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Comparison of furosemide bolus and furosemide continuous in critical patients with fluid overload in ICU

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Abstract

***Introduction*: Fluid overload in critically ill patients represents an adverse condition that affects the clinical outcome of patients in the intensive care unit (ICU). Furosemide is commonly used in the ICU as a diuretic in conditions associated with fluid overload, and there are several furosemide administration methods. There is no general consensus regarding the superiority of the furosemide administration method between bolus or continuous administration. This study was conducted to see the comparison between bolus and continuous administration on the improvement of fluid overload.**

***Methods*: This study used a single-blind, randomized controlled trial (RCT) design, where researchers provided treatment and primary data sources obtained directly from examinations of patients in the ICU. The selected population was randomly divided into the bolus and continuous furosemide groups. Fluid overload assessment was carried out using cumulative fluid balance (CFB), urine output variable (UOP), and central venous pressure (CVP) indicators.**

***Results*: A total of 42 samples were obtained and met inclusion and exclusion criteria. In the measurement of fluid overload indicators CFB, UOP, and CVP, there were significant changes in each group before and after furosemide administration with a p-value <0.05. However, there was no significant difference in the final results of each CFB, UOP, or CVP indicator in comparing bolus furosemide and continuous furosemide with a p-value >0.05. There was no difference in mortality rates between bolus furosemide and continuous furosemide during 72 hours of monitoring with a p-value of 0.54.**

***Conclusion*: Bolus furosemide and continuous furosemide administration improved fluid overload in the critically ill population in the ICU, but there was no superior method between the two.**

Key words: Fluid overload, furosemide, CFB, UOP.

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Introduction

Critically ill patients are defined by the type and severity of organ dysfunction. Critically ill patients admitted to the intensive care unit often receive resuscitation with large amounts of intravenous fluids of crystalloids, colloids, or blood products to correct the situation of low blood flow arising from life-threatening processes such as trauma, bleeding, and infection. Administration of intravenous fluids is one of the main steps performed in the resuscitation of critically ill patients with impaired organ perfusion. Potential adverse mechanisms of resuscitation include shearing injury to the endothelial glycocalyx, a fragile barrier structure that functions to retain fluid in the intravascular space, vasodilation, and decreased adrenergic responsiveness, (1) while

fluid accumulation can result in hemodilution, increased venous pressure with subsequent decreased perfusion pressure gradients, and interstitial edema that impacts oxygen diffusion between capillaries and cells. (2)

Fluid overload in critically ill patients is defined as an increase in cumulative fluid balance (CFB) of 10% of body weight and represents an adverse condition that affects the clinical course and outcome of patients in the intensive care unit (ICU). (3,4) Intensive care patients receive large amounts of fluid during resuscitation, such as maintenance fluids, solvent fluids, medications, and nutrients. Large fluid inputs, capillary leakage, and acute kidney injury (AKI) with accompanying oliguria often lead to the accumulation of sodium chloride and water causing fluid overload. A large iatrogenic sodium load contributes to the development of fluid overload. Sodium intake is mainly due to isotonic maintenance fluid therapy and sodium-containing fluids used as drug solvents. (5)

According to the 2020 Systematic Review and Meta-Analysis study by Messmer et al. on six observational and three randomized controlled trials, a total of 31,076 ICU patients met the inclusion criteria. Fluid overload and cumulative fluid balance were associated with mortality: the relative risk after 3 days in ICU for fluid overload was 8.83 (95% CI, 4.03-19.33), and for cumulative fluid balance 2.15 (95% CI, 1.51-3.07), the relative risk over time for fluid overload was 2.79 (95% CI, 1.55-5.00), and 1.39 (95% CI, 1.15-1.69) for cumulative fluid balance. This suggests that fluid overload and cumulative fluid balance are positively associated with increased mortality in the general population and subgroups of critically ill patients. (6) Furosemide is commonly used in the ICU as a diuretic in conditions associated with fluid overload or pulmonary edema, including acute lung injury. Co-administration of albumin with diuretics can improve hemodynamic stability and diuresis. (7) The furosemide stress test (FST) can be performed in oliguric patients; 1 or 1.5 mg/kg furosemide is administered, and urine output 2 hours later is assessed. A dose of 1 mg/kg is given to patients who have not previously received furosemide and 1.5 mg/kg to those who have. (8)

Whatever the ideal cut-off value of 2-hour urine volume, FST should not delay definitive treatment with renal replacement therapy (RRT). Patients with symptomatic fluid overload and stage III of acute kidney injury (AKI) plus indications for conventional RRT initiation such as hyperkalemia, uremia, acidosis, or fluid overload complications, and those likely to respond poorly to pharmacotherapy, should receive RRT immediately. (9) In the systematic review and meta-analysis by Ng et al., several studies have reported that continuous infusion of furosemide correlated with lower mortality rates and shorter LOS (length of stay) compared with bolus administration. The largest multi-center randomized controlled trial (RCT) comparison conducted by Felker et al. found no significant difference in mortality and other clinical endpoints between continuous infusion or bolus furosemide in heart failure patients. Some trials showed a higher incidence of potentially harmful adverse events with continuous infusion, namely hypotension, electrolyte disturbances, and AKI. Although there was no difference in mortality, the continuous group had a longer LOS than the bolus group. However, there were no significant changes in serum creatinine and estimated glomerular filtration rate (eGFR) in either the bolus or continuous groups. (10)

The purpose of this study was to determine the comparison of bolus and continuous furosemide in critical patients with fluid overload in the ICU.

Methods

This study was an RCT single-blind, where researchers who provided treatment took and processed primary data sources obtained directly from examinations on patients in the ICU of H. Adam Malik Central General Hospital, Medan, North Sumatra University Hospital, Dr. Pirngadi Regional General Hospital, and Hajj General Hospital, Medan, and was started when ethical clearance has been approved. Subjects were collected from critical patients in the ICU and divided into two groups, one group would receive bolus furosemide and the other group would receive continuous furosemide. The subjects met the inclusion and exclusion criteria. All samples had data on (a) demographics, (b) estimated severity of illness using the Sequential Organ Failure Assessment (SOFA) score, (c) ICU admission diagnosis, (d) vasopressor used, and (e) blood pressure and heart rate which would be statistically calculated. The research subjects were part of the population and were expected to be able to represent the population in the study (21 patients in each group). This study has received approval from the Health Research Ethics Committee of the University of North Sumatra No. 387/KEPK/USU/2023. In this study, the statistical relationship was assessed using the independent t-test.

Results

Table 1 shows the characteristics of the research subjects. In the bolus furosemide group, there were

7 (33.3%) men and 14 (66.7%) women. There were 10 (47.6%) men and 11 (52.4%) women in the continuous furosemide group. In the chi-square test, the p-value was 0.346, indicating that there was no significant difference in the gender of the two groups.

Table 2 shows a normality test carried out on the variables before the action was taken to see the data distribution of the research subjects in order to determine the type of comparative test to be carried out. In the CFB variable before the intervention, the average value in the bolus group was 4904.52±834.65 ml with a p-value of 0.261 and 4720.00±702.59 ml in the continuous group with a p-value of 0.083. In the urine output (UOP) variable before the intervention, the average value in the bolus group was 60.57±8.78 ml/hour with a p-value of 0.996 and 64.09±14.64 ml/hour in the continuous group with a p-value of 0.948. From central venous pressure (CVP) measurements taken before the intervention, the CVP value was 11.89±2.33 cmH2O in the bolus group with a p-value of 0.530 and 11.26±3.82 cmH2O in the continuous group with a p-value of 0.090. In assessing the normality test of the variables, the Shapiro-Wilk test was performed, and the p-value>0.05 was obtained in all variables to be tested. This indicated that all variables of the initial characteristics of the fluid overload indicator to be tested were normally distributed.

Table 3 shows a comparative test of fluid overload indicators in the two groups measured before furosemide administration. In the measurement of CFB, the average value in the bolus group was 4904.52 (95% CI 4524.59-5284.45) ml and the average value in the continuous group was 4720.00 (95% CI 4400.18-5039.81) ml with a p-value of 0.433. In the measurement of UOP, the average amount of urine before intervention in the bolus group was 60.57 (95% CI 56.57-64.56) ml/hour, and in the continuous group 64.09 (95% CI 57.42-70.76) ml/hour with a p-value of 0.35. In CVP measurements, the average CVP value before intervention in the bolus group was 11.89 (95% CI 10.82-12.95) cmH2O and in the continuous group was 11.26 (95% CI 9.51-13.00) cmH2O with a p-value of 0.52.

Table 4 shows the normality test carried out on the fluid overload indicator variable after the intervention in each group in order to determine the type of comparative test to be carried out. CFB variable after furosemide administration in the bolus group was found to be 1955.23±942.31 ml with a p-value of 0.198 and in the continuous group 1712.52±11129.09 ml with a p-value of 0.054. In the variable of UOP, after furosemide administration in the bolus group, the UOP was 225.85±39.73 ml/hour with a p-value of 0.119, and in the continuous group, it was 229.57±33.71 ml/hour with a p-value of 0.411. After furosemide administration, CVP was measured, and the CVP value in the bolus group was 6.28±2.88 cmH2O with a p-value of 0.967, and in the continuous group, it was 5.61±2.40 cmH2O with a p-value of 0.590.

Table 5 shows the changes in CFB values before and after furosemide administration in each bolus furosemide and continuous furosemide group. In the bolus group, the average CFB value before intervention was 4904.52 (95% CI 4524.59-5284.45) ml and after intervention was 1955.23 (95% CI 1526.29-2384.17) ml with a p-value of 0.001, while in the continuous group, the average CFB value before intervention was 4720.00 (95% CI 4400.18-5039.81) ml and after intervention was 1712.52 (95% CI 1198.56-2226.48) ml with a p-value of 0.001. In the bolus group, there was a decrease in CFB value of 2949.28±563.31 ml; in the continuous group, there was a decrease in CFB of 3007.47±948.39 ml.

Table 6 shows the comparison of CFBs after furosemide administration in the bolus group and the continuous group. The comparison of the bolus group with an average value of 1955.23 (CI 1526.29-2384.17) ml and the continuous group with an average value of 1712.52 (CI 1198.56-2226.48) ml obtained p-value of 0.454 indicated that the comparison of the two variable groups gave an insignificant difference. This suggests that CFBs in the bolus and continuous groups were not statistically different.

Table 7 shows UOP changes before and after administration of furosemide in the bolus and continuous furosemide groups. The bolus group obtained an average UOP before the intervention of 60.57 (CI 56.57-64.5) ml/hour and after the intervention of 225.85 (CI 207.76-243.94) ml/hour with a p-value of 0.001, while in the continuous group, the average UOP before the intervention was 64.09 (CI 57.42-70.76) ml/hour and after the intervention 229.57 (CI 214.22-244.91) ml/hour with a p-value of 0.001. In the bolus group, there was an increase in UOP of 165.28±37.93 ml/hour, while in the continuous group, an increase in UOP of 165.47±37.70 ml/hour was obtained.

Table 8 shows a comparative test carried out on the UOP variable after administration of furosemide in the bolus group and continuous group. Comparison of UOP of the bolus group, with a mean value of 225.85 (CI 207.76-243.94) ml/hour, and the continuous group, with a mean value of 229.57 (CI 214.22-244.91) ml/hours (p-value 0.746), indicating that the comparison of UOP between the two groups provided an insignificant difference.

Table 9 shows changes in CVP values before and

after administering furosemide in the bolus and continuous groups. In the bolus group, the average CVP value before intervention was 11.89 (CI 10.82-12.95) cmH2O, and after the intervention was 6.28 (CI 4.96-7.59) cmH2O, with a p-value of 0.001; while in the continuous group the average CVP value before the intervention was 11.26 (CI 9.51-13.00) cmH2O and after the intervention was 5.61 (CI 4.52-6.70) cmH2O, with a p-value of 0.001. In the bolus group, the CVP value decreased by 5.60±3.88 cmH2O; in the continuous group, the CVP value decreased by 5.64±3.82 cmH2O.

Table 10 carries out a comparative test on the CVP variable after administration of furosemide in the bolus and continuous groups. Comparison of CVP values after administration of furosemide in the bolus group, with a mean value of 6.28 (CI 4.96-7.59) cmH2O, and the continuous group, with a mean value of 5.61 (CI 4.52-6.70) cmH2O, obtained a p-value of 0.421, which indicated that the comparison of CVP values after administering furosemide in the two groups provided an insignificant difference. This showed that the CVP values after administration of furosemide in the bolus and continuous groups were not statistically different.

Table 11 shows the mortality data of the study subjects collected from the start of the intervention until 72 hours thereof. In the bolus group, there was a mortality rate of 1 (2.4%) person; in the continuous group, there was a mortality rate of 2 (4.8%) people. The comparative test of the two groups found a p-value of 0.549, which meant there was no significant difference. This indicated that mortality in the bolus and continuous groups was not statistically different.

Table 12 shows the changes in hemodynamic and laboratory values of research subjects before and after they were given furosemide bolus intervention. In the hemodynamic assessment, systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate were measured. SBP before and after furosemide bolus showed an average decrease of 15.76 (CI 9.08-22.43) mmHg with a p-value of 0.001. DBP before and after furosemide bolus administration showed an average decrease of 10.19 (CI 8.11-12.26) mmHg with a p-value of 0.001. Changes in heart rate before and after furosemide bolus administration showed an average decrease of 0.33 (CI -2.34-3.02) beats/min with a p-value of 0.798. In the tests carried out, significant differences were found in systolic and diastolic blood pressure values, but no significant differences were found in pulse rate values.

Laboratory values showed a decrease in the average sodium value of 7.85 (CI 3.79-11.91) mmol/l with a p-value of 0.001. Changes in potassium before and after bolus administration of furosemide showed an average decrease of 1.21 (CI 0.89-1.53) mmol/l with a p-value of 0.001. Changes in urea before and after bolus administration of furosemide showed an average decrease of 18.09 (CI 9.98-26.20) mg/dl with a p-value of 0.001. Changes in creatinine before and after bolus administration of furosemide showed an average decrease of 0.12 (CI -0.29-0.54) mg/dl with a p-value of 0.509. Changes in albumin levels before and after bolus administration of furosemide showed an average increase of 0.18 (CI -0.32- (-0.43)) g/dl with a p-value of 0.013. In the tests carried out, significant differences were found in sodium, potassium, urea, and albumin before and after bolus administration of furosemide. However, no significant differences were found in changes in creatinine levels.

Table 13 shows the changes in hemodynamic and laboratory values of subjects before and after they were given continuous furosemide intervention. In the hemodynamic assessment, SBP, DBP, and pulse rate were measured. Changes in SBP before and after continuous administration of furosemide showed an average decrease of 10.52 (CI 7.05-13.98) mmHg with a p-value of 0.001. DBP before and after continuous furosemide administration showed an average decrease of 11.42 (CI 9.07-13.78) mmHg with a p-value of 0.001. Changes in heart rate before and after continuous administration of furosemide showed an average increase of 1.61 (CI -4.48-1.25) beats/minute with a p-value of 0.253. In the rigid test, significant differences were found in systolic and diastolic blood pressure values, but no significant differences were found in heart rate.

Laboratory values showed a decrease in the average sodium value of 0.23 (CI -3.21-3.69) mmol/l with a p-value of 0.911. Changes in potassium before and after continuous administration of furosemide showed an average decrease of 1.06 (CI 0.76-1.36) mmol/l with a p-value of 0.001. Changes in urea before and after continuous administration of furosemide showed an average decrease of 10.09 (CI 6.85-13.33) mg/dl with a p-value of 0.001. Changes in creatinine before and after continuous administration of furosemide showed an average increase of 0.05 (CI -0.30-0.18) mg/dl with a p-value of 0.626. Changes in albumin before and after continuous administration of furosemide showed an average increase of 0.07 (CI -0.21-0.06) g/dl with a p-value of 0.273. In the tests carried out, significant differences were found in changes in potassium and urea before and after continuous administration of furosemide. However, no significant differences were found in sodium, creatinine, and albumin

changes.

Discussion

The age distribution was found to be uneven in the study subject population which was dominated by old age. When viewed from age, this might be because there were comorbidities in the elderly and the body's immune system degrades with age. The pathophysiology of this is very complex and multifactorial. In the elderly, the cell-mediated and humoral immune systems experience functional instability where the thymus organ, a major organ in the adaptive cell-mediated immune system, is atrophied so that the immune response produced is limited. In addition to T cells, B cells also decrease with age. Macrophages also experience changes in function where there is a decrease in antigen processing into T cells, causing reduced bactericidal activity. In addition to macrophages, cells that play a role in innate immunity such as neutrophils and natural killer cells are also impaired. (11,12)

Furosemide is often used in the treatment of patients with diuresis and natriuresis indications to overcome fluid overload conditions. Changes in fluid overload indicators in bolus and continuous furosemide administration showed that there were statistically significant differences after 24 hours in the critically ill population with fluid overload undergoing ICU treatment in the hospital. This shows that both bolus and continuous methods are equally effective in achieving adequate diuresis. The study of Ostermann et al. also showed that bolus and continuous furosemide administration achieved diuresis targets and improved fluid overload in the first 24 hours (5.4 liters and 5.3 liters, p-value 0.640). (13)

In addition, hemodynamic and laboratory changes in both furosemide administration methods were analyzed. A decrease in systolic and diastolic blood pressure was found in the bolus method, while the pulse rate had insignificant changes. In the bolus method, there was a significant decrease in sodium, potassium, and ureum, and a significant increase in albumin values. In contrast, no significant changes were found in creatinine levels. In the continuous method, there was also a decrease in systolic and diastolic blood pressure with insignificant changes in pulse rate. Laboratory examinations showed a significant decrease in potassium and ureum. In contrast, there were no significant differences in sodium, creatinine, and albumin levels. (13)

Based on the results of our study, bolus furosemide and continuous furosemide administration provided significant improvement in fluid overload in the critically ill population in the ICU, but there was no superior method between the two.

Conclusion

In this study, bolus and continuous furosemide were conducted in critical patients with fluid overload in the ICU of H. Adam Malik Central General Hospital, Medan, North Sumatra University Hospital, Dr. Pirngadi Regional General Hospital, and Hajj General Hospital, Medan, and then examined (a) demographics, (b) estimated disease severity using SOFA score, (c) ICU admission diagnosis, (d) vasopressor use, and (e) blood pressure and heart rate. This study concluded that bolus furosemide and continuous furosemide provided significant improvement in fluid overload in the critically ill population in the ICU, and there was no superior method between the two.

Conflict of interest

The authors declare no conflict of interest in the writing of this article.

Table 1. The characteristics data of research subjects

Characteristics	Bolus group	Continuous group	p-value
Gender, n (%) - Male - Female	 7 (33.3) 14 (66.7)	 10 (47.6) 11 (52.4)	 0.346*
Age	58.28±8.27	57.66±10.07	0.811**
Body weight	53.19±5.52	53.52±5.42	0.845***
Systolic blood pressure	120.19±12.11	119.95±10.07	0.948***
Diastolic blood pressure	81.14±10.69	78.23±10.27	0.375***
Heart rate	99.85±3.58	97.90±4.40	0.123***
SOFA ccore	9±2	9.04±2.24	0.943***
Albumin	2.51±0.26	2.50±0.28	0.911***
Ureum	48.61±15.59	53.71±14.56	0.615***
Creatinine	2.02±0.79	1.49±0.53	0.016***
Sodium	140.66±5.57	136.66±6.06	0.032***
Potassium	4.58±0.60	4.58±0.72	0.982***
Vassopresor - Yes - No	 16 (76.2) 5 (23.8)	 14 (66.7) 7 (33.3)	 0.495*
Disease, n (%) - Sepsis - Respiratory failure - Surgical - AKI - Gastrointestinal diseases - Neurological disease	 11 (26.2) 5 (11.9) 2 (4.8) 2 (4.8) 0 (0) 1 (2.4)	 13 (31.0) 3 (7.1) 2 (4.8) 1 (2.4) 1 (2.4) 1 (2.4)	 NA****

Legend: SOFA=Sequential Organ Failure Assessment; AKI=acute kidney injury.
*Chi-square test; **Mann-Whitney test; ***Independent t-test; ****Not applicable.

Table 2. Normality test of initial characteristics

Variable	Bolus group	p-value	Continuous group	p-value
CFB pre	4904.52±834.65	0.261*	4720.00±702.59	0.083*
UOP pre	60.57±8.78	0.996*	64.09±14.64	0.948*
CVP pre	11.89±2.33	0.530*	11.26±3.82	0.090*

Legend: CFB=cumulative fluid balance; UOP=urine output; CVP=central venous pressure.
*Shapiro-Wilk test.

Table 3. Overview of baseline characteristics

Variable	Bolus group		Continous group		p-value
	Mean	95% CI	Mean	95% CI	
CFB pre	4904.52	4524.59-5284.45	4720.00	4400.18-5039.81	0.443*
UOP pre	60.57	56.57-64.56	64.09	57.42-70.76	0.350*
CVP pre	11.89	10.82-12.95	11.26	9.51-13.00	0.524*

Legend: CFB=cumulative fluid balance; UOP=urine output; CVP=central venous pressure; CI=confidence interval.
*Independent t-test.

Table 4. Fluid overload indicator normality test

Variable	Bolus	p-value	Continous	p-value
CFB post	1955.23±942.31	0.198*	1712.52±1129.09	0.054*
UOP post	225.85±39.73	0.119*	229.57±33.71	0.411*
CVP post	6.28±2.88	0.967*	5.61±2.40	0.590*

Legend: CFB=cumulative fluid balance; UOP=urine output; CVP=central venous pressure.
*Shapiro-Wilk test.

Table 5. Changes in CFB on bolus and continuous furosemide

Variable	Before		Mean paired differences	After		p-value
CFB	Mean	95% CI		Mean	95% CI	
Bolus	4904.52	4524.59-5284.45	2949.28±563.31	1955.23	1526.29-2384.17	0.001*
Continous	4720.00	4400.18-5039.81	3007.47±948.39	1712.52	1198.56-2226.48	0.001*

Legend: CFB=cumulative fluid balance; CI=confidence interval.
*Paired t-test.

Table 6. Comparison of CFB after administration of furosemide

Variable	Bolus group		Continuous group		p-value
CFB	Mean	95% CI	Mean	95% CI	
Post	1955.23	1526.29-2384.17	1712.52	1198.56-2226.48	0.454*

Legend: CFB=cumulative fluid balance; CI=confidence interval.
*Independent t-test.

Table 7. Changes in UOP before and after furosemide administration

Variable	Before		Mean paired differences	After		p-value
UOP	Mean	95% CI		Mean	95% CI	
Bolus	60.57	56.57-64.56	-165.28±37.93	225.85	207.76-243.94	0.001*
Continuous	64.09	57.42-70.76	-165.47±37.70	229.57	214.22-244.91	0.001*

Legend: UOP=urine output; CI=confidence interval.
*Paired t-test.

Table 8. Comparison of UOP after furosemide administration

Variable	Bolus group		Continuous group		p-value
UOP	Mean	95% CI	Mean	95% CI	
Post	225.85	207.76-243.94	229.57	214.22-244.91	0.746*

Legend: UOP=urine output; CI=confidence interval.
*Independent t-test.

Table 9. Changes in central venous pressure values

Variable	Before		Mean paired differences	After		p-value
CVP	Mean	95% CI		Mean	95% CI	
Bolus	11.89	10.82-12.95	5.60±3.88	6.28	4.96-7.59	0.001*
Continuous	11.26	9.51-13.00	5.64±3.82	5.61	4.52-6.70	0.001*

Legend: CVP=central venous pressure; CI=confidence interval.
*Paired t-test.

Table 10. Comparison of CVP values after administration of furosemide

Variable	Bolus group		Continuous group		p-value
CVP	Mean	95% CI	Mean	95% CI	
Post	6.28	4.96-7.59	5.61	4.52-6.70	0.421*

Legend: CVP=central venous pressure; CI=confidence interval.
*Independent t-test.

Table 11. Mortality

Variable	Bolus group	Continous group	p-value
Mortality			0.549*
- Life	20 (47.6)	19 (45.2)	
- Death	1 (2.4)	2 (4.8)	

Legend: *Chi-square test.

Table 12. Hemodynamic and laboratory changes in the bolus group

Variable	Paired differences				
	Mean	Standard deviation	95% CI		p-value
			Lower	Upper	
Hemodynamic					
- Systolic	15.76	14.66	9.08	22.43	0.001*
- Diastolic	10.19	4.56	8.11	12.26	0.001*
- Heart rate	0.33	5.89	-2.34	3.01	0.798*
Laboratory					
- Sodium	7.85	8.91	3.79	11.91	0.001*
- Potassium	1.21	0.70	0.89	1.53	0.001*
- Ureum	18.09	17.80	9.98	26.20	0.001*
- Creatinine	0.12	0.92	-0.29	0.54	0.509**
- Albumin	-0.18	0.31	-0.32	-0.43	0.013*

Legend: CI=confidence interval.
*Paired t-test; **Wilcoxon signed rank test.

Table 13. Changes in hemodynamic and laboratory values in the continuous group

Variable	Paired differences				
	Mean	Standard deviation	95% CI		p-value
			Lower	Upper	
Hemodynamic					
- Systolic	10.52	7.61	7.05	13.98	0.001*
- Diastolic	11.42	5.17	9.07	13.78	0.001*
- Heart rate	-1.61	6.30	-4.48	1.25	0.253*
Laboratory					
- Sodium	0.23	7.58	-3.21	3.69	0.911**
- Potassium	1.06	0.66	0.76	1.36	0.001*
- Ureum	10.09	7.11	6.85	13.33	0.001*
- Creatinine	-0.05	0.53	-0.30	0.18	0.626*
- Albumin	-0.07	0.30	-0.21	0.06	0.273*

Legend: CI=confidence interval.
*Paired t-test; **Wilcoxon signed rank test.

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