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PREDICTORS OF TIME-DEPENDENT SURVIVAL IN SEPTIC SHOCK PATIENTS UNDERGOING EXTRACORPOREAL BLOOD PURIFICATION: A PARAMETRIC SURVIVAL ANALYSIS

PREDIKTORI VREMENSKI ZAVISNOG PREŽIVLJAVANJA KOD PACIJENATA SA SEPTIČKIM ŠOKOM KOJI SE PODVRGAVAJU EKSTRAKORPORALNOM PREČIŠĆAVANJU KRVI: PARAMETRIJSKA ANALIZA PREŽIVLJAVANJA

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Summary

Background: Sepsis remains associated with high mortality despite advances in organ support, including extracorporeal blood purification. Conventional prognostic tools rely on static endpoints and do not capture dynamic mortality risk. We aimed to identify predictors of time-dependent survival in sepsis patients.
Methods: We conducted a retrospective, single-centre study of adults with sepsis or septic shock who received continuous renal replacement therapy with CytoSorb® or oXiris®. Demographic, clinical, and laboratory data were extracted. Survival was analysed using Kaplan-Meier estimates, Cox proportional hazards regression, and parametric survival models. Multivariable analyses estimated independent effects, and the final parametric model was used to derive survival probabilities and median survival times conditional on covariates.

Kratak sadržaj

Uvod: Sepsa je i dalje povezana sa visokom stopom smrtnosti uprkos napretku u potpori funkcije organa, uključujući ekstrakorporalno prečišćavanje krvi. Konvencionalni prognostički alati se oslanjaju na statične ishode i ne obuhvataju dinamički rizik od smrtnosti. Cilj ovog istraživanja bio je da se identifikuju prediktori vremenski zavisnog preživljavanja kod pacijenata sa sepsom.
Metode: Sprovedena je retrospektivna, jednocentrična studija odraslih pacijenata sa sepsom ili septičkim šokom koji su lečeni kontinuiranom bubrežnom nadomesnom terapijom uz primenu CytoSorb® ili oXiris® filtera. Prikupljeni su demografski, klinički i laboratorijski podaci. Preživljavanje je analizirano Kaplan-Mejerovom metodom, Cox-ovom regresijom proporcionalnih hazarda i parametrijskim modelima preživljavanja. Multivarijantne analize korišćene su za procenu nezavisnih efekata, dok

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List of abbreviations: AIC, Akaike Information Criterion; AKI, acute kidney injury; AL, albumin; BIC, Bayesian Information Criterion; CMP, cardiomyopathy; COPD, chronic obstruction pulmonary disease; Cr, creatinine; CRP, C-reactive protein; CRRT, continuous renal replacement therapy; Hb, haemoglobin; HR, hazard ratio; ICU, Intensive Care Unit; IL-6, interleukin-6; IQR, interquartile range; LDH, lactate dehydrogenase; Lact, lactate; MICU, Medical Intensive Care Unit; PLT, platelets; RCT, randomized controlled trial; SAPS II, Simplified Acute Physiology Score II; SD, standard deviation; SOFA, Sequential Organ Failure Assessment; WBC, white blood cells.

Results: Of 94 patients, 42 died. In multivariable Cox analysis, higher D-dimer, lactate (Lact), and SAPS II were independent predictors. Each 10 μg/mL increase in D-dimer was associated with a 15% higher hazard, each 1 mmol/L increase in Lact with 12%, and each 1-point increase in SAPS II with a 3% higher hazard. The log-normal parametric model confirmed these predictors were associated with shorter expected survival.
Conclusion: D-dimer, lactate, and SAPS II independently predict mortality in ICU patients with sepsis or septic shock undergoing extracorporeal blood purification. These findings provide a dynamic, quantitative framework for risk stratification and clinical decision-making. Prospective multicentre studies are needed to validate these results.

Keywords: survival model, septic shock, hemadsorption, biomarkers, outcome

Rezultati: Od ukupno 94 pacijenta, 42 je preminulo. U multivarijantnoj Cox analizi, viši nivoi D-dimera, laktata (Lact) i SAPS II skora identifikovani su kao nezavisni prediktori. Svako povećanje D-dimera za 10 μg/mL je bilo povezano sa porastom hazarda za 15%, svako povećanje laktata za 1 mmol/L sa porastom od 12%, a svako poveć anje SAPS II skora za 1 poen sa porastom hazarda od 3%. Log-normalni parametrijski model potvrdio je da su ovi prediktori povezani sa kraćim očekivanim preživljavanjem.
Zaključak: D-dimer, laktat i SAPS II skor nezavisno predviđaju smrtnost kod pacijenata u jedinici intenzivne nege sa sepsom ili septičkim šokom koji se podvrgavaju ekstrakorporalnom prečišćavanju krvi. Ovi nalazi pružaju dinamički, kvantitativni okvir za stratifikaciju rizika i donošenje kliničkih odluka. Potrebne su prospektivne multicentrične studije radi potvrde ovih rezultata.

Ključne reči: model preživljavanja, septički šok, hemoadsorpcija, biomarkeri, ishod

Introduction

Sepsis remains one of the leading causes of mortality in intensive care units (ICUs) worldwide, with septic shock representing its most severe form and carrying mortality rates exceeding 40% despite advances in antimicrobial therapy and organ support (1–3). The condition is characterized by a dysregulated host response to infection, involving endothelial dysfunction, microcirculatory impairment, and profound metabolic disturbances driven by an uncontrolled release of inflammatory mediators. In the most critically ill patients, these complex pathophysiological processes often limit the effectiveness of conventional therapies, contributing to persistent organ failure, especially acute kidney injury (AKI) and poor outcomes (4, 5). In this context, extracorporeal blood purification techniques have gained increasing attention as potential adjunctive therapies in the management of sepsis and septic shock. These approaches include hemoadsorption, high-cut-off membranes, and adsorptive filters integrated into continuous renal replacement therapy (CRRT) modalities, which aim to remove circulating inflammatory mediators, endotoxins, and other deleterious molecules from the bloodstream (6, 7). In clinical practice, the most widely used systems include hemoadsorption devices and adsorptive membranes, such as CytoSorb® and the oXiris® filters, which are increasingly applied in patients with septic shock, particularly in the presence of sepsis-associated AKI. Although these techniques have been associated with a reduction in inflammatory biomarker levels and improvements in hemodynamic parameters, evidence from recent meta-analyses and observational cohort studies has not consistently demonstrated a significant reduction in mortality, highlighting the need for adequately powered randomized controlled trials (RCTs) (8–10). ICU mortality is a key indicator of healthcare quality and the effectiveness of critical care management. Yet, it remains a major global challenge despite advances in medical technology and evidence-based therapies. A complex interaction between disease severity, comorbidities, physiological reserve, and organizational factors within the ICU determines patient outcomes. Conventional prognostic tools provide static estimates of mortality risk but fail to capture the dynamic evolution of a patient's condition over time. This has driven growing interest in predictive models that integrate routinely collected clinical and laboratory data to generate time-dependent survival estimates, with the potential to improve individualized care and clinical decision-making (11–13). Despite extensive research on prognostic markers in sepsis, there is currently a lack of approaches that translate routinely available clinical and laboratory data into time-dependent survival estimates and proportional risk of death, particularly in patients with septic shock undergoing extracorporeal blood purification (EBP).

The main aim of this study was to develop and apply a parametric survival modelling framework to quantify time-dependent survival in critically ill patients with sepsis undergoing extracorporeal blood purification, moving beyond conventional static mortality endpoints.

Materials and Methods

Patients, study design, and ethics

This retrospective, single-centre, observational study was conducted in the Medical Intensive Care

Unit (MICU) of the University Clinical Centre of the Republic of Srpska, a tertiary-level, university-affiliated hospital. The study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (14). The study period extended from January 1, 2023, to December 31, 2024. The study protocol was reviewed and approved by the Ethics Committee of the University Clinical Centre of the Republic of Srpska (approval no. 01-19-373-2/23). It was conducted in accordance with the Declaration of Helsinki. Due to the study's retrospective, observational nature, the ethics committee waived the requirement for informed consent. All consecutive adult patients (≥18 years) admitted to the MICU with a diagnosis of sepsis and septic shock, defined according to the Sepsis-3 criteria (15), and treated with CRRT incorporating either an oXiris® membrane or CytoSorb® hemoadsorption in conjunction with conventional CRRT were eligible for inclusion. According to the local protocol, EBP was initiated in patients with septic shock complicated by AKI (anuria or severe oliguria, rising nitrogen waste products, and persistent metabolic acidosis), in the presence of clinical and laboratory signs of hyperinflammation and endotoxemia. In addition, clinical deterioration, even in the absence of all the above criteria, could also prompt initiation of EBP. The choice of EBP modality and device type was made at the treating intensivist's discretion. Patients were excluded if sepsis was not the primary diagnosis, or if they had active malignancy, a history of heparin-induced thrombocytopenia, or a documented heparin allergy. Management of sepsis and septic shock, including antimicrobial therapy, fluid resuscitation, vasopressor support, and renal replacement therapy, was performed according to institutional protocols and current international guidelines.

Continuous renal replacement therapy and hemoadsorption

CRRT was performed using the Prismaflex® system (Baxter International Inc., USA). Although several CRRT modalities were available, continuous venovenous hemodiafiltration (CVVHDF) was the predominant mode used in this study. The oXiris® haemofilter (Baxter International Inc., USA) is based on an AN69 membrane composed of acrylonitrile and sodium methallyl sulfonate copolymer fibres, surface-treated with polyethyleneimine and pre-grafted with heparin to provide adsorptive capacity and antithrombogenic properties. The membrane has an effective surface area of 1.5 m^2. It enables simultaneous removal of inflammatory mediators and endotoxins while providing renal replacement therapy. The CytoSorb® cartridge (CytoSorbents Corporation, USA) is a sterile, single-use hemoadsorption device containing highly porous polymer beads designed to remove hydrophobic inflammatory mediators and cytokines up to approximately 55 kDa through size-exclusion and hydrophobic interactions. The cartridge was integrated in series into the CRRT circuit and positioned in the post-filter venous line, in accordance with the manufacturer's recommendations (16). CRRT modality, prescribed dose, treatment duration, and anticoagulation strategy were standardized according to institutional protocols and were comparable between patients treated with the CytoSorb® cartridge and those treated with the oXiris® membrane.

Data sources, collection, and laboratory analyses

Clinical data were obtained through a retrospective review of electronic medical records and recorded in a dedicated study database. Laboratory and haematological parameters were routinely collected at two predefined time points: 15–30 minutes before initiation of extracorporeal blood purification therapy and immediately after completion of the treatment session. Each CRRT-based blood purification session was delivered over 24 hours under standardized conditions. Demographic and clinical variables were recorded at MICU admission and at the initiation and completion of extracorporeal blood purification therapy. Collected data included age, sex, comorbidities, source of infection, isolated pathogen, vasopressor use and dosing, duration of vasopressor therapy, duration of mechanical ventilation, MICU length of stay, and MICU and hospital survival. Disease severity was assessed using the Simplified Acute Physiology Score (SAPS) II at MICU admission, while the Sequential Organ Failure Assessment (SOFA) score was recorded on the day of laboratory sampling. Haematological analyses were performed in the hospital's Department of Laboratory Diagnostics using the Sysmex XN-3100™ haematology analyser, which employs fluorescence flow cytometry. Biochemical analyses were performed using the Abbott Alinity C analyser (Abbott Diagnostics, USA) with photometric and potentiometric detection methods.

Statistical analysis

Descriptive statistics were used to summarize patient demographics, clinical characteristics, and laboratory parameters for the entire cohort and for each hemoadsorbent type. Continuous variables are presented as mean ± standard deviation (SD) or median with 25th and 75th percentile (Q1 and Q3, respectively), depending on data distribution, which was assessed using the Shapiro-Wilk test. Categorical variables are expressed as counts and percentages.

Time-dependent survival was analysed using a combination of nonparametric, semiparametric, and parametric approaches. Following categorical variables were tested: sex, septic shock, source and pathogen isolated, mechanical ventilation, blood purification techniques (CytoSorb®, oXiris®), co-morbidities such as hypertension, diabetes, cardiomyopathy (CMP), anaemia, chronic obstructive pulmonary disease (COPD), chronic kidney disease, liver disease; while continuous included: age, white blood cells (WBC), platelets (PLT), haemoglobin (Hb), C-reactive protein (CRP), creatinine (Cr), urea, procalcitonin (PCT), D-dimer, lactate (Lact), IL-6, SAPS II score, SOFA score. Non-parametric survival estimates were obtained using the Kaplan-Meier method. Initially, Cox proportional hazards regression was performed univariably to evaluate the association between each covariate and survival, with proportionality assessed via Schoenfeld residuals. Hazard ratios (HRs) and their 95% confidence intervals were estimated to quantify the relative effect of covariates on the instantaneous risk of death over time, under the assumption of proportional hazards. Covariates demonstrating statistical significance or clinical relevance were subsequently entered into multivariable survival models to estimate their independent effects on the hazard of death. Selection of variables for multivariable modelling was guided by clinical plausibility, assessment of multicollinearity, and improvement in model fit. Further analysis focused on characterizing the shape of the underlying hazard function (), while adjusting for relevant covariates. Within the parametric survival framework, several candidate hazard distributions (Weibull, exponential, log-normal, log-logistic, and Gompertz) were compared. The model with the lowest Akaike Information Criterion (AIC) and/or Bayesian Information Criterion (BIC)was chosen as the best-fitting model. Survival probabilities were derived directly from the cumulative hazard function () using the relationship: , representing the probability of survival at a given time, conditional on covariates. Median survival times were estimated from the final fitted parametric model, which included the combination of clinically significant covariates. Statistical significance was defined as $p<0.05$. All analyses were performed in R (version 4.5.1), RStudio 2025.09.0, using the survival and flexsurv packages.

Results

Data from 94 patients with sepsis admitted to MICU were included in a study, out of 106 screened. Demographic and baseline clinical characteristics and laboratory parameters of the cohort are summarized in *Table I*. Correlation analysis among continuous variables revealed the highest correlation between urea and Cr (r=0.87), followed by CRP and PCT (r=0.52); all other pairwise correlations were below 0.50, indicating limited multicollinearity.

The overall median survival time of the cohort was 22 days. In univariable Cox proportional hazards regression, several covariates were significantly associated with patient survival (*Table II*). Variables demonstrating statistical significance or clinical relevance were subsequently entered into multivariable Cox regression models in stepwise analyses. Elevated D-dimer, Lactate, and higher SAPS II score remained independently associated with an increased hazard of death (*Table III*), while other covariates showed weaker or non-significant effects. These variables were subsequently considered for inclusion in a multivariate parametric survival model.

The duration of mechanical ventilation was initially associated with survival but was excluded from multivariate analysis due to survivorship bias, as longer ventilation inherently reflects prolonged survival rather than predicts it. Similarly, anaemia showed a significant univariate association (*Table II*). Still, it was not included in further modelling due to its counterintuitive interpretation. Patients with anaemia often receive more intensive management (e.g., transfusions, closer monitoring), while non-anaemic patients who die early may not undergo such interventions, potentially biasing the observed association. Following a stepwise procedure, multivariate Cox models identified higher D-dimer, Lact, and SAPS II scores as independent predictors of mortality (*Table III*). The log-normal model demonstrated a good overall fit (likelihood ratio $\chi^2=24.44$, $df=3$, $p<0.001$). Consistent results were observed in the log-normal parametric model, in which these variables were associated with shorter survival times, indicating a higher death rate (*Table III*).

In our multivariate Cox proportional hazards model, higher D-dimer, lactate, and SAPS II scores were associated with increased risk of death (Table III). Using the final log-normal model, we generated predicted survival probability curves for septic patients across representative combinations of D-dimer, lactate, and SAPS II scores (*Figure 1)*.

Figure 2 shows predicted survival times (in days) for MICU patients with sepsis or septic shock across combinations of D-dimer, Lactate, and SAPS II values, illustrating how higher values of these key prognostic variables are associated with shorter expected survival.

Table I Patients' demographic and clinical characteristics.

Variables, units	All patients (N=94)	CytoSorb® (N=72)	oXiris® (N=22)
	median (Q1, Q3) or mean ± SD / n (%)		
Age, years	59 (45, 68)	60 (47, 68)	55(40, 68)
Sex, male	64 (68.1)	49 (68.1)	15 (68.2)
Route of ICU admission			
Emergency department	43 (45.7)	34 (47.2)	9 (40.9)
General ward	51 (54.3)	38 (52.8)	13 (59.1)
Sepsis and septic shock	41 (43.6)	28 (38.9)	13 (59.1)
SAPS II score	51.35±20.07	52.04±20.00	49.09±20.62
SOFA*	9 (6, 11)	10 (8, 11)	6 (6, 10)
Event, death	42 (44.68)	34 (47.22)	8 (36.36)
Comorbidity			
Essential hypertension	48 (51.1)	37 (51.4)	11 (50.0)
Diabetes	25 (26.6)	18 (25.0)	7 (31.8)
Cardiomyopathy	23 (24.5)	21 (29.2)	2 (9.1)
Chronic anaemia	65 (69.1)	47 (65.3)	18 (81.8)
Chronic obstructive pulmonary disease (COPD)	8 (8.5)	6 (8.3)	2 (9.1)
Chronic kidney disease	12 (12.8)	9 (12.5)	3 (13.6)
Chronic liver diseases	24 (25.5)	18 (25.0)	6 (27.3)
Isolated pathogen in the blood			
Gram-negative bacteria	19 (28.8)	15 (31.2)	4 (22.2)
Gram-positive bacteria	17 (25.8)	12 (25.0)	5 (27.8)
Other (including unknown)	41 (62.1)	28 (58.3)	13 (72.2)
None	28 (29.8)	24 (33.3)	4 (18.2)
Invasive mechanical ventilation	78 (83.0)	61 (84.7)	17 (77.3)
Norepinephrine before EBP	86 (91.5)	67 (93.1)	19 (86.4)
Vasopressin on ICU admission	8 (8.5)	5 (6.9)	3 (13.6)
Laboratory parameters			
White blood cells (WBC), $x10^9/L$	11.5(6.7, 17.4)	11.1 (6.6, 17.1)	13.7(6.9, 20.1)
Haemoglobin (Hb), g/L	111.5 (95.3, 131.0)	111.5 (92.2, 141.2)	111.0(91.7, 119.7)
Platelets (PLT), $x10^9/L$	149.5(88.7, 252.5)	162(88.0, 247.0)	130(101.7, 258.5)
C-reactive protein (CRP), mg/L	212.1 (90.1, 311.9)	207.4(92.6, 309.8)	224.1(69.3, 334.3)
Procalcitonin (PCT), ng/mL	6.85(1.90, 27.74)	7.31(1.67, 25.59)	5.49(3.23, 40.77)
D-dimer, mg/mL	5.14 (2.25, 13.69)	5.14 (2.30, 13.99)	5.63 (1.59, 11.30)
Creatinine (Cr), µmol/L	174.5 (95.7, 401.7)	203.0(105.7, 402.2)	145.5(64.5, 332.7)
Urea, mg/dL	13.4 (7.4, 22.9)	13.4 (7.5, 21.8)	13.6 (7.3, 27.3)
Lactate (Lact), mmol/L	2.90 (1.59, 5.10)	2.87 (1.60, 5.10)	3.45 (1.53, 5.45)
Interleukin-6 (IL6), pg/mL*	Missing: 20 (20.28) 337.5 (116.5, 1384.8)	Missing: 16 (22.22) 576.0 (193.2, 1722.8)	Missing: 4 (18.18) 118.0 (27.5, 416.0)

*$p<0.05$ between CytoSorb® and oXiris® subgroups

Table II Univariable Cox proportional hazards regression analysis of covariates associated with survival in patients with sepsis (N=94).

Variable	Comparison / Unit	Hazard ratio, HR (95% CI)	*p-value*
Isolated microorganism	*Staph. aures, Staph. epidermidis, other vs Acinetobacter spp, Klebsiella spp*, multiple microorganisms, none isolated	2.50 (1.35–4.64)	0.0037
Septic shock	Yes vs No	2.76 (1.36–5.63)	0.00513
Anaemia	Yes vs No	0.42 (0.22–0.79)	0.00734
Diabetes	Yes vs No	1.92(1.00–3.68)	0.0493
D-dimer	per unit increase	1.012 (1.005–1.019)	$6.04\ 10^{-4}$
Lactate (Lact)	per unit increase	1.15 (1.06–1.24)	8 10-4
Interleukin-6 (IL-6)	per unit increase	1.0 (1–1)	0.0165
SOFA score	per unit increase	1.15 (1.05–1.25)	0.00301
SAPS II score	per unit increase	1.03 (1.01–1.05)	$8.77\ 10^{-4}$

HR, hazard ratio; SAPS II, Simplified Acute Physiology Score II; SOFA, Sequential Organ Failure Assessment.

Table III Results from multivariate survival analyses including a Cox proportional hazards model and a log-normal parametric model (N=94).

Variable	Cox proportional hazard model		log-normal parametric model	
	HR (95% CI)	p-value	TR (95% CI)	p-value
D-dimer	1.014 (1.006–1.022)	0.0002	0.991 (0.985–0.998)	0.0062
Lactate	1.122 (1.03–1.22)	0.0096	0.911 (0.835–0.994)	0.0352
SAPS II	1.030 (1.01–1.05)	0.0022	0.970 (0.953–0.987)	0.0015

HR-hazard ratio; TR-time ratio.

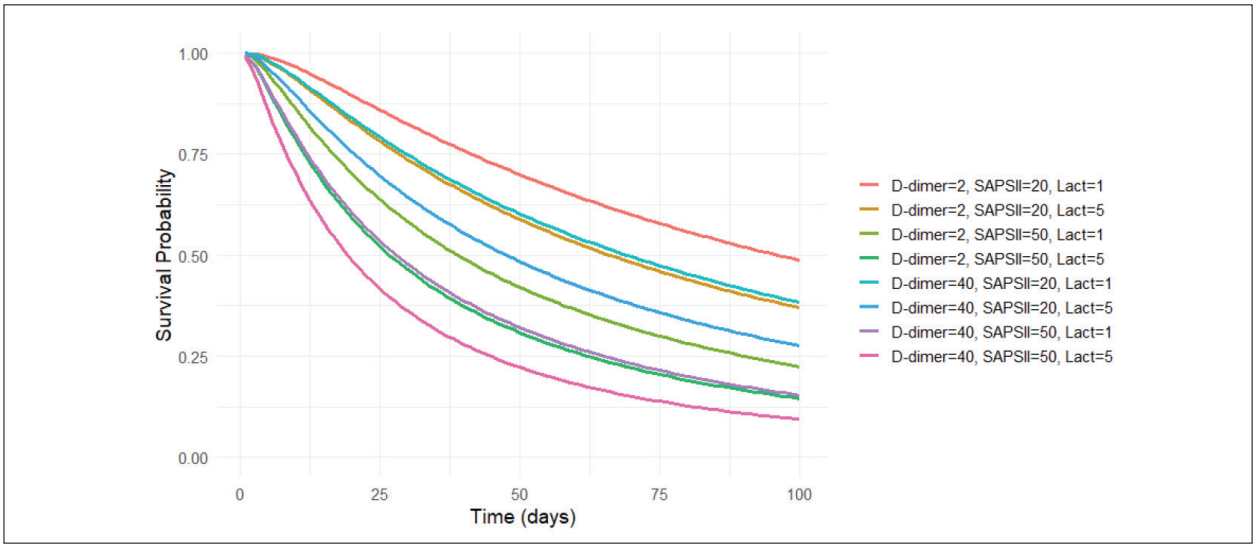

Figure 1 Predicted survival probability curves based on the log-normal model.

Survival curves were generated for representative combinations of D-dimer (μg/mL), lactate – Lact (mmol/L), and Simplified Acute Physiology Score (SAPS) II value.

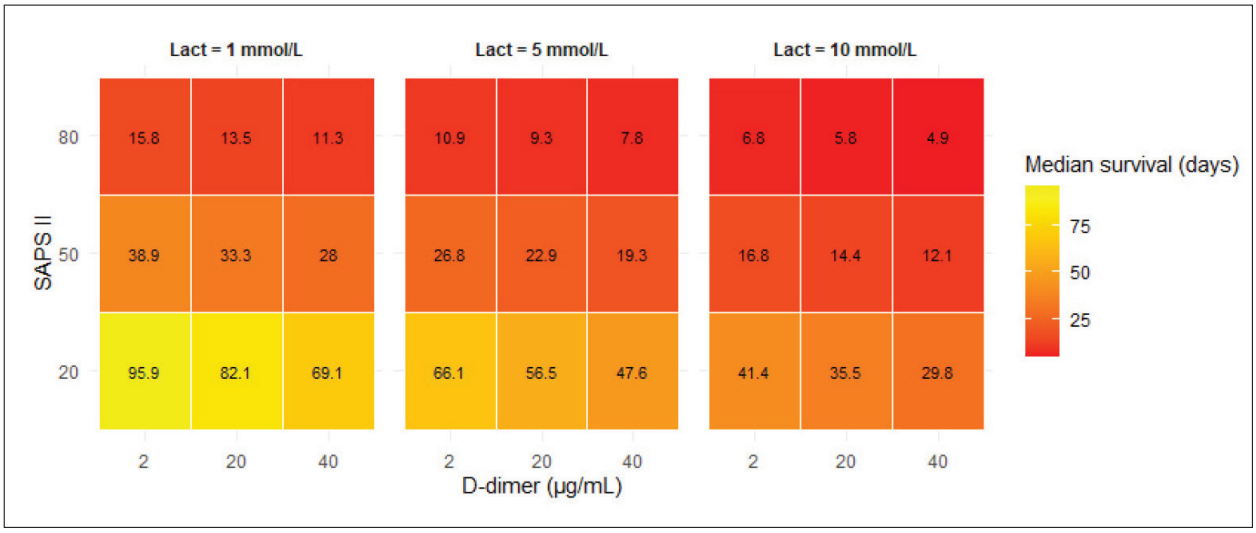

Figure 2 Predicted median survival (days) by the combination of three levels of D-dimer, lactate (Lact), and Simplified Acute Physiology Score (SAPS) II values in patients with sepsis.

Discussion

Our findings show that higher D-dimer, Lact, and SAPS II values are independently linked to increased risk of death of patients with sepsis or septic shock undergoing extracorporeal blood purification. Specifically, each 10 µg/mL increase in D-dimer corresponded to an approximately 15% higher hazard, each 1 mmol/L increase in Lact to a 12% higher hazard, and each 1-point increase in SAPS II score to a 3% higher hazard (*Table III*). Consistent results were observed in the log-normal model, where the same predictors were associated with shorter survival times: a 10 µg/mL increase in D-dimer corresponded to ~9% shorter expected survival, each 1 mmol/L increase in Lact to ~9% shorter survival, and each 1-point increase in SAPS II score to ~3% shorter survival (*Table III*). Our results highlight the combined prognostic impact of coagulation abnormalities, tissue hypoxia, and overall illness severity on survival in ICU patients with sepsis or septic shock. To our knowledge, this is the first survival model in patients with sepsis or septic shock undergoing extracorporeal blood purification that quantifies both the risk of death over time and the expected change in survival associated with key prognostic variables. Literature on D-dimer as a predictor of mortality in patients with septic shock treated with extracorporeal blood purification methods like CytoSorb® or oXiris® is limited. However, several studies have examined the predictive value of D-dimer for mortality in critically ill patients with sepsis and septic shock. Zhan et al. (17) reported that elevated D-dimer levels independently predicted 28-day mortality, with a high discriminative ability (AUC≈0.88), similar to established severity scores in septic patients. Han et al. (18) found that higher D-dimer levels were significantly associated with in-hospital mortality among ICU patients. Predictive accuracy was affected by clinical factors, including vasopressor use. More recently, Qu et al. (19) showed that a 1 µg/mL increase in baseline D-dimer was linked to a 6% higher risk of 30-day mortality after adjusting for other factors, which aligns with our results. Additional research analysing D-dimer, along with other biomarkers such as the D-dimer–albumin ratio or the D-dimer–lymphocyte ratio, further supports its association with adverse outcomes (17–21). Data on lactate, a prognostic biomarker in septic shock patients treated with extracorporeal blood purification techniques, remain scarce; however, numerous studies have demonstrated that lactate is a predictor of mortality in critically ill patients with sepsis or septic shock in general. Our findings align with recent evidence from critically ill septic populations receiving extracorporeal support. In a contemporary ICU cohort of patients with septic shock treated with continuous renal replacement therapy (CRRT), Chang et al. (22) demonstrated that peak lactate within the first 24 hours was independently associated with 28-day mortality, with each 1 mmol/L increase corresponding to an approximately 18% higher risk of death. Similarly, Chu et al. (23) analysing outcomes in patients with sepsis requiring extracorporeal membrane oxygenation (ECMO) and/or CRRT, identified elevated lactate levels as a significant determinant of mortality, underscoring the prognostic importance of metabolic derangement in patients requiring advanced extracorporeal support. Furthermore, real-world data from the COSMOS registry evaluating hemoadsorption therapy in septic shock patients confirmed the clinical relevance of lactate dynamics, demonstrating that persistently

elevated or insufficiently decreasing lactate levels were associated with worse survival. Although registry data do not establish causality, they provide important external validation of lactate as a robust risk stratification marker in extracorporeal blood purification settings. Taken together, these studies support our observation that higher lactate levels are independently associated with mortality in septic patients undergoing extracorporeal blood purification (24). The magnitude of risk increase observed in our cohort (12% per 1 mmol/L increment) is directionally consistent with prior reports, reinforcing the external validity and clinical relevance of lactate as an integrated marker of severity in this high-risk population (22–25). A growing number of studies have evaluated the prognostic value of SAPS II in patients with septic shock treated with extracorporeal blood purification techniques, such as CytoSorb® or oXiris®. In these cohorts, SAPS II has consistently been used as a marker of disease severity and baseline mortality risk, with higher scores observed among non-survivors and in patient subgroups with worse outcomes. In CytoSorb®- and oXiris®-treated septic patients, SAPS II has primarily been applied for risk stratification and for observed-versus-expected mortality comparisons rather than as a continuous predictor within multivariable survival models; nevertheless, these studies consistently demonstrate increasing mortality with higher SAPS II values. These findings are directionally and qualitatively consistent with our estimate of a 36% increase in mortality hazard per 10-point rise in SAPS II, while our analysis extends the existing literature by providing a quantitative, time-to-event assessment of the prognostic impact of SAPS II in this specific extracorporeal blood purification population (26–28).

Several limitations of this study should be acknowledged. First, the single-centre, retrospective design inherently limits the generalizability of the findings. It is susceptible to selection bias and unmeasured confounding. In addition, the overall sample size was relatively small, which may have reduced the statistical power to detect differences in clinically relevant outcomes, including mortality. Although mortality in septic shock remains unacceptably high and identifying effective therapeutic strategies is of paramount importance, the present study cannot establish causality. While hemoadsorption, as part of our local sepsis management protocol, holds promise for mitigating inflammation-mediated organ dysfunction and potentially improving outcomes, these findings should be interpreted with caution. Future large-scale, multicentre RCTs are warranted to define its impact on ICU mortality better and identify patient subgroups most likely to benefit from this intervention.

Conclusions

Using a parametric survival modelling approach, this study moves beyond static mortality endpoints. It provides dynamic survival estimates based on routinely available variables. In patients with sepsis undergoing extracorporeal blood purification, D-dimer, lactate, and SAPS II scores were jointly incorporated into time-dependent survival models, with higher values of each parameter associated with reduced survival and increased mortality risk over time. These findings underscore the prognostic importance of coagulation abnormalities, tissue injury, and overall disease severity in this population. Prospective multicentric studies are needed to validate these results and clarify their clinical implications.

Authors' contribution

Study concept and design: D.M., P.K. Acquisition and collection of data: D.M., P.K., B.Z., M.J., S.D., N.Š., T.K., N.Š., Analysis and interpretation of data: D.M., P.K. Drafting of the manuscript: P.K., K.V., D.M. Statistical analysis: K.V., T.K. Supervision: P.K. Revision of the final manuscript: D.M., P.K, NS, KV, SD, DM, B.Z., M.J., T.K., N.Š., P.K. All authors read and approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Institutional review board statement

The study followed the principles of the Declaration of Helsinki. It was approved by the local Ethical Committee of the University Clinical Centre of the Republic of Srpska (approval no. 01-19-373-2/23).

Informed consent statement

Given the study's retrospective, observational design, the Ethics Committee of the University Clinical Centre of the Republic of Srpska waived the requirement for informed consent.

Data availability statement

The data supporting the findings of this study are not publicly available due to ethical and privacy restrictions, but are available from the corresponding author upon reasonable request.

Conflict of interest statement

All the authors declare that they have no conflict of interest in this work.

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