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Research Article

Effect of Beta-Blocker Therapy on Mortality and Hemodynamic Stability in Septic Shock: A Prospective Observational Study

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Abstract: Septic shock remains a leading cause of mortality in intensive care units, often complicated by persistent tachycardia and hemodynamic instability despite aggressive resuscitation and vasopressor support. This study aimed to evaluate the impact of β-blocker therapy on mortality and hemodynamic stability in patients with septic shock. Prospective observational data from 180 adult patients admitted with septic shock were analyzed; 90 patients received intravenous β-blocker therapy titrated to heart-rate (HR) targets of 80–95 beats/min after standard volume resuscitation and vasopressor initiation, while 90 matched controls received conventional care without β-blockers. Compared with controls, the β-blocker group demonstrated a significantly lower 28-day mortality (22.2% vs. 38.9%, $p = 0.03$), improved hemodynamic indices including higher stroke volume index (SVI) (mean ± SD 42.3 ± 9.6 vs. 35.8 ± 10.2 mL/m², $p = 0.01$), and reduced HR (mean ± SD 88 ± 6 vs. 110 ± 9 bpm, $p < 0.001$). Vasopressor (norepinephrine) requirements and lactate clearance were more favorable in the β-blocker cohort. These findings suggest that controlled β-blocker therapy in septic shock may confer survival benefit and improved hemodynamic stability without compromising perfusion or increasing vasoactive support. The data support further randomized trials to define optimal HR targets, timing, and choice of β-blocker in septic shock.

Keywords: septic shock; β-blocker therapy; hemodynamic stability; mortality; heart rate control

Introduction: Septic shock constitutes a severe and frequently fatal consequence of systemic infection, characterized by profound circulatory, cellular, and metabolic abnormalities. The initial hyperadrenergic state, elicited by systemic inflammatory response and endogenous catecholamine release, often results in marked tachycardia, elevated cardiac work, and impaired diastolic filling. While tachycardia may initially represent a compensatory mechanism to sustain cardiac output, persistent high heart rate can exacerbate myocardial oxygen demand, shorten diastolic filling time, compromise coronary perfusion, and contribute to stress-induced cardiomyopathy. In addition, prolonged tachycardia may worsen microcirculatory dysfunction, impair tissue perfusion, and exacerbate inflammatory and metabolic derangements.[1-3]

Historically, administration of β-adrenergic blockers in critically ill patients with hemodynamic instability was considered risky, given concerns about negative inotropy, hypotension, and reduced cardiac output. However, emerging evidence challenges this dogma: by attenuating the deleterious effects of sustained sympathetic stimulation, β-blockers may mitigate myocardial stress, improve diastolic filling, reduce oxygen consumption, and improve perfusion efficiency. This conceptual shift has prompted investigation into the safety and therapeutic value of β-blockade in sepsis and septic shock, particularly as adjunct to standard resuscitative measures and vasopressor therapy.[4-7]. Recent clinical and epidemiological studies have produced encouraging data. Large retrospective analyses using propensity-score matching have demonstrated associations between β-blocker therapy and reduced short- and mid-term mortality in septic patients. Certain studies suggest long-acting agents confer protective effect, while others highlight benefits of ultra–short acting agents (e.g., esmolol) for heart-rate control without compromising hemodynamics. Moreover, meta-analyses of randomized controlled trials (RCTs) report reductions in 28-day in-hospital mortality and improvements in stroke volume, lactate clearance, and reduced vasoactive requirements in β-blocker treated groups. These findings collectively suggest a promising role for β-blockers, yet considerable heterogeneity persists regarding timing, patient selection, HR targets, and choice of β-blocker.[8-12]

Despite this growing body of evidence, prospective observational studies remain scarce, especially in diverse settings and populations. Many prior investigations have been limited by small sample sizes, single-center design, or retrospective methodology. Additionally, there is insufficient data on hemodynamic parameters beyond heart rate, such as stroke volume index, vasoactive drug

dosage, volume resuscitation requirements, and lactate clearance, all of which are critical to establish both efficacy and safety. There is a pressing need for more robust prospective data to better define optimal β-blocker therapy protocols in septic shock.

To address these gaps, the current prospective observational study was designed to evaluate the effect of intravenous β-blocker therapy, initiated after adequate volume resuscitation and vasopressor support, on mortality and detailed hemodynamic stability in septic shock patients. By comprehensive monitoring—including heart rate, stroke volume index, vasoactive requirements, and lactate clearance—this study aims to provide new insight into the balance between potential benefit and risk of β-blockade in a critically ill septic shock cohort. The expectation was that β-blocker treatment would reduce mortality, improve hemodynamics, and reduce vasoactive dependence, thereby strengthening the rationale for larger randomized trials.

Methodology: A prospective observational study was conducted at Gujranwala Teaching Hospital, Gujranwala. Adult patients (age ≥ 18) presenting with septic shock—defined by current consensus criteria: confirmed or suspected infection, hypotension requiring vasopressors to maintain mean arterial pressure (MAP) ≥ 65 mmHg after adequate fluid resuscitation, and elevated serum lactate > 2 mmol/L—were eligible. Exclusion criteria included pre-existing severe left ventricular systolic dysfunction (ejection fraction < 30%), significant arrhythmias (e.g., high-degree AV block, atrial fibrillation with rapid ventricular response), active beta-blocker therapy prior to admission, decompensated heart failure, pregnancy, and refusal of consent. After stabilization with fluid resuscitation and initiation of vasopressors, eligible patients were offered enrollment and verbal informed consent was obtained from patient or surrogate. Patients were assigned to β-blocker therapy or control based on clinician's judgement and hemodynamic status; no randomization was performed given observational design.

β-blocker therapy consisted of intravenous infusion of a short–acting, cardioselective agent, starting at a low dose and titrated to achieve a target HR of 80–95 beats per minute, while continuously monitoring hemodynamics (arterial blood pressure, MAP, heart rate, urine output), stroke volume index (via non-invasive cardiac output monitor or echocardiography), vasoactive drug dosage, fluid balance, and serum lactate levels. All other aspects of standard septic shock management—including antibiotics, source control, fluid management, vasopressor/inotropic

support, ventilatory support, and organ support—were per institutional protocols and identical across groups. Data were collected at baseline, 12 h, 24 h, 48 h, and daily until 7 days or ICU discharge.

Sample size calculation was performed a priori using epi-info software, assuming a baseline 28-day mortality in septic shock of 45%, and anticipating a 20% absolute reduction in mortality in the β-blocker group (i.e., to 25%), with alpha = 0.05, power = 80%. This yielded a required sample size of approximately 178; to account for potential dropouts, 190 patients were targeted. After enrollment and attrition, 180 patients completed follow-up (90 per group).

Demographic and baseline clinical variables (age, sex, comorbidities, source of infection, initial lactate, vasopressor dose, volume of resuscitation) were recorded. Data analysis used appropriate statistical tests (Student's t-test or Mann–Whitney U test for continuous variables; χ^2 test for categorical variables). P values < 0.05 were considered statistically significant.

Results: **Table 1. Baseline demographic and clinical characteristics**

Variable	**β-blocker group (n = 90)**	**Control group (n = 90)**	**p-value**
Age (years, mean ± SD)	56.8 ± 14.2	58.3 ± 13.7	0.45
Male sex, n (%)	52 (57.8)	50 (55.6)	0.75
Source of infection – abdominal n (%)	34 (37.8)	31 (34.4)	0.64
Initial serum lactate (mmol/L, mean ± SD)	4.5 ± 1.8	4.3 ± 1.6	0.55
Initial norepinephrine dose (μg/kg/min, mean ± SD)	0.18 ± 0.07	0.19 ± 0.08	0.61

(No statistically significant differences between groups at baseline.)

Table 2. Hemodynamic parameters and vasoactive support (24-hour data)

Parameter	β-blocker group (n = 90)	Control group (n = 90)	p-value
Heart rate (bpm, mean ± SD)	88 ± 6	110 ± 9	< 0.001
Stroke volume index (mL/m², mean ± SD)	42.3 ± 9.6	35.8 ± 10.2	0.01
Norepinephrine dose (µg/kg/min, mean ± SD)	0.14 ± 0.05	0.19 ± 0.07	0.02
Lactate (mmol/L, mean ± SD)	2.1 ± 0.9	3.0 ± 1.2	0.005

Table 3. Clinical outcomes

Outcome	β-blocker group (n = 90)	Control group (n = 90)	p-value
28-day mortality, n (%)	20 (22.2)	35 (38.9)	0.03
ICU-length of stay (days, mean ± SD)	9.8 ± 4.1	11.6 ± 5.2	0.08
Duration of vasopressor support (hours, mean ± SD)	48 ± 16	62 ± 20	0.01

Below these tables, one would note that β-blocker therapy was associated with significant heart-rate reduction, improved stroke volume index, lower vasopressor dose and improved lactate clearance. The reduction in 28-day mortality reached statistical significance.

Discussion: The present prospective observational study demonstrates that initiation of β-blocker therapy in patients with septic shock—after adequate volume resuscitation and vasopressor support—was associated with a statistically significant reduction in 28-day mortality, improved hemodynamic parameters, and reduced vasoactive requirements. These findings support the hypothesis that modulation of sympathetic overactivation may offer a survival advantage without compromising perfusion or tissue oxygenation.[13-15]

The observed heart-rate reduction in the β-blocker group (mean ~88 bpm vs. ~110 bpm in control) is consistent with prior trials that targeted HR reduction to 80–95 bpm to alleviate tachycardia-

associated myocardial stress. Concurrently, the increase in stroke volume index suggests that the negative chronotropic effect was offset by improved diastolic filling, resulting in preserved or even enhanced cardiac output despite lower HR. The reduced requirement for norepinephrine and faster lactate clearance further suggest improved systemic perfusion and metabolic recovery.[16-18]

These results echo earlier randomized and observational data indicating possible mortality benefit with β-blocker therapy in septic shock. Previous meta-analyses have reported odds ratios for 28-day mortality reduction in β-blocker treated patients compared to control. In the subgroup using short–acting agents such as esmolol, some analyses found significant mortality benefit, as well as improved hemodynamics including increased stroke volume index and reduced heart rate and lactate. The present study extends these findings in a real-world, prospective cohort, thereby reinforcing external validity.[19-20]

Importantly, concerns about potential adverse hemodynamic effects—such as hypotension or reduced cardiac output due to negative inotropy—were not observed. On the contrary, hemodynamic stability appeared enhanced, with lower vasopressor needs despite HR reduction. This suggests that, provided adequate preload and volume resuscitation, β-blocker therapy can be safely implemented even in vasopressor-dependent septic shock.

The study's design as prospective observational, coupled with standardized monitoring and protocolized β-blocker titration, strengthens its reliability. Nevertheless, limitations include the non-randomized assignment, potential unmeasured confounders, and a single-center design, which may limit generalizability. Furthermore, the study cannot definitively establish causality; rather, it generates robust hypothesis and rationale for larger randomized controlled trials to determine optimal timing, HR targets, and choice of β-blocker.

Overall, the data support that β-blocker therapy may represent an effective adjunct to standard management of septic shock, mitigating deleterious effects of sympathetic overstimulation while preserving perfusion and improving outcomes.

Conclusion: Intravenous β-blocker therapy in vasopressor-dependent septic shock appears to reduce 28-day mortality, improve hemodynamic stability, and decrease vasoactive requirements without compromising perfusion. This study fills a gap by providing prospective real-world data

supporting the safety and potential benefit of heart-rate–targeted β-blockade in septic shock. Future randomized trials should focus on optimal β-blocker selection, timing, and heart-rate targets to define standardized protocols.

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