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Early noninvasive assessment of the severity of myocardial dysfunction in sepsis: a retrospective observational study

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Abstract

INTRODUCTION: Early and rapid assessment of the severity and prognosis of severe sepsis is an essential part of sepsis intensive care. It determines the pace and intensity of treatment measures and the routing process of patients in the first hours after hospitalization. **OBJECTIVE:** To identify early, prognostically significant signs of severe myocardial dysfunction in abdominal sepsis. **MATERIALS AND METHODS:** A total of 40 patients with abdominal sepsis were retrospectively examined. General clinical and laboratory parameters, circulatory parameters, echocardiography data, and hospitalization outcomes were recorded. Depending on the outcome, patients were divided into 2 groups. To assess the separating ability of independent variables, ROC analysis was performed, including only the indicators that differed between the groups. **RESULTS:** Predictors of unfavorable outcome of sepsis were high heart rate (HR; AUC = 0.7, cut-off > 93, 95% CI: 0.524–0.844, p = 0.027), decreased left ventricular ejection fraction (LVEF, AUC = 0.68, cut-off < 52 %, 95% CI: 0.495–0.822, p = 0.027), SOFA scale value (AUC = 0.69, cut-off > 6, 95% CI: 0.519–0.825, p = 0.034) and lactate level (AUC = 0.87, cut-off > 3.74, 95% CI: 0.706–0.968, p = 0.0001). A new index was identified — the ratio of HR to LVEF (HR/LVEF), which has advantages over standard parameters. The proposed indicator significantly (p = 0.0003) differed between the groups (1.29 [1.16–1.53] min^{-1} with a favorable outcome and 1.87 [1.55–2.49] min^{-1} with an unfavorable outcome). When analyzing the ROC curve of the effect of this index on the treatment outcome, the area was 0.86 (95% CI: 0.696–0.954), p < 0.0001; cut-off value > 1.61 min^{-1} (sensi-

Ранняя неинвазивная оценка тяжести миокардиальной дисфункции при сепсисе: ретроспективное наблюдательное исследование

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Реферат

АКТУАЛЬНОСТЬ: Ранняя прогностически ориентированная оценка тяжести клинического состояния играет ключевую роль при сепсисе, определяя лечебную тактику, маршрутизацию, выбор и последовательность мер интенсивной терапии. **ЦЕЛЬ ИССЛЕДОВАНИЯ:** Определить ранние, прогностически значимые признаки тяжелой миокардиальной дисфункции при абдоминальном сепсисе. **МАТЕРИАЛЫ И МЕТОДЫ:** Ретроспективно обследовали 40 больных абдоминальным сепсисом. Регистрировали общеклинические и лабораторные показатели, параметры кровообращения, данные эхокардиографии, исходы госпитализации. В зависимости от исхода пациенты были разделены на 2 группы. Для оценки разделительной способности независимых переменных был выполнен анализ ROC-кривых (receiver operating characteristic — кривая получаемых рабочих характеристик), включая только показатели, различающиеся между группами. **РЕЗУЛЬТАТЫ:** Предикторами неблагоприятного исхода сепсиса оказались: высокая частота сердечных сокращений (ЧСС) (площадь под кривой [ППК] = 0,7, cut-off [точка отсечения] > 93, 95%-й доверительный интервал [95% ДИ] = 0,524–0,844; p = 0,027); снижение фракции изгнания левого желудочка (ФИЛЖ) (ППК = 0,68, cut-off < 52 %, 95% ДИ = 0,495–0,822; p = 0,027); значение шкалы SOFA (Sequential Organ Failure Assessment) (ППК = 0,69; cut-off > 6; 95% ДИ = 0,519–0,825; p = 0,034) и уровень лактата (ППК = 0,87; cut-off > 3,74; 95% ДИ = 0,706–0,968; p = 0,0001). Выявили новый индекс — отношение ЧСС к ФИЛЖ, который имеет преимущества перед стандарт-

tivity — 75 %, specificity — 90 %). **CONCLUSIONS:** Early signs of an unfavorable course of abdominal sepsis are tachycardia, decreased LVEF, increased SOFA scale values, but the most reliable ($p < 0.001$) is hyperlactatemia. Calculating the HR/LVEF ratio allows us to qualitatively improve the information content of echocardiographic screening.

KEYWORDS: sepsis, septic shock, critical care

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ными параметрами. Предлагаемый показатель качественно ($p = 0{,}0003$) различался между группами: 1,29 (1,16–1,53) мин$^{-1}$ при благоприятном и 1,87 (1,55–2,49) мин$^{-1}$ при неблагоприятном исходе. При анализе ROC-кривой влияния данного индекса на исход лечения площадь составила 0,86 (95% ДИ = 0,696–0,954), $p < 0{,}0001$, значение cut-off > 1,61 мин$^{-1}$ (чувствительность — 75 %, специфичность — 90 %). **ВЫВОДЫ:** Ранними признаками неблагоприятного течения абдоминального сепсиса являются тахикардия, снижение ФИЛЖ, повышенные значения шкалы SOFA, но наиболее достоверно ($p < 0{,}001$) — гиперлактатемия. Вычисление отношения ЧСС/ФИЛЖ позволяет качественно улучшить информативность эхокардиографического скрининга.

КЛЮЧЕВЫЕ СЛОВА: шок, сепсис, интенсивная терапия

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Introduction

The early and rapid assessment of severity and prognosis is a critical component of the intensive care management of sepsis. This initial evaluation dictates the pace of therapeutic interventions and guides patient triage during the crucial first hours after hospitalization [1]. In daily clinical practice, intensivists traditionally rely on scoring systems such as the Sequential Organ Failure Assessment (SOFA) to quantify organ dysfunction and the Acute Physiology and Chronic Health Evaluation (APACHE) to determine disease severity and predict mortality in ICU patients [2, 3]. Concurrently, significant attention is devoted to optimizing hemodynamic management. A widely adopted strategy follows an escalation approach — "from simple to complex". Within this paradigm, the diagnostic value of invasive thermodilution techniques, notably transpulmonary thermodilution, is well-established and uncontroversial [4–7]. In contrast, the clinical utility of a common and simple point-of-care tool — focused bedside echocardiography — remains inadequately defined. Some studies explicitly note the underutilization of echocardiography in sepsis [4], while others report conflicting data on the prevalence and prognostic impact of left ventricular ejection fraction (LVEF) alterations [1, 4, 8]. A reduced LVEF is often interpreted as sepsis-induced myocardial dysfunction, whereas a persistently elevated LVEF in the context of ongoing relative hypovolemia may indicate a secondary

response to vasoplegic shock and capillary leakage [6–8]. This hemodynamic heterogeneity likely reflects the widely acknowledged polymorphism of the septic process [9], which manifests through diverse clinical and hemodynamic phenotypes [1–7].

Consequently, the absence of a straightforward, non-invasive method for the initial hemodynamic assessment of septic patients represents a significant clinical gap. Therefore, developing a simple tool for early risk stratification and prediction of adverse outcomes in abdominal sepsis is a matter of considerable relevance.

Objective

To identify early, prognostically significant signs of severe myocardial dysfunction in abdominal sepsis.

Materials and methods

A pilot retrospective observational study of the prognostic impact of baseline clinical, laboratory and echocardiographic parameters on the outcome of abdominal sepsis treatment was conducted. This study, based on archived patient medical records, did not require any interventions. All data used were anonymized. The study was approved by the local Ethics Committee of the State Budgetary Healthcare Institution City Clinical Hospital named after S.S. Yudin, protocol No. 5 dated March 2, 2022. Based on the design of the planned study, the sample size required for intergroup comparative analysis was determined. With a significance level (α) of 0.05 and a criterion power (1–β) of 0.80, the minimum size of each group sufficient for a correct assessment was $n = 18$, the total minimum sample size was $n = 36$.

The following inclusion criteria were used: age over 18 years, the presence of abdominal sepsis according to the criteria of the clinical guidelines «Septic shock in adults» 2024 of the Ministry of Health of the Russian Federation [10], procalcitonin values > 2, SOFA > 1, APACHE II > 10, lactate > 2 mmol/L, noradrenaline requirement > 0.1 mcg/kg/min. Exclusion criteria were defined sepsis or shock of any other genesis. Non-inclusion criteria were lethal outcome within 6 hours of hospitalisation.

According to the specified criteria, 40 patients (22 males and 18 females) aged from 57 to 74 years with an average of 64 years were included in the study. All the patients were transported by ambulance. The diagnoses and surgical interventions performed during the study are presented in the Table 1 and Table 2.

On the inclusion of patients in the study there was performed the registration of general clinical laboratory parameters, namely: complete blood count, C-reactive protein, procalcitonin, lactate. In addition, parameters of non-invasive circulatory monitoring were used: blood pressure, heart rate (HR), echocardiogram registration, heart rate evaluation. There were recorded duration and outcomes of hospitalisation. All the patients underwent focal echocardiography ("Point Of Care Ultrasound") and after there were recorded the following parameters: end-diastolic volume, end-systolic volume, end-diastolic dimension, end-systolic dimension, LVEF, LV posterior wall and interventricular septum thickness; pulmonary artery systolic pressure (PASP). To determine the volumetric parameters there was used the Simpson disc method, and PASP was determined as the time derivative of the Doppler flow acceleration in the pulmonary artery.

All patients received: infusion with balanced crystalloid solutions, antibacterial therapy, and, if necessary, vasopressor support in accordance with the protocol of clinical guidelines

"Septic shock in adults" 2024 of the Ministry of Health of the Russian Federation [10, 11]. Accordingly, 34 (85 %) patients received vasopressor and/or inotropic support (target mean arterial pressure was > 65 mmHg) with norepinephrine, epinephrine or dobutamine, which were administered intravenously, 6 (15 %) patients did not require sympathomimetic therapy [10]. Norepinephrine was used as the drug of choice for vasopressor support. In patients with septic shock accompanied by impaired myocardial contractility or with high doses of norepinephrine (more than 0.5 mcg/kg/min), epinephrine was used as an intravenous infusion at a dose of 0.03–0.8 mcg/kg/min as a second-line sympathomimetic drug to restore mean arterial pressure. Dobutamine was also used for inotropic support in patients with septic cardiomyopathy — an intravenous infusion at a dose of 3–8 mcg/kg/min. Antibacterial therapy was carried out based on the recommendations of the antimicrobial therapy control strategy (ASCT) [12], then adjusted based on the results of microbiological studies. All antibacterial drugs were administered intravenously, the doses were adjusted in accordance with the glomerular filtration rate. Patients stratified by SCAT I received antibacterial therapy with ampicillin + sulbactam. According to SCAT II, antibacterial therapy was with cefepime + sulbactam. According to ASCT III, antibacterial therapy was with imipenem + cilastatin. Respiratory support was required in 26 (65 %) patients, the remaining 14 (35 %) were respiratory stable. At the same time, 19 (47.5 %) patients received artificial ventilation in a protective mode (oxygen fraction (FiO_2) — 30–40 %, positive pressure at the end of expiration — 6–8 cm H_2O, tidal volume — 6 ml/kg of ideal body weight). Three (7.5 %) patients received noninvasive mechanical ventilation with the following parameters: FiO_2 — 40–50 %, positive end-expiratory pressure — 8–10 cm H_2O, support pressure — 10–12 cm H_2O; 4 (10 %) patients received oxygen insufflation at a flow rate of 5–7 l/min. Extended hemodiafiltration was performed in 8 (20 %) patients.

Statistical analysis. Archiving and processing of the obtained data were performed by using Microsoft Office

Excel and MedCalc v14.8.1. The conformity of data distribution to normal was determined by using the Shapiro—Wilk and Shapiro—Frank criteria. The data that had normal distribution were presented as arithmetic mean (M) and standard deviations (σ). For non-normal distribution, the data were presented as median (Me) and interquartile range (P25–P75). There was also calculated the mean frequency of signs (p). Depending on the nature of data distribution, the intergroup differences were evaluated using Student's t-test (in normal distribution) or the Mann—Whitney U-test (in non-normal distribution). Correlations between the indicators were assessed by calculating Pearson's coefficients (r). By using logistic regression there was assessed the influence of independent variables on the dependent variable coded binary. To assess the characteristics of the separating ability of independent variables, there was conducted a ROC-curve analysis with determination of the area under the ROC-curve (AUC), 95% confidence interval (CI), cut-off threshold (according to the Youden Index) and its sensitivity and specificity. The intergroup differences, relationships and dependencies were considered significant at $p < 0.05$.

Results

The fatal outcome group (Group 2), compared with the discharged patients (Group 1), had a higher SOFA score, tachycardia, decreased LVEF ($p < 0.05$), and statistically significantly increased lactate levels ($p < 0.001$). The remaining clinical, laboratory, hemodynamic, and echocardiographic parameters (Table 3) did not differ ($p > 0.05$) between the groups. It is worth noting only the trend ($p < 0.1$) towards an older age in Group 2.

The lethal group (Table 1, Group 2) compared to discharged patients (Table 1, Group 1) had a higher SOFA score, tachycardia, decreased LVEF ($p < 0.05$) and a highly significantly elevated lactate level ($p < 0.001$). The remaining clinical, laboratory, haemodynamic and echocardiographic parameters (see Table 1) did not differ ($p > 0.05$) between the groups. It may just be noted that there is a tendency ($p < 0.1$) to an older age in Group 2.

Furthermore, parameters differing between the groups were included in the ROC-curve analyses of the effect on treatment outcome. It was found that all of these parameters (SOFA, HR, LVEF, and lactate) had a significant effect on treatment outcome (Figures 2–5; ROC > 0.6; $p < 0.05$). In this case, lactate had the most significant effect (PPC = 0.88; $p = 0.0001$).

The following Table 4 shows the results of the ROC analysis of the dependence of the outcome on the value of the analyzed parameters.

As part of further scientific search, the authors of this article proposed a new haemodynamic parameter, which is HR/LVEF ratio. There were analysed the values of HR/LVEF ratio in the selected groups (Figure 5) and found a significant ($p < 0.001$) increase of this index in Group 2 (with further adverse outcome).

Table 1. Diseases in the examined patients

Abdominal cavity disorders	*n* (%)
Cancer-associated intestinal obstruction	13 (32.5%)
Adhesive intestinal obstruction	2 (5%)
Acute destructive pancreatitis	6 (15%)
Hollow viscus perforation (stomach,intestines)	5 (12.5%)
Mesenteric blood supply disorders	5 (12.5%)
Acute cholangitis	9 (22.5%)

Table 2. Surgical interventions in the examined patients

Surgeries	*n* (%)
Endoscopic stenting of tumour-induced stenosis	8 (18.5 %)
Adhesiolysis	2 (5 %)
Suturing of the hollow viscus defect, sanation, drainage of the abdominal cavity	5 (13 %)
Obstructive resection of the necrotic part of the intestine and subsequent anastomosis (the second stage)	4 (11 %)
Stoma exteriorisation	6 (15 %)
Retrograde cholangiopancreatography	9 (22.5 %)
Drainage of abdominal abscesses/fluid accumulations under ultrasound guidance	6 (15 %)

Table 3. Clinical, echocardiographic and laboratory parameters on admission to hospital

Parameters	Group 1	Group 2	*p*
SOFA, scores	6 (2–8)	8 (6–8.5)	0.034
APACHEII, scores	16.5 (14.3–20)	21 (18–27)	0.122
Height, cm	169.5 (160–179)	170 (162–170)	0.99
Weight, kg	70.5 (65–80)	74 (64–80)	0.47
Age, years	62 (42.5–68)	67 (59–80)	0.071
Norepinephrine, mcg/kg/min	0.8 (0.37–0.9)	0.8 (0.55–1.2)	0.67
Mean BP, mmHg	73.5 (72.9–77.8)	86 (71.5–93.5)	0.551
HR, min^{-1}	85 (80.75–91.5)	103 (80–120)	0.038
LVEF, %	63.5 (59.25–64.4)	59 (47.5–66)	0.027
LV EDD, cm	4.5 (4–4.8)	5 (4.47–5.57)	0.786
LV ESD, cm	2.6 (2.55–3)	3 (2.8–4.25)	0.093
IS, cm	1 (1.0–1.35)	1.29 (1.12–1.3)	0.667
LVPW, cm	1.05 (0.93–1.4)	1.1 (0.98–1.27)	0.754
LA1, cm	3.8 (3.47–4.25)	4.2 (3.6–4.5)	0.162
LA2, cm	4.7 (4.2–5)	4.8 (4.6–5.3)	0.165
RA1, cm	3.6 (3.45–3.7)	3.6 (3.5–4.05)	0.187
RA2, cm	4.5 (4.25–4.6)	4.6 (4.27–4.8)	0.906
PASP, mmHg	32.5 (29.3–44)	37 (27.2–40.5)	0.782
Lactate, mmol/L	2.6 (2–3.5)	8 (4–13)	0.0002
Hemoglobin, g/L	86 (75–98.5)	90.5 (73.5–118.5)	0.258
Leukocytes, $\times 10^9$/L	12.8(10.25–21.65)	17 (9.3–19.8)	0.822
Thrombocytes, 1000/mcL	224 (166–367)	77 (58–116)	0.0735

Note: The SOFA (Sequential Organ Failure Assessment) scoring system is used to assess organ failure, risk of mortality and sepsis in intensive care unit (ICU) patients. The APACHE (Acute Physiology and Chronic Health Evaluation) scoring system is designed to measure severity of illness in adult patients admitted to the ICU and to predict mortality; HR — heart rate; LVEF — left ventricular ejection fraction; LV — left ventricle; EDD — end-diastolic diameter; ESD — end-systolic diameter; IS — interventricular septum; LVPW — left ventricular posterior wall; LA — left atrium (sizes 1 and 2); RA — right atrium (sizes 1 and 2).

Table 4. Results of ROC-analysis of outcome dependence on the value of the analysed parameters

Parameters	AUC	CI	*p*	Cut-off	Sensitivity	Specificity
SOFA, scores	0.69	0.519–0.825	0.034	> 6	67 %	67 %
LVEF, %	0.68	0.495–0.822	0.027	< 52	39 %	100 %
HR , min^{-1}	0.7	0.524–0.844	0.027	> 93	72 %	80 %
Lactate, mmol/L	0.87	0.706–0.968	0.0001	> 3.4	80 %	90 %

Table 5. The results of ROC-analysis of adverse outcome dependence on HR/LVEF ratio value

Parameter	AUC	CI	*p*	Cut-off	Sensitivity	Specificity
HR/LVEF	0.83	0.696–0.942	< 0.0001	> 1.61 min^{-1}	70 %	90 %

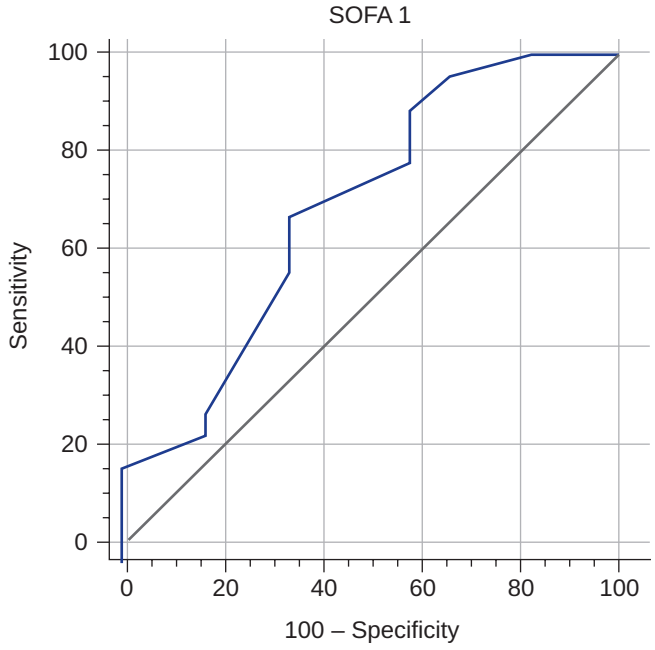

Fig. 1. ROC-curve of outcome dependence on SOFA value

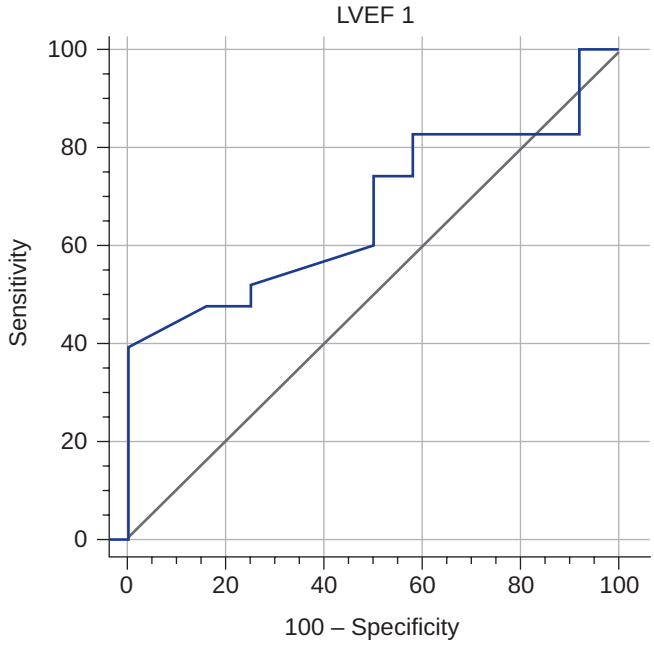

Fig. 2. ROC-curve characterising adverse outcome dependence on decrease in LVEF

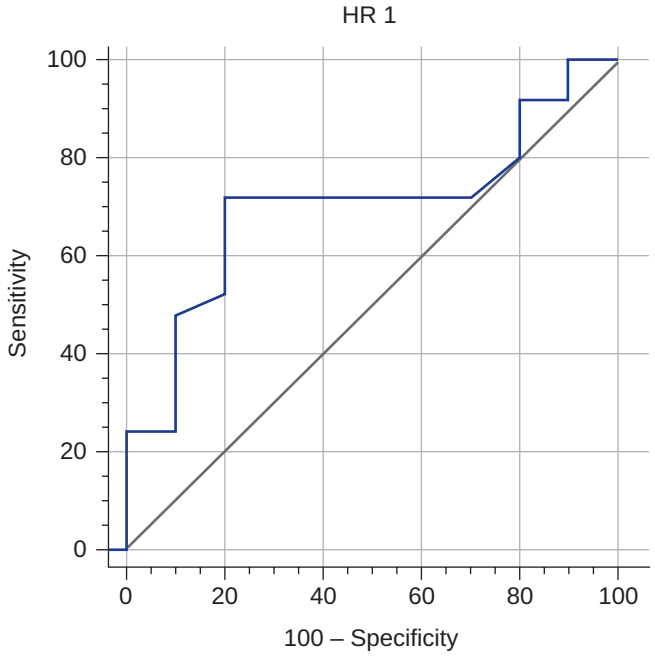

Fig. 3. ROC-curve of adverse outcome dependence on HR

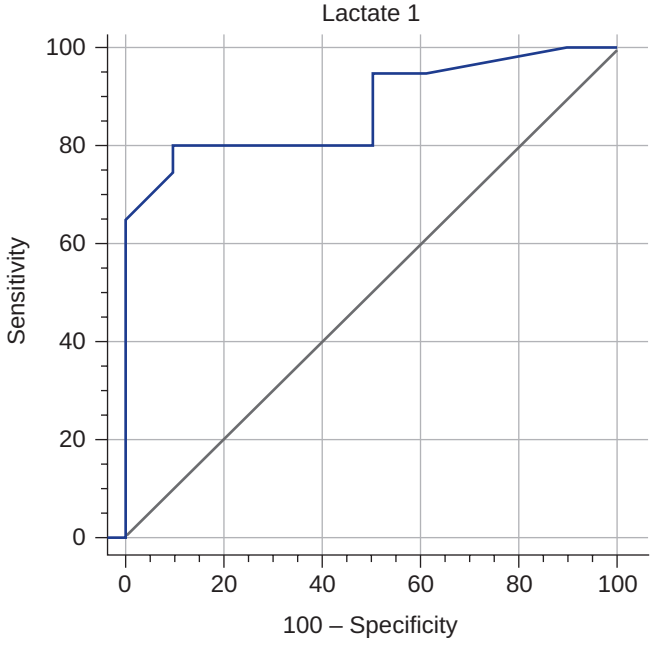

Fig. 4. ROC-curve characterising adverse outcome probability dependence on lactate value

Then the authors plotted and analyzed the ROC-curve of outcome dependence on HR/LVEF ratio (Figure 6). As a result there was found a highly significant dependence (ROC = 0.86; $p < 0.0001$).

Thus, only lactate level and HR/LVEF ratio allow to plot ROC-curves predicting the outcome with very good quality (AUC > 0.8). Moreover, the AUC under the ROC-curves of lactate and HR/LVEF index are significantly ($p < 0.05$) larger than under the ROC-curves of other parameters (LVEF, HR, SOFA). At the same time, the linear correlation between lactate level and HR/LVEF ratio (Figure 7), although reliable ($p = 0.021$), is weak ($r = 0.44$), which makes it impossible to consider these variables interchangeable.

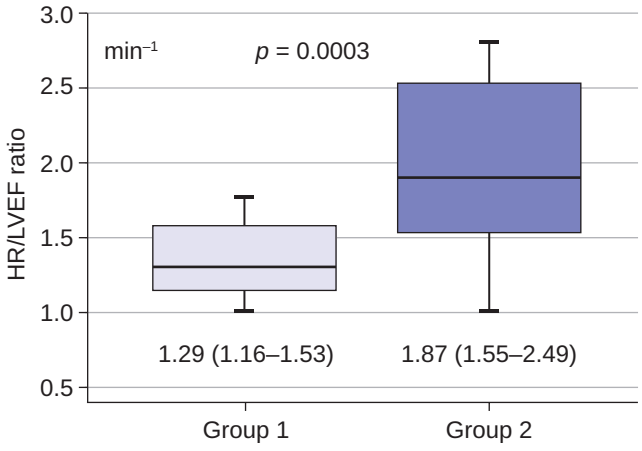

Fig. 5. Comparative intergroup analysis of HR/LVEF ratio

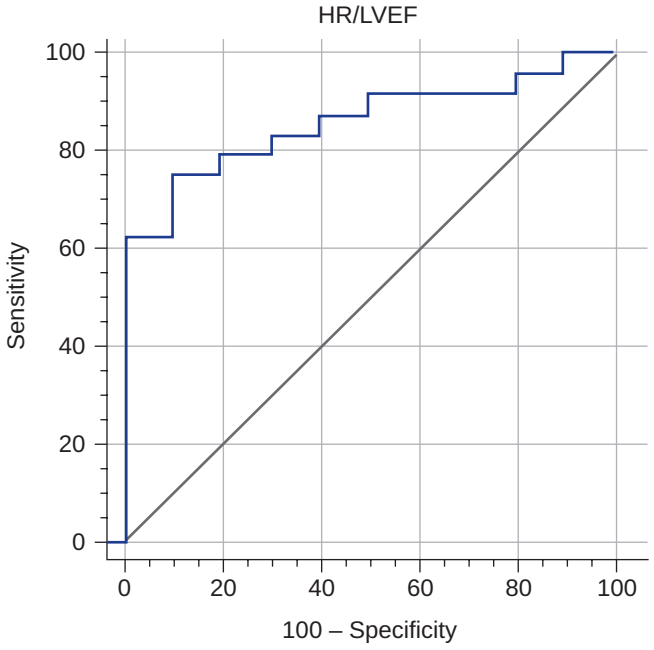

Fig. 6. ROC-curve of adverse outcome dependence on value of HR/LVEF ratio

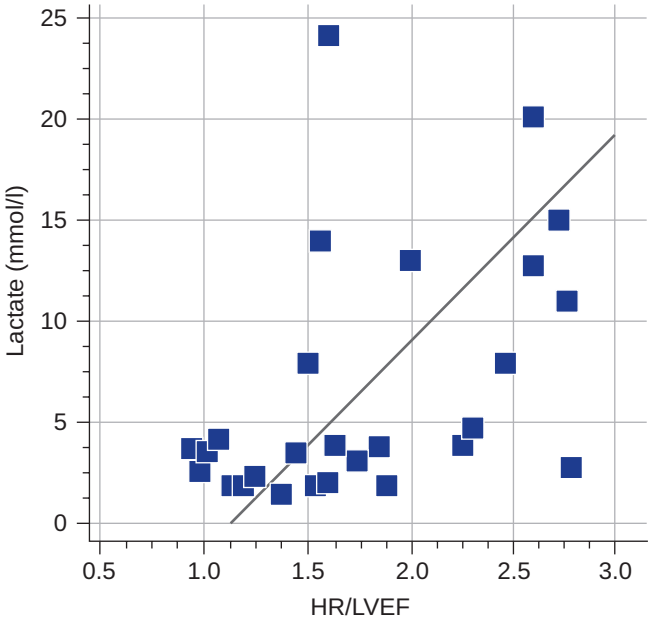

Fig. 7. Linear correlation between lactate level (Y) and HR/LVEF ratio (X): $r = 0.44$; 95% CI: 0.07–0.704 ($p = 0.021$)

Discussion

Abdominal sepsis is a common yet unpredictable condition that necessitates rapid therapeutic decision-making. Its management is complex, involving challenges such as determining the urgency of surgical intervention, the need for re-laparotomy, cavity sanitization, the application of extracorporeal detoxification methods, and aggressive antibiotic therapy. Circulatory failure in sepsis, driven primarily by systemic inflammatory response syndrome, impairs tissue perfusion. Coupled with coagulopathy, this often leads to multiple organ dysfunction syndrome. A significant independent risk factor for poor outcomes is the development of septic cardiomyopathy, which can cause severe contractility and rhythm disturbances [1–11].

Early assessment of the risk and severity of hemodynamic impairment in sepsis remains a critical, though long-debated, challenge [1, 4–8]. While echocardiography is increasingly integrated into the daily practice of anesthesiologists and intensivists [1, 8], its prognostic value in sepsis is not fully established [4]. Our data suggest a negative prognostic value for a reduced left ventricular ejection fraction (LVEF). However, applying this finding is complicated by the fact that LVEF values in our cohort often remained within the normal range. Consequently, defining a reduced LVEF as less than 52 % in this context is clinically unconventional, highlighting the need for a more effective and simplified echocardiographic screening tool.

The negative prognostic impact of tachycardia in abdominal sepsis was an expected finding, consistent with previous reports [8, 11–15]. However, strategies to control heart rate (HR) using modern beta-blockers have yielded conflicting results, with studies showing both benefit [13] and no clear advantage [14–16]. A key point in this debate is the recommendation to interpret heart rate in the context of simultaneous echocardiographic findings [8]. The presence of a hyperdynamic left ventricle [17, 18] may be particularly important for the effective and safe administration of beta-blockers.

We propose that the ratio of heart rate to LVEF (HR/LVEF) may be a more informative parameter than either measure alone. This hypothesis is mathematically grounded in the combination of two reliable but relatively weak predictors: a numerator (HR) that is consistently elevated and a denominator (LVEF) that is consistently depressed. Our analysis confirmed that the HR/LVEF index demon-

strated superior predictive performance compared to standard parameters, showing a significantly higher degree of reliability in both comparative analysis and ROC curve construction. This index could facilitate the use of echocardiography for early risk stratification in sepsis. Hypothetically, it may also provide a safe target parameter for guiding hemodynamic management, including the use of sympatholytics, fluid infusion, or other interventions. Conversely, extreme values of the HR/LVEF ratio could serve as a marker of severe sepsis, indicating the need for treatment intensification [19].

Conclusion

In conclusion, our results demonstrate that, in addition to known predictors of adverse outcomes in abdominal sepsis — such as tachycardia, reduced LVEF, elevated SOFA score, and hyperlactatemia — the HR/LVEF ratio is a novel and robust prognostic marker. Its stability is comparable to that of lactate ($p < 0.001$). The calculation of the HR/LVEF ratio significantly enhances the informational value of echocardiographic screening, providing a practical tool for early risk assessment and potentially guiding therapeutic decisions.

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Author contribution. All authors according to the ICMJE criteria participated in the development of the concept of the article, obtaining and analyzing factual data, writing and editing the text of the article, checking and approving the text of the article.

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