

ORIGINAL RESEARCH

INTENSIVE CARE

Correlation between central venous pressure and acute kidney injury in septic patients

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Abstract

Background & objective: Sepsis is a medical emergency that requires quick and adequate treatment. In various epidemiological studies it is said that 11–60 % of sepsis patients may suffer from acute kidney injury (AKI). The incidence is 23% in the severe sepsis and 51–64 % in septic shock patients. A number of studies reported that a high value of central venous pressure (CVP) is associated with high incidence and morbidity of AKI in sepsis. We conducted this study to compare a cutoff point of 8 mmHg of CVP with the incidence of AKI in sepsis patients admitted in ICU.

Methodology: This study is an observational analytical cohort prospective study. The sampling was done by consecutive sampling technique. Patients were assigned into 2 groups with each group consisting of 41 samples. CVP measurement was done manually. AKI were assessed by measuring the serum creatinine twice and examining the patient's urine. To analyze the relationship between CVP and the frequency of AKI, chi-square test was performed.

Results: Of the 41 subjects with CVP \geq 8 mmHg, 29 of them (60.4%) were diagnosed with AKI. Chi-square test revealed a significant correlation between target CVP and AKI incidence ($p = 0.025$). Also, age, sex, norepinephrine use and type of infection did not correlate with AKI incidence ($p > 0.05$). The only factor related to AKI significantly was CVP with RR 1.526 (95% CI: 1.04-2.24) and p-value of 0.025

Conclusion: In conclusion, a CVP target value of 8 mmHg or higher has a higher risk of AKI. The use of fluid therapy in managing sepsis requires strict fluid monitoring and evaluation.

Key words: Acute kidney injury; AKI, Central venous pressure; Fluid therapy; sepsis

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1. Introduction

Sepsis is a medical emergency that requires quick and adequate treatment. Currently sepsis is believed to be the body's systemic immunological response to infectious processes that can lead to end-stage organ dysfunction and death. Despite significant advances in the understanding of sepsis pathophysiology, hemodynamic monitoring, and resuscitation measures, sepsis remains one of the main causes of morbidity and mortality in critically ill patients. The mortality rate of sepsis is even greater than that of acute coronary syndrome or stroke.

The mortality reaches 30% in sepsis and 80% in sepsis shock.¹

Acute *Kidney Injury* (AKI) is a syndrome consisting of several clinical conditions, due to impaired renal function that occurs suddenly (within a few hours to several days) causing retention of residual nitrogen metabolism (urea-creatinine) and non-nitrogen with or without oliguria and it is influenced by the underlying disease.² The most common causes of AKI in patients with critical illness are sepsis and sepsis shock which contribute to more than 50% of AKI cases in the ICU.³ The incidence of Sepsis and AKI in critical patients

increases gradually and both showed a poor prognosis.^{3,4} Various epidemiological studies said that AKI in occurs in 11 - 60 % septic patients, 23 % severe septic patients and 51 - 64% in septic shock patients.²⁻⁴

In the Surviving Sepsis Campaign (SSC) Guidelines stated that one of the sepsis therapy targets is MAP \geq 65 mmHg and the central venous pressure target (CVP) 8 to 12 mmHg.⁵ Currently, however, there has been a lot of evidence suggesting the use of higher CVP values ultimately increases afterload resistance and renal backflow, resulting in a decrease in renal perfusion pressure that will eventually lead to the incidence and morbidity of AKI in sepsis.⁶⁻⁸ Previous studies, also revealed that an increase in CVP of 1 mmHg increases the chance of AKI incidence by 6%.⁹

On that account we conducted study to compare CVP $<$ 8 mmHg with CVP \geq 8 mmHg relating to the incidence of AKI in sepsis patients in ICU.

2. Methodology

This study was conducted in ICU of Dr. Moewardi General Hospital, Surakarta, by collecting patient data from July to December 2020. This is an observational analytical cohort prospective study to compare the incidence of AKI in sepsis patients with central venous pressure's target $<$ 8 mmHg to sepsis patients with central venous pressure target \geq 8 mmHg.

2.1. Subjects

The study samples were sepsis patients treated in the ICU of Dr. Moewardi General Hospital, Surakarta, from July to December 2020. The sampling was done by consecutive sampling technique. Patients were assigned into 2 groups with each group consisting of 41 samples. Group A was for sepsis patients with a target CVP $<$ 8 mmHg and Group B was for sepsis patients with a target CVP \geq 8 mmHg and monitored every 6 hours for 24 hours.

We included patients aged 19 - 64 years who had been diagnosed with sepsis either using QSOFA criteria or SOFA Score \geq 2. Patients with history of kidney disease, hypertension, and diabetes mellitus were excluded. Patients who died in less than 24 hours were dropped out from the study.

2.2. CVP Measurement

Measurement and monitoring of CVP were done manually following by determining the zero point manometer according to the height of the right atrium (estimated point as high as 4th intercostal space) in the midaxillary line, rotating the three-way so that the infusion fluid flows into the manometer to a limit of 20 - 25 cmH₂O, rotating the three-way so that the fluid in the manometer flows towards / into the patient's blood vessels.¹⁰ Observing fluid fluctuations contained in the

manometer, determine the amount of central venous pressure where the liquid moves steadily (this is the central venous pressure) expressed in cmH₂O then converted into mmHg (mmHg = cmH₂O/1.36) and returning to its original position.¹⁰ The CVP target we use is according to the Surviving Sepsis Campaign (SSC) Guidelines which stated that one of the sepsis therapy targets is MAP \geq 65 mmHg and the central venous pressure target (CVP) 8 to 12 mmHg.⁵

We also performed CVP measurement and monitoring using Transducer.¹⁰ Tool kits used to install transducers were heparin, infusion set, monitoring kit, transducer Edwards Lifesciences Services GmbH Efishonstrasse 6, three way, and pressure bag. We placed the patient in supine position and place the monitoring kit parallel to the right atrium (estimated as high as 4th intercostal space) at the line of right middle axilla, ensure no position changing in order to obtain accurate results. The infusion of the saline solution containing heparin was connected to monitoring kit, then to the transducer and to the monitor screen. Finally we connected the monitoring kit to the central venous catheter using three way. We made sure there was no air in the hose. We performed zeroing action on the monitor by closing the three way. We reopened the three way so that the big CVP value could be seen on the monitor.¹⁰

2.3. AKI Assessment

We followed the AKI definition by Kidney Disease Improving Global Outcome (KDIGO),¹¹ AKI is defined as any of the following: 1) increase in serum creatinine level \geq by 0.3 mg/dl within 48 hours; or 2) urine volume $<$ 0.5 ml/kg/h for 6 hours.¹¹ We examined serum creatinine level at least twice, when the patient was admitted to the ICU and 24 hours later, through venous blood. We monitored urine output every 6 and 24 hours to determine the severity of AKI.

2.4. Statistical Analysis

The data analysis was performed with SPSS ver. 22. Univariate analysis was done descriptively. *Chi-square* test was used for bivariate analysis.

4. Results

Eighty two patients diagnosed with sepsis treated in the ICU of Dr. Moewardi General Hospital, Surakarta were included in this study. Most study subject were over 40 years old (81.7%) with the mean age of 52.32 ± 12.39 y. The subjects were dominantly males (56.1%). Most subjects used vasopressor (54.9%). The most common type of infection was gastrointestinal infection (61%) (Table 1).

Of the 41 subjects with CVP \geq 8 mmHg, 29 (60.4%) of them were diagnosed with AKI. Subjects with CVP \geq 8 mmHg had a risk of AKI by 1.526 times greater than

Table 1: Cross-tabulation between AKI and characteristics of samples. Data given as n (%).

Characteristics	Total	AKI (n= 48)	Non-AKI (n=34)	p-value*
Age	> 40 years old	67 (81.7)	40 (83.3)	0.651
	≤ 40 years old	15 (18.3)	8 (16.7)	
Sex	Male	46 (56.1)	26 (54.2)	0.675
	Female	36 (43.9)	22 (45.8)	
Norepinephrine use	Yes	45 (54.9)	22 (53.7)	0.824
	No	37 (45.1)	19 (46.3)	
Type of Infection	Gastrointestinal	50 (61)	29 (64.4)	0.902
	Non-gastrointestinal	32 (39)	19 (39.6)	

Table 2: Cross-tabulation between CVP and AKI

CVP	AKI (n=48)	Non-AKI (n=34)	RR (95% CI)	p*
≥ 8 mmHg	29 (60.4)	12 (35.3)	1.526 (1.04 - 2.24)	0.025
< 8 mmHg	19 (39.6)	22 (64.7)		

*Chi-square test. Significant at $\alpha = 5\%$ ($p < 0.05$). Data given as n (%)

those with CVP < 8 mmHg (RR 1.526; 95% CI: 1.04 – 2.24). Chi-square test revealed a significant correlation between target CVP and AKI incidence ($p = 0.025$) (Table 2).

Bivariate analysis showed that age, sex, norepinephrine use and type of infection did not correlate with AKI incidence ($p > 0.05$). The only factor related to AKI significantly was CVP with RR 1.526 (95% CI: 1.04-2.24) and p-value of 0.025.

5. Discussion

Sepsis and sepsis shock have become the major health problems worldwide. This can be seen from the high mortality rate because of them. Efforts in resuscitation approaches for treating early disorders in sepsis patients have begun in 2001, SSC 2012, until the emergence of SSC 2018 from a series of 3 hours, 6 hours, to the initial 1 hour.⁵ This change is expected to be an initial change in resuscitation management, especially in the treatment of hypotension in septic shock.^{3,5}

Central venous pressure installation is commonly used as assessment of fluids, medications, parenteral nutrition, medicinal products and a measuring instrument to guide the administration of fluids for postoperative patients and critical patients.^{5,12,13} Monitoring is required for the use of CVP as a measurement of fluid administration.¹³ In the Surviving Sepsis Campaign Guidelines stated that one of the

Table 3: Bivariate analysis between factors related to AKI

Factors	Relative Risk (95%CI)	p*
Age	1.119 (0.670-1.869)	0.651
Sex	0.925 (0.643-1.330)	0.675
Norepinephrine use	1.098 (0.763- 1.579)	0.618
Type of Infections	0.977 (0.674-1.416)	0.902
CVP	1.526 (1.040-2.240)	0.025#

Data given as 95%CI (lower and upper limits)

targets of sepsis therapy is the target of central venous pressure (CVP) 8 to 12 mmHg, while the normal value of CVP is 0–5 mmHg.⁵

Legrand *et al.*¹⁴ in his study reported that CVP value was associated with the risk of developing AKI with OR 1.22 (95% CI 1.08-1.39; $p = 0.002$) and there was a correlation between CVP and AKI improvement in sepsis patients. The paradigm that targeting a high CVP can reduce the incidence of AKI should be evaluated.¹⁴

Many published reviews and clinical studies on Guyton theory in resuscitation reported that Guyton theory is indeed true, based on retrospective studies.¹⁵ In essence CVP is not an indicator of fluid adequacy or the final

indicator of resuscitation but an indicator of the occurrence of congenital organs - distal organs of the body in addition to a hint of a decrease in venous blood flow so that cardiac output decreases.^{15,16} If CVP increases steadily above normal then the pressure gradient will shrink so that the flow from the distal body will be difficult to enter the right heart which will cause a decrease in venous blood flow and decrease of cardiac output. Its impact causes congestion or obstruction in the distal organs that leads to AKI.^{15,16}

A study conducted by Chen *et al.*⁹ found that high CVP value can inhibit venous blood flow to the heart and disrupt microcirculation blood flow resulting in tissue congestion and organ failure. Increased CVP value will mainly harm renal hemodynamics and increase the risk of acute kidney injury.^{8,9} A CVP value greater than 8 mmHg increases the risk of AKI and death, especially in septic or septic shock patients, thus maintaining the lowest possible CVP value can prevent and treat AKI especially in patients with septic shock, heart surgery and intra-abdominal hypertension.^{7,9,14}

Huang et al (2020) in his study including 916 septic patients revealed that fluid administration for septic patients should be controlled and monitored. Since high fluid accumulation is very dangerous for kidney function and increases the risk of AKI incidence.⁷ In Indonesia, Wira¹⁷ study on CVP as a predictor of acute kidney injuries in critical patients in the ICU conducted at Adam Malik Hospital Medan stated that the incidence rate of AKI with a CVP value of ≥ 11.5 mmHg is much greater than CVP < 11.5 mmHg. In our study, it was found that CVP value ≥ 8 mmHg has a risk of AKI by 1,526 times compared to CVP value < 8 mmHg. This is possibly due to excessive fluid administration especially at the time of resuscitation of sepsis patients.^{7-9,12}

6. Limitations

This study is limited by CVP measurement technique. We did the measurement manually and did not do it continuously. The monitoring was only carried out for 24 hours. This is also a single center study thus its results cannot be generalized.

7. Conclusion

In conclusion, CVP target value of 8 mmHg and greater has higher risk of AKI. The use of fluid therapy in managing sepsis requires strict fluid monitoring and evaluation.

8. Conflict of interests

The study was supported by the Faculty of Medicine of Sebelas Maret University and Dr. Moewardi General

Hospital Surakarta. No party other than those mentioned were involved in this study.

9. Authors contribution

The idea, writing, research, and report making is done by the first author. The second author assists in drafting ideas, giving direction in research, as well as improving reports.

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