

## How to manage sepsis in the Emergency Department leading to a decreased mortality in ICU - the Critical Care Cascade

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Patients with sepsis, severe sepsis and/or septic shock are at increased risk of death and organ dysfunction.

While morbidity and mortality of patients with severe traumatic injury, acute myocardial infarction or stroke have been significantly reduced during recent years by the implementation of well-coordinated approaches to apply evidence-based therapies, mortality in patients with sepsis remains high. The awareness of the high death toll of sepsis is not adequately acknowledged in the population and by healthcare providers.

A large body of knowledge to treat bacterial infections and sepsis has accumulated, but is often not adequately provided from healthcare providers. This ineptitude to apply current knowledge of sepsis management in the emergency department (ED) may be overcome by a structured way of diagnostics and treatment protocols.

We report the implementation of sepsis care bundles and demonstrate that hospital mortality of sepsis patients treated in our intensive care unit (ICU) significantly decreased by about 30 % after implementation of our program in the ED.

In conclusion, patients with severe sepsis presenting to the ED display high hospital mortality. Early detection of patients with sepsis in the ED and early treatment in a coordinated manner significantly reduce mortality of affected patients.

## Background

Patients with sepsis, severe sepsis and/or septic shock are at increased risk of death and organ dysfunction, and the number of affected patients increases worldwide [1, 2].

Diagnostic criteria for sepsis include documented or suspected infection in addition to the presence of systemic inflammatory response syndrome of the organism (Table I). Sepsis is the 10th leading cause of death in industrialized countries and accounts for at least 1 of 5 admissions to an intensive care unit (ICU), posing tremendous costs to the healthcare system [1].

Septic shock results in approx. 250,000 deaths per year in the United States and comparable numbers are estimated for Europe [3]. The incidence of affected patients is probably rising due to an aging population,

a higher proportion of patients with a compromised immune system and patients who undergo high-risk surgery [4].

While mortality and morbidity of patients with severe traumatic injury, acute myocardial infarction or stroke have been significantly reduced during recent years by

### Infection (documented or suspected), and some of the following:

#### **General variables**

Fever (core temperature >38.3 °C) Hypothermia (core temperature <36.0 °C) Heart rate >90/min or >2SD above the normal value for age Tachypnea (respiratory rate >20/min) Altered mental status Significant edema or positive fluid balance (>20 mL/kg over 24 hrs) Hyperglycemia (plasma glucose >120 mg/dL or 7.7 mmol/L) in the absence of diabetes

#### Inflammatory variables

Leukocytosis (white blood cell count >12,000/µL) Leukopenia (white blood cell count <4000/µL) Normal white blood cell count with >10 % immature forms Plasma C-reactive protein >2SD above the normal value Plasma procalcitonin >2SD above the normal value

#### Hemodynamic variables

Arterial hypotension (systolic blood pressure <90 mmHg, mean arterial pressure <70 mmHg, or a decrease of systolic blood pressure >40 mmHg in adults) Mixed venous oxygen saturation <70 % Cardiac index >3.5 L/min/m2

#### Organ dysfunction variables

Arterial hypoxemia (pO2(a)/FO2(I) <300) Acute oliguria (urine output <0.5 mL/kg/hr) Creatinine increase >0.5 mg/dL Coagulation abnormalities (INR >1.5 or aPTT >60 sec) Ileus (absent bowel sounds) Thrombocytopenia (platelet count <100,000/µL) Hyperbilirubinemia (plasma total bilirubin >4 mg/dL or 70 mmol/L)

#### **Tissue perfusion variables**

Hyperlactatemia (>1 mmol/L)

Decreased capillary refill or mottling

TABLE I. Diagnostic criteria for sepsis (SD, standard deviation; modified from [18])

the implementation of a well-coordinated approach to apply evidence-based therapies, mortality in patients with sepsis remains high.

The awareness of the high death toll of sepsis is not adequately acknowledged in the population and by healthcare providers. Therefore, an international effort ("The Surviving Sepsis Campaign" [2]) to improve the knowledge about detection and treatment of patients with sepsis has the goal to:

- Build awareness of sepsis
- Improve early and acute diagnosis
- Increase the use of appropriate treatments and interventions
- Improve access to post-ICU care
- Develop global standards of care for patients with sepsis

Conceptually, the care of a critically ill patient should be a well-coordinated continuum beginning with the emergency care providing crews and continuing with hospital destination decisions including disposition to ICU treatment ("The Critical Care Cascade"; [5]).

There is strong evidence to support the need for a series of time-dependent actions in sepsis management [6]. Hospital-based emergency medicine in Germany and other European countries is not well established. We report our effort to implement modern concepts of sepsis management in the emergency department (ED).

## Concepts of sepsis management

The treatment of severe sepsis and septic shock in critical care medicine is challenging due to the complexity of sepsis syndrome and the often unclear symptoms of affected patients at presentation to the ED.

Although the pathophysiology of sepsis is better understood in the meantime due to outstanding basic research [7], new treatment options including sophisticated approaches such as immune modulation have been disappointing. Blocking proinflammatory cytokines or anti-lipopolysaccharide therapy has proven ineffective.

Moreover, the modification of involved signaling or coagulation pathways has not considerably improved survival among patients with sepsis [3].

In contrast, there is convincing evidence that mortality is significantly reduced by a timely application of basic therapies, which should include aggressive volume management and application of calculated anti-microbial therapy (Fig. 1; [8-10]).



FIG. 1: Overview of the effects of the implementation of sepsis care bundles on mortality (modified from [10])

The proof of concept of a bundled approach of a goal-directed treatment algorithm has been made by the milestone work of Rivers *et al.* [6], who controlled the initial phase of volume resuscitation by defining goals such as normalization of central venous oxygen saturation and central venous pressure.

Several investigators have convincingly shown that a goal-directed, protocol-based treatment of sepsis patients significantly reduces mortality by 30-50 % [10].

#### Sepsis management in the ED

In healthcare institutions, an obvious imbalance between discovery and delivery of health services exists, suggesting a considerable gap among best evidence and best practice [11].

Gorovitz and MacIntyre suggested that the main reasons for fallibility in medicine are a) the ignorance of a medical problem and b) the ineptitude to apply stateof-the-art knowledge.

What does this mean to us for sepsis management? Before the discovery of penicillin in 1928, bacterial infection could not be treated.

Due to the "ignorance" of the pathophysiology of sepsis and the unavailability of antibiotics, treatment of sepsis was not possible at former times. In the meantime, a large body of knowledge to treat bacterial infections and sepsis has accumulated, but is often not adequately provided.

This ineptitude to apply current knowledge of sepsis management in the ED may be overcome by a structured way of diagnostics and treatment protocols [10, 12].

# Sepsis management program in Nürnberg city hospital

At the beginning of the sepsis management program in our institution, an important observation was that emergency physicians and nurses rated their quality of delivering care to patients as high. However, evaluation of key performance indicators of sepsis management in our institution at that time revealed that a considerable number of our emergency care providers were not aware of 1) the definition of sepsis, 2) clinically important diagnostic criteria and 3) sepsis bundles as recommended by the Surviving Sepsis Campaign [2].

In the deep belief that an optimum of sepsis care in an ED can only be provided by a team approach, we developed an educational program for both emergency physicians and nurses. In this program, aspects of the pathophysiology and evidence-based treatment bundles of sepsis were presented.

Since lectures have been shown to be largely ineffective to transport theory into practice, small working groups were formed and most contents were presented as case discussion and simulations [13].

In contrast to acute myocardial infarction or stroke, signs and symptoms of patients with sepsis presenting to the ED are often obscure and ambiguous. According to the approaches of Funk *et al.* [14] we developed simple checklists, which had to be fulfilled at the time of presentation of patients in the ED:

Vital parameters were systematically measured in every patient, nurse-driven triage was introduced [15] and cutpoints were defined at which patients had to be seen immediately by an emergency physician (Table II).

If indicated, vitals were timely supplemented by point-of-care measurement of blood gases, including measurement of electrolyte and lactate levels.

If at least one parameter of this evaluation was out of range, a more thorough examination followed by dedicated emergency physicians to rule in or rule out sepsis as the probable cause of the patient's signs or symptoms.

If severe sepsis or septic shock was identified, a bundled approach of aggressive, goal-directed resuscitation including several therapeutic interventions in the ED followed (Table III).

Ten signs of vitality	Triggering parameter
Temperature	≤36 °C
Heart rate	<50/min or >100/min
Pain	New or significant increase
Respiratory rate	<6/min or > 20/min
O <sub>2</sub> -saturation	<90 % and increased FO2(I) necessary
Blood pressure	BPsys <90 mmHg or MAP <60 mmHg
Level of consciousness	Lethargy, agitation, apathy, anxiety, coma
Capillary refill	>3 sec (Capillary Refill Time)
Urinary output	<100 mL/4 hr (=prerenal AKI) (no clue for renal or post-renal AKI)
ScvO <sub>2</sub> /base deficit (BE)	<65 % or base deficit <-5 or lactate >2 mmol/L

TABLE II. Structured evaluation of patients with sepsis presenting to the emergency department (as suggested by Funk et al. [14])

#### A irway

- **O** xygen (application of nasal oxygen)
- V entilation Support (NIV, invasive ventilation)
- I nfuse volume aggressively (1000 mL/30 min)
- P ressors support of blood pressure
- P harmacologic interventions (i.e. early antibiotics, activated protein C)
- **S** pecific invasive therapies on ICU

TABLE III. AOVIPPS algorithm: Basic sepsis bundle to treat sepsis patients presenting to the emergency department [14]

Only basic treatment bundles were initiated at the ED and immediate transfer to our intensive care unit was established to start more sophisticated, goal-directed therapy (Table III).

Every day, a technician checked patients with sepsis treated on our ICU using a dedicated quality management standard form to evaluate the efforts to provide state-of-the-art sepsis management in our institution.

## First results

Analysis of our performance indicators of sepsis management (rate of lactate levels measured in the ED; rate of patients receiving 1000 mL of volume (e.g. 0.9 % NaCl solution) within 1 hour after presentation to the ED; rate of patients receiving antibiotic therapy within 1 hour after presentation) showed that the performance of sepsis management considerably improved.

The hospital mortality of sepsis patients treated in our intensive care unit significantly decreased by about 30 % after implementation of our program (Fig. 2).

Moreover, the ICU stay of patients with communityacquired pneumonia was significantly decreased by 3 days. However, analysis of our sepsis management program also showed that the quality of sepsis management decreased during the year and repetitive educational efforts have been necessary to improve quality of care.



FIG.2: Mortality of patients with sepsis treated in the intensive care unit of the Nürnberg city hospital. Sepsis care bundles were implemented at the end of 2008. Hospital mortality is displayed for the years 2007 (blue bar), 2008 (red bar), 2009 (green bar) and 2010 (orange bar).

## Barriers to sepsis bundle implementation in the ED

During the initiation and implementation of above initiative for improvement of care in patients with sepsis or severe sepsis presenting to the ED, several barriers to translating evidence into practice have become evident [13]:

A lack of providers' awareness that specific guidelines exist, a lack of agreement within the team and how to apply optimal care to patients, and the lack of the teams' ability to implement those recommendations into routine were main obstacles for improvement of healthcare in several settings.

The ability to overcome the inertia to change previous practice, the obstacles to identify process improvement as a major contribution for outcome improvement, and the presence of external barriers (lack of equipment, inadequate resources, etc.) may have been relevant barriers for care amendment [13, 16].

Possibly, this is due to the fact that recent research and efforts have mainly focused on the understanding of the pathophysiology of sepsis and on the identification of effective "isolated" therapies. Moreover, research on how to deliver those therapies has mainly focused on physicians but not ED teams or other caregivers [13].

Above-described barriers to translating modern sepsis management in our ED were present in reality. In order to convince our team about the quality of care applied to patients, we analyzed key performance measures of sepsis bundle application.

This analysis revealed that a large proportion of patients did not receive antibiotic treatment within suggested time intervals [2] and the principles of aggressive, goal-directed volume resuscitation were not adequately provided to patients with sepsis [6].

Further analysis showed that patients admitted from the ED displayed long door to ICU times and relevant steps of basic sepsis management have not been appropriately started in the ED, probably leading to the observed delay of sepsis bundle application to affected patients [17].

Several discussions within the team followed and opinion leaders within the team were chosen to establish a local adaptation of care bundles for the diagnosis and treatment of patients presenting with sepsis or severe sepsis in the ED. These efforts included:

- Evidence-based medicine and clinical practice guidelines
- Professional education and development
- Assessment and accountability
- Patient-centered care
- Total quality management

Finally, knowledge and suggested process improvement strategies were communicated within the team using interactive forms of education, small-group learning and case discussions.

## Conclusion - the critical care cascade

Patients with severe sepsis, who have to be treated on an ICU, display high hospital mortality.

Early detection of patients with sepsis in the ED and early action in a coordinated manner significantly reduce mortality of affected patients. In conclusion, critical care medicine is not a location but a need, and should be initiated in the ED.

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