

The Effect of Implementing Acute Kidney Injury Care Bundle on Clinical Outcomes of Critically Ill Patients

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Abstract

Background: Healthcare quality and cost are major driving forces in healthcare delivery system. Evidence-based bundle of care, is a concept usually involves three to five structured interventions based on scientific evidence based, which when carried out consistently improve patient outcomes. AKI is one of the major complications of critical illness and its management, prevention and management can be achieved through AKI care bundle which aims to manage and prevent newly developed AKI in critically ill patients. **Objective:** To determine the effect of implementing acute kidney injury care bundle on clinical outcomes of critically ill patients. **Settings:** The study was carried out in the General ICUs namely; Casualty unit (unit I), General ICU (unit II, III) at Alexandria Main University Hospital, Egypt. **Subjects:** A convenient sample of 70 newly admitted adult patients aged 18-<60 years were included in this study. Patients who had preexisting AKI, chronic kidney disease and/or on renal replacement therapy were excluded from the study. The sample was equally assigned into two equal groups: group I, the control group (35 patients) and group II, the study group (35 patients). **Tools:** Two tools were used. Tool one: "ICU acquired AKI risk assessment". Tool two: "Clinical outcomes assessment tool". **Results:** The study showed that neither patients in the study group nor the control group had AKI on 1st day (baseline), however during 2nd to 7th day 0.0%, 14.3%, 8.6%, 0.0%, 0.0% and 0.0% of patients in the study group developed AKI compared to 14.3%, 42.9%, 45.7%, 20.0%, 28.6% and 22.9% of patients in the control group. **Conclusion:** Implementation of AKI care bundle interventions significantly decreased the occurrence of ICU acquired AKI. **Recommendations:** Critical care nurses should conduct a baseline assessment to identify high risk patients for development of ICU acquired AKI.

Keywords: Acute kidney injury, Care bundles, Clinical outcomes, Critically ill patients.

Introduction

Healthcare quality and cost are major driving forces in healthcare delivery system. Evidence-based bundle of care, is a concept developed by the Institute for Healthcare Improvement usually involves three to five structured interventions based on scientific

evidence based, which when carried out consistently improve patient outcomes. Many of these bundles have focused on reduction and prevention of hospital acquired infections. These bundles include ventilator associated pneumonia, catheter related blood stream infections, bed sores,

sepsis and acute kidney injury (AKI), which are considered preventable. Since AKI is

one of the major complications of critical illness, prevention and management can be achieved through AKI care bundle which aims to manage and prevent newly developed AKI in critically ill patients (Schiffl, 2018; Yazici & Bulut, 2018).

Acute kidney injury is one of complications that affect kidney structure and function in critically ill patients, affecting >50% of critically ill patients in ICUs (Kebar et al., 2018). ICU-acquired AKI is an abrupt reduction of glomerular filtration rate within 48 hrs of ICU admission. Critically ill patients are at increased risk for developing AKI during their ICU stay specifically due to critical illnesses and their management. Anemia, blood transfusion, hypertension, hypercholesterolemia, hypoalbuminemia, infection, sepsis, high risk surgery, and hemodynamic instability are common pathological causes affect critically ill patients and increase risk for ICU acquired AKI. Mechanical ventilation, nephrotoxin, use of inotropes, and contrast media (CM) are a common iatrogenic factors inducing ICU acquired AKI. A better understanding of the risk of ICU-acquired AKI and the identification of potentially pathological and iatrogenic causes is essential role of critical care nurses to reduce the global burden of AKI in critically ill patients (Huang et al., 2020; Kebar et al., 2018).

Importantly, an episode of AKI even mild is not only associated with short-term adverse outcomes but also long-term adverse outcomes. These adverse outcomes are include fluid overload, acid-base, electrolyte derangement, immune dysfunction and bleeding complications, development or progression of chronic kidney disease, end-stage kidney disease and

increased rates of mortality. (Broyles et al., 2021; Ostermann et al., 2020).

Current management guidelines for patients with AKI include early recognition of AKI risks and augmentation of supportive care to limit AKI progression. AKI care bundles consists of asset of evidence based interventions that is used to rapidly identification of patients at risk for AKI, therefore preventive measures can be started immediately to ensure adequate perfusions, maintain hemodynamic stability, prevent nephrotoxicity of drugs, adjust medication doses for renal clearance, control blood glucose level, and consider alternative to CM based imaging (Schiffl, 2018; Selby et al., 2021).

Although, AKI bundle is feasible, cost effective and easily implemented interventions in the ICUs, their applications are often limited secondary to difficulties in hourly monitoring and accurately recording UO, poor recognition of AKI in early stages in ICUs, and lack of knowledge and training of ICU health team about AKI care bundle. In most countries in the developing world, the number of nephrologists is insufficient (Logan et al., 2018). Therefore, AKI bundle provides collaborative interventions that can be easily implemented by primary care physicians, nurses and health care team who manage AKI patients using the collaborative measures included in AKI bundle (Schiffl, 2018; Selby et al., 2021). Up to our knowledge, there is no national studies tested the efficacy of AKI care bundle in critically ill patients. Therefore, this study conducted to determine the effect of implementing acute kidney injury care bundle on clinical outcomes of critically ill patients.

Aims of the Study

This study aims to determine the effect of implementing acute kidney injury care

bundle on clinical outcomes of critically ill patients.

Operational definitions in this study include primary outcomes such as:

▪ **Renal related outcomes:**

- Serum creatinine.
- Urine output.
- Cumulative fluid balance.

Research hypotheses

Critically ill patients who are subjected to AKI care bundle interventions exhibit decrease in development of AKI than those who are not subjected.

Materials and Method

Materials

Design: A quasi experimental research design was used to conduct this study.

Settings: This study was carried out in the General ICUs namely; Casualty unit (unit I), General ICU (unit II, III) at the Alexandria Main University Hospital. The general ICUs; Unit I, unit II and Unit III beds capacity is 12, 9 and 16 beds respectively.

Subjects: A convenient sample of 70 newly admitted adult patients aged 18-<60 years were included in this study. Patients who had preexisting AKI, chronic kidney disease and/or on renal replacement therapy were excluded from the study. The sample was randomly and equally assigned into two equal groups: group I, the control group (35 patients) and group II, the study group (35 patients). The study sample size was calculated by power analysis using (Epi-Info 7 program), population size=75 for 3 months, confidence level=95%, margin of error=5%, prevalence of the problem=50%, minimum sample size =65, and final sample size=70.

Tools: Two tools were utilized for data collection in this study.

Tool one: "ICU acquired AKI risk assessment"

It is developed by the researcher after reviewing the related literatures (Logan et al., 2018; Broyles et al.,2021) to assess critically ill patients for presence of factors predisposing to AKI such as hypovolemia, previous episode of AKI, and co-morbidities. Each element is scored on a dichotomous scale of yes (present) and no (not present).

Tool two: "Clinical outcomes assessment tool":

It is used to assess clinical outcomes of critically ill patients at risk for AKI. It consists of two parts.

Part I: "Renal related outcomes".

It is adopted from the Kidney Improved Disease Global Outcomes (KIDGO) (2020) to assess severity of AKI in critically ill patients. The KIDGO criteria classify AKI into three stages according to changes in serum creatinine level, urine output and need for CRRT. The KIDGO score is classified according to the severity labels into: mild: stage 1, moderate: stage 2, severe: stage 3.

Part II:" perfusion related outcomes".

It is developed by the researcher after reviewing the related literatures (Koeze, et al., 2020; Selby et al., 2021) to assess critically ill patients' perfusion status. Clinical variables used for assessing perfusion status include critically ill patients' level of consciousness, mean arterial pressure (MAP), capillary refill time, skin turgor, urine output and fluid loss.

Method

Approval from the Ethical Research Committee, Faculty of Nursing, Alexandria University was obtained. Permission to conduct the study was obtained from the administrative authorities of the previously

mentioned settings after explanation the aim of the study.

Part I of tool two was adopted from the Kidney Improved Disease Global Outcomes (KIDGO) (2020). While part II of tool one was developed by the researcher after reviewing the related literatures (Koeze et al., 2020; Broyles et al., 2021). Acute kidney injury care bundle implementation checklist was developed by the researcher in order to check the implementation of acute kidney injury care bundle. Part II of tool one was tested for content validity by five experts in the field of the study; three staff members from critical care and emergency nursing department, one staff members from clinical pharmacology department and one staff members from critical care medicine. The necessary modifications were done. A pilot study was carried out on eight patients who were admitted to intensive care units to test clarity and applicability of the study tools. Reliability of the tools were done using Cronbach's alpha test and results were 0.712 which is acceptable.

Data collection:

Data were collected by the researcher over a period of 7 consecutive months (from August 2021 to February 2022). All newly admitted patients were included in this study. Patient with preexisting AKI, chronic renal failure and/or on renal replacement therapy were excluded from the study. An informed written consent was obtained from conscious patients or witness consent for unconscious patients. It included the aim of the study, potential benefits, risks, discomforts from participation or withdraw from the study at any time, and the right to refuse to participate in the study. Patients' privacy, anonymity and confidentiality of the collected data were maintained during the implementation of the study. Data were collected from the control group firstly and after its completion, data were collected from the study group to prevent the

contamination between the control and study group that might affect the study results.

The study was conducted in three phases:

Phase I: Assessment phase

For both groups:

- The bio-demographic data of the studied patients was obtained and recorded upon admission.
- Critically ill patients were assessed for presence of factors predisposing to ICU acquired AKI; previous episode of AKI was assessed once on patients' admission and signs of volume depletion such as decreased responsiveness, tachycardia with systolic blood pressure ≤ 90 mmHg and MAP ≤ 60 mmHg and oliguria were assessed daily and recorded using part I of tool one.

Phase II: Implementation phase

For the control group:

- Patients were left to receive the routine hospital care which includes daily monitoring of urine output, renal function and discontinue of nephrotoxic antibiotics after rising in creatinine level.

For the study group:

- Patients were subjected to AKI care bundle started from admission to ICU and for 7 consecutive days through implementation of the following intervention:
- Critically ill patients arterial blood gases, serum lactate, cultures and urine for blood or protein were monitored daily and recorded using part I of tool two.
- Critically ill patients were assessed daily for new development of AKI in ICUs or progression of AKI stage using part I of tool two.
 - o The protective measures were started immediately by the researcher in collaboration with resident physician for critically ill patients who didn't develop

- AKI but at high risk. These measures include: -
- Fluid replacement with rapid infusion of 30ml/kg of isotonic crystalloid solution to quickly restore tissue perfusion in hypovolemic patients due to fluid losses.
 - Early norepinephrine infusion was started in combination with volume expansion in patients who had MAP \leq 60mmHg.
 - Antihypertensive drugs were discontinued in patients who developed relative hypotension (SBP \leq 90mmHg).
- The supportive measures were started immediately by the researcher in collaboration with resident physician for critically ill patients who developed ICU acquired AKI after their admission. These measures include: -
- Empirically nephrotoxic antibiotics were stopped and alternative non-nephrotoxic antibiotics were prescribed matching with local policies of the hospital.
 - Doses of renally excreted drugs were adjusted through two major approaches; lengthen the interval between doses or reduce the dose, or both
 - Glucose levels were monitored and insulin therapy was initiated.

Phase III: Evaluation phase

- Patients' outcomes were assessed daily for 7 consecutive days for both group.
- **Renal related outcomes** including new development of AKI after ICU admission were assessed and recorded using part I of tool two.
- **Perfusion related outcomes** including MAP, glasgow coma scale

and skin turgor were assessed and recorded using part II of tool two.

Statistical analysis

- Data were fed to the computer and analyzed using statistical package for social science (SPSS/version 20.0) software. Count and percentage were used to describe and summarize qualitative data. Mean and standard deviation used to describe quantitative data. Student t-test used to compare two sample means. The significance of the results was at the 5% level of significance.

Ethical considerations

- Written informed consent was obtained from patients. It includes the aim of the study potential benefits, risks and discomforts from participation and the right to refuse to participate in the study was emphasized to subjects. Patients' privacy and confidentiality of the collected data was maintained during implementation of the study. The patient has the right to withdraw from the study at any time.

Results

Table I represents **the distribution of the studied groups according to demographic data**. Concerning patients' age, this table shows that 42.9% of patients in the study group aged 50- \leq 60 years compared to 57.1% of patients in the control group. The mean age was 44.31 \pm 12.41 for the study group compared to 47.71 \pm 15.57 for the control group. In relation to **gender**, this table shows that 51.4 % of patients in the study group were males compared to 65.7% of patients in the control group with no statistical difference between two the two groups (p=0.225).

Table II represents **the distribution of the studied groups according to comorbidities**. It can be noted from this table that 54.3% of patients in the study group had hypertension compared to 42.9% of patients in the control group. In relation to DM, this table shows that 11.4% of patients in the study group had DM compared to 31.4% of patients in the control group with no statistical difference between the two groups ($p=0.126$). Regarding **previous episodes of AKI**, this table shows that 94.3% of patients in the study group didn't have previous episodes of AKI compared to 85.7% of patients in the control group with no statistical difference between the two groups ($p=0.232$).

Table III represents **the distribution of the studied groups according to the severity of illness**. As regard **EWS score**. It can be noted from this table that the mean score was 3.74 ± 1.54 for patients in the study group compared to 5.0 ± 1.59 for patients in the control group. In relation to **APACHE II score**, it can be noted that the mean score was 24.37 ± 4.52 for patients in the study group compared to 23.89 ± 4.56 for patients in the control group with no statistical difference between the two groups ($p=0.656$).

Table IV represents **the distribution of the studied groups according to fluid volume depletion over the seven consecutive days**. It can be noted from this table on 1st day (baseline) that 5.7% of patients in the study group had fluid loss compared to 5.7% of patients in the control group with no statistical difference between the two groups ($p=>0.999$).

Table V represents **the distribution of the studied groups according to the incidence of ICU acquired AKI over the seven consecutive days**. It can be noted from this table that neither patients in the study group nor the control group had AKI on 1st day (baseline), however during 2nd to

7th day 0.0%, 14.3%, 8.6%, 0.0%, 0.0% and 0.0% of patients in the study group developed AKI compared to 14.3%, 42.9%, 45.7%, 20.0%, 28.6% and 22.9% of patients in the control group. The differences between the study and control group regarding incidence of AKI on the days 2nd, 3rd, 4th, 5th and 6th were found to be a statistical significance where ($p=0.020$, $p=0.008$, $p=0.008$, $p=0.008$ and $p<0.001$ and) respectively.

Table IV represents **the distribution of the studied groups according to perfusion related outcomes over the seven consecutive days**. In addition to **perfusion related outcomes**, it can be noted that the mean MAP in the 1st day (baseline) was (87.14 ± 13.87) for the study group compared to (82.0 ± 16.27) for the control group. After implementation of AKI care bundle interventions, the mean MAP was 89.0 ± 35.34 for the study group compared to (84.0 ± 10.94) for the control group with a statistical significance differences between the two groups ($p=0.059$). In relation to GCS score, it can be noted that the mean GCS score in the 1st day was (12.49 ± 3.37) for the study group compared to (10.63 ± 4.33) for the control group. After implementation of AKI care bundle interventions, the mean GCS was (13.11 ± 2.83) compared to (10.97 ± 4.15) for the control group with a statistical significance differences between the two groups ($p=0.029$).

Regarding skin turgor, it can be noted that the mean skin turgor in the 1st day was (1.06 ± 0.24) for the study group compared to (1.19 ± 0.42) for the control group. After implementation of AKI care bundle interventions the mean skin turgor was (1.0 ± 0.0) for the study group compared to (1.22 ± 0.38) for the control group with a statistical significance differences between the two groups ($p=0.004$). As regard to SCVO₂, it can be noted that the mean

SCVO₂ on the 1st day was (66.57±1.63) for the study group compared to (64.29±2.15) for the control group. After implementation of AKI care bundle interventions, the mean SCVO₂ was (66.55±1.31) for the study group compared to (65.89±1.52) for the control group with a statistical significance differences between the two groups (p<0.001).

Discussion

Acute kidney injury is a growing problem worldwide, consuming a lot of resources and can be variable between high and low income countries (Fuhrman et al., 2018; Schaubroeck et al., 2021).

The findings of the present study showed that most of studied patients in both the study and control group were males and aged more than fifty years old. Most of them were admitted to ICU with central nervous disorders and respiratory disorder.

As regard **co-morbidities**, the current study findings showed that approximately half of the studied patients were hypertensive and majority of them had not previous episodes of AKI. In relation to the **severity of illness**, the current study findings showed that approximately half of the studied patients had low risk for organ failure and mortality when assessed using APACHE II, EWS and SOFA score.

As regard **fluid volume depletion**, the present study findings showed that the majority of the studied patients didn't have fluid volume depletion at the baseline and throughout the study time. The absence of fluid volume depletion throughout the study time may be due to continuous daily assessment of signs and symptoms of fluid volume depletion such as decreased responsiveness, tachycardia with systolic blood pressure ≤ 90 mmHg and mean arterial pressure ≤ 60 mmHg, oliguria, slow capillary refill time, dry mucous membranes, decreased skin turgor, cold clammy skin, and weak peripheral pulses by

the researcher with immediate fluid replacement after discussion with the resident physician. Also, the resident physician monitors signs and symptoms of fluid volume depletion and implement measures to maintain adequate fluid volume.

Regarding **renal outcomes**, the present study findings showed that the **occurrence of AKI** decreased in the study group throughout the study time compared to the control group. Decreased occurrence of new onset AKI in the study group may be explained by performing baseline (on admission) and daily assessment of high-risk patients for developing AKI using renal angina index, early monitoring of signs and symptoms of fluid volume depletion and rapid correction of hypovolemia by the researcher in collaboration with the resident physician. In addition to daily monitoring of renal function, serum electrolytes and acid base balance.

Also, this may be due to timely accurate intake & output charting. The nephrotoxic drugs were discontinued early and dosages for renally excreted drugs were reviewed in high risk critically ill patients based on renal angina index score in collaboration with resident physician.

The findings of the current study are supported with the result of Koeze et al. (2020) who conducted a prospective observational study to determine the effect of AKI care bundles in critically ill patients. They concluded that critically ill patients in the control group developed stage III AKI compared to those the intervention group who developed stage I AKI when subjected to SAVE THE KIDNEY care bundle.

Also, the findings of this study are contradictory to Schaubroeck (2021) who conducted a meta-analysis and concluded that the occurrence of AKI was not significantly decreased in patients exposed to an AKI care bundle compared to standard of care. Importantly, occurrence of more

severe stages of AKI was less frequent after implementation of AKI care bundle.

As regard *perfusion related outcomes*, the current study findings revealed that there was a significant difference between the study and control group throughout the study time. This may be explained by rapid replacement of fluid and early initiate of inotropic drugs by the researcher in collaboration with resident physician in delay response to fluid therapy.

The findings of the current study are similar to the result of Khanna et al. (2019) who conducted a retrospective cohort study to assess the association between lowest mean arterial pressure on each intensive care day. They concluded that increasing amounts of hypotension were strongly associated with renal injury in critically ill patients.

Conclusion

Based on the results of this study, it can be concluded that the implementation of AKI care bundle interventions significantly decreased the occurrence of ICU acquired AKI and significantly stabilized hemodynamic status of critically ill patients.

Recommendations

Based on the findings of this study, it can be recommended that:

- Critical care nurses should conduct a baseline assessment to identify high risk patients for development of ICU acquired AKI.
- Outreach Systems should emphasize on monitoring of renal function before and after hospital discharge as expanded role of critically care nurses.
- Replication of this study on a larger sample is needed to allow generalization of the finding.

Table (I) Comparison between the studied groups according to the demographic data

Demographic data		Groups				Test of significance
		Study (n=35)		Control (n=35)		
		N	%	N	%	
Age	<40	14	40.0%	11	31.4%	X ² =1.47 P=0.478
	40-49	6	17.1%	4	11.4%	
	50-≤60	15	42.9%	20	57.1%	
	Mean ±SD	44.31±12.41		47.71±15.57		t=1.01 p=0.316
Gender	Male	18	51.4%	23	65.7%	X ² =1.47 P=0.225
	Female	17	48.6%	12	34.3%	

χ²: Chi square test t: Student t-test p: p value for comparing between the studied groups

Table (II) Comparison between the studied groups according to co-morbidities.

Co-morbidities		Groups				Test of significance
		Study (n=35)		Control (n=35)		
		N	%	N	%	
None		12	34.3%	7	20.0%	X ² =7.19 P=0.126
Hypertension		19	54.3%	15	42.9%	
Diabetes mellitus		4	11.4%	11	31.4%	
Others		0	0.0%	2	5.7%	
Previous episode of AKI	No	33	94.3%	30	85.7%	X ² =1.43 P=0.232
	Yes	2	5.7%	5	14.3%	

Table (III) Comparison between the studied groups according to the severity of illness.

Severity of illness		Groups				Test of significance
		Study (n=35)		Control (n=35)		
		N	%	N	%	
Early warning score	Low risk (1-4)	20	57.1%	15	42.9%	X ² =1.44 P=0.487
	Intermediate risk (5-6)	11	31.4%	15	42.9%	
	High risk (≥7)	4	11.4%	5	14.3%	
	Mean ±SD.		3.74±1.54		5.0±1.59	
APACHE II	Low risk (≤25)	22	62.9%	22	62.9%	X ² =0.25 p=0.884
	Intermediate risk (25- <35)	10	28.6%	11	31.4%	
	High risk (≥35)	3	8.6%	2	5.7%	
	Mean ±SD.		24.37±4.52		23.89± 4.56	

APACHE II : Acute Physiology and Chronic Health Evaluation II

Table (IV) Comparison between the studied groups according to fluid volume depletion over the seven consecutive days.

Fluid volume depletion		Day													
		1 st (baseline)		2 nd		3 rd		4 th		5 th		6 th		7 th	
		N	%	N	%	N	%	N	%	N	%	N	%	N	%
No	Study (n=35)	33	94.3%	35	100.0%	35	100.0%	35	100.0%	35	100.0%	35	100.0%	35	100.0%
		2	5.7%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Yes	Control (n=35)	33	94.3%	32	91.4%	33	94.3%	33	94.3%	35	100.0%	34	97.1%	35	100.0%
		2	5.7%	3	8.6%	2	5.7%	2	5.7%	0	0.0%	1	2.9%	0	0.0%
Test of sig.		X ² =0.00 p>0.999		X ² =3.13 p=0.077		X ² =2.06 p=0.151		X ² =2.06 p=0.151		X ² =N/A -		X ² =1.01 p=0.314		X ² =N/A -	

Table (V) Comparison between the studied groups according to occurrence of ICU acquired AKI over the seven consecutive days

Occurrence of ICU acquired AKI		Day													
		1 st (baseline)		2 nd		3 rd		4 th		5 th		6 th		7 th	
		N	%	N	%	N	%	N	%	N	%	N	%	N	%
No	Study (n=35)	35	100.0%	35	100.0%	30	85.7%	32	91.4%	35	100.0%	35	100.0%	35	100.0%
Yes		0	0.0%	0	0.0%	5	14.3%	3	8.6%	0	0.0%	0	0.0%	0	0.0%
No	Control (n=35)	35	100.0%	30	85.7%	20	57.1%	19	54.3%	28	80.0%	25	71.4%	27	77.1%
Yes		0	0.0%	5	14.3%	15	42.9%	16	45.7%	7	20.0%	10	28.6%	8	22.9%
Test of sig.		X ² =N/A -		X ² =5.39 p=0.020*		X ² =7.00 p=0.008*		X ² =7.00 p=0.008*		X ² =7.00 p=0.008*		X ² =12.21 p<0.001*		X ² =0.20 p=0.656	

Table (IV) Comparison between the studied groups according to perfusion related outcomes throughout the study time

Clinical outcomes	Baseline assessment		Intervention (2 nd to 7 th day)		Test of sig
	Study (n=35)	Control (n=35)	Study (n=35)	Control (n=35)	
MAP(mmHg) Mean ±SD.	87.14±13.87	82.0±16.27	89.03±5.34	84.0±10.94	F=2.948 p=0.059*
GCS score Mean ±SD.	12.49±3.37	10.63±4.33	13.11±2.83	10.97±4.15	F=3.737 p=0.029*
Skin turgor (per sec) Mean ±SD.	1.06±0.24	1.19±0.42	1.0±0.0	1.22±0.38	F=5.92 p=0.004*
Capillary refill (per sec) Mean ±SD.	2.11±1.35	2.26±1.17	2.1±1.32	2.38±1.27	F=0.821 p=0.444
SCVO2% Mean ±SD.	66.57±1.63	64.29±2.15	66.55±1.31	65.89±1.52	F=12.567 p<0.001*

F: F-value computed from 2-way ANOVA for repeated measures (MANOVA) MAP: mean arterial pressure GCS: glasgow coma scale SCVO2%: central venous oxygen saturation

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