Journal of Intensive Medicine 3 (2023) 165–170

Contents lists available at ScienceDirect

Journal of Intensive Medicine

journal homepage: www.elsevier.com/locate/jointm

Original Article

# Optimization of central venous pressure during the perioperative period is associated with improved prognosis of high-risk operation patients

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ARTICLE INFO

*Keywords:*
Perioperative
Central venous pressure
Fluid management
Acute renal injury

ABSTRACT

*Background:* While central venous pressure (CVP) measurement is used to guide fluid management for high-risk surgical patients during the perioperative period, its relationship to patient prognosis is unknown.

*Methods:* This single-center, retrospective observational study enrolled patients undergoing high-risk surgery from February 1, 2014 to November 31, 2020, who were admitted to the surgical intensive care unit (ICU) directly after surgery. Patients were divided into the following three groups according to the first CVP measurement (CVP1) after admission to the ICU: low, CVP1 <8 mmHg; moderate, 8 mmHg≤ CVP1 ≤ 12 mmHg; and high, CVP1 >12 mmHg. Perioperative fluid balance, 28-day mortality, length of stay in the ICU, and hospitalization and surgical complications were compared across groups.

*Results:* Of the 775 high-risk surgical patients enrolled in the study, 228 were included in the analysis. Median (interquartile range) positive fluid balance during surgery was lowest in the low CVP1 group and highest in the high CVP1 group (low CVP1: 770 [410, 1205] mL; moderate CVP1: 1070 [685, 1500] mL; high CVP1: 1570 [1008, 2000] mL; all $P$ <0.001). The volume of positive fluid balance during the perioperative period was correlated with CVP1 ($r$=0.336, $P$ <0.001). The partial arterial pressure of oxygen($PaO_2$)/fraction of inspired oxygen($FiO_2$) ratio was significantly lower in the high CVP1 group than in the low and moderate CVP1 groups (low CVP1: 400.0 [299.5, 443.3] mmHg; moderate CVP1: 362.5 [330.0, 434.9] mmHg; high CVP1: 335.3 [254.0, 363.5] mmHg; all $P$ <0.001). The incidence of postoperative acute kidney injury (AKI) was lowest in the moderate CVP1 group (low CVP1: 9.2%; moderate CVP1: 2.7%; high CVP1: 16.0%; $P$=0.007). The proportion of patients receiving renal replacement therapy was highest in the high CVP1 group (low CVP1: 1.5%; moderate CVP1: 0.9%; high CVP1: 10.0%; $P$=0.014). Logistic regression analysis showed that intraoperative hypotension and CVP1 >12 mmHg were risk factors for AKI within 72 h after surgery (adjusted odds ratio[aOR]=3.875, 95% confidence interval[CI]: 1.378–10.900, $P$=0.010 and aOR=1.147, 95%CI: 1.006–1.309, $P$=0.041).

*Conclusions:* CVP that is either too high or too low increases the incidence of postoperative AKI. Sequential fluid therapy based on CVP after patients are transferred to the ICU post-surgery does not reduce the risk of organ dysfunction caused by an excessive amount of intraoperative fluid. However, CVP can be used as a safety limit indicator for perioperative fluid management in high-risk surgical patients.

## Introduction

Perioperative fluid management is difficult for two reasons: (1) absolute or relative volume deficiency often occurs postoperatively in patients due to preoperative fasting, intraoperative bleeding, and non-dominant fluid loss caused by vasodilation and fluid redistribution caused by anesthesia; and (2) insufficient fluid infusion can lead to increased postoperative organ complications and poor wound healing. Adequate and goal-oriented hemodynamic monitoring combined with early and appropriate treatment can improve the prognosis of high-risk surgical patients.[1,2]

Hemodynamic monitoring plays an important role in fluid management, and central venous pressure (CVP), a clinical hemodynamic parameter, can be easily obtained in the perioperative period. CVP is a dual indicator of tissue perfusion: decreased CVP may reflect insufficient volume, which can lead to low tissue perfusion, whereas elevated CVP can reduce venous

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https://doi.org/10.1016/j.jointm.2022.06.003
Received 21 May 2022; Received in revised form 18 June 2022; Accepted 24 June 2022. Managing Editor: Jingling Bao
Available online 5 August 2022

return, leading to tissue edema. However, the most appropriate CVP for perioperative patients undergoing high-risk surgery has not been established. The present retrospective study examined the relationship between CVP and postoperative complications and the prognosis of high-risk surgical patients. Patients aged ≥18 years who underwent non-cardiac surgery requiring postoperative care in the intensive care unit (ICU) were included.[3] As the criteria for postoperative intensive care are not standardized across intensive care centers, all patients with this indication were considered to be high-risk.

## Methods

### *Study population*

This single-center, retrospective observational study enrolled patients undergoing high-risk surgery from February 1, 2014 to November 31, 2020, who were admitted to the surgical (S)ICU directly after surgery. The inclusion criteria were as follows: (1) age ≥18 years; (2) patients who underwent surgery and were admitted to the ICU directly afterward; (3) ICU stay longer than 48 h; and (4) CVP catheter removed >48 h after ICU admission. The exclusion criteria were as follows: (1) pregnant patients; (2) age >80 years; (3) patients who underwent cardiac surgery; (4) chronic kidney disease; and (5) incomplete hospitalization information. This study was retrospectively registered on October 15, 2020 (trial registration no. NCT04596332).

### *CVP measurement and grouping*

All enrolled patients underwent central venous catheterization during surgery. The catheter was placed by the anesthesiologist and confirmed by bedside chest X-ray. The CVP value was displayed on a monitor via a pressure transducer with a connecting tube and cable. The pressure sensor was maintained at the "0" point horizontally and aligned with the midaxillary line of the patient and the intersection point of the fourth rib. The continuous and stable CVP waveform and value were obtained by rotating the three-way knob and zeroing. CVP values were continuously monitored immediately after admission and recorded automatically every hour. The initial CVP within the first hour after ICU admission was defined as the first CVP measurement (CVP1). Patients were divided into the following three groups according to CVP1:[4] low, CVP1 <8 mmHg; moderate, 8 mmHg≤ CVP1 ≤ 12 mmHg; and high, CVP1 >12 mmHg.

### *Clinical variables and outcomes*

All demographic data including age, sex, operation(s), comorbidities, mean arterial pressure (MAP), Sequential Organ Failure Assessment score, Acute Physiology and Chronic Health Evaluation Scoring System II score, lactate levels, intraoperative fluid balance, and fluid balance from admission to 6 h and 24 h after operation were obtained from electronic medical records. Fluid balance was defined as total input (including fluids, medications, and blood products) minus total output (including urine volume, feces, and drainage). In a recent large epidemiologic study of patients undergoing major non-cardiac surgery in ICUs in Brazil, 30% of patients experienced postoperative complications, with acute kidney injury (AKI) being the second most common.[3] We thus speculated that perioperative AKI is common and warrants attention. The primary outcome in this study was the incidence of postoperative AKI, and secondary outcomes included 28-day mortality, length of stay in the ICU, and length of hospitalization.

### *Statistical analysis*

Data are presented as the mean ± standard deviation or median (interquartile range), as determined using the Kolmogorov–Smirnov test. Analysis of variance was used to compare normally distributed data for the three groups and the nonparametric test was used to compare non-normally distributed data for the three groups. Pearson's chi-squared test or Fisher's exact probability method were used to assess differences in categorical data. A correlation analysis was performed to evaluate correlations between different variables. Binary logistic regression analysis was performed to identify factors affecting the incidence of postoperative acute renal injury. $P$ values <0.050 were considered indicative of statistical significance. All statistical analyses were performed using SPSS v24 statistical software package (IBM, Armonk, NY, USA).

## Results

Of the 775 high-risk surgical patients enrolled in the study, 228 were included in the analysis. The flow diagram of patient selection is shown in Figure 1. The demographic and clinical characteristics of all enrolled patients are shown in Table 1. There were no differences in age, sex, complications, cardiac function, or type of operation among the three groups. The CVP1 >12 mmHg group had a significantly higher incidence of intraoperative hypotension than the other two groups. There were significant differences in cumulative intraoperative fluid balance among the three groups. Fluid balance during surgery was significantly higher in the high CVP1 group than in the low and moderate CVP1 groups. At the time of ICU admission, the partial arterial pressure of oxygen($PaO_2$)/fraction of inspired oxygen($FiO_2$) ratio of patients in the high CVP1 group was lower than that of patients in the other two groups.

Significant differences in short-term volume management between the three groups were observed (Table 2). There were no differences in intraoperative crystal fluid input and colloidal fluid input among groups. Cumulative fluid balance was higher in the low CVP1 group than in the moderate and high CVP1 groups, and the high CVP1 group maintained a negative fluid balance during the first 6 h and 24 h in the ICU. Fluid balance during surgery and within 6 h and 24 h after ICU admission were significantly correlated with CVP1 ($r$=0.336, −0.536, and −0.472, respectively; $P$ <0.001, Table 3).

Postoperative AKI was evaluated according to the Acute Kidney Injury Network criteria.[5] Overall, 7.5% of patients experienced postoperative AKI (Table 2). Interestingly, both the low and high CVP1 groups had significantly higher incidences of postoperative AKI than the moderate CVP1 group. However, the proportion of patients receiving renal replacement therapy was higher in the high CVP1 group than in the low CVP1 group. The duration of mechanical ventilation was significantly higher in the moderate CVP1 group than in the low CVP1 group. Other clinical outcomes including 28-day mortality, total length of hospital stay, and length of ICU stay did not differ significantly across groups. Intraoperative hypotension and CVP1 >12 mmHg

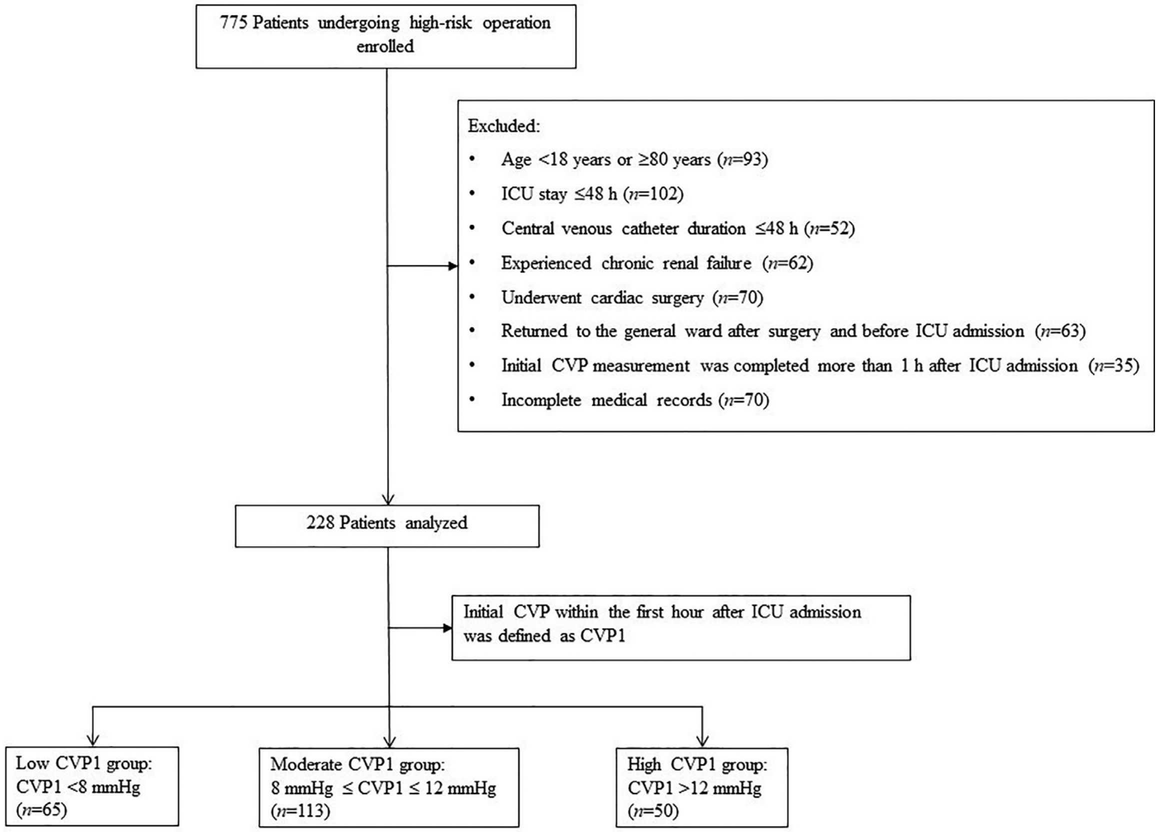


**Figure 1.** Flowchart of patient selection and grouping.
CVP: Central venous pressure; CVP1: Initial central venous pressure value within 1 h after ICU admission; ICU: Intensive care unit.

were risk factors for AKI in high-risk surgical patients within 72 h after surgery (adjusted odds ratio[aOR]= 3.875, 95% confidence interval[CI]: 1.378–10.900, $P$=0.010 and aOR=1.147, 95%CI: 1.006–1.309, $P$=0.041) (Table 4).

## Discussion

The results of our study demonstrate that the initial postoperative CVP value after admission to the ICU was related to the volume of positive fluid balance during the operation. Additionally, patients with a CVP of 8–12 mmHg had the lowest incidence of AKI, while CVP >12 mmHg was a risk factor for AKI within 72 h after surgery as well as renal replacement therapy and impaired oxygenation function after ICU admission. However, there was no association between CVP and length of ICU stay or 28-day mortality.

Monitoring CVP remains the most common method used by clinicians to guide fluid therapy; however, it is not without controversy. Venous return is determined by mean systemic filling pressure and CVP gradient according to the venous return theory proposed by Guyton.[4,6] Perioperative infusion can increase cardiac output by increasing mean circulatory filling pressure. However, the right side of the heart—especially the ventricle—has a thin and tapered wall and a lower tolerance for afterload than the left side.[7] Elevated mean or maximum CVP was shown to be correlated with poor outcomes and prolonged treatment in critical care settings.[6] In our study, the high CVP1 group had the highest positive intraoperative fluid balance but a negative fluid balance within 24 h after surgery. In contrast, the low CVP1 group had the lowest intraoperative positive fluid balance but the highest postoperative positive fluid balance. We also found that the incidence of postoperative AKI and rate of renal replacement therapy were lower in the moderate CVP1 group than in the low or high CVP1 group. The intraoperative positive balance caused CVP to be >12 mmHg, which resulted in a higher incidence of AKI and increased the need for renal replacement therapy in the three groups; however, clinicians optimized the management of liquid based on initial CVP after admission to the ICU.

Low CVP levels suggested that the body was likely to be in a state of insufficient circulatory perfusion, and the function of volume-sensitive organs such as the kidneys was compensated by vasoconstriction. Even if MAP was normal, the organs were already in a state of low perfusion and impaired renal function. However, when CVP is too high, peripheral venous reflux resistance increases greatly, which can lead to increased renal afterload and obstruction of renal perfusion.[8] Many factors are related to the occurrence of AKI[9–18] and mean CVP was shown to be related to acute renal injury,[19–22] suggesting that high CVP makes the kidney prone to dysfunction. We found that the risk of postoperative AKI increased even if a negative balance was corrected in a timely manner after surgery in high-risk surgical patients with a large volume of intraoperative positive balance.

It has been suggested that CVP fails to reflect the risk of pulmonary edema development, which depends on capillary pressure and hence on left atrial pressure, and pulmonary artery

**Table 1**
Demographic and clinical characteristics of 228 patients undergoing high-risk operation.

| Variables | Total (*n*=228) | Low CVP1 group* (*n*=65) | Moderate CVP1 group* (*n*=113) | High CVP1 group* (*n*=50) | *P*-value |
|---|---|---|---|---|---|
| Female sex | 67 (29.3) | 23 (35.3) | 26 (23.0) | 18 (36.0) | 0.111 |
| Age (years) | 58.0 (44.0, 67.0) | 55.0 (41.5, 69.5) | 59.0 (46.0, 67.0) | 53.0 (44.0, 67.3) | 0.791 |
| Comorbidities | | | | | 0.968 |
| 0–1 | 191 (83.8) | 56 (86.2) | 94 (83.2) | 41 (82.0) | |
| 2–3 | 33 (14.5) | 8 (12.3) | 17 (15.0) | 8 (16.0) | |
| ≥4 | 4 (1.8) | 1 (1.5) | 2 (1.8) | 1 (2.0) | |
| NYHA functional class | | | | | 0.121 |
| I | 213 (93.4) | 61 (93.8) | 108 (95.6) | 44 (88.0) | |
| II | 8 (3.5) | 3 (4.6) | 1 (0.9) | 4 (8.0) | |
| III | 7 (3.1) | 1 (1.5) | 4 (3.5) | 2 (4.0) | |
| Information on operations | | | | | 0.148 |
| Neurosurgery | 138 (60.5) | 33 (50.8) | 72 (63.7) | 33 (66.0) | |
| Thoracic surgery | 3 (1.3) | 0 (0) | 2 (1.8) | 1 (2.0) | |
| Abdominal surgery† | 64 (28.1) | 17 (26.2) | 33 (29.2) | 14 (28.0) | |
| Orthopedic surgery | 18 (7.9) | 10 (15.4) | 6 (5.3) | 2 (4.0) | |
| Operation duration (min) | 167.5 (107.0, 230.0) | 161.0 (90.0, 245.0) | 170.0 (110.0, 230.0) | 161.5 (103.8, 230.0) | 0.787 |
| Fluid input during surgery (mL) | 1470 (970, 2470) | 1270 (720, 2255)‡ | 1470 (945, 2445) | 1720 (1133, 2495)§ | 0.029 |
| Crystal fluid input during surgery (mL) | 1000 (500, 1360) | 750 (500, 1200) | 1000 (500, 1315) | 1000 (675, 1500) | 0.070 |
| Colloid fluid input during surgery (mL) | 500 (200, 1000) | 500 (0, 950) | 500 (225, 1000) | 500 (150, 1000) | 0.506 |
| Fluid output during surgery (mL) | 340 (123, 900) | 400 (207, 1000)‡ | 390 (125, 900) | 200 (97, 663)§ | 0.015 |
| Fluid balance during surgery (mL) | 1050 (650, 1600) | 770 (410, 1205)‡,¶ | 1070 (685, 1500)‡,§ | 1570 (1008, 2000)§,¶ | <0.001 |
| Emergent surgery | 119 (52.2) | 36 (55.4) | 57 (50.4) | 26 (52.0) | 0.817 |
| Intraoperative hypotension | 51 (22.4) | 12 (18.5)‡ | 21 (18.6)‡ | 18 (36)§,¶ | 0.032 |
| Intraoperative blood transfusion history | 64 (28.1) | 19 (29.2) | 34 (30.1) | 11 (22) | 0.553 |
| ICU admission status | | | | | |
| SOFA score | 4.0 (3,6. 8.0) | 4.0 (2.0, 6.5) | 4.0 (3.0, 7.0) | 4.0 (3.0, 6.0) | 0.610 |
| APACHE II score | 10.0 (6.3, 16.0) | 10.0 (7.0, 16.0) | 10.0 (6.0, 17.0) | 8.5 (6.0, 13.0) | 0.080 |
| MAP (mmHg) | 77.0 (74.0, 84.8) | 77.0 (71.0, 82.0) | 78.0 (74.0, 84.5) | 77.5 (73.8, 86.3) | 0.696 |
| Serum lactate level (mmol/L) | 1.7 (1.1, 2.3) | 1.9 (1.3, 3.1)¶ | 1.5 (1.0, 2.2)§ | 1.7 (1.2, 2.2) | 0.018 |
| $PaO_2/FiO_2$ ratio (mmHg) | 356.3 (318.1, 434.3) | 400.0 (299.5, 443.3)‡ | 362.5 (330.0, 434.9)‡ | 335.3 (254.0, 363.5)§,¶ | 0.002 |
| CVP at 24 h after ICU admission (mmHg) | 10.0 (8.0, 12.0) | 10.0 (7.0, 12.0) | 10.0 (8.0, 12.0) | 10.5 (8.0, 12.3) | 0.209 |

Data are expressed as median(interquartile range), or *n* (%).
* Patients were divided into three groups according to CVP1: low, CVP1 <8 mmHg; moderate, 8 mmHg ≤ CVP1 ≤ 12 mmHg; and high, CVP1 >12 mmHg.
† Abdominal surgery included hepatobiliary surgery, pancreas surgery, spleen surgery, gastrointestinal surgery, and urology surgery.
‡,§,¶ Statistically significant results compared with high, low and moderate CVP1 groups, respectively.
APACHE II: Acute Physiology and Chronic Health Evaluation Scoring System II; CVP: Central venous pressure; CVP1: Initial central venous pressure value within 1 h after ICU admission; $FiO_2$: Fraction of inspired oxygen; ICU: Intensive care unit; MAP: Mean arterial pressure; NYHA: New York Heart Association; $PaO_2$: Partial arterial pressure of oxygen; SOFA: Sequential Organ Failure Assessment.

**Table 2**
ICU treatment and clinical outcomes.

| Variables | Total (*n*=228) | Low CVP1 group* (*n*=65) | Moderate CVP1 group* (*n*=113) | High CVP1 group* (*n*=50) | *P*-value |
|---|---|---|---|---|---|
| ICU treatment | | | | | |
| Fluid balance within 6 h after ICU admission (mL) | 245 (−243, 472) | 454 (295, 688)†,‡ | 182 (−179, 444)§,‡ | −333 (−528, 206)§,† | <0.001 |
| Fluid balance within 24 h after ICU admission (mL) | 417 (−336, 908) | 762 (327, 1256)†,‡ | 568.0 (−215, 923)§,‡ | −541 (−1023, 215)§,† | <0.001 |
| Duration of ventilation (h) | 9.0 (0, 54.4) | 3.0 (0, 33.5)† | 13.0 (1.0, 66.0)§ | 9.3 (0, 37.9) | 0.046 |
| Renal replacement therapy | 7 (3.1) | 1 (1.5)‡ | 1 (0.9)‡ | 5 (10.0)†,§ | 0.014 |
| Partial postoperative complications | | | | | |
| $PaO_2/FiO_2$ ratio <300 mmHg within 24 h after ICU admission | 32 (14.0) | 11 (16.9) | 10 (8.8) | 11 (22.0) | 0.061 |
| AKI‖ within 48 h after ICU admission | 17 (7.5) | 6 (9.2)† | 3 (2.7)§,‡ | 8 (16.0)† | 0.007 |
| Clinical outcomes | | | | | |
| Mortality on day 28 | 2.7 (11.8) | 6 (9.2) | 13 (11.5) | 8 (16.0) | 0.531 |
| Length of hospitalization (days) | 27.0 (17.0, 34.8) | 28.0 (18.5, 33.0) | 24.0 (16.0, 36.0) | 27.0 (17.8, 35.0) | 0.738 |
| Length of ICU stay (days) | 13.0 (7.0, 24.0) | 12.0 (6.0, 25.0) | 14.0 (8.0, 23.5) | 11.5 (6.0, 24.0) | 0.485 |

Data are expressed as median(interquartile range)or *n* (%).
* Patients were divided into three groups according to CVP1: low, CVP1 <8 mmHg; moderate, 8 mmHg ≤ CVP1 ≤ 12 mmHg; and high, CVP1 >12 mmHg.
†,‡,§ Statistically significant results compared with moderate, high and low CVP1 groups, respectively.
‖ The diagnosis of AKI was based on Acute Kidney Injury Network criteria published in 2007.[5]
AKI: Acute kidney injury; CVP1: Initial central venous pressure value within 1 h after ICU admission; $FiO_2$: Fraction of inspired oxygen; ICU: Intensive care unit; $PaO_2$: Partial arterial pressure of oxygen.

occluded pressure is preferred as a safety variable for the lungs and/or measurement of extravascular lung water to estimate the severity of lung edema.[8] However, since venous return and cardiac output must be identical in a closed system,[23] increased CVP can also increase left atrial volume load and left atrial pressure to some extent. In our study, there were no differences in smoking history, chronic pulmonary disease, or positive end-expiratory pressure among the groups, and the high CVP1 group had the lowest $PaO_2/FiO_2$ ratio and longest duration of mechanical ventilation. Therefore, postoperative “restrictive” infusion

**Table 3**
Correlation analysis of perioperative fluid balance and CVP1.

| Variables* | *r* | *P*-value |
|---|---|---|
| Fluid balance during surgery | 0.336 | <0.001 |
| Fluid balance within 6 h after ICU admission | −0.536 | <0.001 |
| Fluid balance within 24 h after ICU admission | −0.472 | <0.001 |

* Fluid balance=Total input (including fluids, medications, and blood products)−Total output (including urine volume, feces, and drainage) during a given period.
CVP1: Initial central venous pressure value within 1 h after ICU admission; ICU: Intensive care unit.

**Table 4**
Logistic regression analysis of clinical factors associated with the development of AKI* within 72 h after surgery.

| Variable | Univariate conditional logistic regression | | | Multivariable conditional logistic regression | | |
|---|---|---|---|---|---|---|
| | OR | 95% CI | *P*-value | Adjusted OR | 95% CI | *P*-value |
| Age | 0.970 | 0.941–1.000 | 0.053 | – | – | – |
| Sex | 0.723 | 0.227–2.303 | 0.583 | – | – | – |
| Hypertension | 1.680 | 0.622–4.539 | 0.306 | – | – | – |
| Diabetes mellitus | 0 | 0–0 | 0.999 | – | – | – |
| Malignant tumor | 0 | 0–0 | 0.999 | – | – | – |
| Basal serum creatinine | 1.006 | 0.983–1.029 | 0.626 | – | – | – |
| Basal urea nitrogen | 1.059 | 0.929–1.207 | 0.391 | – | – | – |
| Emergency surgery | 3.219 | 1.017–10.195 | 0.047† | – | – | 0.087 |
| Intraabdominal general surgery | 0.774 | 0.243–2.470 | 0.666 | – | – | – |
| Surgical duration | 0.994 | 0.988–1.000 | 0.057 | – | – | – |
| Intraoperative hypotension | 4.527 | 1.648–12.436 | 0.003† | 3.875 | 1.378–10.900 | 0.010 |
| Intraoperative blood transfusion | 0.527 | 0.146–1.899 | 0.327 | – | – | – |
| CVP1 >12 mmHg | 1.178 | 1.034–1.341 | 0.014† | 1.147 | 1.006–1.309 | 0.041 |
| APACHE II score | 0.953 | 0.874–1.038 | 0.270 | – | – | – |
| Fluid balance during surgery | 1.000 | 1.000–1.001 | 0.505 | – | – | – |
| Fluid balance within 6 h after ICU admission | 1.000 | 0.999–1.001 | 0.934 | – | – | – |
| Fluid balance within 24 h after ICU admission | 1.000 | 0.999–1.000 | 0.569 | – | – | – |

* The diagnosis of AKI was based on Acute Kidney Injury Network criteria published in 2007.[5]
AKI: Acute kidney injury; APACHE II: Acute Physiology and Chronic Health Evaluation Scoring System II; CI: Confidence interval; CVP1: Initial central venous pressure value within 1 h after ICU admission; ICU: Intensive care unit; OR: Odds ratio.

is undoubtedly more beneficial for patients with abnormally high CVP, especially high-risk surgical patients.

There were several limitations to this study. First, this was a single-center retrospective study and the sample size was small. Second, because of the retrospective nature, the accuracy of CVP measurement cannot be guaranteed – for example, the zero position of the pressure transducer may have influenced the measured value. Third, given the continuity and dynamic characteristics of hemodynamics, the impact of continuous CVP *vs.* CVP1 monitoring after admission on the prognosis of critically ill patients remains unclear. Clinicians can make sound judgments according to multiple indicators to improve the accuracy of fluid therapy.

## Conclusions

CVP that is too high or too low increases the incidence of postoperative AKI. Sequential fluid therapy based on CVP after patients were transferred to the ICU following surgery did not reduce the incidence of organ dysfunction caused by excessive amounts of intraoperative fluid. Therefore, maintaining CVP at an intermediate value may be a better strategy for perioperative fluid management in patients undergoing high-risk surgery, although this remains to be confirmed in prospective studies.

## Ethics Statement

All methods were carried out in accordance with relevant guidelines and regulations. The research protocol was approved by the ethics committee of Fujian Provincial Hospital (ethics code K2018-09-006). Given its retrospective nature, this study was exempted from the requirement of written, informed consent from participants by the Ethics Committee of Fujian Provincial Hospital.

## Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Funding

The protocol was financially supported by high-level hospital foster grants from Fujian Provincial Hospital, Fujian Province, China [Grant number: (2020) HSJJ14].

## Conflicts of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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