A SIRS-BASED AUTOMATED ALARM SYSTEM FOR THE DIAGNOSIS OF SEPSIS AFTER BURN INJURY

ALARME AUTOMATIQUE BASÉE SUR LES PARAMÈTRES DE SIRS POUR LE DIAGNOSTIC DE SEPSIS APRÈS BRÛLURE

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SUMMARY. The present study examined the effectiveness of an automated systemic inflammatory response syndrome (SIRS)-based alarm system for the early detection of sepsis in adult burn patients. In addition, the relevance of the sepsis criteria from the American Burn Association (ABA) and the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) for this patient group was determined. In this prospective observational study, we included 41 consecutive patients who were admitted to our burn ICU within a one-year period. SIRS alarms were calculated for these patients according to predefined criteria using the PREDEC ALARM automated alarm system and alarms generated according to ABA criteria and daily Sequential Organ Failure Assessment (SOFA) results. The alarms were not visible to the treating doctors and nurses. The alarms identified were related to episodes of sepsis with positive blood cultures. Twenty-one sepsis events were recorded in 41 patients. The receiver operating characteristic (ROC) curve revealed an area under the curve (AUC) of 0.72 for alarms using 2 SIRS criteria, 0.77 for 3 SIRS criteria, and 0.61 for 4 SIRS criteria. AUC values of 0.53 and 0.59 were calculated for the ABA criteria and Sepsis-3 definition, respectively. An alarm system using 3 SIRS criteria proved to be suitable for the early detection of sepsis in burn patients. The frequent number of false alarms requires further refinement of the alarm system. Based on the results of our study, the ABA criteria and the Sepsis-3 definition provide no advantages over the SIRS criteria in the early diagnosis of sepsis after burn injury.

Keywords: burns, sepsis, SIRS, SOFA, alarm

RÉSUMÉ. *Cette étude évalue l'efficacité d'un système automatique fondé sur les paramètres de SIRS pour la détection précoce du sepsis chez des adultes brûlés. En outre, il étudie la pertinence des critères d'infection de l'ABA et des critères de sepsis selon la conférence Sepsis-3 chez ces patients. Nous avons inclus 41 patients consécutifs, admis dans notre USI pour brûlés, dans cette étude observationnelle prospective. Les alarmes du système automatique PREDEC ALARM ont été calibrées selon les critères de l'ABA et le score SOFA et comparés aux 21 épisodes septiques à hémocultures positives. Elles étaient cachées aux médecins et infirmières. Les aires sous courbes ROC étaient de 0,72 pour les alarmes basées sur 2 critères de SIRS ; 0,77 pour 3 critères et 0,61 pour 4 critères. Elles étaient de 0,53 pour les critères ABA et 0,59 pour les critères Sepsis-3. Une alarme basée sur 3 critères de SIRS semble donc être utilisable pour détecter précocement un sepsis chez les brûlés, mais le nombre élevé de faux positif nécessite un affinement du système. Les critères ABA et Sepsis-3 ne semblent pas plus efficaces dans ce but.*

Mots-clés: *brûlure, sepsis, SIRS, SOFA, alarme*

Introduction

Septic multi-organ failure is the main cause of death for severely injured patients who have survived the resuscitation period.[1] In a study by Wang et al., patients with sepsis exhibited a 7.17-fold increase in mortality compared to patients without sepsis.[2] In patients with a greater than 40% burned total body surface area (TBSA), sepsis is the cause of death in 75% of cases.[3] Compared with other patient groups, burn-injured patients have a particularly high risk of infection during the course of their treatment.[4] The main reasons for this increased risk include microbial colonization of the burns and immunosuppression, in addition to inhalation injury, intubation, longer ventilation times and the need for multiple devices.[5] Thus, 8 to 65% of burn-injured patients suffer from sepsis[6] during treatment of their burn injury. Recognition of the corresponding clinical symptoms of sepsis is difficult for burn patients due to chronic hypermetabolism and associated changes. Hypermetabolism results from high stress hormone levels (catecholamines, glucagon and cortisone) and proinflammatory mediators released from the burn wound, and from high heat and evaporative fluid losses.[7] The increase in metabolism can

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increase the basic turnover by up to two-fold and can last for weeks.[8] This metabolic increase results in changes that correspond to a systemic immune response syndrome (SIRS) and are very similar to the clinical picture of infection.[9]

In 1992, the American College of Chest Physicians and Society of Critical Care Medicine established the first international definition of sepsis. At least two of the criteria listed in *Table I* must be met to determine the presence of SIRS of an infectious genesis with organ complications or of SIRS with a non-infective genesis with or without organ complications.[10] A valuation with respect to the forecast is not defined according to the number of fulfilled SIRS criteria. However, as shown in a study by Sprung et al., the risk of organ failure and subsequent mortality increases as the number of positive SIRS criteria increase.[11]

Table I - SIRS criteria[10]

1. Temperature: > 38°C or < 36°C
2. Heart rate: > 90 beats per min
3. Respiratory rate: > 20 breaths/min or partial pressure of CO_2 ($PaCO_2$) < 32 mm Hg
4. White blood cell count: > 12,000 or < 4000 cells/mm³
SIRS, systemic inflammatory response syndrome

The SIRS criteria proposed by Bone et al. were confirmed in a second consensus conference in 2001 and supplemented with further clinical symptoms and laboratory parameters.[12] However, this extension was not universally accepted, and the original sepsis definition was used in the absence of alternatives.[13] The Third International Consensus Definitions for Sepsis and Septic Shock[14] were released in February 2016. This new definition ("Sepsis-3") was based on a retrospective analysis of large cohorts of patients with sepsis and focused on sepsis-related organ dysfunction. Biomarkers were not integrated. Sepsis is therefore defined as a life-threatening organ dysfunction caused by a dysregulated response of the organism to an infection. Organ dysfunction is recorded using the Sequential Organ Failure Assessment (SOFA) score (*Table II*). An infection-related increase of ≥ 2 points within 24 hrs is a possible indication of sepsis and has been associated with hospital mortality greater than 10%.[14] The extent to which the SOFA score can actually replace the existing SIRS criteria in the diagnosis of sepsis is currently controversial.[15,16] However, the authors of the Sepsis-3 definition note that the SIRS criteria may remain useful for the identification of infection.[14] The Sepsis-3 definition is currently recognized by two intensive care societies (Society of Critical Care Medicine (SCCM) and European Society of Intensive Care Medicine (ESICM)). However, no current data on the significance of the Sepsis-3 definition in burn patients are available.

Currently, no consensus exists on the signs of sepsis in burn patients.[18] In addition to the above-mentioned general, intensive medical definitions of sepsis, recommendations from national associations have a variety of different criteria.[19,20,21] For example, the criteria of the American Burn Association (ABA) formulated in 2007 within the framework of a Consensus Conference[19] are listed in *Table III*. Although only a weak

Table III - ABA sepsis criteria.[19] Sepsis should be considered when three or more of the criteria are met

1. Temperature: > 39°C or < 36.5°C
2. Progressive tachycardia: > 110 beats per min
3. Progressive tachypnoea: a. > 25 breaths per minute, not ventilated b. Minute ventilation > 12 l/min, ventilated
4. Thrombocytopenia (not applied until 3 d after initial resuscitation): < 100.000 cells/µl
5. Hyperglycaemia (in the absence of pre-existing diabetes mellitus) a. Untreated plasma glucose levels > 200 mg/dl or the equivalent in mM/l b. > 7 units of insulin/hr by intravenous drip c. Significant resistance to insulin (> 25% increase in insulin requirement over 24 hr)
6. Inability to continue enteral feedings > 24 hr a. Abdominal distension b. High gastric residuals (residuals two times the feeding rate) c. Uncontrollable diarrhoea (0.2500 ml/d)
In addition, documented infection must be identified through one of the following tests: A. Culture-positive infection B. Identification of the pathological tissue source, or C. Clinical response to antimicrobials

Table II - The SOFA score[17]

Organ system	SOFA score			
	1	2	3	4
Cardiovascular system Blood pressure, mmHg Catecholamines	Mean arterial pressure (MAP) < 70	Dobutamine	Adrenaline ≤ 0.1 µg/kg/min or noradrenaline ≤ 0.1 µg/kg/min	Adrenaline > 0.1 µg/kg/min or noradrenaline > 0.1 µg/kg/min
Respiratory system partial oxygen pressure (PaO_2)/fraction of inspired oxygen (FiO_2), mmHg	< 400	< 300	< 200*	< 100*
Central nervous system (CNS) Glasgow Coma Scale	13-14	10-12	6-9	< 6
Coagulation Platelets, Gpt/l	< 150	< 100	< 50	< 20
Hepatic system Bilirubin, µmol/l	20-32	33-101	102-204	> 204
Renal system Creatinine, µmol/l Urine output (UO), ml/ d	100-170	171-299	300-440 or < 500 (UO)	> 440 or < 200 (UO); dialysis
* Values are for patients receiving respiratory support.				

correlation between the ABA criteria and sepsis was reported in burn patients,[22,18] these criteria gained widespread use in studies on this topic.[23,24,25]

Regarding the diagnosis of sepsis, the importance of automated alarm systems has been minimally investigated to date. The parameters that are suitable for such alarm systems are also unclear. The aim of an alarm system is to enable the early and specific detection of a septic infection event, because early diagnosis and initiation of an adequate antibiotic therapy may be significant prognostic factors for septic patients.[26,27,28] Studies of an automated alarm system using modified SIRS criteria revealed good sensitivity and specificity but did not show any benefit in terms of therapy initiation and important prognostic parameters compared with the control group.[29,30] Data on burn-injured patients and automated alarm systems are not available.

The aim of the present study is to test the significance of the SIRS criteria within an automated alarm system for the early detection of sepsis in burned patients. In addition, the sensitivity and specificity of the ABA criteria and of the Sepsis-3 definition are assessed regarding the diagnosis of sepsis.

Materials and methods

Study population

Approval of the Ethics Commission of the Saxonion Chamber of Physicians was issued by a vote on July 8, 2011 (EK-BR-33/11-1). The prospective study included all patients admitted to the ICU of a regional burn centre from September 2011 until August 2012. Exclusion criteria included patient age <18 years, palliative care upon admission and < 3 days of ICU stay.

Data collection

The collected data included demographics, injury characteristics (*Table IV*), vital parameters such as blood pressure and temperature, respiratory rate, and routine laboratory variables, including white blood cell (WBC) count. These data were collected from a patient data management system (PDMS, ICU Data, IMESO, Gießen, Germany) and patient medical records. All patients were evaluated at admission using the Acute Physiology and Chronic Health Evaluation II (APACHE II) score and the SOFA score.[17] The SOFA score was calculated daily during the investigation period. The SOFA score on day 1 was defined as the measurement at 0600 hrs on the day following admission. All subsequent scores were recorded at 0600 hrs at 24-hr intervals.

Infection criteria

The definition of sepsis is the result of clinical suspicion and confirmed positive blood cultures. These criteria were selected to achieve the maximum reliability of the diagnosis of sepsis. The suspicion of sepsis within our institution arises through clinical experience, including observation of the following: deterioration of the patient's general condition, rapid increase in temperature, new tachycardia, bounding pulse, increased capillary refill time, hemodynamic instability without other reason, increasingly labored breathing, altered mental state without other reason, inability to receive enteral feeding in combination with laboratory values (new alteration of blood glucose, increase in biomarkers such as white blood cell count, increase of lactate and negative base excess). Clinical "suspicion" would trigger synchronous blood culture sampling. Onset of sepsis was defined as time of blood culture sampling. In case of recurrent sepsis, all events were recorded and analyzed.

Alarm criteria

Using the automated alarm system PREDEC ALARM (Löser Medizintechnik GmbH, Leipzig, Germany), SIRS alarms were calculated according to different criteria. A SIRS alarm was triggered if at least 2, 3, or 4 SIRS criteria **(***Table I*) were met for at least 30, 60, or 120 minutes, resulting in 9 different settings for SIRS. These settings were used to exclude specific points, such as tachycardia, in the context of physiotherapy or endotracheal suction. The SIRS alarm was valid until the defined number of SIRS criteria were no longer met for 30, 60 and 120 minutes. The SIRS criteria must have been present at the same time (temperature, heart rate, respiratory rate and hypocapnia) or remain effective (WBC count). The alarm system used data from central monitoring (Intellivue, Philips Healthcare, Hamburg, Germany) and PDMS (ICU Data, IMESO GmbH, Giessen, Germany). The data were recorded without a time delay and were not dependent on input by the staff.

An ABA alarm was triggered if at least 3 ABA criteria were met. The SOFA score was recorded automatically as described above. According to the Sepsis-3 definition, we retrospectively examined whether an infection-induced increase in the SOFA score of ≥ 2 occurred within a 24-hour window on the day the infection was diagnosed.

Sensitivity and specificity were calculated daily. For each individual day, we determined whether an alarm or an infection event occurred. The computed alarms were compared with the diagnosis of sepsis according to the infection criteria described above. The alarms were not visible to the treating physicians and nurses. In the evaluation, all alarms were rejected up to 5 days after a sepsis event, assuming that the alarms were associated with sepsis. In addition, all alarms generated within 48 hours after admission to the hospital were excluded. This exclusion was based on the assumption that a trauma-associated SIRS could be expected during the resuscitation period and that infection events tend to be the exception.

Time intervals were defined to determine the association of an alarm with a septic event. An alarm was viewed as occurring simultaneously to sepsis if it occurred within 2 hours before or up to 2 hours later. Thus, an alarm was considered earlier when it occurred 2 to 24 hours prior to the event and later when it appeared 2 to 24 hours after the sepsis event detected by the physician. Alarms that occurred 24 hours prior to the event were not considered related to sepsis.

Burn care protocol

Subjects were treated in a standardized manner, and practice patterns were not changed during the study period. The initial fluid infusion rate was calculated according to the Rule of TEN.[31] This infusion rate was titrated to maintain a urine output of 0.5 ml/kg BW/hr. In the event of unstable cardiovascular function, 20% human albumin was infused as required to maintain a serum albumin concentration greater than 25.0 g/l. In cases of persistent cardiovascular instability, patients received vasopressor support, such as noradrenaline. Enteral nutrition was normally initiated within 6 hrs of admission or at the earliest opportunity thereafter. Wound excision and grafting were initiated within 72 hrs after burn injury. Approximately 20–25% of the burned surface was excised and grafted in one procedure, and operations were repeated every 2-3 days. No prophylactic antibiotics were used.

Statistical analysis

The results are presented descriptively as medians (50th percentile) and interquartile ranges (i.e., the interval between the 25% and 75% quartiles). The sensitivities and specificities of the alarms of the settings are displayed in one receiver operating characteristic (ROC) plot. Sensitivity indicates the proportion of sepsis days that are correctly identified as such (true positive rate). Specificity measures the proportion of non-sepsis days that are correctly identified as such (true negative rate). Fisher's exact test was applied to test the null hypothesis of independence of rows and columns in the contingency table, resulting in P-values, 95 percent confidence intervals and odds ratios for each setting. The alarms were computed using Microsoft Visual C++ and Excel VBA (Microsoft Cooperation, Redmond, USA). The statistical evaluation was performed using R for Windows version 3.3.2.

Results

The study included 41 patients. Seven patients were excluded due to primary palliative therapy or < 3 days of ICU stay (*Fig. 1*).

The causes of burn were flames in 30 cases (73.2%), explosions in 6 cases (14.6%), and scalds in 4 cases (9.8%). One patient suffered an electrical burn. Demographic and biometric data, burn characteristics and outcome parameters are summarized in *Table IV.*

A total of 1076 patient days were entered into the analysis. In 15 patients (34.1%) a total of 21 sepsis episodes were recorded. Two events were recorded in 4 patients, and 3 events were recorded in one patient. The median timing of sepsis occurrence was day 13 [6; 23] after burn injury. The microbiological characteristics (blood cultures) are summarized in *Table V*.

During the course of treatment, 21 patients (51.2%) received beta-blockers. Forty patients (97.6%) received metamizole as part of pain therapy, and 6 patients (14.6%) received clonidine. All patients with sepsis received therapy with a beta-blocker and metamizole at the time of the infection. Diabetes mellitus was a pre-existing condition in 3 patients (7.3%).

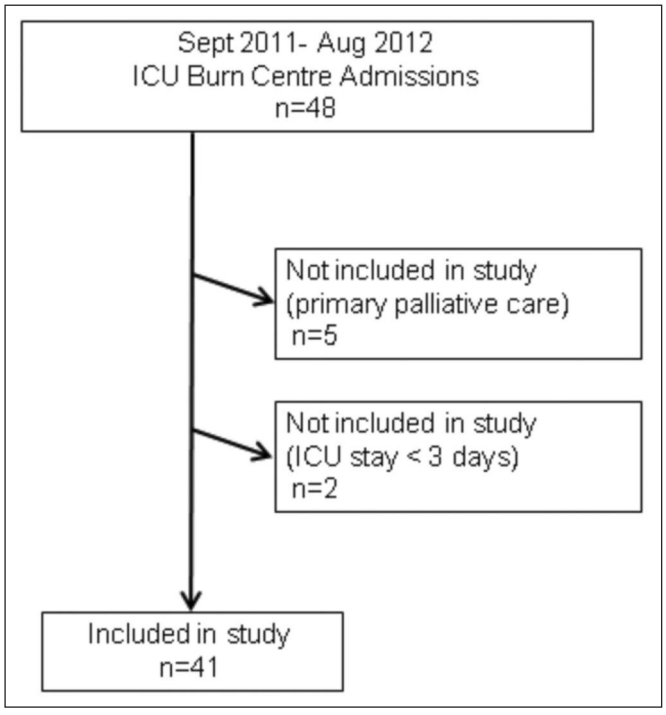

Fig. 1 - Flowchart of patients included in this study.

Table IV - Patients, injury characteristics and outcome parameters

n = 41	Median [range], n (%)
Age (yrs)	44 [31; 60]
Gender, male	28 (68.3)
Body weight (kg)	80 [70; 89]
TBSA (%)	21 [14; 29]
Full thickness burn (%)	12 [4; 27]
ABSI	7 [5; 8]
Baux score	69 [53; 85]
No. of inhalation injuries	8 (19.5)
APACHE II day 1	13 [11; 14]
SOFA at admission	2 [1; 4]
Mechanical ventilation	21 (51.2)
Mechanical ventilation (h)	2 [0; 6]
CRRT	1 (2.4)
Days of ICU stay	18.7 [8.7; 32.7]
Days of hospital stay	27 [15; 41]
Outcome, death	1 (2.4)

TBSA = total body surface area, ABSI = Abbreviated Burn Severity Index, Baux score = age (y) + TBSA (%), APACHE II = Acute Physiological and Chronic Health Evaluation II, SOFA = Sequential Organ Failure Assessment, CRRT = continuous renal replacement therapy, ICU = intensive care unit

Table V - Microbiological results of blood cultures

	n = 21
Gram-positive	
Staphylococcus aureus	3
Coagulase-negative *Staphylococcus*	1
Enterococcus faecalis	1
Streptococcus agalactiae	1
Streptococcus pneumonia	1
Gram-negative	
Pseudomonas aeruginosa	9
Escherichia coli	4
Serratia marcescens	2
Klebsiella pneumonia	1
Enterobacter cloacae	1
Proteus mirabilis	2
Yeast	
Candida albicans	1

Alarms for SIRS criteria

In daily observations over the observed 1067 patient days, 2 SIRS criteria exceeding 30 minutes resulted in 576 alarms, SIRS criteria exceeding 60 minutes resulted in 477 alarms and SIRS criteria exceeding 120 minutes resulted in 401 alarms. When 3 SIRS criteria were fulfilled, 236 alarms were observed at 30 minutes, 172 at 60 minutes, and 132 at 120 minutes. Regarding the fulfilment of 4 SIRS criteria at 30 minutes, 60 minutes and 120 minutes, 48, 32 and 22 alarms were generated, respectively. For the three scenarios, the statistical parameters of diagnostic performance regarding the detection of sepsis are summarized in *Table VI.*

A sensitivity of 86.7% and specificity of 47.1% was recorded for a SIRS alarm with 2 SIRS criteria fulfilled over 60 min. With 3 SIRS criteria specificity and sensitivity were 83% and 60%.

Table VI - Parameters used to assess the diagnostic performance of SIRS criteria for sepsis[10]

	2 SIRS criteria			3 SIRS criteria			4 SIRS criteria		
Time to fulfil the criteria (min)	30	60	120	30	60	120	30	60	120
Sensitivity (%)	93.3	86.7	86.7	73.3	60.0	53.3	26.7	20.0	6.7
Specificity (%)	33.9	47.1	57.3	77.3	83.0	87.5	96.0	96.9	97.9
AUC (ROC analysis)	0.72			0.77			0.61		
95% confidence interval (AUC)	0.587 – 0.782			0.676 – 0.817			0.48 – 0.692		

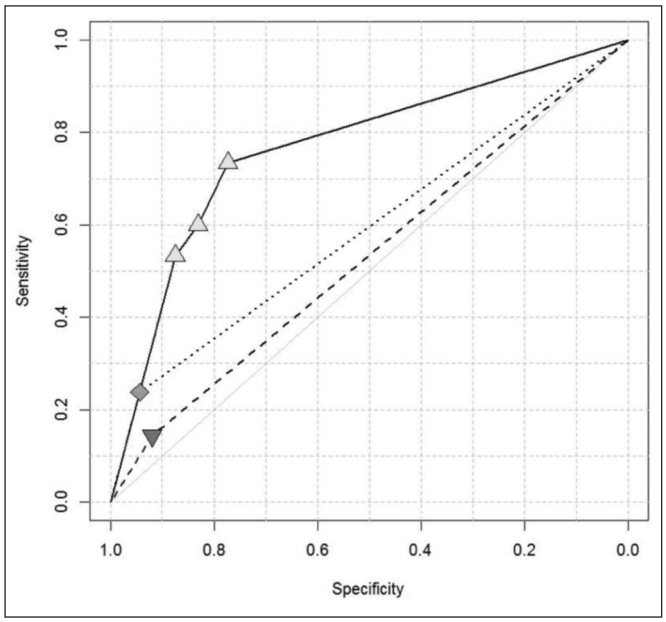

Fig. 2 - ROC curves displaying the performance of the criteria used to diagnose sepsis. 3 SIRS criteria (line with green triangles, AUC 0.77), ABA criteria (broken line with a blue cone, AUC 0.53) and Sepsis-3 definition (dotted line with a red diamond, AUC 0.59).

At the time of sepsis, alarms were generated in 90.5% of events (19 episodes) for the 2 SIRS criteria/60 min scenario and in 61.9% of events (13 episodes) for the 3 SIRS criteria/60 min scenario. A simultaneous alarm was generated for the 2 SIRS/60 min scenario in 5.3% of events. The alarms occurred earlier in 94.7% of events and later in 0% of events. For the 3 SIRS /60 min scenario, alarms were reported at the time of sepsis in 46.2% of events. In contrast, 53.8% of alarms were registered earlier, and 7.7% were registered after the diagnosis of sepsis.

Alarms for ABA criteria

For the ABA criteria, a sensitivity of 14.3% and a specificity of 92.0% with an AUC 0.53 (*Table VII* and *Fig. 2*) were identified. The required minimum of 3 criteria was met in 3 of the 21 sepsis episodes (14.3%). The ABA criteria were fulfilled as follows: temperature 52.4% (11 episodes), tachycardia 57.1% (12 episodes), tachypnoea 42.7% (9 episodes), thrombocytopenia 9.5% (2 episodes), hyperglycaemia 9.5% (2 episodes), and inability to continue enteral feeding >24 hrs 0%.

Sepsis-3 criteria

A total of 66 alarms were recorded using the Sepsis-3 definition, i.e., suspected infection and an increase in the SOFA score of at least 2 points. The retrospective analysis revealed a sensitivity of 23.8% and a specificity of 94.4% with an AUC of 0.591 (*Table VII* and *Fig. 2*).

Table VII - Parameters used to assess the diagnostic performance of the ABA criteria for sepsis[19] and the Sepsis-3 definition[14]

	ABA	Sepsis-3 definition
Sensitivity (%)	14.3	23.8
Specificity (%)	92.0	94.4
AUC (ROC analysis)	0.53	0.59
95% confidence interval (AUC)	0.46 – 0.817	0.527 – 0.654

Discussion

The timely recognition of changes in a patient's condition depends on the level of education, experience and the number of medical and nursing staff.[18] An automatic, continuously screening alarm system allows these changes to be identified, regardless of these factors. Thus, this alarm system may help medical staff identify a possible septic infection at an early stage. In the present study, an automated alarm system based on the SIRS criteria was suitable for the early detection of sepsis after severe burn injury. In the investigation of different alarm scenarios, the scenario with 2 SIRS criteria over 60 min and 3 SIRS criteria over 60 min exhibited the best relationship between sensitivity and specificity, corresponding to an AUC of 0.72 for 2 SIRS criteria and 0.77 for 3 SIRS criteria. In total, 94.7% and 53.8% of the alarms generated using the criteria listed above were active before the clinical diagnosis of sepsis. Diagnostic and therapeutic measures could have been initiated earlier in these cases. In our study, the lack of a control group does not allow any statement about possible improvement in outcomes. Although automated sepsis alerts may improve the care process, until now there has been no evidence they improve mortality.[32] Nevertheless, earlier recognition of sepsis and subsequent early initiation of treatment can only be considered as beneficial. Importantly, this system is not used for the automated diagnosis of sepsis but rather for the automated detection and utilization of infection-type changes. The alerting tool by no means replaces the clinical view of the medical staff but serves to support the daily routine.

In previous investigations on SIRS criteria, daily observations or a rolling 24hr window was considered.[11,29,30,33] The SIRS criteria were considered fulfilled if at least 2 SIRS criteria were met within this time window. However, patients were not necessarily required to simultaneously meet these criteria. In a study of burn patients with a similar design, the SIRS criteria were met in approximately all cases in non-septic patients.[18] In contrast to this approach, in the present study the SIRS criteria had to be satisfied simultaneously over a defined period of time. This feature ensured that the SIRS criteria referred to each other and to a possible case of sepsis. In addition, adulteration by artefacts and short-term reactions were excluded, e.g. increase in heart rate during physiotherapy or endotracheal

suction. This circumstance seems to be very important for the enhanced performance of the SIRS criteria in our patient cohort. In a study by Hogan et al., many patients met the SIRS criteria in the absence of infection.[22] Notably, 88% of the non-septic patients entered their study within 24 hours after admission. These patients were therefore still in the resuscitation period and exhibited trauma-associated changes in SIRS parameters. Within this period, SIRS criteria are indeed not considered appropriate. Our study did not assess alarms occurring during the first 48 hours after admission due to their limited clinical impact. In burn patients, a very early onset of sepsis would be most uncommon. In the present study, sepsis occurred on day 13 (median) [6; 23] after trauma. In a large retrospective study of 2364 patients, a blood stream infection occurred on day 7 (median) after burn trauma.[34] A further difference between the present study and that of Hogan et al. was the less severe burn size (21% burned TBSA). We postulate that trauma-induced SIRS played a lesser role. Burn-related SIRS is expected to involve greater than 25% burned TBSA.[35] In this context, the greater burned TBSA reported in Hogan's study may be a further explanation for the high rate of false-positive SIRS alarms. An average of 14.8% burned TBSA was reported for patients treated in German burn centres in 2015,[36] which is comparable to the current study. Thus, the application of our findings may be limited to the German domestic situation. However, the German situation compares well with that reported for other countries.[37,38,39,40]

Within an alarm system, sensitivity shows a higher value than specificity. The main task is reliable alarming. Alternatively, a low specificity indicates a high rate of false alarms and the risk that personnel will ignore the alarm.[41] Within the setting of the current study, the assignment of a traffic light system for the alarms may be favourable. The constellation of 2 SIRS criteria over 60 minutes could serve as a yellow signal with good sensitivity and accepted low specificity, and 3 SIRS criteria over 60 minutes could serve as a red signal corresponding to lower sensitivity but good specificity. Improved specificity may be achieved by integrating additional parameters. These parameters should also be recorded automatically and allow for differentiation from non-septic events. Which criteria remains unclear. These may include parameters emphasizing organ dysfunction, lactate level, base excess in the context of regularly collected blood gas analyses, an MAP < 60 mmHg and/or the need for catecholamine treatment. Mann-Salinas et al. suggested six parameters that reflect shock occurrence and the dysregulation of temperature and blood glucose levels. Using these criteria, a satisfactory differentiation between septic and non-septic patients was achieved with an AUC of 0.77.[18] However, the results were not better than the results obtained under the simpler scenario with 3 SIRS criteria in our study (AUC 0.77). In the present study, only a weak correlation was observed between ABA criteria and sepsis (AUC 0.53). The previously mentioned study by Hogan et al. also reported a weak correlation (AUC 0.64) between the ABA criteria and sepsis. The multivariate analysis did not reveal any significant relationship between the ABA criteria and sepsis for patients beginning on the 3rd day after admission. The authors also criticize the blurring of some ABA criteria, which makes their clear assignment in clinical practice more difficult.[22] Mann-Salinas et al. reported an inadequate discrimination between septic patients and patients without suspected infection for the ABA criteria. A high rate of false-positive results was noted.[18] In our patient population, the problem was more likely to be the high rate of false-negative values, as 86% of the septic patients met less than 3 ABA criteria. Overall, according to the results of our study and the present literature,[22,18] the suitability of the ABA criteria for the early diagnosis of sepsis is questionable.

Notably, accompanying medications are problematic for the application of both SIRS and ABA criteria. All patients included in the present study received therapy with a beta-blocker and antipyretics at the time of sepsis. These medications may attenuate the burn-induced hypermetabolism as a therapeutic target but may also conceal clinical signs of infection. We can only speculate on whether the significance of the corresponding parameters in infections will increase again.

The criteria for the SOFA-based Sepsis-3 definition were only present in 23.8% of patients with a clinical suspicion of sepsis and positive blood culture. Furthermore, not all elements of the SOFA score can be assessed automatically (e.g., Glasgow Coma Scale), which limits their application within an automated alerting tool. According to our results, the Sepsis-3 definition does not appear to be suitable for definition or use within an alerting tool for the detection of sepsis in burned patients. Of interest, even the authors of the Sepsis-3 definition consider the SIRS criteria to continue to have a high priority in the detection of infection.[14,15,16] Therefore, the SIRS criteria are still considered valuable as a screening tool for sepsis and should not be replaced by the SOFA score.[15,16] The SOFA score is primarily associated with sepsis as a prognosis parameter[13] and high specificity is achievable with the Sepsis-3 definition (increase in the SOFA score of ≥ 2 points) as also shown in our study. However, cellular damage that has already been sustained at the beginning of the therapy prior to diagnosis using these criteria is a concern; thus, the chances of a successful treatment may be reduced.[42]

One of the strengths of this study is the prospective and non-visible recording of the alarms. Therefore, we avoided influencing the behaviour of the staff regarding the different alarm settings. The most important aspect is the condition that the fulfilled alarm criteria must have been met simultaneously over a defined period of time. Our study differs from all previous studies on this topic. The present study is limited by a small patient cohort from a single burn centre. Due to the relatively low burned TBSA, no conclusions can be reached regarding patients with extensive burns. The results can only be transferred to comparable patient groups. We defined very strict sepsis criteria. Bacteraemia was selected as an indispensable precondition in cases of clinically suspected sepsis, given its fidelity in this context. Thus, only clear sepsis episodes were considered, at a risk of missing sepsis without a microbiologically proven infection.

Conclusion

The contribution of automated medical systems to the monitoring, alert support and effective management of patients in the ICU setting is well established. Alarms with high specificity and sensitivity employing reliable parameters can allow early recognition and initiation of treatment of sepsis. Ideally, researchers should consider data parameters that use simple software requiring no additional workload to clinical personnel. Such systems are currently not available to the severe

burns patient. The present study highlights current routinely available parameters used in SIRS criteria that may be considered for such alarm systems in the future. Based on the results of this study, the fulfilment of 2 or 3 positive SIRS criteria over a defined period of time is more appropriate for the detection of sepsis than the ABA criteria or the Sepsis-3 definition. Further studies with supplementary parameters in order to increase specificity and sensitivity are needed prior to translation into routine daily practice, but the findings of the current study are encouraging.

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