

SUPPLEMENTAL DIGITAL CONTENT

Table S1. Characteristics of the participating hospitals and ICUs.

HOSPITALS	
Nº of participating hospitals	10
Type	
University	5
Community	5
Nº of hospital beds	
< 400	3
400-600	2
600-800	2
> 800	3
ICUs	
Nº of participating ICUs	11
Nº of ICU beds	154
Type of ICU	
Medical	0
Medical-Surgical	11
ICUs with coronary unit	7

Types of ICUs definitions:

1. **Medical:** $\geq 80\%$ of admissions are medical pathology.
2. **Surgical:** $\geq 80\%$ of admissions are surgical pathology.
3. **Medical – Surgical:** $> 20\%$ and $< 80\%$ of admissions are medical or surgical pathology, mixed admission.
4. **Trauma:** $\geq 80\%$ of admissions are trauma pathology.

All of the ICUs are attending full-time by Intensive Care Especialists, 24 hours 7 days per week.

TABLE S2. Surviving Sepsis Campaign bundles 2008 edition [21].

RESUSCITATION BUNDLE (Recommendations to achieve in first 6 hours)
<ol style="list-style-type: none">1. To measure serum lactate as soon as possible.2. Obtain blood cultures prior antibiotic administration.3. Early broad spectrum antibiotics administration (Within first 3h for emergency room admission and 1 h for non emergency department or ICU admissions)4. In case of hypotension or lactate \geq 4mmol/l:<ol style="list-style-type: none">a. Deliver 20ml/kg bolus of crystalloids (or equivalent dose of colloids)b. Administer vasopressors to achieve MAP > 65mmHg in the event of persistent hypotension despite fluid infusion (septic shock).5. In case of septic shock: (insert central venous line)<ol style="list-style-type: none">a. Achieve Central Venous Pressure (CVP) > 8mmHgb. Achieve Central Venous oxygen saturation (SvO₂) > 70%
MANAGEMENT BUNDLE (Recommendations to complete in first 24 hours)
<ol style="list-style-type: none">1. Administer intravenous low dose steroids (300mg hydrocortisone/day) to patients with refractory hypotension despite adequate fluid resuscitation and vasopressors.2. Consider Protein C activated administration in patients with septic shock and \geq 2 sepsis induced organ failures, with no contraindications.3. Maintain glucose control greater than lower normal limit but lower than 150 mg/dl.4. Maintain Plateau Pressure < 30cmH₂O in mechanically ventilated patients

Table S3. Characteristics of septic episodes included in 2011 cohort.

VARIABLE	GRECIA Cohort 2011 (231 Episodes)
	Mean (SD)
AGE(years)	66.87 (14.22)
APACHE II	21.92 (6.67)
LOD	5.6 (3.28)
SOFA D1	8.06 (3.58)
	N (%)
SEPTIC SHOCK (episodes)	176 (76.2%)
GENDER (Male)	153 (66.2)
McCABE INDEX	
0	64 (27.8)
1	101 (44)
2	56 (24.34)
3	9 (4)
CATEGORY	
Medical	152 (66.09)
Urgent surgery	54 (23.48)
Scheduled surgery	15 (6.52)
Trauma	9 (3.91)
ORIGIN	
Medical Ward	84 (37)
Surgical Ward	40 (17.62)
Operating room	21 (9.25)
Emergency room	69 (30.40)
Other ICU	4 (1.76)
Other	9 (3.96)
COMORBIDITIES	
AIDS	2 (0.86)
Immunosuppression	50 (21.64)
Cancer	15 (6.5)
Heart Failure	15 (6.5)
Chronic Renal insufficiency	15 (6.5)
Chronic Respiratory insufficiency	28 (12.12)
Chronic Liver inssufficiency	7 (0.3)
Diabetes Mellitus	27 (11.68)
Alcohol abuse	16 (6.92)
Hypercoagulability disease	1 (0.43)
Increased Bleeding risk	31 (13.42)
NUMBER OF COMORBIDITIES	
0	89 (38.53)
1	91 (39.4)
2	40 (17.32)
3 or more	11 (4.76)
NUMBER OF ORGAIN FAILURE	
0	29 (12.9)
1	68 (30.22)
2	86 (38.22%)
3	32 (14.22%)
4	9 (4%)
5	1 (0.44%)
ORGAN FAILURE	
Neurologic	16 (7.1%)
Respiratory	98 (43.5%)
Cardiovascular	176 (76.2%)
Renal	46 (20.4%)
Haematologic	31 (13.7%)
Liver	11 (4.9%)

Table S4. Characteristics of infection.

INFECTION CHARACTERISTICS	N(%)
ORIGIN OF INFECTION	
Community	136 (59.13%)
Nosocomial	76 (33.04%)
Intra-ICU	18 (7.83%)
SOURCE OF INFECTION	
Abdominal	75 (32.47%)
Lung	69 (29.87%)
Urinary tract	35 (15.15%)
Surgical wound	2 (0.87%)
Bloodstream, Catheter	15 (6.49%)
Soft tissues	12 (5.19%)
Others	23 (9.96%)