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Appendix

Management of sepsis: from evidence to clinical practice

Riccardo Gerloni, Luciano Mucci, Carlotta Casati, Andrea Crociani, Ombretta Para, Elisabetta Benetti, Paola Gnerre, Anna Bovero, Elisa Romagnoli, Nicola Tarquinio, Clelia Canale, Davide Brancato, Laura Massarelli, Salvatora Piras

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Appendix Table 1. Diagnostic criteria for sepsis.

Infection, documented or suspected, and some of the following:
General variables
Fever (>38.3°)
Hypothermia (<36.0°)
Heart rate >90/m or more than 2 SD above the normal value for age
Tachypnea (> 20/m)
Altered mental status (lethargic or aggressive)
Stress hyperglycemia
Inflammatory variables
Leukocytosis (WBC >12,000 μL) or leukopenia (WBC <4000 μL)
Elevated plasma C-reactive protein
Elevated procalcitonin
Hemodynamic variables
Arterial hypotension (SBP <90 mmHg, MAP <70 mmHg or SBP decrease >40 mmHg in adults or less than 2 SD below normal for age)
Organ dysfunction variables
Arterial hypoxemia (PaO_2/FiO_2 <300)
Acute oliguria (urine output <0,5 mL/kg/h for at the least 2 h despite adequate fluid resuscitation) or creatinine increase
Coagulation abnormalities (INR > 1.5 or aPTT >60 s) or hyperbilirubinemia
Ileus
Thrombocytopenia (platelets count <100,000/μL)
Tissue perfusion variables
Hyperlactatemia
Decreased capillary refill

MAP, mean arterial pressure; SBP, systolic blood pressure; WBC, white blood count; INR, international normalized ratio; aPTT, activated partial thromboplastin time. Adapted from Dellinger *et al*.[1]

Appendix Table 2. Diagnostic criteria for severe sepsis.

Infection that causes any of the following:
Hypotension
Elevated lactate
Urinary output < 0.5 mL/kg/h for more than 2 h despite adequate fluid resuscitation
Creatinine >2 mg/dL
Acute lung injury with PaO_2/FiO_2 <250 in the absence of pneumonia as infection source
Acute lung injury with PaO_2/FiO_2 <200
Hyperbilirubinemia
Platelet count <100,000 μL
Coagulopathy (international normalized ratio >1.5)

Adapted from Dellinger *et al*.[1]

Appendix Table 3. Features to search in the sonographic study of kidney and urinary tract.

Presence of the kidney in the renal loggia
Dimension and symmetry (main measure is the longitudinal diameter normally between 10 and 12 cm (more or less 1 cm in extreme heights); a difference of more than 1.5 cm between the two kidneys should always be considered abnormal)
Profile and morphology of the kidneys
Structure (presence of an echoic renal cortex (1.5-2 cm) and hypo- or anechoic renal medullary pyramids. Cortical abnormalities can be observed in chronic nephropathies or inflammatory diseases)
Presence of dilatation of calices and renal sinus (hydronephrosis)
Presence of dilatation of the ureter
Presence of renal stones
Presence of other lesions (cyst, abscess, tumor)
Vascular renal abnormalities (main arterial and venous renal vessels, intraparenchymal vascularization, resistive index)
Bladder and filling status

Appendix Table 4. Bacterial and mycotic abscesses.

Single or multiple lesions ranging in size from 1 cm to largest and confluent nodules. Usually at the right hepatic lobe
Bacterial abscesses: ultrasound findings
Initial or pre-suppurative stage: Hypoechoic or normal echogenic, irregular, vanishing shape Mild posterior reverberation artifact Increased Doppler signals
Suppurative stage: Hypo or anechoic with low-level suspended echoes, irregular edges Strong posterior reverberation artifact Outer increased Doppler signals
Resolution: Hypo/hyperechoic up to calcific scare, more regular shape Reduced/absent
Mycotic abscess: ultrasound findings
Initial stage: typical *wheels-within-wheels* with central hypo or anechoic area (necrotic tissue), echoic intermediate ring and hypoechoic outer ring
Possible evolution: target lesions, hypo or hyperechoic lesions

Appendix Table 5. Location of free abdominal effusions.

Epigastric view: pericardial effusion
Intercostal right view (10-12° rib): Morrison's pouch and right pleural effusion
Intercostal left view (9-11° rib): perisplenic space, interface between left kidney and spleen, left kidney effusion
Pelvic view: few centimeters above the pubis: pouch of Douglas
Free fluid between gut

Appendix Table 6. Inferior vena cava: ultrasound measurement and intravascular status assessment.

IVC size	Respiratory change	CVP	Volume status
<1.5 cm	Total collapse	0-5 mmHg	Severe hypovolemia
1.5-2 cm	>50 % collapse	5-10 mmHg	Mild hypovolemia or normal volume status
1.5-2 cm	33-50% collapse	10-15 mmHg	Normal volume status
2-2.5 cm	0-33% collapse	15-20 mmHg	Hypervolemia
>2.5 cm	No change	>20 mmHg	Severe hypervolemia

Normal value: diameter <2-2, 5 cm
reduction in inspiration: 30-40%
Variations of inferior vena cava are calculated as caval index.
Caval index = 100 x (expiratory diameter-inspiratory diameter)/ expiratory diameter

Appendix Table 7. PCWP.

E/E'	PCWP	Evaluation
<10	< 14 mmHg	Normal
10-14	15-18 mmHg	Abnormal
>15	>18 mmHg	Pathological

Appendix Table 8. Recommendations for initial resuscitation.

1) Protocolized, quantitative resuscitation of patients with sepsis-induced tissue hypoperfusion (definited as hypotension persisting after the initial fluid challenge or blood lactate concentration ≥ 4 mmol/L). Goals during the first 6 hours of resuscitation:
a) Central venous pressure 8-12 mmHg
b) Mean arterial pressure (MAP) ≥ 65 mmHg
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 evidence)
2) In patients with elevated lactate levels targeting resuscitation to normalize lactate (grade 2C)

Adapted from Dellinger *et al*.[1]

Appendix Table 9. Surviving sepsis campaign bundles.

To be completed within 3 h

1) Measure lactate level
2) Obtain blood cultures prior to administration of antibiotics
3) Administer broad spectrum antibiotics
4) Administer 30 mL/kg crystalloid for hypotension or lactate ≥4 mmol/L

To be completed within 6 h

5) Apply vasopressor (for hypotension that does not respond to initial fluid resuscitation) to maintain a mean arterial pressure (MAP) ≥65 mmHg
6) In the event of persistent arterial hypotension despite volume resuscitation (septic shock) or initial lactate ≥4 mmol/L (36 mg/dL): - Measure central venous pressure (CVP) - Measure central venous oxygen saturation (ScvO2)

Adapted from Dellinger *et al*.[1]

Appendix Table 10. Use of vasopressors recommendations.

1. We recommend that vasopressor therapy initially target a MAP of 65 mmHg (grade 1 C)
2. We recommend norepinephrine as the first-choice vasopressor (grade 1B)
3. We suggest epinephrine (added to and potentially substituted for norepinephrine) when an additional agent is needed to maintain adequate blood pressure (grade 2B)
4. Vasopressin (up to 0.03 U/min) can be added to norepinephrine with the intent of raising MAP to target or decreasing norepinephrine dosage (UG).
5. Low-dose vasopressin is not recommended as a single initial vasopressor for the treatment of sepsis-induced hypotension, and vasopressin doses higher than 0.03-0.04 U/min should be reserved for salvage therapy
6. We suggest dopamine as an alternative vasopressor agent to norepinephrine only in highly selected patients (*e.g.*, patients with low risk of tachyarrytmias and absolute or relative bradycardia) (grade 2C)
7. Phenylephrine is not recommended in the treatment of septic shock except in the following circumstances: (a) norepinephrine is associated with serious arrhythmias, (b) cardiac output is known to be high and blood pressure persistently low, or (c) as salvatage therapy when combined inotrope/vasopressor drugs and low-dose vasopressin have failed to achieve the MAP target (grade 1C).
8. We recommend that low-dose dopamine not be used for renal protection (grade 1A)

Adapted from Dellinger *et al*.[1]

Reference

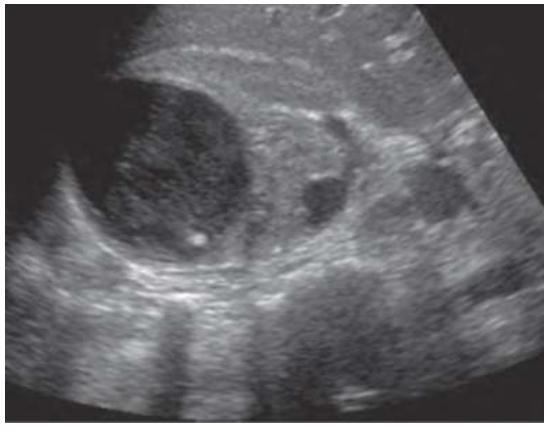
1. Dellinger RP, Levy MM, Rhodes A et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock, 2012. Intensive Care Med 2013;39:165-228.

Appendix Figure 1. Mild hydronephrosis.

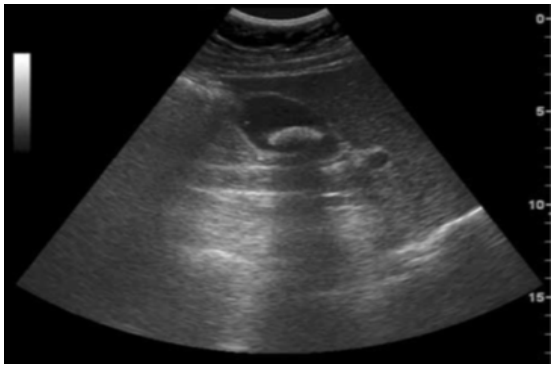
Appendix Figure 2. Moderate hydronephrosis.

Appendix Figure 3. Severe hydronephrosis.

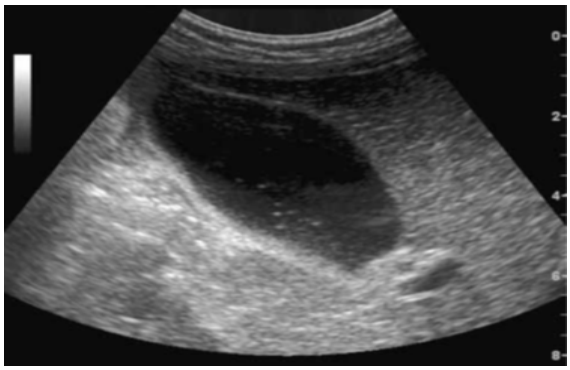
Appendix Figure 4. Renal enlargement in acute pyelonephritis.



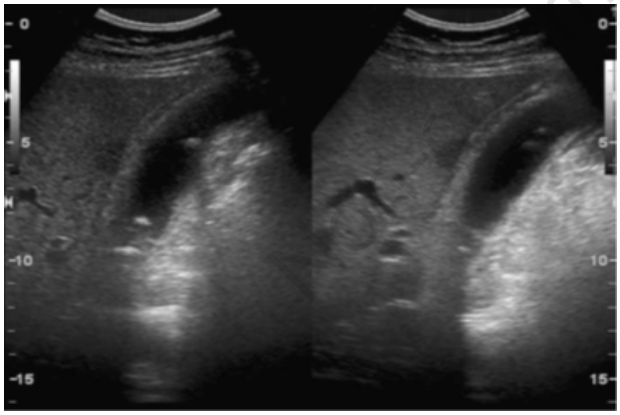
Appendix Figure 5. Focal area (renal abscess).



Appendix Figure 6. Gallstone.



Appendix Figure 7. Sludge in the gallbladder.

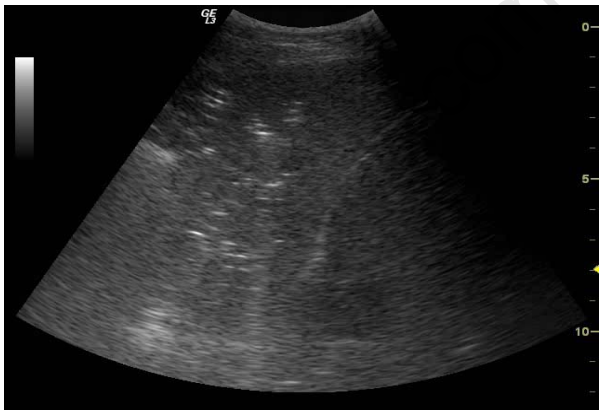


Appendix Figure 8. Thickening of the gallbladder wall, striated with a hypoechoic intermediate layer.

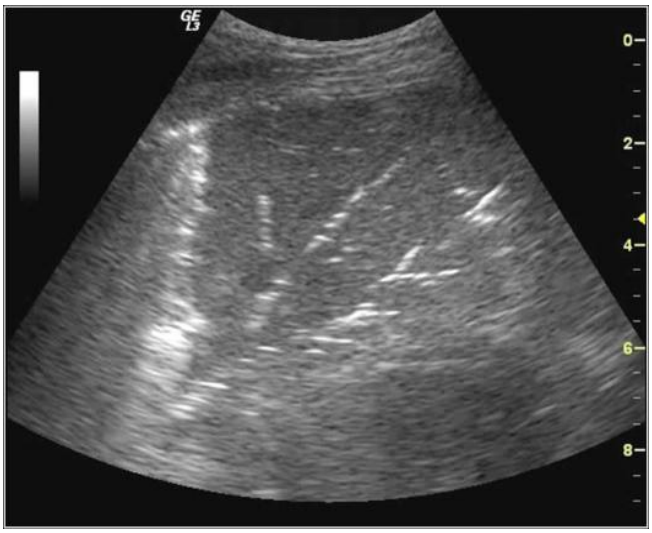
Appendix Figure 9. Pre-suppurative stage.

Appendix Figure 10. Suppurative stage.

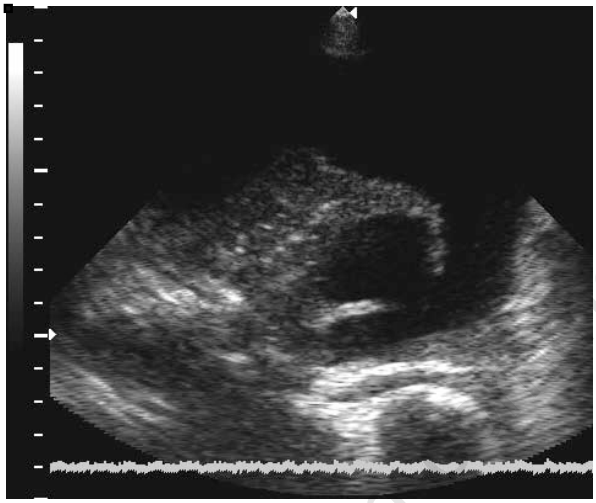
Appendix Figure 11. Resolution.



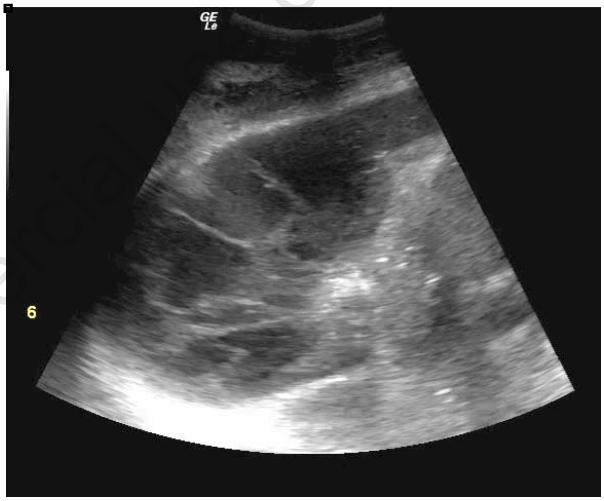
Appendix Figure 12. Pulmonary consolidation.



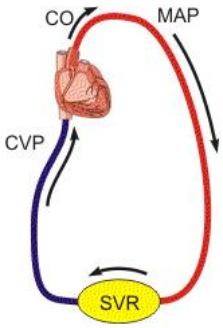
Appendix Figure 13. Dynamic air bronchogram.



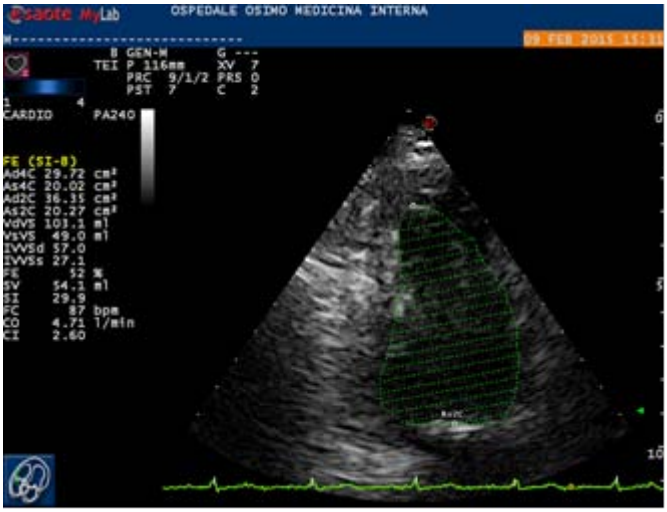
Appendix Figure 14. Free effusion.



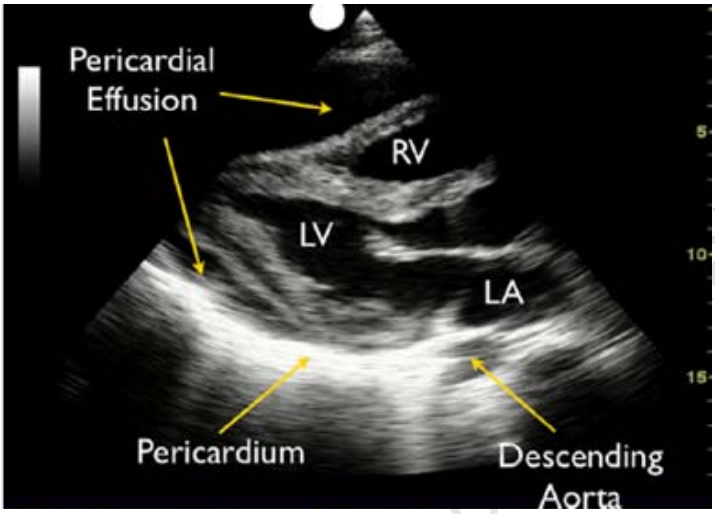
Appendix Figure 15. Organized effusion.



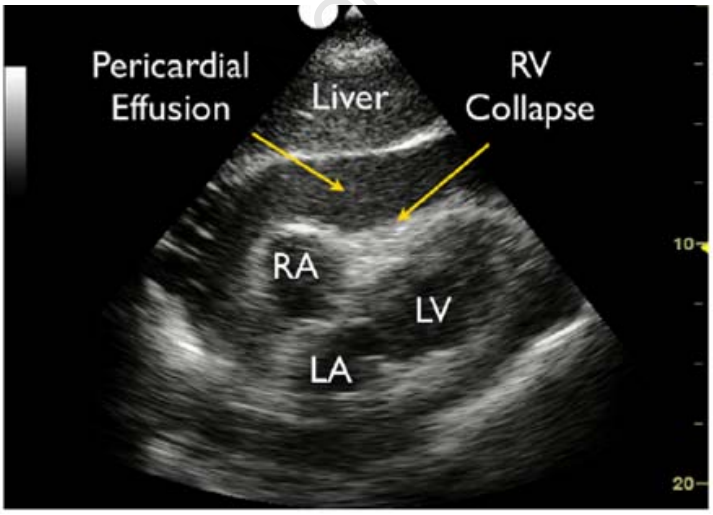
Appendix Figure 16. Physiological variables interconnected in critical patient.



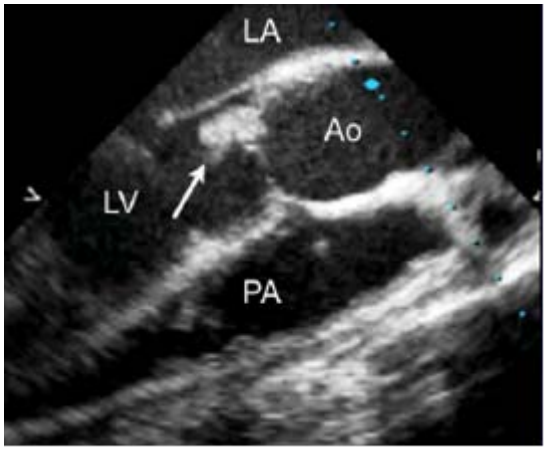
Appendix Figure 17. Left ventricle in the apical route for calculation of ejection fraction.



Appendix Figure 18. Parasternal long.axis view: large pericardial effusion.

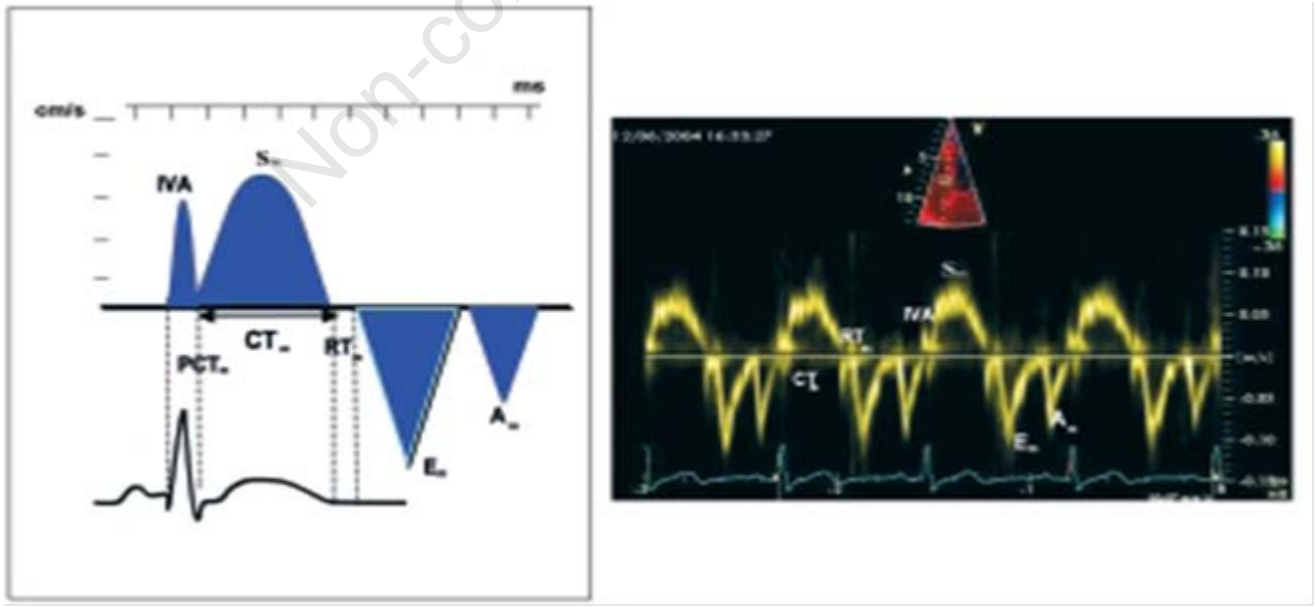


Appendix Figure 19. Subxiphoid view; cardiac tamponade.



Appendix Figure 20. Endocarditis.

Appendix Figure 21. Inferior vena cava.



Appendix Figure 22. Pattern of pulsed Doppler tissue (left) and equivalent pattern recorded at mitral annulus lateral (right).

Appendix Figure 23. Staging sepsis.