Septisches Kreislaufversagen –

Was sagen die Guidelines?

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Universitätsklinik für Innere Medizin I

Surviving Sepsis Campaign

Surviving Sepsis Campaign

Richtlinien für das Management der Schweren Sepsis und des Septischen Schocks

Ziel:
Reduktion der Mortalität der schweren Sepsis / des septischen Schocks

Dellinger et al.: Crit Care Med 32: 858 (2004) und Intensive Care Med 30: 536 (2004)

Dellinger et al.: Crit Care Med 36: 296 (2008) und Intensive Care Med 34: 17 (2008)

Dellinger et al.: Crit Care Med 41: 580 (2013) und Intensive Care Med 39: 165 (2013)

Rhodes et al.: Crit Care Med 45: 381 (2017) und Intensive Care Med 43: 304 (2017)

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Daten

Surviving Sepsis Campaign

Surviving Sepsis Campaign

Februar 2013 — **März 2017**

- EGDT
- ß-Blocker
- Transfusionstrigger
- Temperaturmanagement
- Abgrenzung zu HPS
- Beatmungstherapie
- S3 - Analgesie, Sedierung, Delir
- Humanalbumin
- Blutdruckziele
- Thiamin
- Sepsis 3
- .....

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Sepsis-3

Special Communication | CARING FOR THE CRITICALLY ILL PATIENT

The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

Mervyn Singer, MD, FRCP; Clifford S. Deutschman, MD, MS; Christopher Warren Seymour, MD, MSc; Manu Shankar-Hari, MSc, MD, FFICM; Djillali Annane, MD, PhD; Michael Bauer, MD; Rinaldo Bellomo, MD; Gordon R. Bernard, MD; Jean-Daniel Chiche, MD, PhD; Craig M. Coopersmith, MD; Richard S. Hotchkiss, MD; Mitchell M. Levy, MD; John C. Marshall, MD; Greg S. Martin, MD, MSc; Steven M. Opal, MD; Gordon D. Rubenfeld, MD, MS; Tom van der Poll, MD, PhD; Jean-Louis Vincent, MD, PhD; Derek C. Angus, MD, MPH

Peer Review von 31 Fachgesellschaften, incl. ESICM/SCCM

Singer et al. JAMA 2016

Sepsis-3: Definition

„Sepsis wird definiert als lebensbedrohliche Organdysfunktion, die durch eine fehlregulierte Wirtsantwort auf eine Infektion hervorgerufen wird."

Laiendefinition:

„Sepsis ist eine lebensbedrohliche Erkrankung bei der die Reaktion des Körpers auf eine Infektion zur einer Schädigung der eigenen Gewebe und Organe führt."

Singer et al. JAMA 2016, Übersetzung lt. DGIIN

Sepsis-3: klinische Kriterien

Sepsis = Verdacht auf Infektion und Zunahme des SOFA Scores um ≥ 2 Punkte

Singer et al. JAMA 2016

Sepsis-3 = ≥ 2 SOFA Punkte plus Infektion

Table 1. Sequential [Sepsis-Related] Organ Failure Assessment Score[a]

System	Score 0	1	2	3	4
Respiration					
Pao_2/Fio_2, mm Hg (kPa)	≥400 (53.3)	<400 (53.3)	<300 (40)	<200 (26.7) with respiratory support	<100 (13.3) with respiratory support
Coagulation					
Platelets, $\times 10^3/\mu L$	≥150	<150	<100	<50	<20
Liver					
Bilirubin, mg/dL (μmol/L)	<1.2 (20)	1.2-1.9 (20-32)	2.0-5.9 (33-101)	6.0-11.9 (102-204)	>12.0 (204)
Cardiovascular	MAP ≥70 mm Hg	MAP <70 mm Hg	Dopamine <5 or dobutamine (any dose)[b]	Dopamine 5.1-15 or epinephrine ≤0.1 or norepinephrine ≤0.1[b]	Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1[b]
Central nervous system					
Glasgow Coma Scale score[c]	15	13-14	10-12	6-9	<6
Renal					
Creatinine, mg/dL (μmol/L)	<1.2 (110)	1.2-1.9 (110-170)	2.0-3.4 (171-299)	3.5-4.9 (300-440)	>5.0 (440)
Urine output, mL/d				<500	<200

Singer et al. JAMA 2016, adaptiert nach Vincent et al. ICM 1996

qSOFA (q=quick, 3 Variablen)

1.	Atemfrequenz	≥ 22 /min
2.	Glasgow Coma Scale	< 15
3.	Blutdruck systolisch	< 100 mmHg

- Positiv, wenn 2 von 3 Kriterien positiv
- 2 Kriterien positiv: 3-fach erhöhte Sterblichkeit (10%)
- 3 Kriterien positiv: 14-fach erhöhte Sterblichkeit
- Screening Tool (prähospital, NFA, Normalstation, NICHT ICU)

Singer et al. JAMA 2016; Seymour et al. JAMA 2016

Septischer Schock: Definition

„Untergruppe der Sepsis, bei der die vorliegenden zirkulatorischen, zellulären und metabolischen Störungen so ausgeprägt sind, dass die Sterblichkeit substantiell zunimmt."

Singer et al. + Shankar-Hari et al. JAMA 2016; Übersetzung lt. DGIIN

Septischer Schock: klinische Kriterien

Sepsis

+

Vasopressoren notwendig, um MAP ≥ 65 mmHg zu halten

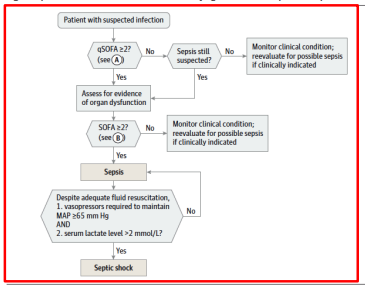
+

Laktat > 2 mmol/L
(trotz adäquater Volumengabe)

Singer et al. JAMA 2016; Übersetzung lt. DGIIN

Diagnose Algorithmus Sepsis / septischer Schock

Figure. Operationalization of Clinical Criteria Identifying Patients With Sepsis and Septic Shock



A qSOFA Variables
Respiratory rate
Mental status
Systolic blood pressure

B SOFA Variables
PaO_2/FiO_2 ratio
Glasgow Coma Scale score
Mean arterial pressure
Administration of vasopressors with type and dose rate of infusion
Serum creatinine or urine output
Bilirubin
Platelet count

The baseline Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score should be assumed to be zero unless the patient is known to have preexisting (acute or chronic) organ dysfunction before the onset of infection. qSOFA indicates quick SOFA; MAP, mean arterial pressure.

Singer et al. JAMA 2016; Seymour et al. JAMA 2016

B. Screening for Sepsis

2012	Änderungen	2016
1. Routine screening of potentially infected seriously ill patients for severe sepsis to allow earlier implementation of therapy (grade 1C). 2. Hospital–based performance improvement efforts in severe sepsis (UG).		We recommend that hospitals and hospital systems have a performance improvement program for sepsis, including sepsis screening for acutely ill, high-risk patients (BPS).

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www.esicm.org/sepsis ; Surviving Sepsis Guidelines 2016 Intensive Care Medicine, Appendix II

C. Diagnosis

Änderungen

2012

1. Cultures as clinically appropriate before antimicrobial therapy if no significant delay (> 45 mins) in the start of antimicrobial(s) (grade 1C). At least 2 sets of blood cultures (both aerobic and anaerobic bottles) be obtained before antimicrobial therapy with at least 1 drawn percutaneously and 1 drawn through each vascular access device, unless the device was recently (<48 hrs) inserted (grade 1C).

2. Use of the 1,3 beta-D-glucan assay (grade 2B), mannan and anti-mannan antibody assays (2C), if available and invasive candidiasis is in differential diagnosis of cause of infection.

3. Imaging studies performed promptly to confirm a potential source of infection (UG).

2016

1. We recommend that appropriate routine microbiologic cultures (including blood) be obtained before starting antimicrobial therapy in patients with suspected sepsis or septic shock if doing so results in no substantial delay in the start of antimicrobials (BPS).

D. Antimicrobial Therapy

Änderungen

2012

1. Administration of effective intravenous antimicrobials within the first hour of recognition of septic shock (grade 1B) and severe sepsis without septic shock (grade 1C) as the goal of therapy.

2a. Initial empiric anti-infective therapy of one or more drugs that have activity against all likely pathogens (bacterial and/or fungal or viral) and that penetrate in adequate concentrations into tissues presumed to be the source of sepsis (grade 1B).

2b. Antimicrobial regimen should be reassessed daily for potential deescalation (grade 1B).

3. Use of low procalcitonin levels or similar biomarkers to assist the clinician in the discontinuation of empiric antibiotics in patients who initially appeared septic, but have no subsequent evidence of infection (grade 2C).

4a. Combination empirical therapy for neutropenic patients with severe sepsis (grade 2B) and for patients with difficult-to-treat, multidrugresistant bacterial pathogens such as Acinetobacter and Pseudomonas spp. (grade 2B). For patients with severe infections associated with respiratory failure and septic shock, combination therapy with an extended spectrum beta-lactam and either an aminoglycoside or a fluoroquinolone is for P. aeruginosa bacteremia (grade 2B). A combination of beta-lactam and macrolide for patients with septic shock from bacteremic Streptococcus pneumoniae infections (grade 2B).

4b. Empiric combination therapy should not be administered for more than 3–5 days. De-escalation to the most appropriate single therapy should be performed as soon as the susceptibility profile is known (grade 2B).

5. Duration of therapy typically 7–10 days; longer courses may be appropriate in patients who have a slow clinical response, undrainable foci of infection, bacteremia with S. aureus, some fungal and viral infections or immunologic deficiencies, including neutropenia (grade 2C).

6. Antiviral therapy initiated as early as possible in patients with severe sepsis or septic shock of viral origin (grade 2C).

7. Antimicrobial agents should not be used in patients with severe inflammatory states determined to be of noninfectious cause (UG).

2016

1. We recommend that administration of IV antimicrobials be initiated as soon as possible after recognition and within 1 h for both sepsis and septic shock (strong recommendation, moderate quality of evidence; grade appropriate conditions).

2. We recommend empiric broad-spectrum therapy with one or more antimicrobials for patients presenting with sepsis or septic shock to cover all likely pathogens (including bacterial and potentially fungal or viral coverage) (strong recommendation, moderate quality of evidence).

3. We recommend that empiric antimicrobial therapy be narrowed once pathogen identification and sensitivities are established and/or adequate clinical improvement is noted (BPS).

4. We recommend against sustained systemic antimicrobial prophylaxis in patients with severe inflammatory states of noninfectious origin (e.g., severe pancreatitis, burn injury) (BPS).

5. We recommend that dosing strategies of antimicrobials be optimized based on accepted pharmacokinetic/ pharmacodynamic principles and specific drug properties in patients with sepsis or septic shock (BPS).

6. We suggest empiric combination therapy (using at least two antibiotics of different antimicrobial classes) aimed at the most likely bacterial pathogen(s) for the initial management of septic shock (weak recommendation, low quality of evidence).

7. We suggest that combination therapy not be routinely used for ongoing treatment of most other serious infections, including bacteremia and sepsis without shock (weak recommendation, low quality of evidence).

8. We recommend against combination therapy for the routine treatment of neutropenic sepsis/bacteremia (strong recommendation, moderate quality of evidence).

9. If combination therapy is initially used for septic shock, we recommend de-escalation with discontinuation of combination therapy within the first few days in response to clinical improvement and/ or evidence of infection resolution. This applies to both targeted (for culture-positive infections) and empiric (for culture-negative infections) combination therapy (BPS).

10. We suggest that an antimicrobial treatment duration of 7–10 days is adequate for most serious infections associated with sepsis and septic shock (weak recommendation, low quality of evidence).

11. We suggest that longer courses are appropriate in patients who have a slow clinical response, undrainable foci of infection, bacteremia with S. aureus , some fungal and viral infections, or immunologic deficiencies, including neutropenia (weak recommendation, low quality of evidence).

12. We suggest that shorter courses are appropriate in some patients, particularly those with rapid clinical resolution following effective source control of intra-abdominal or urinary sepsis and those with anatomically uncomplicated pyelonephritis (weak recommendation, low quality of evidence).

13. We recommend daily assessment for de-escalation of antimicrobial therapy in patients with sepsis and septic shock (BPS).

14. We suggest that measurement of procalcitonin levels can be used to support shortening the duration of antimicrobial therapy in sepsis patients (weak recommendation, low quality of evidence).

15. We suggest that procalcitonin levels can be used to support the discontinuation of empiric antibiotics in patients who initially appeared to have sepsis, but subsequently have limited clinical evidence of infection (weak recommendation, low quality of evidence).

E. Source Control

Änderungen

2012

1. A specific anatomical diagnosis of infection requiring consideration for emergent source control be sought and diagnosed or excluded as rapidly as possible, and intervention be undertaken for source control within the first 12 hr after the diagnosis is made, if feasible (grade 1C).

2. When infected peripancreatic necrosis is identified as a potential source of infection, definitive intervention is best delayed until adequate demarcation of viable and nonviable tissues has occurred (grade 2B).

3. When source control in a severely septic patient is required, the effective intervention associated with the least physiologic insult should be used (eg, percutaneous rather than surgical drainage of an abscess) (UG).

4. If intravascular access devices are a possible source of severe sepsis or septic shock, they should be removed promptly after other vascular access has been established (UG).

2016

1. We recommend that a specific anatomic diagnosis of infection requiring emergent source control be identified or excluded as rapidly as possible in patients with sepsis or septic shock, and that any required source control intervention be implemented as soon as medically and logistically practical after the diagnosis is made (BPS).

2. We recommend prompt removal of intravascular access devices that are a possible source of sepsis or septic shock after other vascular access has been established (BPS).

A. Initial Resuscitation

Änderungen

2012	2016
1. Protocolized, quantitative resuscitation of patients with sepsis- induced tissue hypoperfusion (defined in this document as hypotension persisting after initial fluid challenge or blood lactate concentration ≥ 4 mmol/L). Goals during the first 6 hrs of resuscitation: a) Central venous pressure 8–12 mm Hg b) Mean arterial pressure (MAP) ≥ 65 mm Hg c) Urine output ≥ 0.5 mL/kg/hr d) Central venous (superior vena cava) or mixed venous oxygen saturation 70% or 65%, respectively (grade 1C). 2. In patients with elevated lactate levels targeting resuscitation to normalize lactate (grade 2C).	1. Sepsis and septic shock are medical emergencies, and we recommend that treatment and resuscitation begin immediately (BPS). 2. We recommend that, in the resuscitation from sepsis-induced hypoperfusion, at least 30 mL/kg of IV crystalloid fluid be given within the first 3 h (strong recommendation, low quality of evidence). 3. We recommend that, following initial fluid resuscitation, additional fluids be guided by frequent reassessment of hemodynamic status (BPS). 4. We recommend further hemodynamic assessment (such as assessing cardiac function) to determine the type of shock if the clinical examination does not lead to a clear diagnosis (BPS). 5. We suggest that dynamic over static variables be used to predict fluid responsiveness, where available (weak recommendation, low quality of evidence). 6. We recommend an initial target mean arterial pressure (MAP) of 65 mm Hg in patients with septic shock requiring vasopressors (strong recommendation, moderate quality of evidence). 7. We suggest guiding resuscitation to normalize lactate in patients with elevated lactate levels as a marker of tissue hypoperfusion (weak recommendation, low quality of evidence).

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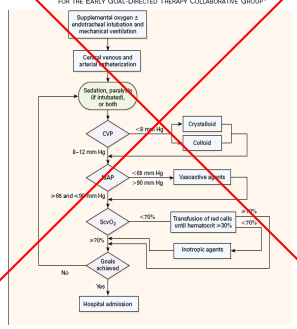
www.esicm.org/sepsis ; Surviving Sepsis Guidelines 2016 Intensive Care Medicine, Appendix II

The New England Journal of Medicine 345: 1368 (2001)

EARLY GOAL-DIRECTED THERAPY IN THE TREATMENT OF SEVERE SEPSIS AND SEPTIC SHOCK

Emanuel Rivers, M.D., M.P.H., Bryant Nguyen, M.D., Suzanne Havstad, M.A., Julie Ressler, B.S., Alexandria Muzzin, B.S., Bernhard Knoblich, M.D., Edward Peterson, Ph.D., and Michael Tomlanovich, M.D., for the Early Goal-Directed Therapy Collaborative Group*



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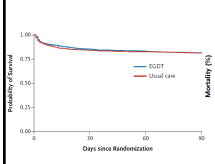
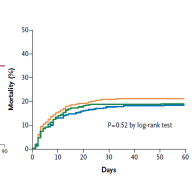
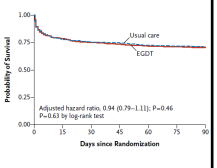
EGDT versus Standard

796 EGDT vs. 804 Standard Septischer Schock	439 EGDT vs. 446 Protocol Standard vs. 456 Free Standard Septischer Schock	630 EGDT vs. 630 Standard Septischer Schock
90-d-Mortalität: 18.6 %	90-d-Mortalität: 19.3 %	90-d-Mortalität: 29.3 %







ARISE, New Engl J Med 2014 | PROCESS, New Engl J Med 2014 | ProMISe, New Engl J Med 2015

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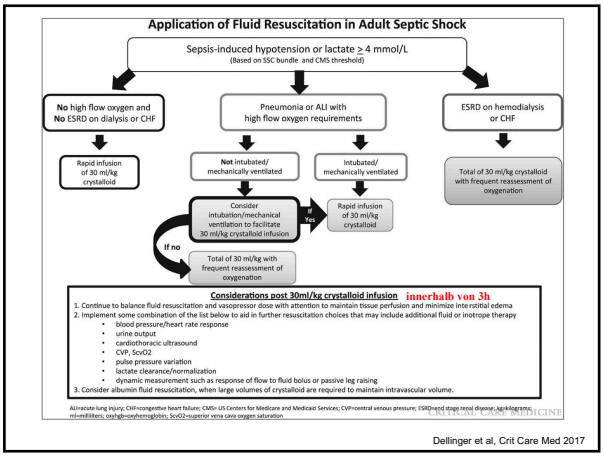

Dellinger et al, Crit Care Med 2017

F. Fluid Therapy

Änderungen

2012	2016
1. Crystalloids as the initial fluid of choice in the resuscitation of severe sepsis and septic shock (grade 1B).	1. We recommend that a fluid challenge technique be applied where fluid administration is continued as long as hemodynamic factors continue to improve (BPS).
2. Against the use of hydroxyethyl starches for fluid resuscitation of severe sepsis and septic shock (grade 1B).	2. We recommend crystalloids as the fluid of choice for initial resuscitation and subsequent intravascular volume replacement in patients with sepsis and septic shock (strong recommendation, moderate quality of evidence).
3. Albumin in the fluid resuscitation of severe sepsis and septic shock when patients require substantial amounts of crystalloids (grade 2C).	3. We suggest using either balanced crystalloids or saline for fluid resuscitation of patients with sepsis or septic shock (weak recommendation, low quality of evidence).
4. Initial fluid challenge in patients with sepsis-induced tissue hypoperfusion with suspicion of hypovolemia to achieve a minimum of 30 mL/kg of crystalloids (a portion of this may be albumin equivalent). More rapid administration and greater amounts of fluid may be needed in some patients (grade 1C).	4. We suggest using albumin in addition to crystalloids for initial resuscitation and subsequent intravascular volume replacement in patients with sepsis and septic shock when patients require substantial amounts of crystalloids (weak recommendation, low quality of evidence).
5. Fluid challenge technique be applied wherein fluid administration is continued as long as there is hemodynamic improvement either based on dynamic (eg, change in pulse pressure, stroke volume variation) or static (eg, arterial pressure, heart rate) variables (UG).	5. We recommend against using hydroxyethyl starches (HESs) for intravascular volume replacement in patients with sepsis or septic shock (strong recommendation, high quality of evidence).
	6. We suggest using crystalloids over gelatins whenresuscitating patients with sepsis or septic shock (weak recommendation, low quality of evidence).

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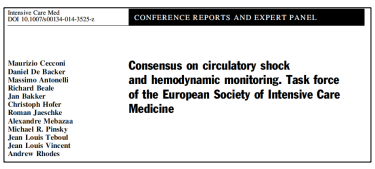
Individualisierte Flüssigkeitszufuhr


Intensive Care Med
DOI 10.1007/s00134-014-3525-z

CONFERENCE REPORTS AND EXPERT PANEL

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Consensus on circulatory shock and hemodynamic monitoring. Task force of the European Society of Intensive Care Medicine

Fluid Responsiveness:

- Steigt der Cardiac Output durch Flüssigkeitszufuhr?
- Monitoring durch Echo (TTE, TEE), Pulskontur, Dilutionstechniken
- Möglich ohne einen einzigen Tropfen! (Echo Indizes, PLR)

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Passive Leg Raising (PLR)

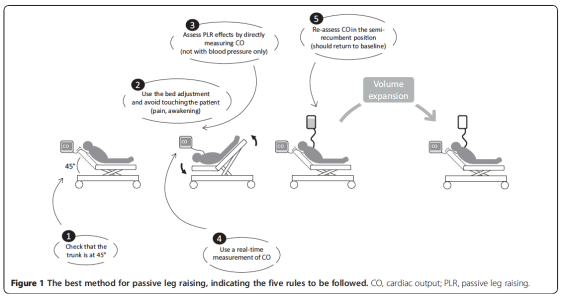


Figure 1 The best method for passive leg raising, indicating the five rules to be followed. CO, cardiac output; PLR, passive leg raising.

G. Vasoactive Medications

Änderungen

2012

1. Vasopressor therapy initially to target a mean arterial pressure (MAP) of 65 mm Hg (grade 1C).

2. Norepinephrine as the first choice vasopressor (grade 1B).

3. Epinephrine (added to and potentially substituted for norepinephrine) when an additional agent is needed to maintain adequate blood pressure (grade 2B).

4. Vasopressin 0.03 units/minute can be added to norepinephrine (NE) with intent of either raising MAP or decreasing NE dosage (UG).

5. Low dose vasopressin is not recommended as the single initial vasopressor for treatment of sepsis-induced hypotension and vasopressin doses higher than 0.03-0.04 units/minute should be reserved for salvage therapy (failure to achieve adequate MAP with other vasopressor agents) (UG).

6. Dopamine as an alternative vasopressor agent to norepinephrine only in highly selected patients (eg, patients with low risk of tachyarrhythmias and absolute or relative bradycardia) (grade 2C).

7. Phenylephrine is not recommended in the treatment of septic shock except in circumstances where (a) norepinephrine is associated with serious arrhythmias, (b) cardiac output is known to be high and blood pressure persistently low or (c) as salvage therapy when combined inotrope/vasopressor drugs and low dose vasopressin have failed to achieve MAP target (grade 1C).

8. Low-dose dopamine should not be used for renal protection (grade 1A).

9. All patients requiring vasopressors have an arterial catheter placed as soon as practical if resources are available (UG).

2016

1. We recommend norepinephrine as the firstchoice vasopressor (strong recommendation, moderate quality of evidence).

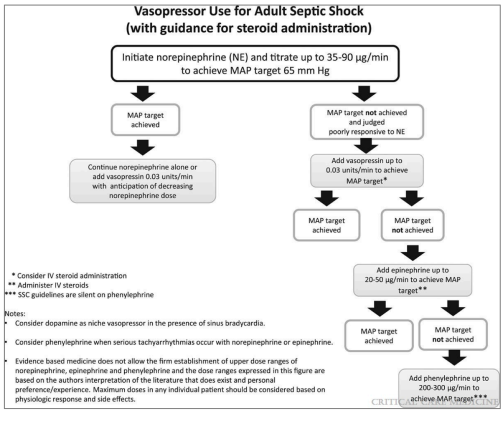
2. We suggest adding either vasopressin (up to 0.03 U/min) (weak recommendation, moderate quality of evidence) or epinephrine (weak recommendation, low quality of evidence) to norepinephrine with the intent of raising MAP to target, or adding vasopressin (up to 0.03 U/min) (weak recommendation, moderate quality of evidence) to decrease norepinephrine dosage.

3. We suggest using dopamine as an alternative vasopressor agent to norepinephrine only in highly selected patients (e.g., patients with low risk of tachyarrhythmias and absolute or relative bradycardia) (weak recommendation, low quality of evidence).

4. We recommend against using low-dose dopamine for renal protection (strong recommendation, high quality of evidence).

5. We suggest using dobutamine in patients who show evidence of persistent hypoperfusion despite adequate fluid loading and the use of vasopressor agents (weak recommendation, low quality of evidence).

6. We suggest that all patients requiring vasopressors have an arterial catheter placed as soon as practical if resources are available (weak recommendation, very low quality of evidence).



Dellinger et al, Crit Care Med 2017

H. Corticosteroid

Änderungen

2012	2016
1. Not using intravenous hydrocortisone to treat adult septic shock patients if adequate fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability (see goals for Initial Resuscitation). In case this is not achievable, we suggest intravenous hydrocortisone alone at a dose of 200 mg per day (grade 2C).	1. We suggest against using IV hydrocortisone to treat septic shock patients if adequate fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability. If this is not achievable, we suggest IV hydrocortisone at a dose of 200 mg per day (weak recommendation, low quality of evidence).
2. Not using the ACTH stimulation test to identify adults with septic shock who should receive hydrocortisone (grade 2B).	
3. In treated patients hydrocortisone tapered when vasopressors are no longer required (grade 2D).	
4. Corticosteroids not be administered for the treatment of sepsis in the absence of shock (grade 1D).	
5. When hydrocortisone is given, use continuous flow (grade 2D).	

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I. Blood Products

Änderungen

2012	2016
1. Once tissue hypoperfusion has resolved and in the absence of extenuating circumstances, such as myocardial ischemia, severe hypoxemia, acute hemorrhage, or ischemic coronary artery disease, we recommend that red blood cell transfusion occur when the hemoglobin concentration decreases to < 7.0 g/dL to target a hemoglobin concentration of 7.0 to 9.0 g/dL in adults (grade 1B).	1. We recommend that RBC transfusion occur only when hemoglobin concentration decreases to <7.0 g/dL in adults in the absence of extenuating circumstances, such as myocardial ischemia, severe hypoxemia, or acute hemorrhage (strong recommendation, high quality of evidence).
2. We recommend not using erythropoietin as a specific treatment of anemia associated with severe sepsis (grade 1B).	2. We recommend against the use of erythropoietin for treatment of anemia associated with sepsis (strong recommendation, moderate quality of evidence).
3. We suggest that fresh frozen plasma not be used to correct laboratory clotting abnormalities in the absence of bleeding or planned invasive procedures (grade 2D).	3. We suggest against the use of fresh frozen plasma to correct clotting abnormalities in the absence of bleeding or planned invasive procedures (weak recommendation, very low quality of evidence)
4. We recommend against antithrombin administration for the treatment of severe sepsis and septic shock (grade 1B).	4. We suggest prophylactic platelet transfusionwhen counts are <10,000/mm3 in the absence of apparent bleeding and when counts are <20,000/mm3 if the patient has asignificantrisk of bleeding. Higher platelet counts ≥ 50,000/mm3 are advised for active bleeding, surgery, or invasive procedures (weak recommendation, very low quality of evidence). when counts are <10,000/mm3) in the absence of apparent bleeding and when counts are <20,000/mm3 if the patient has a significant risk of bleeding. Higher platelet counts [≥50,000/mm3) are advised for active bleeding, surgery, or invasive procedures (weak recommendation, very low quality of evidence).
5. In patients with severe sepsis, we suggest that platelets be administered prophylactically when counts are ≤ 10,000/ mm3 (10 Â~ 109 /L) in the absence of apparent bleeding, as well when counts are ≤ 20,000/mm3 if the patient has a significant risk of bleeding. Higher platelet counts (≥ 50,000/mm3) are advised for active bleeding, surgery, or invasive procedures (grade 2D).	

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J. Immunoglobulins

Keine wesentliche Änderung

2012	2016
1. Not using intravenous immunoglobulins in adult patients with severe sepsis or septic shock (grade 2B).	1. We suggest against the use of IV immunoglobulins in patients with sepsis or septic shock (weak recommendation, low quality of evidence).

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Blood Purification

2012	NEU	2016
----		We make no recommendation regarding the use of blood purification techniques.

L. Anticolagulants

2012	Keine wesentliche Änderung	2016
		1. We recommend against the use of antithrombin for the treatment of sepsis and septic shock (strong recommendation, moderate quality of evidence). 1. We make no recommendation regarding the use of thrombomodulin or heparin for the treatment of sepsis or septic shock.

M. Mechanical Ventilation

2012	Änderungen	2016
1. Target a tidal volume of 6 mL/kg predicted body weight in patients with sepsis-induced ARDS (grade 1A vs. 12 mL/kg). 2. Plateau pressures be measured in patients with ARDS and initial upper limit goal for plateau pressures in a passively inflated lung be ≤30 cm H2O (grade 1B). 3. Positive end-expiratory pressure (PEEP) be applied to avoid alveolar collapse at end expiration (atelectotrauma) (grade 1B). 4. Strategies based on higher rather than lower levels of PEEP be used for patients with sepsis- induced moderate or severe ARDS (grade 2C). 5. Recruitment maneuvers be used in sepsis patients with severe refractory hypoxemia (grade 2C). 6. Prone positioning be used in sepsis-induced ARDS patients with a Pao2/Fio2 ratio ≤ 100 mm Hg in facilities that have experience with such practices (grade 2B). 7. That mechanically ventilated sepsis patients be maintained with the head of the bed elevated to 30-45 degrees to limit aspiration risk and to prevent the development of ventilator-associated pneumonia (grade 1B). 8. That noninvasive mask ventilation (NIV) be used in that minority of sepsis-induced ARDS patients in whom the benefits of NIV have been carefully considered and are thought to outweigh the risks (grade 2B). 9. That a weaning protocol be in place and that mechanically ventilated patients with severe sepsis undergo spontaneous breathing trials regularly to evaluate the ability to discontinue mechanical ventilation when they satisfy the following criteria: a) arousable; b) hemodynamically stable (without vasopressor agents); c) no new potentially serious conditions; d) low ventilatory and end-expiratory pressure requirements; and e) low Fio2 requirements which can be met safely delivered with a face mask or nasal cannula. If the spontaneous breathing trial is successful, consideration should be given for extubation (grade 1A). 10. Against the routine use of the pulmonary artery catheter for patients with sepsis-induced ARDS (grade 1A). 11. A conservative rather than liberal fluid strategy for patients with established sepsis-induced ARDS who do not have evidence of tissue hypoperfusion (grade 1C). 12. In the absence of specific indications such as bronchospasm, not using beta 2-agonists for treatment of sepsis-induced ARDS (grade 1B).		1. We recommend using a target tiddal volume of 6 mL/kg predicted body weight compared with 12 mL/kg in adult patients with sepsis-induced acute respiratory distress syndrome (ARDS) (strong recommendation, high quality of evidence). 2. We recommend using an upper limit goal for plateau pressures of 30 cm H2O over higher plateau pressures in adult patients with sepsis-induced severe ARDS (strong recommendaon, moderate quality of evidence). 3. We suggest using higher posive end-expiratory pressure (PEEP) over lower PEEP in adult patients with sepsis-induced moderate to severe ARDS (weak recommendation, moderate quality of evidence). 4. We suggest using recruitment maneuvers in adult patients with sepsis-induced severe ARDS (weak recommendation, moderate quality of evidence). 5. We recommend using prone over supine position in adult patients with sepsisinduced ARDS and a PaO2/FIO2 ratio < 150 (strong recommendaon, moderate quality of evidence). 6. We recommend against using high-frequency oscillatory ventilation in adult patients with sepsis-induced ARDS (strong recommendation, moderate quality of evidence). 7. We make no recommendation regarding the use of noninvasive ventilation for patients with sepsis-induced ARDS. 8. We suggest using neuromuscular blocking agents for ≤ 48 hours in adult patients with sepsis-induced ARDS and a PaO2/FIO2 ratio < 150 mm Hg (weak recommendation, moderate quality of evidence). 9. We recommend a conservative fluid strategy for paents with established sepsis-induced ARDS who do not have evidence of sue hypoperfusion (strong recommendation, moderate quality of evidence). 10. We recommend against the use of E-2 agonists for the treatment of patients with sepsis-induced ARDS without bronchospasm (strong recommendation, sepsis-induced ARDS (grade 1A). 11. We recommend against the routine use of the pulmonary artery catheter for patients with sepsis-induced ARDS (strong recommendation, high quality of evidence). 12. We suggest using lower tidal volumes over higher tidal volumes in adult patients with sepsis-induced respiratory failure without ARDS (weak recommendation, low quality of evidence). 13. We recommend that mechanically ventilated sepsis patients be maintained with the head of the bed elevated between 30 and 45 degrees to limit aspiration risk and to prevent the development of ventilator-associated pneumonia (strong recommendation, low quality of evidence). 14. We recommend using spontaneous breathing trials in mechanically ventilated patients with sepsis who are ready for weaning (strong recommendation, high quality of evidence). 15. We recommend using a weaning protocol in mechanically ventilated patients with sepsis-induced respiratory failure who can tolerate weaning (strong recommendation, moderate quality of evidence).

N. Sedation and Analgesia

Änderungen

2012	2016
1. Continuous or intermittent sedation be minimized in mechanically ventilated sepsis patients, targeting specific titration endpoints (grade 1B). 2. Neuromuscular blocking agents (NMBAs) be avoided if possible in the septic patient without ARDS due to the risk of prolonged neuromuscular blockade following discontinuation. If NMBAs must be maintained, either intermittent bolus as required or continuous infusion with train-of-four monitoring of the depth of blockade should be used (grade 1C). 3. A short course of NMBA of not greater than 48 hours for patients with early sepsis-induced ARDS and a Pao2/Fio2 < 150 mm Hg (grade 2C).	1. We recommend that continuous or intermitent sedadation be minimized in mechanically ventilated sepsis patients, targeting specific titration end points (BPS).

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O. Glucose Control

Keine wesentliche Änderung

2012	2016
1. A protocolized approach to blood glucose management in ICU patients with severe sepsis commencing insulin dosing when 2 consecutive blood glucose levels are >180 mg/dL. This protocolized approach should target an upper blood glucose ≤180 mg/dL rather than an upper target blood glucose ≤ 110 mg/dL (grade 1A). 2. Blood glucose values be monitored every 1–2 hrs until glucose values and insulin infusion rates are stable and then every 4 hrs thereafter (grade 1C). 3. Glucose levels obtained with point-of-care testing of capillary blood be interpreted with caution, as such measurements may not accurately estimate arterial blood or plasma glucose values (UG).	1. We recommend a protocolized approach to blood glucose management in ICU patients with sepsis, commencing insulin dosing when two consecutive blood glucose levels are > 180 mg/dL. This approach should target an upper blood glucose level ≤ 180 mg/dL rather than an upper target blood glucose level ≤ 110 mg/dL (strong recommendation, high quality of evidence). 2. We recommend that blood glucose values be monitored every 1 to 2 hours until glucose values and insulin infusion rates are stable, then every 4 hours thereafter in patients receiving insulin infusions (BPS). 3. We recommend that glucose levels obtained with point-of-care testing of capillary blood be interpreted with caution because such measurements may not accurately estimate arterial blood or plasma glucose values (BPS). 4. We suggest the use of arterial blood rather than capillary blood for point-of-care testing using glucose meters if patients have arterial catheters (weak recommendation, low quality of evidence).

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P. Renal Replacement Therapy

Änderungen

2012	2016
1. Continuous renal replacement therapies and intermittent hemodialysis are equivalent in patients with severe sepsis and acute renal failure (grade 2B). 2. Use continuous therapies to facilitate management of fluid balance in hemodynamically unstable septic patients (grade 2D).	1. We suggest that either continuous or intermitent renal replacement therapy (RRT) be used in patients with sepsis and acute kidney injury (weak recommendation, moderate quality of evidence). 2. We suggest using continuous therapies to facilitate management of fluid balance in hemodynamically unstable septic patients (weak recommendation, very low quality of evidence). 3. We suggest against the use of RRT in patients with sepsis and acute kidney injury for increase in creatinine or oliguria without other definitive indications for dialysis (weak recommendation, low quality of evidence).

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Q. Bicarbonate Therapy

Keine wesentliche Änderung

2012	2016
1. Not using sodium bicarbonate therapy for the purpose of improving hemodynamics or reducing vasopressor requirements in patients with hypoperfusion-induced lactic acidemia with pH ≥7.15 (grade 2B).	1. We suggest against the use of sodium bicarbonate therapy to improve hemodynamics or to reduce vasopressor requirements in patients with hypoperfusion-induced lactic acidemia with pH ≥ 7.15 (weak recommendation, moderate quality of evidence).

R. Venous Thromboembolism Prophylaxis

Änderungen

2012	2016
1. Patients with severe sepsis receive daily pharmacoprophylaxis against venous thromboembolism (VTE) (grade 1B). This should be accomplished with daily subcutaneous low-molecular weight heparin (LMWH) (grade 1B versus twice daily UFH, grade 2C versus three times daily UFH). If creatinine clearance is <30 mL/min, use dalteparin (grade 1A) or another form of LMWH that has a low degree of renal metabolism (grade 2C) or UFH (grade 1A). 2. Patients with severe sepsis be treated with a combination of pharmacologic therapy and intermittent pneumatic compression devices whenever possible (grade 2C). 3. Septic patients who have a contraindication for heparin use (eg, thrombocytopenia, severe coagulopathy, active bleeding, recent intracerebral hemorrhage) not receive pharmacoprophylaxis (grade 1B), but receive mechanical prophylactic treatment, such as graduated compression stockings or intermittent compression devices (grade 2C), unless contraindicated. When the risk decreases start pharmacoprophylaxis (grade 2C).	1. We recommend pharmacologic prophylaxis (unfractionated heparin [UFH] or low-molecular weight heparin [LMWH]) against venous thromboembolism (VTE) in the absence of contraindications to the use of these agents (strong recommendation, moderate quality of evidence). 2. We recommend LMWH rather than UFH for VTE prophylaxis in the absence of contraindications to the use of LMWH (strong recommendaon, moderate quality of evidence). 3. We suggest combinaon pharmacologic VTE prophylaxis and mechanical prophylaxis, whenever possible (weak recommendation, low quality of evidence). 4. We suggest mechanical VTE prophylaxis when pharmacologic VTE is contraindicated (weak recommendation, low quality of evidence).

S. Stress Ulcer Prophylaxis

Änderungen

2012	2016
1. Stress ulcer prophylaxis using H2 blocker or proton pump inhibitor be given to patients with severe sepsis/septic shock who have bleeding risk factors (grade 1B). 2. When stress ulcer prophylaxis is used, proton pump inhibitors rather than H2RA (grade 2D). 3. Patients without risk factors do not receive prophylaxis (grade 2B).	1. We recommend that stress ulcer prophylaxis be given to patients with sepsis or septic shock who have risk factors for gastrointestinal (GI) bleeding (strong recommendation, low quality of evidence). 2. We suggest using either proton pump inhibitors or histamine-2 receptor antagonists when stress ulcer prophylaxis is indicated (weak recommendation, low quality of evidence). 3. We recommend against stress ulcer prophylaxis in patients without risk factors for GI bleeding (BPS).

T. Nutrition

Änderungen

2012	2016
1. Administer oral or enteral (if necessary) feedings, as tolerated, rather than either complete fasting or provision of only intravenous glucose within the first 48 hours after a diagnosis of severe sepsis/septic shock (grade 2C). 2. Avoid mandatory full caloric feeding in the first week but rather suggest low dose feeding (eg, up to 500 calories per day), advancing only as tolerated (grade 2B). 3. Use intravenous glucose and enteral nutrition rather than total parenteral nutrition (TPN) alone or parenteral nutrition in conjunction with enteral feeding in the first 7 days after a diagnosis of severe sepsis/septic shock (grade 2B). 4. Use nutrition with no specific immunomodulating supplement	1. We recommend against the administration of early parenteral nutrition alone or parenteral nutrition in combination with enteral feedings (but rather initiate early enteral nutrition) in critically ill patients with sepsis or septic shock who can be fed enterally (strong recommendation, moderate quality of evidence). 2. We recommend against the administration of parenteral nutrition alone or in combination with enteral feeds (but rather to initiate IV glucose and advance enteral feeds as tolerated) over the first 7 days in critically ill patients with sepsis or septic shock for whom early enteral feeding is not feasible (strong recommendation, moderate quality of evidence). 3. We suggest the early initiation of enteral feeding rather than a complete fast or only IV glucose in critically ill patients with sepsis or septoc shock who can be fed enterally (weak recommendation, low quality of evidence). 4. We suggest either early trophic/hypocaloric or early full enteral feeding in critically ill patients with sepsis or septic shock; if trophic/hypocaloric feeding is the initial strategy, then feeds should be advanced according to patient tolerance (weak recommendation, moderate quality of evidence). 5. We recommend against the use of omega-3 fatty acids as an immune supplement in critically ill patients with sepsis or septic shock (strong recommendation, low quality of evidence). 6. We suggest against routinely monitoring gastric residual volumes in critically ill patients with sepsis or septic shock (weak recommendation, low quality of evidence). However, we suggest measurement of gastric residuals in patients with feeding intolerance or who are considered to be at high risk of aspiration (weak recommendation, very low quality of evidence). Remarks: This recommendation refers to nonsurgical critically ill patients with sepsis or septic shock. 7. We suggest the use of prokinetics agents in critically ill patients with sepsis or septic shock and feeding intolerance (weak recommendaton, low quality of evidence). 8. We suggest placement of post-pyloric feeding tubes in critically ill patients with sepsis or septic shock with feeding intolerance or who are considered to be at high risk of aspiratin (weak recommendation, low quality of evidence). 9. We recommend against the use of IV selenium to treat sepsis and septic shock (strong recommendation, moderate quality of evidence). 10. We suggest against the use of arginine to treat sepsis and septic shock (weak recommendation, low quality of evidence).

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U. Setting Goals of Care

Keine wesentliche Änderung

2012	2016
1. Discuss goals of care and prognosis with patients and families (grade 1B). 2. Incorporate goals of care into treatment and end-of-life care planning, utilizing palliative care principles where appropriate (grade 1B). 3. Address goals of care as early as feasible, but no later than within 72 hours of ICU admission (grade 2C).	1. We recommend that goals of care and prognosis be discussed with paents and families (BPS). 2. We recommend that goals of care be incorporated into treatment and end-of-life care planning, utilizing palliative care principles where appropriate (strong recommendation, moderate quality of evidence). 3. We suggest that goals of care be addressed as early as feasible, but no later than within 72 hours of ICU admission (weak recommendaon, low quality of evidence).

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Fazit Sepsis 3

- „SIRS“ obsolet
- „Severe Sepsis“ obsolet
- Sepsis 3 „lebensbedrohliche Organdysfunktion, durch fehlregulierte Wirtsantwort auf Infektion“
- Screening qSOFA ≥ 2 Punkte
- Diagnose SOFA ≥ 2 Punkte
- Sept. Schock Sepsis + Vasopressoren + Laktat > 2 mmol/l

Singer et al. JAMA 2016; Seymour et al. JAMA 2016

Fazit Initial Resuscitation

- EGDT — obsolet — (Ressourcen-intensiv, keine Vor- aber auch keine Nachteile)
- 3h Bundle — bleibt gleich
  1) Laktat Messen
  2) Kulturen
  3) Breitband AB prompt
  4) 30 ml/kg Kristalloide (Hypotension, Laktat >4 mmol/L)
- Verlauf
  - ZVD und SvO_2 *initial* nicht mehr relevant
  - Wenn keine Stabilisierung trotz Flüssigkeit und Vasopressoren
  -> individuelle Verlaufsbeurteilung (ZVD, SvO_2,Laktat, Klinik, Echo, Fluidchallenge)

Singer et al. JAMA 2016

Fazit Implementierung

- Die Implementierung von Sepsis Screening und SOPs rettet Leben!
- Sepsis-3 erlaubt Identifikation besonders gefährdeten Patienten
- Die Implementierung ist Aufwendig!
- Es gibt ausreichende Hilfestellung!
- Man wird es machen müssen!

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