Resuscitation Strategies in Early Septic Shock: A Survey of Puerto Rico Intensive Care Physicians

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Objective: Severe sepsis and Septic Shock may progress in the first hours after presentation and has been associated with an increased mortality. Prompt recognition and treatment of early septic shock (ESS) may improve survival. The purpose of our study was to describe the monitoring and management strategies of ESS, within Intensive Care Units (ICU) in Puerto Rico (PR).

Methods: In order to achieve our objective, a self-administered survey, previously validated by the Canadian Critical Care Trials Group, was administered to 25 physicians during a Critical Care Medicine (CCM) Meeting. Questions about usual monitoring and resuscitation end-points were administered.

Results: Most of the participants were affiliated to community hospitals (84%) and 92% were pulmonary or CCM specialists, with more than 15 years of working experience (80%). Monitoring devices and parameters mostly used by at least 85% of the respondents were: Oxygen Saturation, Foley catheters, Telemetry, Heart Rate, Blood Pressure, and Urinary Output. Intra-arterial lines and Central Venous Pressure were less used. Most use normal saline (96%), as the initial fluid of resuscitation. Only 24% would use inotropes to improve perfusion.

Conclusions: Significant variability exists in the management of ESS among physicians in the ICU in PR. Compared to other studies, fewer physicians in PR use invasive monitoring techniques. These results highlight the need for quality education and training in CCM as well as continuing education in the field. [*P R Health Sci J 2019;38:8-14*]

Key words: Resuscitation Strategies, Early Septic Shock, Early Goal Directed Therapy, Survey

Sepsis is a medical condition caused by an immune response against an infectious process. Hospitalizations in the United States (US) due to sepsis were 1,141,000 in 2008, a 70% increase from 2000 (1). Mortality for severe sepsis and septic shock has been estimated to be between 20 to 50% and 40 to 80% respectively. Sepsis is the tenth leading cause of death in the US (2). The progression in severity of disease develops in the first hours after presentation (3). Early recognition and aggressive treatment increases the chances of survival. These important interventions that would make the difference between survival and death take place either in the emergency department (ED), hospital ward, or intensive care unit (ICU).

In 2001, the concept of early goal directed therapy (EGDT) was introduced by Rivers et al. It combined hemodynamic assessment based on traditional parameters such as vital signs, central venous pressure (CVP), and urinary output (U/O), with the measuring of mixed venous saturation, lactic acid, pH, and base excess (3). Suggested protocol included placing a central venous catheter capable of measuring central venous saturation (ScvO2) and CVP, as well as an arterial line for continuous blood pressure (BP) monitoring. It included administering crystalloid or colloid fluid bolus to achieve a CVP between 8 and 12mmHg. If mean arterial pressure (MAP) is less than 65mmHg, vasopressors were started. If MAP was above 90mmHg, vasodilators were started. If ScvO2 was less than 70%, blood was transfused until hematocrit (Hct) was at least 30%. If ScvO2 persisted below 70% despite Hct above 30%, dobutamine was started. According to Rivers et al, these interventions resulted in a mortality reduction in all patients analyzed and in the septic shock sub-group. This was paired with a decrease in the incidence of sudden cardiovascular collapse (3).

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Recently, there have been several studies questioning the mortality benefit of EGDT, when compared to usual care. These multi-center studies have not found an improvement in outcomes when using protocoled-based resuscitation as compared to usual care (4-6). There was no benefit of the mandated use of central venous catheterization and central hemodynamic monitoring in all patients (4).

Between January and May 2004, a survey was conducted in Canada, among intensivists, to obtain information about monitoring, resuscitation end-points, fluid administration, blood transfusion threshold, and use of inotropes. A self-administered scenario-based questionnaire was used. This survey was validated by 17 members of the Canadian Critical Care Trials Group (CCTG). The study found out that there was substantial variation in the resuscitation practices of adult patients with ESS (7). This finding is consistent with the lack of a definitive recommendation in literature concerning resuscitation strategies. A similar assessment was made in Puerto Rico (PR) when a self-administered questionnaire among physicians in training and attending physician demonstrated there were deficiencies in knowledge of the published guidelines for the management of sepsis (8).

The purpose of this study was to describe the monitoring techniques, resuscitation end-points, fluid administration, blood transfusion threshold, and use of inotropes when managing early septic Shock (ESS) among physicians who work at ICU in PR. Our hypothesis was that significant variability exists in the monitoring, resuscitation end-points, fluid administration, blood transfusion threshold, and use of inotropes when managing ESS among physicians who work at ICU in PR.

Materials and Methods

A self-administered survey, previously validated by the CCTG, was administered to the physicians attending the PR Pneumology Society 2015 meeting. Inclusion criteria were physicians who worked at an adult ICU. Residents, fellows, pediatric intensivists, pediatric emergency physicians, and retired physicians were excluded. A letter explaining the questionnaire and its purpose was handed personally to each physician. All responses were voluntary and anonymous. Surveys were collected in a sealed box. This study was submitted and approved by the Ponce School of Medicine and Health Sciences Institutional Review Board.

The survey consisted of two clinical scenarios of patients with septic shock. The first had three associated questions to evaluate usual monitoring parameters, volume resuscitation end-points, and resuscitation fluid preferences. The second had two associated questions to evaluate hemoglobin threshold for red blood cell (RBC) transfusion and use of inotropes in response to ScvO2. Information on physician and institution characteristics including age, sex, primary specialty (emergency, medical, surgical, anesthesia, or other), years in practice (0 to 5, 6 to 10, 11 to 15, or more than 15), number of weeks (0 to 10, 11 to 20, or >20) worked in the ICU or ED making shifts, and academic affiliation (university, veterans affairs, or community) was also gathered. No identifiable data was collected.

Resuscitation interventions were dichotomized into often/always and sometimes/rarely/never. Monitoring parameters and volume resuscitation end-points were represented using a scale of: often/always, sometimes, and rarely/never. A variable summing the number of more invasive interventions with often/always use was created and recoded into the following categories: 0 intervention, 1-3 interventions and ≥4 interventions.

The characteristics of the participants of the study and their practices were summarized using descriptive statistics, mean (sd) for quantitative data and frequencies and percentages for categorical variables. The relationship between demographic variables and selected interventions with often/always use were evaluated by means of the Fisher's exact test. Multinomial logistic regression was employed to quantify the effect size of the associations between demographic characteristics and use of more invasive methods. Results are expressed as odds ratios (OR) with its corresponding 95% confidence intervals (CI). All statistical tests were two-sided and significance was set at a p-value of 0.05. Data analysis was conducted in Stata (Version 12.1, College Station, TX, USA).

Results

Forty-nine of the 75 physicians who were invited completed the survey. This represents a response rate of 65.3%. The mean age of participants was 50.2 years and 69% were men. Most physicians (91%) were either pulmonary physicians or critical care medicine (CCM) specialists, and had more than 15 years of working experience (69%). Over two-thirds (70%) worked more than 20 weeks each year at the ICU and 18% worked at the ED more than 20 weeks per year. The majority of participants (93%) were affiliated to community hospitals (Table 1).

Interventions recorded by physicians are shown in Table 2. The following monitoring devices or parameters were reported to be used always or often by at least 85% of the respondents: oxygen saturation (100%), Foley catheter (94%), telemetry (98%), HR (98%), BP (100%) and U/O (96%). Intra-arterial lines (30%) and CVP (39%) were used either often or always less frequently. Only one person (2%) used pulmonary catheter with a frequency of always or often. Peripheral perfusion (76%), CVP (36%), sustained CVP (30%), ScvO2 (18%), MVO2 (11%), Cardiac Output/Index (CO/CI) (18%), sonography (6%), pulse pressure variability (6%) and lactic acid measure (4%) were used less frequently either often or always (Figure 1).

In terms of resuscitation interventions, 0.9% normal saline solution (NSS) was used always or often by (98%) of responders as the initial resuscitation fluid. Ringer's lactate (19%) and albumin (4%) was chosen respectively by responders to use it in an often or always basis. No one use pentastarch with these frequencies (Figure 2).

Table 1. Description of study population

	n (%)
Age, mean (sd), n=43	50.2 (7.8) years
Sex, n=45	
Male	31 (69)
Female	14 (31)
Specialty, n=45	
Medicine critical care medicine	15 (33)
Pulmonary medicine	22 (44)
Pulmonary + Critical care medicine	5 (11)
Years in practice, n=45	
0-5	5 (11)
6-10	7 (16)
11-15	2 (4)
>15	31 (69)
Weeks at ICU, n=44	
0-10	9 (20)
11-20	4 (9)
>20	31 (70)
Weeks at ER, n=44	
0-10	35 (80)
11-20	1 (2)
>20	8 (18)
Institution affiliation, n=43	
University	3 (7)
VA	0
Community	34 (79)
University + VA	0
University + Community	3 (7)
VA + Community	3 (7)

Forty-four percent of physicians reported using a RBC transfusion threshold of 7g/dL if the ScvO2 was 50% in a patient who had reduced metabolic demand and optimized intravascular volume and blood pressure, while 11% used a threshold of 10g/dL. Sixty-two percent of respondents said that they would use inotropes, either often or always, if the ScvO2 remained below the set goal after volume resuscitation and blood pressure optimization, minimization of metabolic demand, and administration of RBC to improve oxygen delivery. While 22% of respondents said they rarely/never would use inotropes. With regards to the amount of more invasive interventions used in an often/always basis, 43% of physicians had no interventions of this type, 35% had 1-3 interventions and 22% reported using 4 or more.

When evaluating the relationship between demographic variables and selected interventions, there were no statistically significant associations found, but some results deserve being pointed out. Experience, view as either years of age or years in practice, might be related with physicians' practices. Older physicians were more likely to use Ringer's lactate but were less likely to use a lower RBC transfusion threshold (Hgb ≤7g/dL) and inotropes than younger or less experienced physicians.

The results of the multinomial logistic regressions are shown in table 3 and 4. Relative to the no invasive interventions category, women had a higher odds of using 1-3 and ≥4 interventions than men, although it was no statistically significant [OR (95%CI): 2.45 (0.56-10.68) and 1.50 (0.26-8.64), respectively]. Also, physicians who worked more than

Table 2. Interventions used with either always or often frequencies

	n (%)
ICU monitoring strategies	
Oxygen saturation	49 (100)
Foley catheter, n=48	45 (94)
Telemetry	48 (98)
Intra-arterial blood pressure, n=47	14 (30)
Central venous pressure	19 (39)
CVP with continuous Central venous saturation, n=48	6 (13)
Pulmonary artery catheter, n=48	1 (2)
Fluids	
Normal saline	48 (98)
Ringer's lactate, n=47	9 (19)
5% Albumin, n=48	1 (2)
25% Albumin, n=47	2 (4)
Pentastarch, n=48	0
Other, n=48	0
ICU Resuscitation end points	
Heart rate, n=48	47 (98)
Blood pressure, n=48	48 (100)
Peripheral perfusion, n=45	34 (76)
Urine output, n=49	47 (96)
Central venous pressure, n=47	17 (36)
Sustained rise in CVP, n=46	14 (30)
Central venous saturation, n=45	8 (18)
Mixed venous saturation, n=44	5 (11)
Cardiac output/Cardiac index, n=45	8 (18)
Sonography	3 (6)
Pulse pressure variability	3 (6)
Lactate levels	2 (4)
Hemoglobin threshold for PRBC transfusion (g/dL), n=45	
6	5 (11)
7	20 (44)
8	10 (22)
9	5 (11)
10	5 (11)
11	0
12	0
Inotropes, n=45	28 (62)
More invasive interventions	
0	21 (43)
1-3	17 (35)
≥4	11 (22)

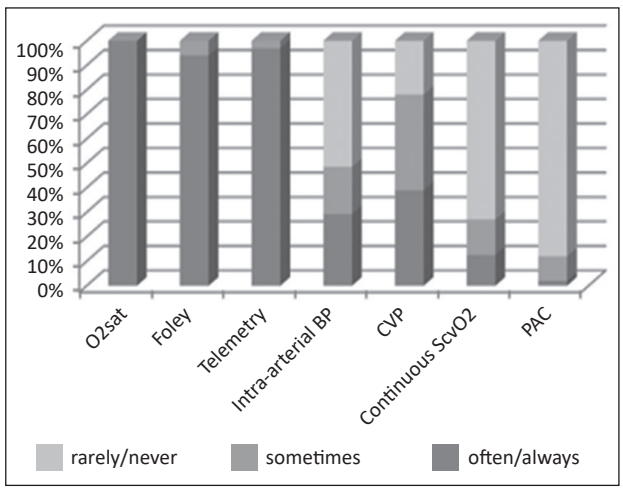

Figure 1. Monitoring Parameters used by Intensive Care Unit Physicians.

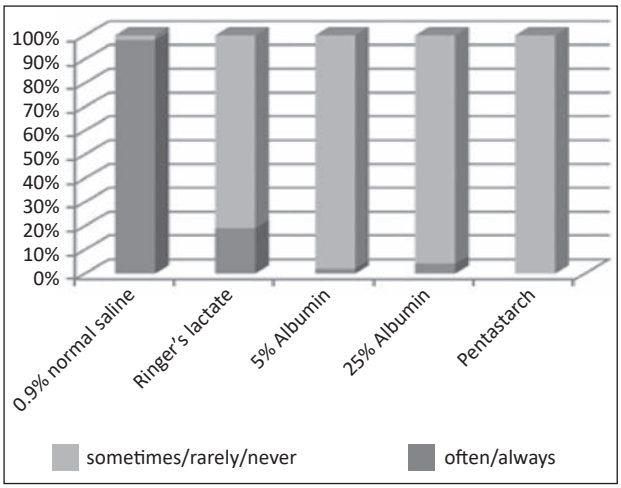

Figure 2. Resuscitation Fluids used by Physicians.

10 weeks at ED per year had a higher odds of using 1-3 and ≥4 interventions than physicians who annually worked 0-10 weeks at ED [OR (95%CI): 11.20 (1.19-105.13) and 1.78 (0.10-31.98), respectively] (Table 3). Considering there might be different working conditions based on physician's affiliation, the same analysis was conducted considering only those respondents with an exclusive appointment to community hospitals. Similar results were observed for the majority of demographic variables, except for years of experience. When evaluating the no interventions category as reference, physicians with more than 15 years in practice had a higher odds of using 4 or more invasive interventions than less experienced physicians [OR (95% CI): 3.50 (0.33-36.86)] (Table 4).

Table 3. Relationship between demographic variables and number of more invasive interventions used with either always or often frequencies

	Number of more invasive interventions				Multinomial logistic regression*	
					1-3 interventions	≥4 interventions
Variable	0	1-3	≥4	p-value	Crude OR (95% CI)	Crude OR (95% CI)
Age						
≤45	5 (36)	5 (36)	4 (29)	0.75	1	1
46-55	4 (27)	7 (47)	4 (27)		1.75 (0.31-10.02)	1.25 (0.19-8.44)
56-60	7 (50)	5 (36)	2 (14)		0.71 (0.13-3.87)	0.36 (0.05-2.77)
Sex						
Male	14 (45)	10 (32)	7 (23)	0.46	1	1
Female	4 (29)	7 (50)	3 (21)		2.45 (0.56-10.68)	1.50 (0.26, 8.64)
Years in practice						
0-15	5 (36)	6 (43)	3 (21)	0.92	1	1
>15	13 (42)	11 (35)	7 (23)		0.71 (0.17-2.96)	0.90 (0.16-4.92)
Weeks at ICU						
0-10	3 (33)	4 (44)	2 (22)	0.89	1	1
>10	15 (43)	12 (34)	8 (23)		0.60 (0.11-3.21)	0.80 (0.11-5.82)
Weeks at ER						
0-10	16 (46)	10 (29)	9 (26)	0.04	1	1
>10	1 (11)	7 (78)	1 (11)		11.20 (1.19-105.13)	1.78 (0.10-31.98)

*Reference category: No intervention

Discussion

Most of the physicians, who work at the ICU in PR, do not strictly abide to the protocol suggested by Rivers et al of EGDT in the treatment of severe sepsis and septic shock (3). Most of them use less invasive techniques to guide therapy in ESS. In addition, they use end points obtained through less invasive means to monitor response to the different interventions. More invasive techniques such as intra-arterial lines CVP, ScvO2, MVO2, and CO/CI are only seldom used. Less than half of the physicians who participated in this study use the CVP or ScvO2 as monitoring strategies with a frequency of often or always. Both of these parameters were pivotal to the EGDT protocol. These management strategies differences are consistent with the later studies (4-6) that have questioned the improvement in mortality that was originally described by Rivers et al protocol (3). It has been argued that early resuscitation, which is the standard of care, is the basis of improved outcomes in mortality, rather than the particular monitoring method being used (9-10). In addition, lack of resources and availability of continuous ScvO2 monitoring may be another reason precluding the consistent use of this monitoring strategy by the surveyed physicians. The need for central venous catheter placement may also contribute the lack of systematic use of continuous ScvO2 as a monitoring strategy and endpoint.

In contrast to similar study by McIntyre et al. conducted among Canadian ICU physicians, using the same survey instrument (7), physicians who work at the ICU in PR use invasive monitoring techniques with less frequency than their Canadian counterparts. While their often/always frequency of using, intra-arterial BP monitoring, CVP, and pulmonary artery catheter (PAC) was 96.6%, 89.2%, and 24.7% respectively (7), PR physicians use it only 29%, 39%, and 2% respectively. Both studies demonstrated rare utilization of continuous ScvO2 (9.8% vs 12.5%). The lack of use of invasive monitoring techniques, have also led to the limited use of resuscitation endpoints obtained by these means. Therefore our results showed that CVP, sustained rise in CVP, and CO/CI are used with a frequency of often or always only by 30%, 36%, and 18% of the physicians respectively, while they are used by 78.7%, 69.3%, and 24.9% respectively, by their Canadian counterparts. The utilization of ScvO2 and MvO2 was low in both populations (18% vs 19.4% and 11% vs 14.9%) (7).

Even though there is no definitive guideline in the literature concerning which should be the initial resuscitation fluid of choice in ESS, there appeared to be consensus in this aspect among the

Table 4. Relationship between demographic variables and number of more invasive interventions used with either always or often frequencies in physicians affiliated to community institutions only

	Number of more invasive interventions				Multinomial logistic regression*	
					1-3 interventions	≥4 interventions
Variable	0	1-3	≥4	p-value	Crude OR (95% CI)	Crude OR (95% CI)
Age						
≤45	5 (45)	4 (36)	2 (18)	0.95	1	1
46-55	4 (33)	4 (33)	4 (33)		1.25 (0.19-8.44)	2.50 (0.29-21.40)
56-60	4 (44)	3 (33)	2 (22)		0.94 (0.13-6.87)	1.25 (0.12-13.24)
Sex						
Male	11 (50)	5 (23)	6 (27)	0.32	1	1
Female	4 (33)	6 (50)	2 (17)		3.30 (0.63-17.16)	0.92 (0.13, 6.56)
Years in practice						
0-15	5 (50)	4 (40)	1 (10)	0.57	1	1
>15	10 (42)	7 (29)	7 (29)		0.88 (0.17-4.47)	3.50 (0.33-36.86)
Weeks at ICU						
0-10	1 (20)	2 (40)	2 (40)	0.48	1	1
>10	14 (50)	8 (29)	6 (21)		0.29 (0.02-3.67)	0.21 (0.02-2.84)
Weeks at ER						
0-10	13 (52)	5 (20)	7 (28)	0.02	1	1
>10	1 (13)	6 (75)	1 (13)		15.60 (1.48-164.38)	1.86 (0.10-34.44)

*Reference category: No intervention

physicians who participated in the survey. Almost all prefer crystalline solutions over colloids, mostly 0.9% NSS, as the initial fluid of resuscitation. Only a minority used colloids, mainly albumin. The use of 0.9% NSS was preferred over albumin even though, according to literature, they may be considered clinically equivalent treatments for intravascular volume resuscitation (11). The preference of using crystalloids over colloids could be mostly due to availability and costs.

When compared to McIntyre's study, our survey demonstrated that physicians who work at the ICU in PR have similar resuscitations fluid predilections. In our study 98% of physicians used 0.9% NSS as the initial fluid of resuscitation with a frequency of either often or always, compared to the 84% obtained in the Canadian survey (7). However, in our study, none of the surveyed physicians chose pentastarch, while in the Canadian counterpart, 51.3% of physicians use it with a frequency of often or always, in the management of ESS (7). This difference could be mostly secondary to costs.

Even though there appears to a consensus in the literature, in terms of that a restrictive transfusion strategy with an Hgb transfusion threshold of 7.0g/dL is as effective and possibly superior to a liberal threshold of 10.0g/dL (12-13), less than half of the survey participants (45%) use 7.0g/dL of Hgb concentration as the lowest transfusion threshold. This finding is similar to the one obtained by McIntyre et al. where only 42.2% use a restrictive transfusion threshold (7).

Sixty-two percent would use inotropes in their patients with a frequency of often or always if the ScvO2 remained below the set goal. However, even though more than half said they would use inotropes in response to a low ScvO2 despite adequate resuscitation with fluids and blood products, only 17% of the physicians answered that they would monitor that parameter frequently. This apparent incongruence has also been described in previous studies (7), and suggests that although seldom used, when available and in some cases, physicians use it to guide therapy.

None of the associations between the demographic characteristics and monitoring strategies, outcomes, choice of resuscitation fluid, PRBC transfusion threshold, or use of inotropes reached statistical significance. However, there are interesting tendencies when the data is analyzed by taking into account years of clinical practice. Older physicians and those with more years of practice were more likely to use Ringer's lactate as the initial fluid of resuscitation, and less likely to use a PRBC transfusion threshold of less than 7g/dL or inotropes, when compared to younger physicians and those with less years of experience. Then tendency toward use of PRBC transfusion thresholds of more than 7g/dL and less use of inotropes might be explained by the fact that the evidence that supports a restrictive transfusion strategy and EGDT is rather recent when compared to the years in practice (more than 15) of the more experienced ICU physicians in the representative sample. These physicians were trained using different thresholds and strategies when managing ESS.

When the community hospital affiliated sample is analyzed as an independent group, physicians with more than 15 years in practice had a higher odds of using 4 or more invasive interventions than less experienced physicians. This tendency might be explained by the recent questioning of the utility of static measures such as CVP and capillary wedge pressure versus dynamic measures in determining fluid status and responsiveness when managing ESS. Physicians with more recent training are less prone to use these more invasive monitoring devices or parameters.

For our study, an acceptable response rate of 60% of the sample was regarded as adequate, considering that the survey was handed personally. Our response rate was 65.3%. A study that analyzed 350 studies of postal or electronic surveys of healthcare workers (1996-2005) described an average response rate of 57.5% in postal surveys among healthcare professionals (14). A previously meta-analysis including 178 studies showed a mean response rate among mail surveys published in medical journals of approximately 60%. However, published surveys of physicians had a mean response rate of only 54%, and those of non-physicians had a mean response rate of 68% (15).

A potential limitation to this study includes the small sample that was obtained. Another potential limitation was that the survey itself may have caused a response bias. The

hypothetical scenario and the available responses, might have led participant physicians to overestimate the use of certain monitoring strategies or endpoints. Another limitation is that the length of the survey, which included clinical scenarios, may have prompted some of the participants not to thoroughly read the questions and responses, affecting the quality and veracity of the responses.

Conclusions

Severe sepsis and septic shock are syndromes with high associated mortality that have been estimated to be as high as 50% and 80% respectively (2). Early recognition and aggressive treatment increases the chances of survival. This survey helped to describe the management of ESS in a representative sample of physicians who work at ICU in PR. However, it might not reflect the actual practice of all the physicians who manage this condition at the ICU, ED, or hospital ward. Further surveys that include physicians who work at ED and hospital wards are needed in order to evaluate the real actual practice of managing ESS, in the settings where it might initially be identified. In addition, further studies should be conducted to establish clear guidelines and standardized the management of ESS.

This survey suggests that physicians who work at the ICU in PR prefer less invasive monitoring techniques and resuscitation endpoints obtained through less invasive approaches to guide resuscitation efforts and evaluate intervention response in patients with ESS. Significant variabilities exist in the management of ESS among physicians. This in partly may be due to the lack of established guidelines and the recent questioning of EGDT. The lack of a specific guideline, and furthermore, the need in PR of a protocol for the management of sepsis have been addressed in the past by other authors (16-18). In addition, literature available at the time of training might influence the management strategies of this condition, thus creating a generational educational gap in CCM. Our data showed differences in management that varied among the years of experience. Vigo et al have previously documented the need for sepsis management awareness, and have proposed to establish treatment protocols (16). The result of our study, highlight the need for quality CCM education in PR. PR houses only one ACGME accredited CCM Training Program since 2001, and two since April 2017. Considering the constant changes in literature and recommendations regarding sepsis management, our study supports there is still need for a consensus in management and may raise awareness in regards of the relevance of continuing education and forums that could promote discussion in the management of the critically ill.

Resumen

Objetivo: La sepsis severa y el choque séptico pueden progresar en las primeras horas después de la presentación inicial y han sido asociados con un aumento de la mortalidad. El reconocer y tratar el choque séptico en estadio temprano (ESS, por sus siglas en inglés) puede mejorar la sobrevida. El propósito de nuestro estudio fue describir las estrategias de monitoreo y manejo de ESS, en las unidades de cuidados intensivos (UCI) en Puerto Rico (PR). Métodos: Para lograr nuestro objetivo, una encuesta auto-administrada, previamente validada por el Grupo Canadiense de Estudios Clínicos en Cuidado Critico, fue administrada a 25 médicos durante una Conferencia de Medicina de Cuidado Crítico (MCC). Se administraron preguntas sobre las metas de monitoreo y resucitación utilizadas. Resultados: La mayoría de los participantes eran afiliados a hospitales de la comunidad (84%) y 92% eran especialistas de Neumología o MCC, con más de 15 años de experiencia (80%). Los dispositivos de monitoreo y parámetros utilizados por al menos el 85% de los encuestados fueron: saturación de oxígeno, sondas Foley, telemetría, frecuencia cardíaca, presión arterial y diuresis. Las líneas intra-arteriales y la presión venosa central fueron menos utilizadas. La mayoría utiliza solución normal salina (96%) como el líquido inicial en la resucitación. Sólo el 24% consideraría utilizar fármacos inotrópicos para mejorar la perfusión. Conclusión: Existe una variabilidad en el manejo de ESS entre los médicos de las UCI en PR. En comparación con otros estudios, los médicos en PR utilizan menos las técnicas de monitoreo invasivas. Estos resultados resaltan la necesidad de una educación de calidad y entrenamiento en MCC, así como la educación continua en el campo.

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