reversal of such alterations [7]. In the study by Rivers and colleagues, demonstrating a better prognosis in the early goal-directed therapy group, close to 14% of patients received dobutamine in the first 6 hours in the interventional group versus 0.8% in the control group [8]. Finally, Rhodes and colleagues, Kumar and colleagues,

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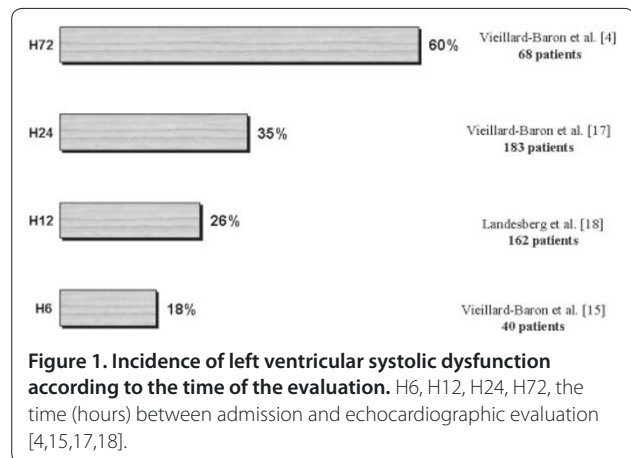
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and Vallet and colleagues reported similar results – a huge decrease in mortality in septic patients who respond to dobutamine in terms of cardiac output [9-11].

More interestingly, however, the article by Huang and colleagues allows us to try to clarify the meaning of LV function in septic shock patients. A lot of confusion exists. In all experimental models of septic shock, LV contractility impairment – called septic cardiomyopathy – has been reported to be constant. In these studies, as in the study by Barraud and colleagues [12], intrinsic contractility is assessed using a parameter that is not dependent on load conditions; that is, systolic elastance. Unfortunately, this assessment requires the generation of pressure/volume loops, something difficult to achieve in human subjects at the bedside. This difficulty is why in clinical practice most intensivists use LV systolic function parameters that are for the most part dependent on load conditions. This dependency is the case for LVEF obtained using echocardiography.

More than 20 years ago, Robotham and colleagues nicely reiterated that LVEF reflects the coupling between LV contractility and LV afterload [13]. In other words, a normal LVEF may be observed when the arterial tone is severely depressed, despite seriously impaired intrinsic LV contractility. Everyone understands that it is crucial to remember this in septic shock, in which arterial tone is initially severely decreased. LV systolic function, evaluated using an echocardiograph or another device, is more a reflection of arterial tone (and its correction) than of intrinsic LV contractility. In a 1990 study, Jardin and colleagues elegantly showed that patients with a normal LVEF had a significantly lower systemic vascular resistance than patients with a low LVEF in whom resistance was corrected [14]. As shown in Figure 1, it is then easy to understand that the incidence of LV systolic dysfunction greatly depends on the time of the evaluation. This dependence only reflects the fact that, during resuscitation and treatment, vasoplegia and then LV afterload are corrected, thus unmasking septic cardiomyopathy.

With these points in mind, we can revisit the results of Margaret Parker and colleagues' study: it is not that the patients with a low EF survived better, but rather that the other patients had an increased mortality due to persistent profound vasoplegia. This was suggested by our group in a study where 100% of patients with a hyperkinetic state (LVEF  $67 \pm 7\%$ ) finally died, compared with 'only' 43% of patients with a hypokinetic state (LVEF  $34 \pm 10\%$ ) [15]. Weng and colleagues showed recently that high peak systolic velocity measured at the mitral annulus by tissue Doppler imaging might be associated with mortality in patients with septic shock, suggesting that profound vasoplegia inducing high contractility is linked to poor prognosis [16].



**Figure 1. Incidence of left ventricular systolic dysfunction according to the time of the evaluation.** H6, H12, H24, H72, the time (hours) between admission and echocardiographic evaluation [4,15,17,18].

In conclusion, it will be very difficult to demonstrate that LV systolic dysfunction is associated with prognosis. Septic cardiomyopathy is constant and LV systolic function is more a reflection of the status of LV afterload. Rather, we have now to demonstrate what the best mortality-reducing strategy is when there is LV systolic dysfunction. Persistence of a hyperkinetic state is a warning signal suggesting that the septic process is not under control and that the patient has a high probability of dying.

#### Abbreviations

EF, ejection fraction; LV, left ventricular.

#### Competing interests

The authors declare that they have no competing interests.

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