

## IMPORTANCE OF EDUCATIONAL ACTION TO IMPROVE ADJUSTMENT TO THE SEPSIS PROTOCOL

<sup>1</sup>Adriana O. L. Veríssimo, <sup>2</sup>Markus B. de Albuquerque, <sup>3</sup>Shirley H. S. Henriques, <sup>4</sup>Isis Jasper, <sup>5</sup>Bruno A. P. Barreto, <sup>6</sup>Katia Kietzer and <sup>7</sup>Edgar B. Sobrinho

<sup>1</sup>Mestre, Fisioterapeuta, Hospital Adventista de Belém, Pará

<sup>2</sup>Mestre, Médico, Hospital Adventista de Belém, Pará

<sup>3</sup>Especialista, Enfermeira, Hospital Adventista de Belém, Pará

<sup>4</sup>Acadêmica de Medicina, Universidade Federal do Pará

<sup>5</sup>Doutor, Médico, Universidade do Estado do Pará

<sup>6</sup>Doutora, Fisioterapeuta, Universidade do Estado do Pará

<sup>7</sup>Mestre, Médico, Hospital Adventista de Belém, Pará

### ARTICLE INFO

#### Article History:

Received 20<sup>th</sup> June, 2018  
Received in revised form  
09<sup>th</sup> July, 2018  
Accepted 16<sup>th</sup> August, 2018  
Published online 30<sup>th</sup> September, 2018

#### Key Words:

Sepsis, Formative feedback,  
Hospital mortality.

### ABSTRACT

**Introduction:** Sepsis is a major global health problem and is responsible for the deaths of thousands of people each year. It is the second leading cause of death in intensive care units, after coronary heart disease. Due to the high mortality rate, sepsis needs to be addressed through evidence-based practice, institutionalized protocols, well-developed clinical strategies, and continuing education. This study analyzed the clinical impact of adherence to an education tool for sepsis control measures at the Adventist Hospital of Belém in Brazil.

**Methodology:** A prospective, quasi-experimental study was carried out from March 2015 to August 2016. The study included 320 patients diagnosed as having selection criteria with suspected sepsis. The patients were divided into periods for better visualization of the results. In August 2015, start the period in which an educational tool was applied for adherence to the hospital sepsis protocol.

**Results:** The best adherence measure, after the tool application, was antimicrobial therapy. There was a reduction in the hospitalization time of the surviving patients from 19.7 days to 7.7 days and the mortality rate decreased from 63.3% to 30.6%.

**Conclusion:** Although adherence to resuscitation packages complet was low, the education tool increased the insight of professionals in the identification of septic patients, resulting in a diagnosis and early treatment that corresponded with a reduction in hospitalization time and a decrease in mortality.

Copyright © 2018, Adriana O. L. Veríssimo et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

**Citation:** Adriana O. L. Veríssimo, Markus B. de Albuquerque, Shirley H. S. Henriques, Isis Jasper, Bruno A. P. Barreto, Katia Kietzer and Edgar B. Sobrinho. 2018. "Importance of educational action to improve adjustment to the sepsis protocol", *International Journal of Development Research*, 8, (09), 22992-22997.

## INTRODUCTION

Sepsis is a major global health problem that affects millions of people every year, leading to the death of one in four people. The incidence of sepsis has increased over time (Dellinger, 2013; Martin, 2009 and Gaiski, 2013). In the United States, there has been an average annual incidence of 300 cases per 100,000 inhabitants, an increase of 13% per year, and mortality ranges from 14.7% to 29.9%.<sup>3</sup> Recently, a study conducted to compare sepsis care in the United States and

Europe found that the gross hospital mortality rate associated with sepsis in Europe is 41% (Levy, 2012). In Brazil, mortality is 50-60%, which is considered among the highest in the world (Kauss, 2010). The SPREAD study, which randomized 231 intensive care units (ICUs) in Brazil, revealed that 30% of the ICU beds in the country were occupied by patients with severe sepsis or septic shock, and 55% of these patients died (AMIB.org, 2015). Sepsis is the second main cause of death in ICUs, after coronary diseases, accounting for 20% of the admissions (Romero, 2013). Although there has been advancement in medical science, both in technology and in therapeutic measures such as the appearance of antibiotics, the mortality of these patients remains high (Mayr, 2015).

\*Corresponding author: Adriana O. L. Veríssimo  
Mestre, Fisioterapeuta, Hospital Adventista de Belém, Pará

**Table 1. Surviving Sepsis Campaign Therapy Packs<sup>1</sup>**

3 hour packages	
1.	Measure the lactate level.
2.	Obtain blood cultures before administration of antibiotics.
3.	Initiation of broad-spectrum antibiotics intravenously within the first hour of diagnosis.
4.	Administer 30 mL/kg of crystalloids or the equivalent of colloids for hypotension or lactate $\geq 4$ .
6 hour packages (Patients with hyperlactatemia or persistent hypotension).	
1.	Apply vasopressors (for hypotension that does not respond to initial resuscitation of liquid to maintain a PAM $\geq 65$ mmHg).
2.	In case of persistent hypotension despite resuscitation of initial volume or lactate of 4 mmol/L (36 mg/dL):
	• Measure central venous pressure (CVP)
	• Measure central venous oxygen saturation (ScvO <sub>2</sub> )
	• Measure the lactate again

<sup>1</sup>Sepsis Survival Campaign: International Guidelines for the Treatment of Severe Sepsis and Septic Shock (2012). PAM = mean arterial pressure.

Due to the seriousness of the problem, the Surviving Sepsis Campaign (CSS) was launched in 2002, where it was recommended that institutions have strategies for detecting sepsis and that they institute update programs to improve care. Evidence shows that the effective implementation of protocols has an impact on the survival of patients (Ilas online.org, 2015). The establishment of protocols in the medical services is an excellent strategy to reduce sepsis since these protocols aim to diagnose in a shorter period of time and treat the disease in a more effective way, according to the needs of individual patients (Pérez, 2012). Studies show that the early implementation of measures to combat sepsis ensures interventions at each stage, allowing the application of strategies to improve therapy. Considering the great importance of protocols, this study aimed to analyze the clinical impact of the use of an education tool in the adherence to the sepsis protocol. Additionally, the study sought to identify the measures with better adherence after the implementation of the tool and to analyze the length of hospitalization and mortality before and after implementation of the tool.

## MATERIALS AND METHODS

This was a prospective, quasi-experimental study conducted from March 2015 to August 2016 in a private, tertiary hospital, a reference center for highly complex cases. The implementation of a health education tool in the sepsis protocol was evaluated. The implementation of the protocol took place in the March 2015. During this process, reference guides were developed and explanatory leaflets and flowcharts with algorithms were distributed throughout the hospital, mainly in the emergency department. The guides were based on the international guidelines of Sepsis and the Brazilian Patient Safety Program (Dellinger, 2012; Ilas online.org, 2015 and Segurançadopaciente.com, 2015). The implementation of the educational tool and feedback letter was performed in August 2015 because there was little adherence to the measures of the protocol, as the protocol was rarely used. All adult patients greater than 18 years of age and diagnosed with sepsis, severe sepsis, and septic shock, admitted from the emergency department or transferred to the ICU within the first 24 hours of the diagnosis, were included in the study. The criteria for defining sepsis were based on the Sepsis Survival campaign (CSS) criteria. Obstetric patients, patients with sepsis referred from other institutions, and patients with organic dysfunctions not considered secondary to a chronic disease were excluded. The compilation of clinical and demographic data was conducted through the patients' clinical histories, using the form designed by the Institute Latin American Sepsis (ILAS) (Ilas online.org, 2015) and adapted by hospital quality management in conjunction with the

Hospital Infection Control Committee (IHCC). From the time that the patient with suspected sepsis was admitted to the hospital, the CCIH team was activated and the data was collected using the pre-designed form. The evaluation was based on compliance with the updated CSS resuscitation package from 2012. The package also includes requirements that must be met within the first three and six hours, which are comprised of diagnostic and therapeutic interventions. The measures were considered adherent to the protocol when they complied with each item of the package (Table 1). Once the evaluation of compliance with the protocol was made, a letter of feedback was sent to the professionals who attended the patient at the time of the suspicion of sepsis, indicating adherence to the measures. Patients were followed up until hospital discharge to determine their vital status.

## Ethical aspects

The investigation began with authorization from the Adventist Hospital of Belém (HAB), Brazil, Amazon region and after the approval of the research ethics committee of the Gaspar Vianna Hospital Clinic Committee (CAAE n° 49443615.2.0000.0016).

## Statistical Analysis

Fisher's Exact Test, G-Test, Student's T-Test, and Mann-Whitney Test were used to compare the characteristics of the patient groups in relation to the demographic characteristics, comorbidities, and clinical situation according to the assumptions of each test. Bioestat<sup>®</sup> 5.0 program was used for all analyses. A significance level of 5% was used for all the work ( $p < 0.05$ ).

## RESULTS

During the study period, 320 patients with suspected sepsis were admitted, of whom 235 met the inclusion criteria, the others were classified as infection. Of this sample, 15 were admitted from March to July 2015, 169 from August to December 2015 and 136 from January to August 2016. There were statistically significant differences higher in the groups in regards to sepsis diagnosis. There were more cases of sepsis in the group August to December 2015 than in the January to August 2016 (58,8% vs.35,3%, respectively). Also had more cases of septic shock (58,8% vs. 35,3%, respectively) (Table 2). Regarding the general characteristics of the patients, we observed that although the groups do not contain an equal number of patients, the sample is relatively homogeneous. There was no statistically significant difference on any of the characteristics considered between the groups (Table 3).

**Table 2. Distribution of patients diagnosed with sepsis admitted to the institution from March to December 2015, Belém – Pará - Brazil**

	Control (n=30)		Case (n=122)		Total (b=152)		P-value
	n	%	n	%	n	%	
Sepsis	1	3.3	33	27.0	34	22.4	< 0.001 <sup>a</sup>
Severe sepsis	18	60.0	78	63.9	96	63.2	
Septic Shock	11	36.7	11	9.0	22	14.5	

Source: Research Protocol. <sup>a</sup>G-Test.**Table 3. General characteristics of patients admitted to the institution from March to December 2015, Belém – Pará – Brazil**

	Control (n=30)		Case (n=122)		P-value
	n	%	n	%	
Sex					
Male	14	46.7	61	50.0	0.843 <sup>a</sup>
Female	16	53.3	61	50.0	
Age (mean ± SD)		70.9 ± 21.9		71.2 ± 18.2	0.942 <sup>b</sup>
Comorbidities					
Alcoholism	0	0.0	3	2.5	>0.99 <sup>a</sup>
HIV/AIDS	0	0.0	2	1.6	>0.99 <sup>a</sup>
Neoplasm	4	13.3	11	9.0	0.50 <sup>a</sup>
Immunosuppressants	6	20.0	20	16.4	0.79 <sup>a</sup>
Diabetes	6	20.0	42	34.4	0.131 <sup>a</sup>
Heart failure	2	6.7	13	10.7	0.743 <sup>a</sup>
Chemotherapy	0	0.0	3	2.5	>0.99 <sup>a</sup>
COPD	4	13.3	13	10.7	0.754 <sup>a</sup>
Chronic renal failure	3	10.0	13	10.7	>0.99 <sup>a</sup>
Radiotherapy	0	0.0	0	0.0	e
Stroke	3	10.0	14	11.5	>0.99 <sup>a</sup>
Systemic arterial hypertension	11	36.7	69	56.6	0.062 <sup>a</sup>
None	7	23.3	17	13.9	0.265 <sup>a</sup>

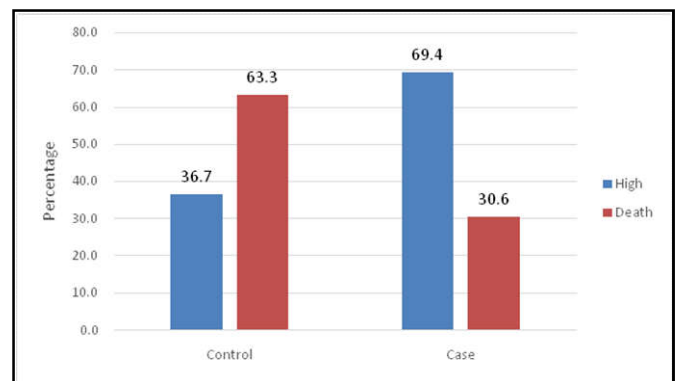
HIV/AIDS - Human immunodeficiency virus/human immunodeficiency syndrome. COPD - Chronic Obstructive Pulmonary Disease. HTA - Systemic arterial hypertension. Source: research protocol. <sup>a</sup> Fisher exact test; <sup>b</sup> Student T-Test.**Table 4. Adherence to sepsis resuscitation packages in the institution. Belém – Pará-Brazil**

	Control (n=27) *		Case (n=93) *		P-value <sup>a</sup>
	n	%	n	%	
1. Lactate	17	63.0	65	69.9	0.641
2. Hemocultures	12	44.4	30	32.2	0.263
3. Antibiotics	15	55.5	76	81.7	0.011
4. Volume/ Glass	7/7	100.0	7/8	87.5	>0.99
5. Collection of 2 <sup>nd</sup> lactate	1/2	50.0	6/7	85.7	0.424
6. Reassessment	8/8	100.0	8/9	88.9	>0.99

\* Patients who were adherent to the measures. <sup>a</sup> Fisher exact test.

All patients who developed sepsis were diagnosed at the institution's emergency department. Regarding the place of sepsis treatment, there was a statistical difference between the groups: in the group August to December 2015, 61% of the patients treated in the emergency department were transferred to the ICU, while in the group January to August 2016 only 33% were transferred ( $p < 0.01$ ). In the majority of patients in all of the groups, the reason for hospitalization was clinical and the type of infection was community-based with statistical difference between them, and pulmonary focused, this with no statistical difference. In the evaluation of SOFA (Sequential Organ Failure Assessment), patients in the groups presented higher scores. When analyzing the institutional performance regarding the time from organic dysfunction to the diagnosis of sepsis, there was a statistical difference between the groups studied in the emergency department. The control group had a mean of 4.4 hours and the case group has a mean of 0.5 hours ( $p = 0.032$ ). The antibiotic therapy time was also statistically different between the ICU groups, the control group with a mean of 0.9 hours and the mean of the case group 0.2 hours ( $p = 0.020$ ). In the analysis of the implementation of different measures proposed in the Surviving Sepsis Campaign Therapy Packs, had a increase adherence to the complete set of measures to the lactate ( $p = 0.0019$ ), Hemocultures ( $p = 0.00001$ ), Volume/ Glass ( $p = 0.0055$ ) and 6 hour packages

( $p = 0.00001$ ) after implementation of the tool. (Table 4). The measurement of hospitalization time from admission to discharge showed a statistical difference between the groups after implementation of the tool.



\*P value for Fisher exact test = 0.0014.

\* High risk

**Figure 1. Lethality of patients admitted to the institution with a diagnosis of sepsis. Belém – Pará – Brazil**

Surviving patients in the groups had a mean of 22,9, 19,7 e 11,3 days respectively ( $p = 0,04$ ). (Figure 3) In the evaluation of the mortality of patients, we noticed a statistical difference

between the groups, with a rate of 33.3% to a rate of 19.5% ( $p = 0,028$ ) (Figure 1).

## DISCUSSION

It has been 14 years since CSS was first launched, when a group of professionals joined the challenge of developing recommendations to improve care, based on good medical practice, with the goal of reducing mortality by 25% in patients with sepsis. However, the incidence of this disease remains high and institutions find great difficulties in adoption and implementation of these protocols because the clinical management of sepsis is so complex (Rhodes, 2015; Vásquez, 2011 and Quintero, 2012). The present study revealed a high incidence of severe sepsis (63.2%) among patients diagnosed with sepsis. A high frequency of severe sepsis (74.9%) was also found in a study performed at the ICU of a Recife hospital, which shows the severity of this pathology (Koury, 2006). After the implementation of the educational tool, a significant difference was observed in the number of patients diagnosed with sepsis without dysfunction ( $p < 0.001$ ). Early diagnosis is crucial considering that when treating this disease its initial development is less severe and its advance may be prevented with treatment.

This may reveal that the improvement in knowledge and practical skills has led to increased sensitivity in recognition of this type of patient after an intervention measure (Armero, 2014 and Girardis, 2009). In this study, there was no association between the presence of sepsis, gender, and comorbidities, consistent with another study performed in a public hospital in the same region (Silva, 2015). However, it is worth noting that the prevalence of sepsis, according to gender and comorbidities, differs according to the sample and the study (Koury, 2006; Ponce, 2008; Yoshihara, 2011). The place of diagnosis and initiation of measures to combat sepsis occurs mainly in the emergency department (Rhodes, 2015 and Peake, 2014). It is important to emphasize that the transfer of patients to the ICU was lower in the case group, which shows that the use of an educational tool and the implementation and execution of a protocol may decrease a patient's severity of illness due to the initial handling of the disease (Pérez, 2012; Armero, 2014 and Girardis, 2009). The most frequent reason for hospitalization was clinical, with a predominance of community infection, with pulmonary focus prevailing in both groups. Studies conducted in different regions confirm this distribution (Rhodes, 2015; Koury, 2006; Peake, 2014; Zanon, 2008).

The literature suggests that there is a strong relationship between the time between organic dysfunction and the diagnosis of sepsis, as well as the time between antibiotic administration and mortality (Ilas online.org, 2016). After the intervention, it was observed that providers in the emergency department made an earlier diagnosis of sepsis, with only 30 minutes from the time of dysfunction until the diagnosis; in the ICU, the time of administration of antibiotics reached approximately 12 minutes. After the educational intervention, there was no increase in adherence to the measures in their entirety, but a better appreciation of the individual components, as other studies show (Pérez, 2012). The use of antibiotic therapy was significantly higher after the use of the tool, increasing from 55.5% to 81.7% ( $p = 0.009$ ). Studies have shown that the administration of antibiotics should be immediate and be a top priority goal in the care of septic

patients, trying to minimize bacterial load (Bloos, 2014 and Tejedo, 2009). Each hour of delay in antibiotic therapy is associated with an increase in mortality. However, it is important to note that antibiotic therapy, initiated before blood culture, delays or prevents the detection of the microorganisms responsible for the infection, which is generally positive in 30% to 50% of patients with sepsis. That is why it is important to emphasize the "time" factor in the different areas of focus in continuing education. Better coordination between those who diagnose the disease (laboratory) and those who administer the drugs (pharmacy) is crucial, so that the early administration of antibiotics does not hinder the results of blood cultures (Dellinger, 2013).

Regarding the lactate measurement, no significant improvement in adherence to the protocol was found. However, it is worth emphasizing a tendency in the improvement of adherence. This is important since the increased lactate value reflects a state of tissue hypoperfusion, which facilitates the diagnosis of subclinical shock, allowing early and adequate administration of intravenous fluids, increasing the survival rate of these patients. An increased lactate level is associated with a worse prognosis, which is why a smaller percentage of patients developed septic shock after the use of the tool (9%) (Zapata, 2010). The average length of stay for patients with sepsis was consistent with previous studies, ranging from 15.3-18.4 days (Clèries, 2016). In another study, the average length of stay before the introduction of the CSS resuscitation packages was 10.5 days in the United States and 22.8 days in Europe.<sup>4</sup>

In this study, after the educational tool was introduced, the average length of stay was 7.7 days, which reflects the benefit for both the patient and the hospital, since shorter stays lead to a decreased costs (Román, 2012). In this study, the identification and early treatment by the use of the training strategy for patients with sepsis allowed a reduction in mortality to 30.6%, a result lower than that found in a cohort in Europe<sup>4</sup>. This study on quality indicators in sepsis treatment has shown that training strategies may motivate professionals to search for and continuously improve their knowledge and ability to solve different situations they face, thus improving the outcomes of patients with sepsis (Salazar, 2012).

## Conclusion

Sepsis is a disease that requires exhaustive and multidisciplinary research. Although it is difficult to adopt and implement a care protocol and apply improvement strategies, it is still the best way to achieve greater adherence and improve patient prognosis. After implementation of the tool, the mortality rate for patients with sepsis was lower and their hospital stays were shorter. Additionally, there was a marked decrease in the transfer of patients with sepsis to the ICU, institutional performance in the detection of the first organ dysfunction increased, and the initial administration of antibiotics improved.

## REFERENCES

AMIB.org [Webpage]. São Paulo: SPREAD- Sepsis Prevalence Assessment Database. (en línea) (Acceded 25 Jul 2015). Available in: <http://www.amib.org.br/detalhe/noticia/estudo-revela-que-brasil-ainda-tem-alta->

- prevalencia-de-mortalidade-por-sepse-infeccao-generalizada-em-todas-as-regioes-do-pais/.
- Armero EG, Yébenes JCR, Vendrell MJB. Implementación de una estrategia en formato código para mejorar el manejo de la sepsis grave comunitaria en hospitales comarcales sin UCI. Universidad Autónoma de Barcelona, 2014 (N. del T.: En español: [tesis]).
- Bloos F, Rüdgel DT, Rüdgel H, Engel C, Schwarzkopf D, Marshall JC, *et al.* Impact of compliance with infection management guidelines on outcome in patients with severe sepsis: a prospective observational multi-center study. *Critical Care*. 2014;18:42.
- Bruhn AC, Pairumani RM, Hernandez GP. Manejo del paciente, en shock séptico. *Revista Médica Clínica Las Condes*. 2011;22(3):293-301.
- Clèries M. Epidemiologia de la Sèpsia Greu a Catalunya. Jornada tècnica sobre el Continu Assistencial en el Maneig de la Sèpsia Greu [en línea]. Actualización: 03 de Julio de 2013. Fecha de consulta: 20 de febrero de 2016. Disponible en: [http://www.gencat.cat/salut/botss/html/ca/dir3667/2013\\_07\\_03\\_m\\_cleries.pdf](http://www.gencat.cat/salut/botss/html/ca/dir3667/2013_07_03_m_cleries.pdf).
- Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, *et al.* Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock. 2012. *Critical Care Medicine and Intensive Care Medicine*. 2013;41:580-637.
- Espichán MM. Strategies for improving survival in patients with severe sepsis. *Acta Médica Peruana*. 2010;27(4):302-309.
- Gaieski DF, Edwards JM, Kallan MJ, Carr BG. Benchmarking the Incidence and Mortality of Severe Sepsis in the United States. *Critical Care Medicine*. 2013;41:1167-1174.
- Girardis M, Rinaldi L, Donno L. 2009. Effects on management and outcome of severe sepsis and septic shock patients admitted to the intensive care unit after implementation of a sepsis program: a pilot study. *Critical Care*. 13(5):143.
- Hernández G, Bruhn A, Castro R, Reguera T. 2012. The holistic view on perfusion monitoring in septic shock. *Critical Care*. 2012;18:280-6.
- Ilas online.org [página de internet]. Características clínicas y factores de riesgo para morbilidad en pacientes sépticos internados en cuidados intensivos de hospitales públicos y privados brasileños. (accedido 15 Feb 2016). Disponible en: <http://www.ilas.org.br/>.
- Ilas online.org [página de internet]. São Paulo: Instituto Latino Americano da Sepse; 2015. (en línea) (Actualizada: 01 Jul 2015; accedido 10 Ago 2015). Available in: <http://www.ilasonline.org.br/index-modal.php#close>.
- Kauss IAM, Grion CMC, Cardoso LTQ, Anami EHT, Nunes LB, Ferreira GL, *et al.* The epidemiology of sepsis in a Brazilian teaching hospital. *Brazilian Journal of Infectious Diseases*. 2010; 14:264-270.
- Koenig A, Picon PD, Feijó J, Silva E, Westphal GA. Estimativa do impacto econômico da implantação de um protocolo hospitalar para detecção e tratamento precoce de sepse grave em hospitais públicos e privados do sul do Brasil. *Revista Brasileira de Terapia Intensiva*. 2010; 22(3):213-219.
- Koury JCA, Lacerda HR, Barros AJN. Characteristics of septic patients in an intensive care unit of a tertiary private hospital from Recife, northeast of Brazil. *Revista brasileira de terapia intensiva*. 2006;18 (1):52-58.
- Levy MM, Artigas A, Phillips GS. Outcomes of the Surviving Sepsis Campaign in intensive care units in the USA and Europe: a prospective cohort study. *The Lancet Infectious Diseases*. 2012;12:919-924.
- Martin JB, Wheeler AP. Approach to the Patient with Sepsis. *Clinics in Chest Medicine Journal*. 2009;30(1):1-16.
- Mayr FB, Yende S, Angus DC. Epidemiology of severe sepsis. *Virulence Journal*, 2014;5:4-11.
- Peake SL, Delaney A, Bailey M, Bellomo R, Cameron PA, Cooper DJ, *et al.* Goal-directed resuscitation for patients with early septic shock. *The New England Journal of Medicine*. 2014;371:1496-1506.
- Pérez AL, Rosell EC, Lacosta MD, Dardet CA, Selles JU, Mendonza CLM. Clinical pathway intervention compliance and effectiveness when used in the treatment of patients with severe sepsis and septic shock at an Intensive Care Unit in Spain. *Revista Latino-Americana de Enfermagem*. 2012;20(4):09.
- Ponce JIL, Vilcapoma FV. Características clínicas de los pacientes con sepsis severa admitidos a una unidad de cuidados intensivos. *Revista Peruana de Medicina Interna*. 2008;21(4):139-142.
- Quintero RA, Martínez CA, Gamba JD, Ortiz I, Jaimes F. Adherence to international guidelines on early management in severe sepsis and septic shock. *Biomedica*. 2012;32:449-56.
- Rhodes A, Phillips G, Beale R, Cecconi M, Chiche JD, De Backer D, *et al.* The Surviving Sepsis Campaign bundles and outcome: results from the International Multicentre Prevalence Study on Sepsis (the IMPReSS study). *Intensive Care Med*. 2015;41(9):1620-8.
- Rivers E, Nguyen HB. Early Goal-Directed Therapy in the treatment of severe sepsis and septic shock. *N Engl J Med*. 2001;345(19):1368-77.
- Rocha LL, Pessoa CMS, Corrêa TD, Pereira AJ, Assunção MSC, Silva E. Current concepts on hemodynamic support and therapy in septic shock. *Revista Brasileira de Anestesiologia*. 2015;65(5):395-402.
- Román IP, Varela AIC, Pérez WQ, Rodríguez MR, Reinoso SA. Sepsis: a strategy of training in Primary Health Care and hospital emergencies. Indicators of quality in the care of patients. *Revista de Ciencias Médicas de Pinar del Río*. 2012;16(3):120-138.
- Romero C, Hernández G. Initial resuscitation bundle and monitoring tissue perfusión in severe sepsis. *Revista Medicina Chile*. 2013;141:1173-1181.
- Romero CP, Cornejo RR, Tobar EA, Gálvez RA, Llanos OV, Castro JO. Reanimación protocolizada del shock séptico. *Revista HCUCH*. 2008;19:127-141.
- Salazar N, Griñen H, Jirón M, *et al.* Impacto del cuidado Multidisciplinario en los desenlaces clínicos [Segurancadopaciente.com](http://segurancadopaciente.com) [página de internet]. São Paulo: Comitê Científico do Programa Brasileiro de Segurança do Paciente – PBSP. (en línea) (Acceded 12 Ago 2015). Available in: <http://www.segurancadopaciente.com/>.
- Silva AQ, Sobrinho EB. Análise de medidas de combate a sepse em Unidade de Terapia Intensiva. Hospital de Clínicas Gaspar Vianna, 2015 (N. del T.: In portuguese: [tesis]).
- Tejedo A, Pazos E, Peters S, Botet C. Implementación de un “Código Sepsis Grave” en un servicio de urgencias. *Emergencias*. 2009; 21:255-61.
- Vásquez AL, Gil CL, Regidor AL. New therapeutic alternatives for severe sepsis in the critical patient. A review. *Medicina Intensiva*. 2011;35(4):236-245.

Vicente M. Escalas pronósticas en la Unidad de Terapia Intensiva. *Revista de Medicina Crítica y Terapia Intensiva*. 2012;26(4):234-241.

Yoshihara JC, Okamoto TY, Queiroz LT, et. al. Análise descritiva dos pacientes com sepse grave ou choque séptico e fatores de risco para mortalidade. *Semina: Ciências Biológicas e da Saúde*. 2011;32(2):127-134.

Zanon F, Caovilla JJ, Michel RS, Cabeda EV. Sepse na Unidade de Terapia Intensiva: Etiologias, Fatores Prognósticos e Mortalidade. *Revista Brasileira de Terapia Intensiva*. 2008;20(2):128-134

Zapata LMM, Jaimes FB. Fisiopatología, importancia y utilidad del lactato en pacientes con sepsis. *IATREIA*. 2010;23(3):278-285.

\*\*\*\*\*