Impact of Septic Shock Hemodynamic Resuscitation Guidelines on Rapid Early Volume Replacement and Reduced M

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Background: *Septic shock is one of the most serious conditions associated with high mortality. We recently developed a modified septic shock management guideline focusing on rapid restoration of hemodynamics by using clinical endpoint. Our aim was to analyze patients' outcomes following the guideline implementation.*
Material and Method: *A retrospective review of hemodynamic data sheet and clinical outcomes of patients admitted to medical ICU and medical Wards and during June 2004 and February 2006.*
Results: *One hundred and four patients' records were retrieved. The patients' mean age was 62.5 ± 18.6 year. Their mean APACHE II score were 24.9 ± 6.7 and the overall mortality was 59%. Sixty eight patients (65.4%) underwent guideline directed therapy (guideline group). The guideline group received higher volume resuscitation from the first hour of resuscitation (1,016.3 ± 675.0 ml vs. 521.4 ± 359.2 ml, p < 0.001) to the forty eighth hour (10,096.9 ± 3,256.1 ml vs. 8,067.3 ± 2,591.9 ml, p = 0.006). More of them achieved the therapeutic goal within 6 hours (86.8% vs. 44.4%, p < 0.001) and their hospital mortality was lower (41.2% vs. 69.4%, p = 0.008). When analyzing differences between those who survived and those who died, more of the surviving patients underwent guideline directed treatment (79.5% vs. 55%, p = 0.012). They received higher volume replacement from the first hour to the end of the twelfth hour (first hour 1,098.0 ± 723.0 vs. 660.9 ± 478.9 ml, p < 0.001; the end of the twelfth hour 3,746.6 ± 1,799 vs. 3,014.1 ± 1,579.9 ml, p = 0.038) and more of them achieved the therapeutic goal within 6 hours (95.5% vs. 55%, p < 0.001). Multivariate analysis of factors associated with mortality disclosed APACHE II score, volume resuscitation more than 800 ml in the first hour and achievement of the therapeutic goal within 6 hours.*
Conclusion: *Implementation of our modified septic shock guideline is associated with rapid initial volume replacement, prompt achievement of therapeutic goal and improved outcomes. Volume resuscitation greater than 800 ml in the first hour is associated with better survival.*

Keyword: *Septic shock, Hemodynamic guideline, Fluid therapy*

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Septic shock is one of the most serious conditions associated with high mortality despite advances in medical technology. Attempts to improve its outcomes have been made and the resulting evidence based information[1-3] was reported in the form of Surviving Sepsis Campaign guidelines. These included early goal directed therapy, early administration of appropriate antibiotics together with source control and organ support. Appropriate uses of corticosteroids, activated protein C are also recommended in patients with specific indications.

Using these evidence based therapies, our institution has developed hemodynamic management guidelines. The purpose is to improve treatment outcomes, namely reduced mortality, reduced organ failure and shortened ICU length of stay. We report here

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the retrospective review of the patients' outcomes following implementation of the guidelines. Factors affecting these outcomes were explored and analyzed.

Material and Method

Patients

The clinical records from the patients with septic shock who were admitted to the hospital during June 2004 and February 2006 were retrieved. Septic shock was defined as shock with evidences of systemic inflammation together with identifiable sources of infection. We excluded the patients who were under 18 years old, patients with "Do not resuscitate" orders, patients with hypovolemic and/or cardiogenic shock, and patients with inappropriate data recording. Basic characteristics of the patients, nature of infection, uses of the guideline, details of volume replacement and uses of inotrope and vasopressor were recorded. The patients' clinical progression and outcomes were noted. During this study period, the decision whether or not to follow the septic shock management guidelines depended on the primary attending physicians.

The hemodynamic management of septic shock guidelines

As shown in Fig. 1, the guidelines emphasize early restoration of tissue perfusion (within 6 hours). First, volume resuscitation with normal saline solution or other isotonic crystalloid is given rapidly at the rate of 500-1000 ml in the first half hour while the patient's blood pressures, jugular venous pressure (JVP) and/or central venous pressure (CVP) are monitored. The goal includes a mean blood pressure of 65 mmHg or greater and a central venous pressure of 8-12 mmHg. Norepinephrine or dopamine is administered to raise the blood pressure towards the goal if intravascular volume proved adequate as judged by the CVP above. Thereafter, signs of adequate tissue perfusion including urine output (> 0.5 ml/kg/hour) and normalization of arterial pH are also assessed and, if abnormal, packed red cell or dobutamine will be started. Pack red cell infusion is indicated in patients with hematocrit below 30%. For

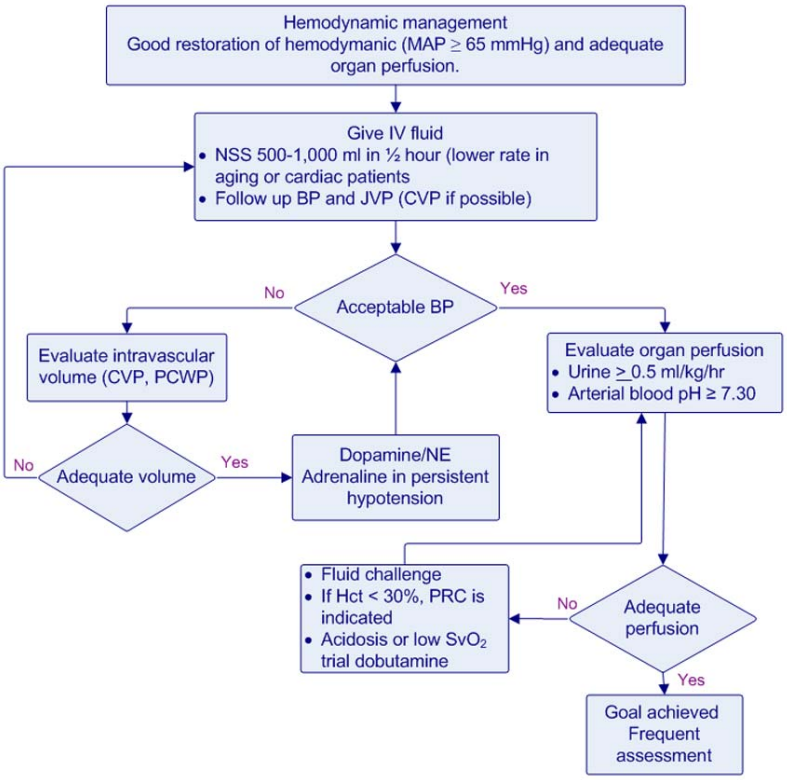

Fig. 1 Hemodynamic management guideline of septic shock (MAP = mean arterial blood pressure, JVP = jugular venous pressure, CVP = central venous pressure, PCWP = pulmonary capillary wedge pressure and NE = nor epinephrine)

those who have a hematocrit of 30% or higher, dobutamine will be given.

Statistical analysis

The data for categorical variables were compared between the patients who underwent guideline directed therapy (guideline group) and those who did not (non guideline-group) by Chi-square method. The comparison of variables from the survivor and non-survivor group was also made. The continuous variables data were summarized with the use of mean ± SD. Statistical tests for continuous variables were performed by independent sample t-test. The multivariate analysis to identify the factors that predict mortality among septic shock patients was performed by Binary logistic regression model analysis. The p-value less than 0.05 was accepted as statistically significant. The SPSS version 11.5 was used for statistical analysis.

Results

One hundred and four patients were included and 44.2% were male. The mean aged was 62.5 ± 18.6 years. The average admission duration was 23.9 ± 24.9 days and the overall mortality rate was 59%. Most of the patients (88.5%) had at least one co-morbid disease, among which malignancy was the leading condition, followed by atherosclerotic disease, hypertension, during immunosuppressive treatment and diabetes mellitus, respectively. No proportional difference was noted between the patients who survived (surviving group) and those who did not (non surviving group). As for the source of infection, respiratory tract was the most common (49.5%), followed by genitourinary tract (19.4%), intra-abdominal infection (9.7%), skin and soft tissue infection (6.8%), bacteremia without identified site of infection (3.9%), catheter related bacteremia (1.0%) and unknown source of infection (9.7%). Bacterial pathogens were identified in 63% of the patients. Of these, gram negative bacteria were the most common 49%, gram positive bacteria 9.7% and other organism 5%. Positive blood cultures were reported in 37.6 percent of patients. There was no significant difference between the surviving and the non-surviving group according to sites and types of bacterial infection. Focusing on the guideline usage, sixty-eight patients underwent this therapeutic scheme (guideline group), while 36 did not (non-guideline group). As shown in Table 1, no difference in baseline characteris-

Table 1. Patients' baseline characteristics according to therapeutic modality

Clinical variables	Non - guideline (n = 36)	Guideline (n = 68)	p
Age (year)	64.6 ± 17.1	61.4 ± 19.4	ns
Body temperature (°c)	38.7 ± 1.7	38.5 ± 1.4	ns
Systolic BP (mmHg)	72.6 ± 11.0	74.8 ± 15.6	ns
Diastolic BP (mmHg)	40.3 ± 14.6	44.9 ± 12.0	ns
Mean arterial BP (mmHg)	51.8 ± 10.8	54.6 ± 12.1	ns
Heart rate (beat/min)	109 ± 16	118 ± 21	0.037
Respiratory rate (/min)	28 ± 6	27 ± 5	ns
Blood urea nitrogen (mg/dl)	44.1 ± 36.5	39.4 ± 29.9	ns
Creatinine (mg/dl)	1.8 ± 1.1	2.0 ± 1.3	ns
Glasgow coma score	10.2 ± 4.4	11.3 ± 4.3	ns
Hematocrit (%)	29.3 ± 7.0	30.7 ± 6.3	ns
Hemoglobin (g/dl)	9.8 ± 2.3	10.1 ± 2.1	ns
White blood cell count (/mm^3)	13,054 ± 8,758	17,955 ± 19,567	ns
Polymorphonuclear cell (%)	74.3 ± 25.7	73.8 ± 20.9	ns
Band form (%)	2.4 ± 5.7	7.2 ± 11.1	ns
Lymphocyte (%)	12.3 ± 16.8	12.8 ± 14.5	ns
Mononuclear cell (%)	3.5 ± 2.8	6.4 ± 7.7	ns
Eosinophil (%)	0.2 ± 0.3	0.7 ± 1.5	ns
Platelet count (per mm^3)	180,158 ± 187,216	209,459 ± 154,768	ns
Albumin (g/dl)	2.4 ± 0.6	2.4 ± 0.6	ns
Organ failure (median)	3	3	ns
APACHE II score	25.4 ± 7.9	24.7 ± 6.5	ns

tics was noted except the heart rate, which was higher in the guideline group. Table 2 demonstrated therapeutic variables and the results. The guideline group received higher volume resuscitation from the first hour of resuscitation (1,016.3 ± 675.0 ml vs. 521.4 ± 359.2 ml, $p < 0.001$) to the forty eighth hour (10,096.9 ± 3,256.1 ml vs. 8,067.3 ± 2,591.9 ml, $p = 0.006$). There was no difference in the uses of dopamine, norepinephrine, dobutamine and hydrocortisone. More patients in the guideline group achieved the therapeutic goal within 6 hours (86.8% vs. 44.4%, $p < 0.001$) and their hospital mortality was lower (41.2% vs. 69.4%, $p = 0.008$). In addition, Kaplan-Meier analysis (Fig. 2) demonstrated that the guideline group had significant lower mortality rate than non-guidelines group [HR, 0.50; 95% CI, 0.10-0.69: $p = 0.006$].

The patients' characteristics and therapeutic variables between the surviving group and the non-surviving group were mostly similar (Table 3), except for the Glasgow Coma Score, number of organ failure and the APACHE II score, which were worse in non-survived group. More survived patients underwent guidelines directed therapy than the non-survived (79.5% vs. 55%, $p = 0.012$). They received higher volume replacement from the first hour of treatment (1,098.0 ± 723 ml vs. 660.9 ± 478.9 ml, $p < 0.001$) to the end of the twelfth hour (3,746.6 ± 1,799 ml vs. 3,014.1 ± 1,579.9 ml, $p = 0.038$). No difference in the uses of vasopressors, inotropes, and steroids was observed (Table 4). Nor epinephrine was prescribed more in the non-surviving group, and the difference was not significant. In addition, more patients in the surviving group achieved the therapeutic goal than the other (95.5% vs. 55% respectively, $p < 0.001$). For prediction of hospital survival with the use of ROC curves (Fig. 3), volume resuscitation in first hour greater than 800 ml had a sensitivity of 67.5% and a specificity of 65.5%. The area under the ROC curve was 0.712 ($p < 0.001$). Moreover, volume resuscitation in first 2 hours of more than 1,300 ml had a sensitivity of 60% and a specificity of 67.3% with the area under the curve which was 0.700 ($p = 0.001$).

Clinical parameters and therapeutic variables

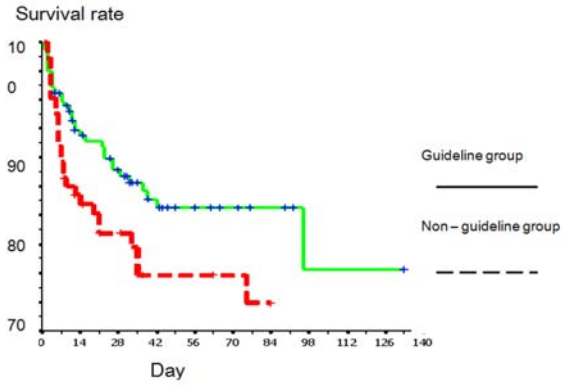

Fig. 2 Kaplan-Meier estimates of survival of the patients in the guideline group and the non-guideline group. There was a significantly lower mortality rate in the guideline group [HR, 0.50; 95% CI, 0.10-0.69: $p = 0.006$]

Table 2. Treatment variables and outcomes of the guideline and non-guideline group

Treatment variables	No guideline (n = 36)	Guideline (n = 68)	p
Volume replacement (from the beginning of resuscitation, ml)			
To the end of the first hour	521.4 ± 359.2	1,016.3 ± 675.0	<0.001
To the end of the second hour	938.8 ± 612.1	1,455.8 ± 872.8	0.003
To the end of the sixth hour	1,840.9 ± 960.3	2,525.3 ± 1,483.6	0.017
To the end of the twelfth hour	2,747.7 ± 1,270.8	3,647.8 ± 1,834.5	0.012
To the end of the twenty fourth hour	4,536.0 ± 1,664.5	6,083.5 ± 2,375.4	0.002
To the end of the forty eighth hour	8,067.3 ± 2,591.9	10,096.9 ± 3,256.1	0.006
Inotrope and vasopressors			
Dopamine (% use)	67.6%	83.8%	0.076
Norepinephrine (% use)	38.2%	33.8%	ns
Dobutamine (% use)	0%	4.4%	ns
Hydrocortisone (% use)	21.9%	36.1%	ns
Outcomes			
Achieved therapeutic goal within 6 hours (%)	44.4%	86.8%	<0.001
Hospital mortality (%)	69.4%	41.2%	0.008

Table 3. Patients' baseline characteristics in non-survived and survived group

	Non-survived group (n = 60)	Survived group (n = 44)	p
Age (years)	63.3 ± 17.6	61.5 ± 20.1	ns
Body temperature (°c)	38.5 ± 1.6	39.7 ± 1.3	ns
Systolic BP (mmHg)	72.0 ± 15.0	76.7 ± 12.4	ns
Diastolic BP (mmHg)	41.5 ± 14.8	45.6 ± 10.0	ns
Mean arterial BP (mmHg)	52.3 ± 13.0	55.6 ± 9.4	ns
Heart rate (beats/min)	114.0 ± 21.1	114.8 ± 17.8	ns
Respiratory rate (/min)	27.9 ± 5.8	26.2 ± 4.3	ns
Glasgow coma score	10.1 ± 4.7	12.1 ± 3.5	0.023
Blood urea nitrogen (mg/dl)	45.9 ± 35.4	34.3 ± 26.3	ns
Creatinine (mg/dl)	2.1 ± 1.3	1.7 ± 1.1	ns
Hemoglobin (g/dl)	9.7 ± 2.2	10.3 ± 2.1	ns
White blood cell (per mm^3)	15,188 ± 13,278	17,446 ± 20,224	ns
Albumin(g/dl)	2.3 ± 0.6	2.6 ± 0.6	ns
Organ failure (median)	3	2	<0.001
APACHE II score	27.2 ± 6.9	22.1 ± 6.1	<0.001

Table 4. Treatment variables of the non-surviving and surviving group

Treatment variables	Non-survived (n = 60)	Survived (n = 44)	p
Guideline use (%)	55%	79.5%	0.012
Volume replacement (from the beginning of resuscitation, ml)			
To the end of the first hour	660.9 ± 478.9	1,098.0 ± 723.0	<0.001
To the end of the second hour	1,038.2 ± 696.0	1,590.6 ± 886.6	0.001
To the end of the sixth hour	1,965.9 ± 1,063.3	2,690.4 ± 1,582.4	0.009
To the end of the twelfth hour	3,014.1 ± 1,579.9	3,746.6 ± 1,799.0	0.038
To the end of the twenty fourth hour	5,269.4 ± 2,213.1	5,933.4 ± 2,327.4	0.160
To the end of the forty eighth hour	9,070.9 ± 3,160.2	9,866.5 ± 3,213.8	0.256
Inotrope and vasopressors			
Dopamine (% use)	74.6%	83.7%	ns
Norepinephrine (% use)	42.4%	25.6%	0.096
Dobutamine (% used)	1.7%	4.7%	ns
Hydrocortisone (% used)	28.3%	35%	ns
Achieved therapeutic goal within 6 hours (%)	55.0%	95.5%	<0.001

associated with mortality of septic shock patients were analyzed (Table 5). Univariate analysis demonstrated the significance of Glasgow coma score, APACHE II score, guideline use, volume replacement greater than 800 ml in the first hour and the achievement of the therapeutic goal within 6 hours of resuscitation. However, when multivariate analysis was made, the significant predictive factors for were limited to APACHE II score (Odds ratio 1.09, 95% CI 1.01-1.18, p = 0.03), volume replacement greater than 800 ml in the first hour (Odds ratio 0.32, 95% CI 0.12-0.86, p = 0.01) and the achievement of the therapeutic goal after resuscitation (Odd ratio 0.13, 95% CI 0.03-0.64, p = 0.02).

Discussion

The above data can be summarized as follows: in our institution, septic shock posed a high mortality risk. The patients who underwent treatment according to the hemodynamic resuscitation guidelines had better treatment outcomes. They got more fluid and achieved the therapeutic goal more than the non guideline group, which led to better survival. On the other hand, the surviving group as a whole had lower disease severity and higher proportion of them received

Table 5. Clinical parameters and therapeutic variables associated with mortality

	Non-survived (60)	Survived (44)	p	Multivariated Odds ratio [95% CI]	p
Glasgow coma score (mean±SD)	10.1±4.7	12.1±3.5	0.023		
APACHE II (mean±SD)	27.2±6.9	22.1±6.1	<0.001	1.09[1.01-1.18]	0.03
Guideline use (%)	55.0	95.5	<0.001		
Receiving volume resuscitation > 800 ml in 1st hr (%)	55.0	79.5	0.012	0.32[0.12-0.86]	0.01
Achieved therapeutic goals within 6 hours (%)	36.8	66.7	0.004	0.13[0.03-0.64]	0.02

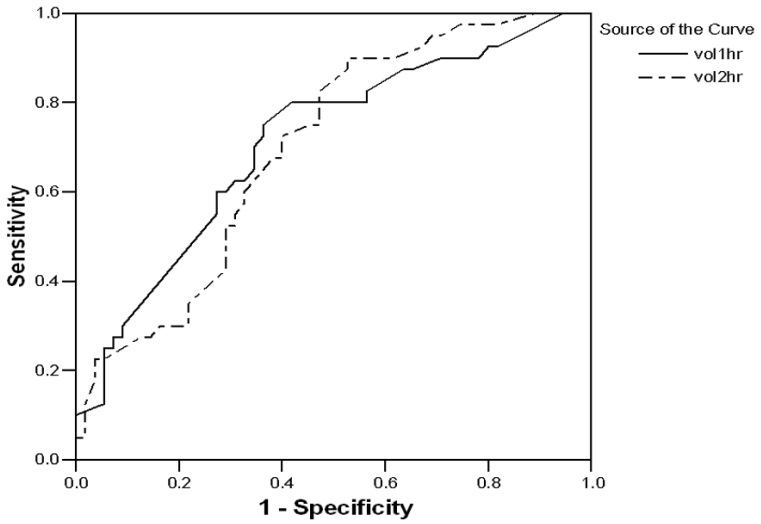

Fig. 3 Receiver operating characteristic (ROC) curve performed to access the accuracy of volume resuscitation during 1st and 2nd hour in predicting in-hospital survival. The areas under the ROC curve of volume resuscitation during first hour (vol 1 hr) and first 2 hours (vol 2 hr) were 0.712 (P<0.001) and 0.700 (P=0.001), respectively.

guidelines directed therapy. They received more volume replacement in the early hours and achieved the therapeutic goal within six hours more often than the non surviving group.

Since the report of early goal directed therapy of septic shock[1] and Surviving Sepsis Campaign[2,3], there have been tremendous changes in septic shock management. Apart from source identification, source control and early administration of antibiotics, local guidelines and bundles aiming to prompt restoration of patients' hemodynamics and tissue perfusion were subsequently developed[4-8]. Despite differences in certain details in various institutions, these reports disclose improved outcomes, and does ours. Patients in whom the guidelines were fully employed (guideline group), namely: initial rapid fluid administration, timely administration of vasopressors and inotropes and usages of the clinical endpoint at which organ perfusion was restored, had better outcomes. The proportion of the patients who achieved the therapeutic goal within 6 hours was higher in the guidelines group than those in whom the guidelines was not fully employed (86.8% vs. 44.4%, p < 0.001) and, also, the mortality was lower (41.2% vs. 69.4%, p = 0.008). Additional important find-

ings, as noted from Table 2, were that the guidelines group received a higher amount of fluid, especially in the first hour (1,016.3 ± 675 ml vs. 521.4 ± 359.2 ml, $p < 0.001$) and this significance continued through the first 48 hours. Thus, guidelines directed therapy resulted in more aggressive fluid therapy and there were more patients attained therapeutic goal achievement which gave rise to better survival. In retrospect, when analyzing differences between those who survived and those who died (Table 3), the severity of illness in the survived group was lower. Again, a higher proportion of the surviving group underwent guidelines directed therapy (55% vs. 79.5%, $p = 0.012$). More fluid was given in this group during the early hours, especially in the first hour (1,098 ± 723 ml vs. 660.9 ± 478.9 $p < 0.001$). Further, difference in proportion of the patients ($p = 0.01$) who received volume replacement greater than 800 ml in the first hour between the survived group and the expired group as judged by multivariate analysis was also identified. Our conclusion regarding guideline use and the survival rate is that guideline directed therapy resulted in lower mortality and the most important intervention associated with the improving outcomes was the amount of fluid given in the early hours. This result not only parallels others[4-8], but also stresses the importance of early fluid replacement. Rapid refill of volume depleted vascular bed is one of the most important parts of hemodynamic support in septic shock. This will further emphasize the need for strict adherence to such guidelines or treatment protocols.

The amount and rate of fluid given initially in septic shock treatment are important major issues. Crystalloid replacement of 500-1000 ml or colloid replacement of 250-500 ml in the first half hour is recommended in most guidelines[2,3,9], with the evidence grading of level E and 1C respectively. In our review, the survivors received higher a amount of fluid from the first hour to 12 hours and more patients who survived received intravenous fluid greater than 800 ml during the first hour. In addition, the Kaplan-Meier curve demonstrated lower mortality in patients who received first-hour volume replacement greater than 800 ml (HR, 0.28; 95% CI, 0.10-0.69: $p = 0.006$). Thus, our findings strongly support the Surviving Sepsis Campaign's recommendation that initial fluid replacement is necessary and an amount of fluid greater than 800 ml in the first hour is critical.

Regarding the end point of resuscitation, which is the point where tissue perfusion is restored, we note that, currently, no precise end point has been defined[10]. In addition to clinical parameters, indexes of global oxygenation, namely arterial pH, mixed venous oxygen saturation (SvO_2), central venous oxygen saturation ($ScvO_2$) and arterial lactate are used in many guidelines[11]. In addition, organ specific perfusion parameters such as gastric tonometry, sublingual capnometry and near infrared spectrometry are also introduced. Some interventions prove beneficial in some studies. In Rivers' early goal directed study[1], mean arterial pressure, central venous pressure and venous oxygen saturation in central veins ($ScvO_2$) were used to define end points. Despite the uses of clinical parameters only (target blood pressures and urine flow of greater than 0.5 ml kg/hour), more patients in the guidelines group reached the therapeutic goal than the others and they had a much lower mortality rate. Thus, the using of clinical end point may be applicable in septic shock resuscitation, except in patients with anuria from acute renal failure or end stage renal disease. The assessment of adding central venous oxygen saturation, lactate dynamics together with clinical end point on patients' outcomes is in process in our institution.

Conclusion

Our findings add more insight to septic shock therapy. Modified hemodynamic management guidelines directed treatment resulted in more fluid administration in the early hours which led to speedy restoration of hemodynamics. This approach improved survival. Intravenous isotonic crystalloid replacement of more than 800 ml in the first hour was associated with lower mortality.

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แนวทางการรักษาภาวะ septic shock, การให้สารน้ำ และผลลัพธ์การรักษา

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ภาวะช็อกจากการติดเชื้อเป็นภาวะที่พบได้บ่อยและมีอัตราตายสูง คณะผู้รายงานได้จัดทำแนวทางการรักษาโดยมุ่งหวังให้ผู้ป่วยพ้นจากภาวะช็อกโดยเร็ว ในการนี้ได้บันทึกการให้สารน้ำการให้ยากระตุ้นหัวใจและยาบีบหลอดเลือดและผลลัพธ์การรักษาในแบบบันทึก คณะผู้ศึกษาได้รวบรวมแบบบันทึกการรักษาของผู้ป่วยในช่วงเดือนมิถุนายน 2547 ถึงเดือนกุมภาพันธ์ 2549 จำนวน 104 ราย ผู้ป่วยมีอายุเฉลี่ย 62.5 ± 18.6 ปี มีค่าเฉลี่ยของ APACHE II score 24.9 ± 6.7 และมีอัตราตายโดยรวม 59% ผู้ป่วย 68 ราย (65.4%) ได้รับการรักษาตามแนวทางที่วางไว้ ผู้ป่วยกลุ่มนี้ได้รับสารน้ำในปริมาณที่มากกว่ากลุ่มที่ไม่ได้รับการรักษาตามแนวทางที่วางไว้ ตั้งแต่ชั่วโมงแรก (1,016.3 ± 675.0 ml vs. 521.4 ± 359.2 ml, p < 0.001) จนถึง 48 ชั่วโมงแรก (10,096.9 ± 3,256.1 ml vs. 8,067.3 ± 2,591.9 ml, p = 0.006) ผู้ป่วยกลุ่มนี้พ้นจากภาวะช็อกภายใน 6 ชั่วโมง ในจำนวนที่มากกว่า (86.8% vs. 44.4%, p < 0.001) และมีอัตราตายต่ำกว่า (41.2% vs. 69.4%, p = 0.008) เมื่อเปรียบเทียบกลุ่มผู้ป่วยที่รอดชีวิตกับกลุ่มที่เสียชีวิตพบว่า ในกลุ่มที่รอดชีวิตมีสัดส่วนของผู้ที่ได้รับการรักษาตามแนวทางที่วางไว้มากกว่า (95.5% vs. 55%, p < 0.001) โดยกลุ่มนี้ได้รับปริมาณสารน้ำมากกว่าตั้งแต่ชั่วโมงแรกจนถึง 24 ชั่วโมง (ชั่วโมงแรก 1,098.0 ± 723.0 vs. 660.9 ± 478.9 ml, p < 0.001; 24 ชั่วโมง 3746.6 ± 1799 vs. 3014.1 ± 1579.9 ml, p = 0.038) การวิเคราะห์ multivariate analysis พบว่า APACHE II score, การให้สารน้ำในชั่วโมงแรกของการรักษามากกว่า 800 ml และการพ้นจากภาวะช็อกภายใน 6 ชั่วโมง เป็นปัจจัยที่มีผลต่อการเสียชีวิตอย่างมีนัยสำคัญ โดยสรุปการใช้แนวทางการรักษาภาวะ septic shock ที่ได้วางไว้ ทำให้แพทย์เริ่มให้สารน้ำแก่ผู้ป่วยอย่างรวดเร็ว ผู้ป่วยพ้นจากภาวะช็อกได้เร็วขึ้นส่งผลให้ผลการรักษาดีขึ้นและอัตราตายลดลง การให้สารน้ำมากกว่า 800 มล. ในชั่วโมงแรกของการรักษาและการที่ผู้ป่วยพ้นจากภาวะช็อกภายใน 6 ชั่วโมงแรกของการรักษาสัมพันธ์กับการรอดชีวิตของผู้ป่วย