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Effect of norepinephrine on cardiac output and preload in septic shock patients

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Introduction Norepinephrine (NE) is a first-line vasopressor used in patients with septic shock. Because of its predominant α-agonist effect, it is assumed to increase vasomotor tone and hence the mean arterial pressure (MAP) without significant effect on the cardiac index (CI). However, a potential beneficial effect on CI can be expected from its venoconstrictor α-agonist-mediated effect combined with an inotropic β_1 agonist effect, provided that the increase in left ventricular afterload is not excessive (high levels of MAP). The aim of our study was to examine the cardiovascular effect of NE when it induces marked changes in MAP.
Methods In an observational study of patients ($n = 37$) resuscitated for septic shock, we analysed hemodynamic PiCCO data at two consecutive time points where the MAP changed by more than 15% in response to either initiation or to change of doses of NE. Two subgroups of patients were identified. The first subgroup (MAPincr) consisted of 21 patients in whom the MAP increased by more than 15% in response to either initiation of NE infusion ($n = 8$) or increase in NE dose (from 1.7 ± 1.7 to 2.2 ± 1.4 mg/hour; $n = 13$). The second subgroup (MAPdecr) consisted of 16 patients in whom the MAP decreased by more than 15% in response to the decrease in NE doses. For both subgroups, the time between the two consecutive sets of measurements did not exceed 2 hours and no other treatments that may alter hemodynamics were administered within this period (fluids, hemofiltration, diuretics or other catecholamines).
Results In the MAPincr subgroup, MAP increased from 56 ± 17 to 84 ± 12 mmHg ($P < 0.05$) while significant increases in CI (from 3.4 ± 1.0 to 3.7 ± 0.9 l/min/m^2), stroke volume index (SVi) (from 37 ± 12 to 41 ± 11 ml/m^2) and global end diastolic volume index (GEDVi) (from 706 ± 203 to 767 ± 225 ml/m^2) were observed. Neither the heart rate nor the global ejection fraction (GEF) significantly changed. In seven patients, the GEF markedly increased by >15% in parallel to the increase in SVi. In the MAPdecr subgroup, MAP decreased from 95 ± 12 to 70 ± 9 mmHg ($P < 0.05$). The CI (from 3.5 ± 1.4 to 3.0 ± 0.9 l/min/m^2) and GEDVi (from 815 ± 319 to 721 ± 253 ml/m^2) decreased significantly, while the heart rate, SVi ($P = 0.07$) and GEF did not change.
Conclusion In our septic shock patients, changes in MAP resulting from increases or decreases in the doses of NE, were associated with changes in CI related to changes in GEDVi (cardiac preload) and in some patients to changes in systolic left ventricular function evaluated by GEF. These findings suggest that administration of NE in septic shock is associated not only with an increase in MAP but also with an increase in systemic blood flow.

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Tissue Doppler imaging suggests an association between endotoxemia and impaired myocardial relaxation

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Introduction Tissue Doppler imaging (TDI) is a novel technique that measures myocardial velocity. The peak early diastolic mitral annulus velocity (*E′*) offers a relatively preload-insensitive measure of LV relaxation. There are scant data regarding its use in sepsis or endotoxemia. This study sought to determine the effect of endotoxemia upon TDI variables.
Methods With ethics committee approval, 10 male Sprague–Dawley rats were studied. Anesthesia was induced with alfaxalone and maintained with isofluorane. Mechanical ventilation was performed via tracheostomy. All rats received 0.9% NaCl 3 ml/hour via a carotid line. Immediately after baseline assessment ($T = 0$), rats received 1 ml/kg i.v. infusion over 30 minutes (study group ($n = 5$), endotoxin 10 mg/ml (*Escherichia coli* O55:B5; Sigma, MO, USA); control group, 0.9% NaCl). Echocardiography was performed (15 MHz transducer, Vivid5; GE Healthcare) at $T = 0$, 60 minutes ($T = 60$) and 2.5 hours ($T = 150$). Measurements included the heart rate, mean arterial pressure (MAP), femoral venous pressure, LV outflow tract diameter and flow (peak velocity (V_{peak}), cardiac output (CO)), peak early diastolic mitral inflow (*E*), peak systolic mitral annulus velocity (*S′*) and *E′*.
Results There was no significant difference in mean ± SD weight (study 539 ± 88 g, control 504 ± 108 g, $P = 0.6$) or hemodynamic variables at $T = 0$. At $T = 60$, only V_{peak} was higher in the study group compared with controls (1.29 ± 0.24 vs 0.86 ± 0.21 m/s, $P = 0.03$). The study group demonstrated lower MAP, *E* and *E′* at $T = 150$ (Table 1).

Table 1 (abstract P38)

	Control	Study	*P*
MAP (mmHg)	118 ± 21	75 ± 35	0.05
CO (l/min)	0.156 ± 0.02	0.181 ± 0.07	0.5
E (m/s)	1.02 ± 0.2	0.76 ± 0.11	0.04
E′ (m/s)	0.095 ± 0.02	0.061 ± 0.02	0.03

Conclusion In this model, endotoxemia was associated with a decrease in *E* and *E′*. This decrease in E′ suggests a decreased rate of myocardial relaxation. This has not previously been reported.

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Hemodynamic and cardiac peptide in septic myocardial depression: the effects of calcium sensitizer

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Introduction The aim of this retrospective study is to evaluate hemodynamic and neurohormonal effects of levosimendan in cardiac patients with sepsis-induced cardiac dysfunction. Septic shock is characterized by profound cardiovascular alterations including myocardial depression. Levosimendan has recently been shown to improve cardiac function in septic shock.
Methods Fifteen patients with myocardial depression related to septic shock were enrolled. All patients had SIRS criteria, culture isolation of one or more pathogens, positive procalcitonin, SBP < 90 mmHg unresponsive to load challenge. We defined myocardial depression as a reduced SvO_2 in the presence of increased brain natriuretic peptide secretion and Troponin I release, and systolic and/or diastolic dysfunction by transoesophageal echo evaluation of ejection fraction and mitral annulus tissue Doppler imaging velocities. All patients received levosimendan infusion for 24 hours at 0.1 μg/kg/min combined with norepinephrine.
Results Data were obtained by evaluating the average of the percentage variation between T_0 (starting infusion) and T_1 (24 hours after infusion), T_2 (48 hours), T_3 (72 hours), T_4 (96 hours), T_5 (120 hours) and T_6 (144 hours). Levosimendan significantly increased SvO_2 and ejection fraction, and decreased