S1 Table. Characteristics of the participating hospitals and Intensive Care Units

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 that had a coronary unit	7

ICU: Intensive Care Unit.

S2 Table. Univariate analysis results of variables related to in-hospital mortality as dependent variable.

	SURVIVORS	NON-SURVIVORS	P
DEMOGRAPHICS			
Age (years) Mean (IC 95%)	65.32 (62.84 – 67.80)	68.72 (65.66 – 71.78)	0.04
	N (%)		
Sex			0.12
• Male	92 (60.1)	61 (39.9)	
• Female	55 (70.5)	23 (29.5)	
Patient´s category			0.71
• Medical	101 (66.5)	51 (33.5)	
• Urgent surgery	35 (64.8)	19 (35.2)	
• Scheduled surgery	7 (46.7)	8 (53.3)	
• Traumatic	4 (44.4)	5 (55.6)	
Origin prior ICU admission			0.25
• Medical ward	51 (60.7)	33 (39.3)	
• Surgical ward	27 (67.5)	13 (32.5)	
• Operating room	11 (52.4)	10 (47.6)	
• Emergency	51 (73.9)	18 (26.1)	
• Other ICU	2 (50)	2 (50)	
• Others	4 (44.4)	5 (55.6)	
PREVIOUS COMORBIDITIES	**N (%)**		
AIDS			0.68
• No	146 (63.8)	83 (36.2)	
• Yes	1 (50)	1 (50)	
Immunosuppression			<.01
• No	125 (69)	56 (31)	
• yes	22 (44)	28 (56)	
Metastatic cancer			0.76
• No	138 (63.9)	78 (36.1)	
• Yes	9 (60)	6 (40)	
Chronic respiratory insufficiency			0.23
• No	132 (65)	71 (35)	
• Yes	15 (53.6)	13 (46.4)	
Chronic heart failure			0.39
• No	139 (64.3)	77 (35.7)	
• Yes	8 (53.3)	7 (46.7)	
Chronic renal failure			0.76
• No	138 (63.9)	78 (36.1)	
• Yes	9 (60)	6 (40)	
Chronic liver insufficiency			0.12
• No	144 (64.3)	80 (35.7)	
• Yes	3 (42.9)	4 (57.1)	
Diabetes Mellitus			0.23
• No	127 (62.3)	77 (37.7)	
• **Yes**	20 (74.1)	7 (25.9)	
Chronic alcohol abuse			0.07
• No	140 (65.1)	75 (34.9)	
• **Yes**	7 (43.7)	9 (56.3)	
Hipercoagulability			0.44
• No	146 (63.5)	84 (36.5)	
• **Yes**	1 (100)	0 (0)	
Increased bleeding risk			0.91
• No	127 (63.5)	73 (36.5)	
• Yes	20 (64.5)	11 (35.5)	
Number of comorbidities			0.01
• 0	65 (73.1)	24 (26.9)	
• 1	52 (57.1)	39 (42.9)	
• 2	27 (67.5)	13 (32.5)	
• 3	3 (37,5)	5 (62,5)	
• 4	0	3 (100)	
McCabe Index			0.09
• 0	47 (73.4)	17 (26.6)	
• 1	64 (63.4)	37 (36.6)	
• 2	32 (57.1)	24 (42.9)	
• 3	3 (33.3)	6 (66.7)	

	SURVIVORS	NON-SURVIVORS	p
INFECTION	**N (%)**		
Acquisition of infection			<.01
• Community	104 (76.5)	32 (23.5)	
• Hospital	35 (46.1)	41 (53.9)	
• Intra-ICU	8 (44.4)	10 (55.6)	
Source of infection			0.05
• Urinary tract	34 (20.48)	5 (7.69)	<.01
• Lung	42 (25.30)	27 (41.54)	0.01
• Abdominal	53 (31.93)	22 (33.85)	0.38
• Bloodstream / catheter related	11 (6.63)	4 (6.15)	0.44
• Others	26 (15.66)	7 (10.77)	0.16
ORGAN FAILURE ON DAY 0	**N (%)**		
Neurologic			0.02
• No	138 (65.7)	72 (34.3)	
• Yes	6 (37.5)	10 (32.5)	
Respiratory			<.01
• No	92 (72.4)	35 (27.6)	
• Yes	51 (52.1)	47 (47.9)	
Cardiovascular			<.01
• No	39 (79.6)	10 (20.4)	
• Yes	104 (59.1)	72 (40.9)	
Hematological			<.01
• No	146 (75.26)	48 (24.74)	
• Yes	16 (51,61)	15 (48,39)	
Renal			0.93
• No	114 (63.7)	65 (36.3)	
• Yes	29 (63.1)	17 (36.9)	
Liver			0.2
• No	138 (64.5)	76 (35.5)	
• Yes	5 (45.4)	6 (54.6)	
Hematological			<.01
• No	130 (67.1)	64 (32.9)	
• Yes			
Number of organ failure			<.01
• 0	25 (86.2)	4 (13.8)	
• 1	50 (73.5)	18 (26.5)	
• 2	50 (58.1)	36 (41.9)	
• 3	14 (43.7)	18 (56.3)	
• 4	4 (44,44)	5 (55,56)	
• 6	0	1 (100)	
	SURVIVORS	**NON-SURVIVORS**	
ORGAN FAILURE SCORES	**Mean (95% CI)**		
LOD	4.95 (4.45 – 5.46)	6.74 (6.01 – 7.48)	<.01
APACHE II	20.03 (19.04 - 21.02)	25.21 (23.8 - 26.61)	<.01
SOFA DO	7.97 (7.42 – 8.52)	9.78 (9.05 – 10.50)	<.01
SOFA D1	7.34 (6.78 – 7.90)	9.39 (8.61 – 10.17)	<.01
Delta SOFA (D3-D1)	1.84 (1.43 – 2.25)	0.55 (0.02 – 1.13)	<.01

ICU: *Intensive Care Unit*; **CI**: *Confidence interval*; **AIDS**: *acquired immune deficiency syndrome; **LOD**: Logistic Organ Dysfunction system**; ***APACHE II*:* Acute Physiology And Chronic Health Evaluation II score; **SOFA**: Sequential Organ Failure Assessment score.

SIF APPENDIX. Definitions of variables used in the study

A. ICU CLASSIFICATION:

Participating ICUs were classified according to the next criteria:

1. **Medical**: if > 80% of admissions are medical pathology.
2. **Surgical:** if > 80 % of admissions are surgical pathology.
3. **Medical-surgical**: if < 80% and > 20% are medical or surgical pathology in both groups.

B. CATEGORY OF PATIENTS:

Patients were classified according to their origin with this criteria:

1. **Medical**: patients not surgical or not operated in 10 days before ICU admission or those that stay in ICU for more than 10 days from surgery.
2. **Surgical**: Patients operated in 10 days before or after ICU admission. Urgent surgery or scheduled surgery.
3. **Traumatic**: Trauma patients

C. COMORBIDITIES

1. **Immunosuppression:** patients in treatment with immunosuppressants drugs, high doses of glucocorticoids, chemotherapy or radiotherapy. Blood malignancies as leukemia, linphoma or **AIDS** (patient with HIV positive, hospitalized for pneumocystis jiroveci pneumonia, Kaposi´s sarcoma, linphoma, toxoplasmosis, tuberculosis or CD4 count < 50/mm^3).
2. **Transplant:** kidney, liver, bone marrow, pancreas, lung, heart transplantation.
3. **Metastatic cancer:** metastasis diagnosed by image findings, surgery or tumoral markers.
4. **Chronic heart failure:** NYHA class IV.
5. **Chronic renal failure:** patients on hemodyalisis program or peritoneal dyalisis.
6. **Chronic respiratory insufficiency:** obstructive, restrictive or vascular disease that limits daily activities. Supplemental oxygen therapy, secondary polycythemia or severe pulmonary hypertension (> 40 mmHg).
7. **Chronic liver insufficiency:** Cirrhosis documented by biopsy or portal hypertension with bleeding history or liver failure, hepatic encephalopathy or coma.
8. **Insulin dependent Mellitus Diabetes:** hyperglycemia as result of insulin reduced secretion, action or both and that needs exogenous insulin administration to maintain adequate levels.
9. **Chronic alcohol abuse:** defined by drinking more than 14 cups / week (400 ml of wine or 750ml of beer) daily in men; and drinking more than 7 cups / week (200 ml of wine or 375 ml of beer) daily in women.
10. **Hypercogulable syndrome:** Hereditary deficit of Protein C, Protein S or Antithrombin III. Anticardiolipin antibodies, antiphospholipid antibodies, lupus anticoagulant or diagnosis of deep

vein thrombosis in 3 months before sepsis episode.

11. **High bleeding risk:** active bleeding in postsurgery period or gastrointestinal bleeding or diathesis in 6 weeks before. Trauma with high risk of bleeding, Brain Trauma or intracranial mass, intracranial surgery or any ischemic or hemorrhagic injury of central nervous system. Surgery 12 hours prior development of septic episode.

D. INFECTION

History, symptons, anamnesis and physical exploration findings that suggest infection and treatment with antibiotics. According to diagnosis way infection was classified as:

1. **Suspected:** clinical syndrome associated with high probability of infection.
2. **Clinical documented:** clinical findings and pus visualization in usually sterile fluid or cavity. Image diagnosis with no microbiologic isolation. Organ perforation.
3. **Microbiologically documented:** Infection with microorganism isolation in at least one culture of tissue or biological fluids and treated with antibiotics, according to CDC standardized definitions.[36]
4. **Community acquired:** infection already present on admission or developed in first 48 hours after admission.
5. **Nosocomial**: Infection developed during hospitalization and developed 48 hours after admission in ward or ICU.

E. SEPSIS DEFINITIONS

1. **Sepsis:** definition according to 2001 International Consensus Conference criteria. [31]
2. **Severe Sepsis**: Sepsis with at least one organ dysfunction, hypoperfusion or arterial hypotension associated with sepsis onset according to 2001 International Consensus Conference criteria. [31]
3. **Septic shock:** severe sepsis plus hypotension refractory to volume infusion and need of vasoactive drugs [31].

G. ORGAN DYSFUNCTION

We used SOFA score [35] to quantify the number of organs and systems in failure at the time of diagnosis of severe sepsis (Day 0), with the clinical and analytical variables collected at the initial time. We defined organ dysfunction as 1 or 2 points and organ failure as 3 or 4 points in each section of SOFA score.

To value the organ failure evolution we used sequential calculation of SOFA score during days 1 to 7, 14 and 28 from the time of severe sepsis diagnosis.