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Effects of modified ultrafiltration and conventional ultrafiltration combination on perioperative clinical outcomes in pediatric cardiac surgery

A meta-analysis

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Abstract

Background: This meta-analysis was performed to review the effects of the addition of modified ultrafiltration (MUF) and conventional ultrafiltration (CUF) to CUF alone on postoperative hemoglobin, surgical and ultrafiltration data, and postoperative clinical outcomes in pediatric patients undergoing cardiac surgery.

Methods: A systematic search was performed to identify randomized controlled clinical trials that compared MUF and CUF combination with CUF alone in pediatric cardiac surgery undergoing cardiopulmonary bypass (CPB) in PubMed, Embase, Cochrane Library, and Web of Science without any language or date limitation in February 2020. For each included trial, the primary outcomes including post-CPB and postoperative hematocrit, surgical and ultrafiltration data, postoperative clinical outcomes including volume of chest tube drainage within 48 hours after surgery and perioperative blood requirement, ventilation support duration, and length of stay day in the intensive care unit (ICU) and hospital were collected and analyzed. The analysis was conducted using STATA version 12.0.

Results: A total of 8 trials encompassing 405 patients were included in this analysis. Analysis indicated that MUF + CUF increased the post-CPB hematocrit (Standard mean difference, SMD = 1.85, 95% confidence interval, 95% CI 0.91–2.79). Meanwhile, ultrafiltration volume was higher in CUF+MUF infants than CUF-alone infants (SMD = 1.46, 95% CI 0.51–2.41, *P* = .003). The clinical outcomes, including postoperative hemodynamic changes, prime volume, blood requirement, chest tube drainage volume, mechanical ventilation duration, and ICU duration, were unclear because of the unstable sensitivity analyses.

Conclusions: Beneficial effects of using MUF and CUF for pediatric cardiac surgery, including increase post-CPB hematocrit and ultrafiltration volume when compared with CUF alone. Meanwhile, MUF and CUF did not significantly influence the postoperative hospital stay duration, CPB, and aortic occlusion duration.

Abbreviations: 95% CI = 95% confidence intervals, AO = aortic occlusion, CPB = cardiopulmonary bypass, CUF = conventional ultrafiltration, ICU = intensive care unit, MUF = modified ultrafiltration, SMD = standard mean difference.

Keywords: conventional ultrafiltration, meta-analysis, modified ultrafiltration, pediatric cardiac surgery

1. Introduction

The prime solution of cardiopulmonary bypass (CPB) circuits can result in an increase in body fluids volume for patients undergoing cardiac surgery. Perioperative hypothermia and hemodilution also contribute to the body fluids augment. Pediatric patients exhibit a poor ability to regulate body fluids content and the excessive tissue water cannot be effectively removed by the kidneys.[1] The body fluids volume excessive increase has stronger adverse effects after surgery in children with lower weight and age compared to adults.[1–3] These effects may result in coagulation disorders, inflammatory response, hemostatic impairment, pulmonary and myocardial edema after cardiac surgery leading to increased morbidity and mortality.[4–7] The CPB circuit sizes were significantly smaller with the technical advances, and priming volumes were minimized now compared with decades ago.[8]

The 2017 European Association for Cardio-Thoracic Surgery and the European Association of Cardiothoracic Anesthesiology Guidelines on patient blood management for adult cardiac surgery recommended that modified ultrafiltration (MUF) may be considered as part of a blood conservation strategy to minimize hemodilution (Class IIb, level B).[9] Conventional

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The datasets generated during and/or analyzed during the current study are publicly available.

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ultrafiltration (CUF) and MUF are used routinely in CPB. CUF is carried during CPB running to maintain moderate hemodilution and minimal venous reservoir blood, and MUF can perform after discontinuation of CPB are used routinely in CPB. However, it remains unclear which should be preferred in pediatric patients between MUF and CUF. Clinical guidelines for the management of patients with transposition of the great arteries with intact ventricular septum suggested both interventions were effective.[10] MUF was performed after the termination of CPB with CUF. The performance of MUF inevitably lengthens the operation time, and needs additional technical management, which can cause errors and accidents.[8] There is no conclusion whether it is time to eliminate MUF in the current era. Meanwhile, the current recommendation is based on expert consensus due to a lack of evidence. Therefore, this study tries to evaluate the addition of MUF to CUF with CUF alone in pediatric cardiac surgery to examine its effects on postoperative hemoglobin, surgical, and ultrafiltration data, and postoperative clinical outcomes.

2. Methods

2.1. Study design

A meta-analysis was conducted following the reporting recommendations of the PRISMA statement and Cochrane Collaboration for systematic reviews and meta-analysis.[11]

This meta-analysis was approved by Xiangya Hospital, Central South University, and the ethical approval and informed consent were not necessary.

2.2. Systematic search

Full articles that compared MUF and CUF combination with CUF alone in pediatric cardiac surgery undergoing CPB were comprehensively searched. A systematic search was performed in PubMed, Embase, Cochrane Library, and Web of Science without any language or date limitation. The following text searches and search headings were used individually and in combination: "pediatric," "cardiopulmonary bypass," "modified ultrafiltration." References listed in relevant articles and textbooks were also searched manually to find other potential studies. The last electronic search was performed in February 2020.

2.3. Study selection, data collection, and quality assessment

The identified papers were reviewed independently by two authors (HJ & LP). Duplicate studies were excluded redundancy, and then titles, abstracts, and full texts were screened to select the trials that matched the inclusion criteria.

We included published randomized controlled clinical trials that compared MUF and CUF combination with CUF alone in pediatric cardiac surgery undergoing CPB. The MUF + CUF group patients should accept both CUF during CPB and MUF after the termination of CPB. The circuit lines of ultrafiltration should from artery cannulation to venous reservoir (VA) or from inferior vena to venous reservoir (VV). All CUF was performed during CPB, and MUF was after the termination of CPB. In the intervention, both the MUF and CUF should be performed on the same patient. Trials that only tested the effect of MUF in the intervention group were excluded. Trials that did not report any analyzable clinical outcomes were also excluded. Trials reported in scientific meetings, correspondence, case reports, and review papers were also excluded. Quality assessments using the Cochrane Collaboration's tool for assessing the risk of bias in randomized trials[12] on the selected published studies were carried out by another investigator.

Two authors (YJ & ZC) independently extracted all the relevant information from each included study using standardized data collection forms. Another 2 authors (HJ & LP) checked the consistency of the extracted data. For each included trial, the following data were collected: the name of the first author, publication year, number of patients, post-CPB and postoperative hematocrit, aortic occlusion (AO) duration, CPB duration, prime volume, ultrafiltration volume, hemodynamic changes, the volume of chest tube drainage within 48 hours after surgery and perioperative blood requirement, ventilation support duration, and length of stay day in the intensive care unit (ICU) and hospital. Continuous variables that were reported as interquartile ranges were estimated to means and standard deviations form as Hozo et al described.[13]

2.4. Statistical analysis

The analysis was conducted using STATA version 12.0. Each analysis was assessed for statistical heterogeneity using Cochran Q and I^2 tests. $P < .10$, and $I^2 > 50\%$ indicated heterogeneity, and a fixed-effect model was used to determine the pooled effect estimates; otherwise, the random-effects model was used. Standard mean differences 1 SMDs) with pertinent 95% confidence intervals (95% CIs) were computed to express the estimators of treatment effects for each analyzed clinical data. Sensitivity analysis was conducted by removing each study individually to assess the quality and consistency of the results.

3. Results

3.1. Literature search findings

A total of 492 potentially relevant articles from our search of the literature were identified. After excluding 484 articles, a total of 8 articles[1,14–20] covering 8 trials published between 1998 and 2018 with 405 patients included (203 received MUF+CUF, and 202 received CUF alone). The circuit lines were VA in all trials except which was VV from Bando et al.[17] All CUFs were performed during CPB, and MUFs were after the termination of CPB. Figure 1 illustrated the eligible studies selection procedure. A summary of the included studies is summarized in Table 1. The quality of the included trials is summarized in Table 2.

3.2. Procedural characteristics

The CPB duration, AO duration, and prime volume were reported to display the procedural characteristics. The CPB duration was reported in all the 8 trials,[1,14–20] and there was no significant heterogeneity ($I^2 = 5.4\%$, $P = .388$). Meta-analysis under fixed model indicated that CUF+MUF had no significant influence in CPB time comparing to CUF alone (SMD = 0.09, 95% CI −0.11 to 0.28, $P = .394$, Fig. 2A). Meanwhile, the sensitivity analysis suggested the pooled result was stable.

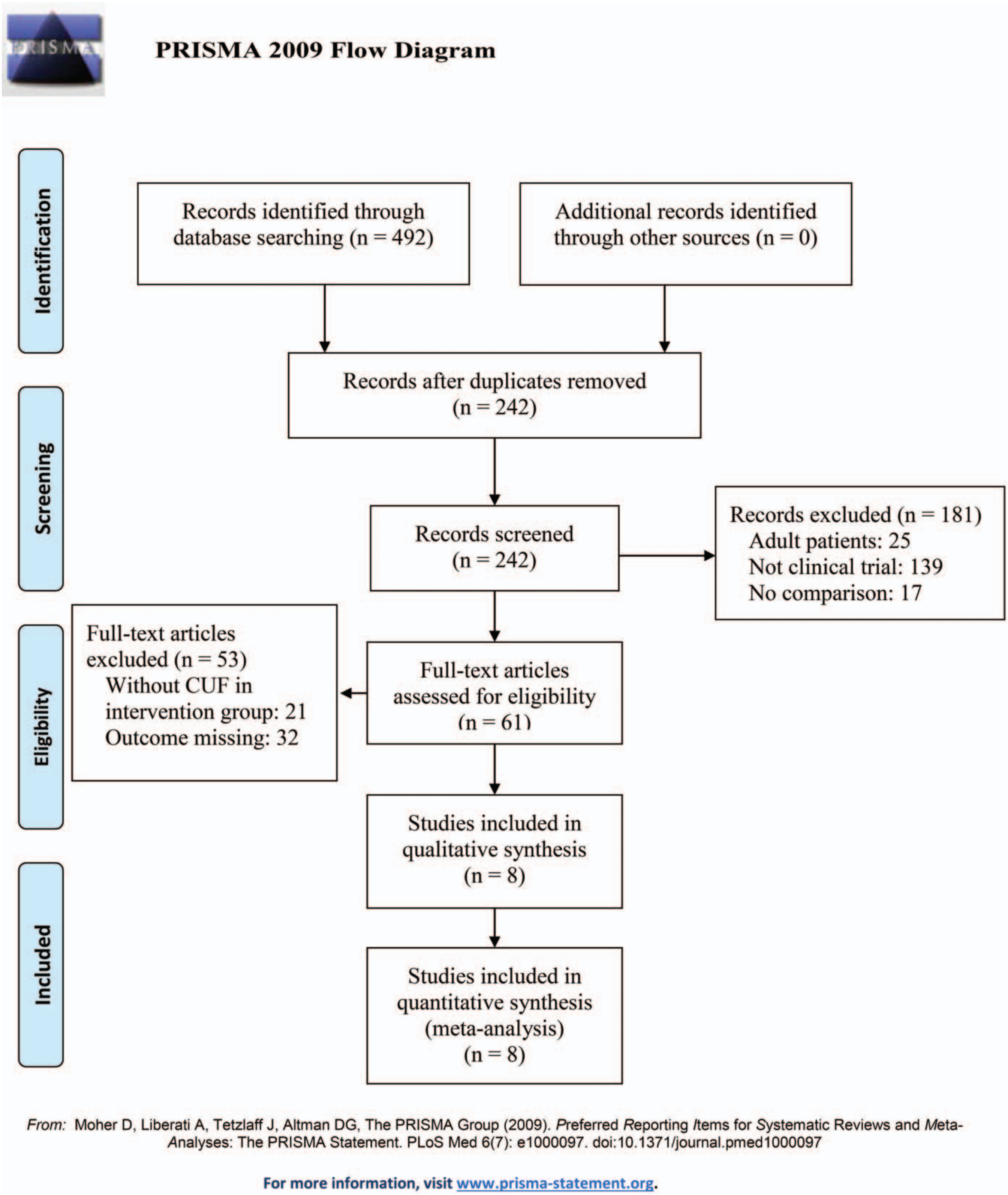

Figure 1. PRISMA flow diagram of eligible studies selection procedure. CUF = conventional ultrafiltration.

Table 1

Basic characteristics of included studies.

		MUF				CUF			
Year	First author	Patients	Age, mo	Weight, kg	Circuit	Patients	Age (Month)	Weight (kg)	Diseases
1998	Bando (A)[17]	50	17.7±20.7	8.5±5.2	VV	50	30.1±42.2	12.8±12.0	Complex CHD
1998	Bando (J)[19]	12	6.0±5.6	5.2±1.3	AV	12	7.4±4.8	7.4±5.0	CHD
2004	Sever[16]	13	9.38±1.94	7.27±0.73	AV	14	12.9±13.0	7.3±1.0	complex CHD
2005	Mahmoud[15]	20	13.1±4.1	7.8±2.1	AV	20	11.8±3.3	8.1±0.4	Biventricular CHD
2006	Williams[14]	21	2.14±2.46	4.52±1.23	AV	19	2.04±2.13	4.27±1.29	CHD
2007	Aggarwal[1]	15	30.0±20.8	10.0±3.8	AV	15	33.6±13.9	10.8±2.9	ASD, AVSD, TOF
2016	Ziyaeifard[18]	23	15.0±4.2	8.1±14	AV	23	17.0±6.3	8.5±1.2	CHD
2018	Milovanovic[20]	49	5.33±5.3	6.2±2.9	AV	49	6.53±5.63	6.7±3.0	CHD

Data are expressed as mean±SD; Bando (A): published in *Ann Thorac Surg* by Bando; Bando (J): published in *J Thorac Cardiovasc Surg* by Bando.

ASD=atrial septal defect, AV=artery- venous, AVSD=atrioventricular septal defect, CHD=congenital heart disease, CUF=conventional ultrafiltration, MUF=modified ultrafiltration, TOF=tetralogy of fallot, VSD=ventricular septal defect, VV=venous- venous.

AO duration was also listed in all the 8 trials,[1,14–20] and data from including trials were homogeneous by the Cochran's Q and I^2 tests ($I^2<0.01\%$, $P=.839$). The pooled result indicated that CUF and MUF combination had no significant difference in CPB time compared with CUF alone (SMD=−0.06, 95% CI −0.26 to 0.14, $P=.549$, Fig. 2B). The combined result was reliable according to the sensitivity analysis.

The prime volume was weighted by the weight of infants with a unit of mL/kg. Priming volume was tested in these 4 trials,[14,16,18,20] and the Cochran's Q and I^2 tests showed that there was homogeneous ($I^2<0.1\%$, $P=.594$), so fixed model was selected for analysis. The merged result showed that there was no difference in prime volume between the CUF+MUF infants and CUF alone infants (SMD=0.25, 95% CI −0.03 to 0.52, $P=.076$, Fig. 2C). When Ziyaeifard et al[18] were removed from the analysis, prime volume was higher in CUF+MUF infants (SMD= 0.33, 95% CI 0.03–0.62). So, a clear conclusion could not be reached basing on current clinical evidence concerning the prime volume.

3.3. Post-CPB and postoperative hematocrit

Post-CPB hematocrit, which was tested after the termination of CPB or MUF and postoperative hematocrit, which was assessed after the termination of the operation were both analyzed. There were 2 trials that were both published in 1998 By Bando et al[17,19]; we marked the trial published in *Ann Thorac Surg*[17,19] as Bando (A) and published in *J Thorac Cardiovasc Surg*[19] as Bando (J). Four trials[1,16,17,20] reported the post-CPB hematocrit. Significant heterogeneity was revealed ($I^2=88.4\%$, $P<.0001$), so we pooled the post-CPB hematocrit result under a random model. The result showed that post-CPB hematocrit significantly increased in CUF+MUF infants when compared with CUF alone ones (SMD=1.85, 95% CI 0.91–2.79, $P<.001$, Fig. 3). Removal of individual trials did not significantly alter the pooled result on post-CPB hematocrit. Only 1 trial[16] listed the postoperative hematocrit, so the effect of MUF on postoperative hematocrit is still unclear basing on current evidence.

3.4. Ultrafiltration volume

There were 4 studies that reported the outcome of ultrafiltration volume,[14,17,19,20] which was adjusted by weight of infants, and heterogeneity analysis found that there was significant heterogeneity ($I^2=90.3\%$, $P<.001$). The merged result indicated that the ultrafiltration volume was higher in CUF+MUF infants than CUF-alone infants under the random model (SMD=1.46, 95% CI 0.51–2.41, $P=.003$, Fig. 4). At the same time, the removal of the individual trial did not significantly alter the pooled result of ultrafiltration volume.

3.5. Post-CPB and postoperative hemodynamic changes

Post-CPB hemodynamic changes were tested at the end of CPB in the CUF group and the end of MUF in the MUF+CUF group, and postoperative hemodynamic changes were tested at the end of the

Table 2

Risk of bias assessment for evaluation the quality of each included trials.

Year	First author	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
1998	Bando (J)[19]	UR	UR	LR	LR	LR	LR	UR
2004	Sever[16]	UR	LR	UR	UR	LR	LR	UR
2005	Mahmoud[15]	UR	LR	UR	UR	LR	LR	LR
2006	Williams[14]	UR	LR	LR	LR	LR	LR	LR
2007	Aggarwal[1]	UR	LR	UR	UR	LR	LR	LR
2016	Ziyaeifard[18]	UR	LR	LR	LR	LR	LR	UR
2018	Milovanovic[20]	LR	UR	UR	LR	LR	LR	LR

Bando (A): published in *Ann Thorac Surg* by Bando; Bando (J): published in *J Thorac Cardiovasc Surg* by Bando.

HiR=high risk, LR=low risk, UR=unclear risk.

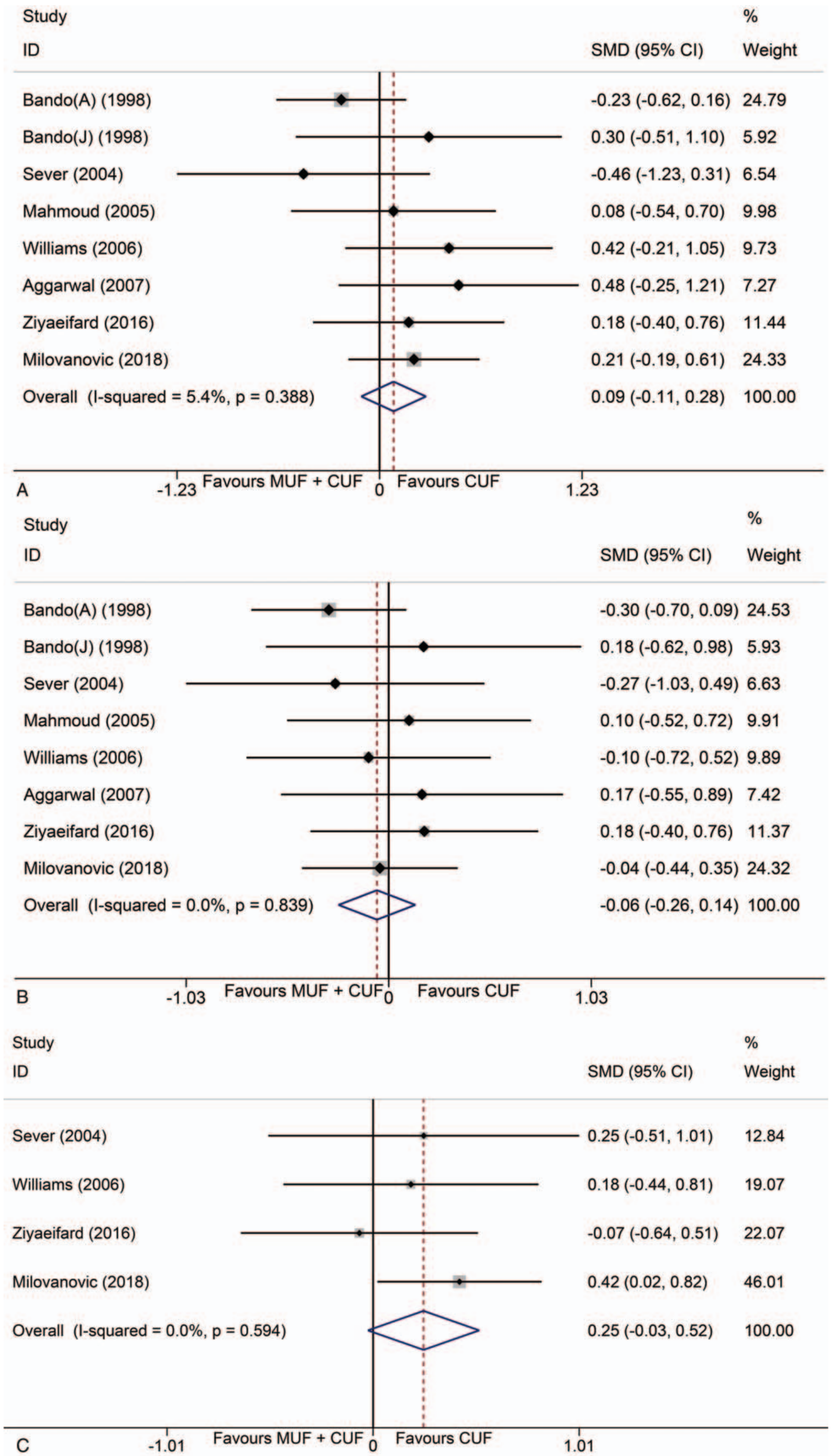

Figure 2. Forest plot of duration of CPB and AO duration, prime volume between MUF plus CUF and CUF alone in pediatric cardiac surgery. (A) Forest plot of duration of CPB duration between MUF plus CUF and CUF alone. (B) Forest plot of duration of AO duration between MUF plus CUF and CUF alone. (C) Forest plot of amount of prime volume between MUF plus CUF and CUF alone. Bando (A): published in *Ann Thorac Surg* by Bando; Bando (J): published in *J Thorac Cardiovasc Surg* by Bando. CI = confidence interval, CUF = conventional ultrafiltration, MUF = modified ultrafiltration, SMD = standard mean difference.

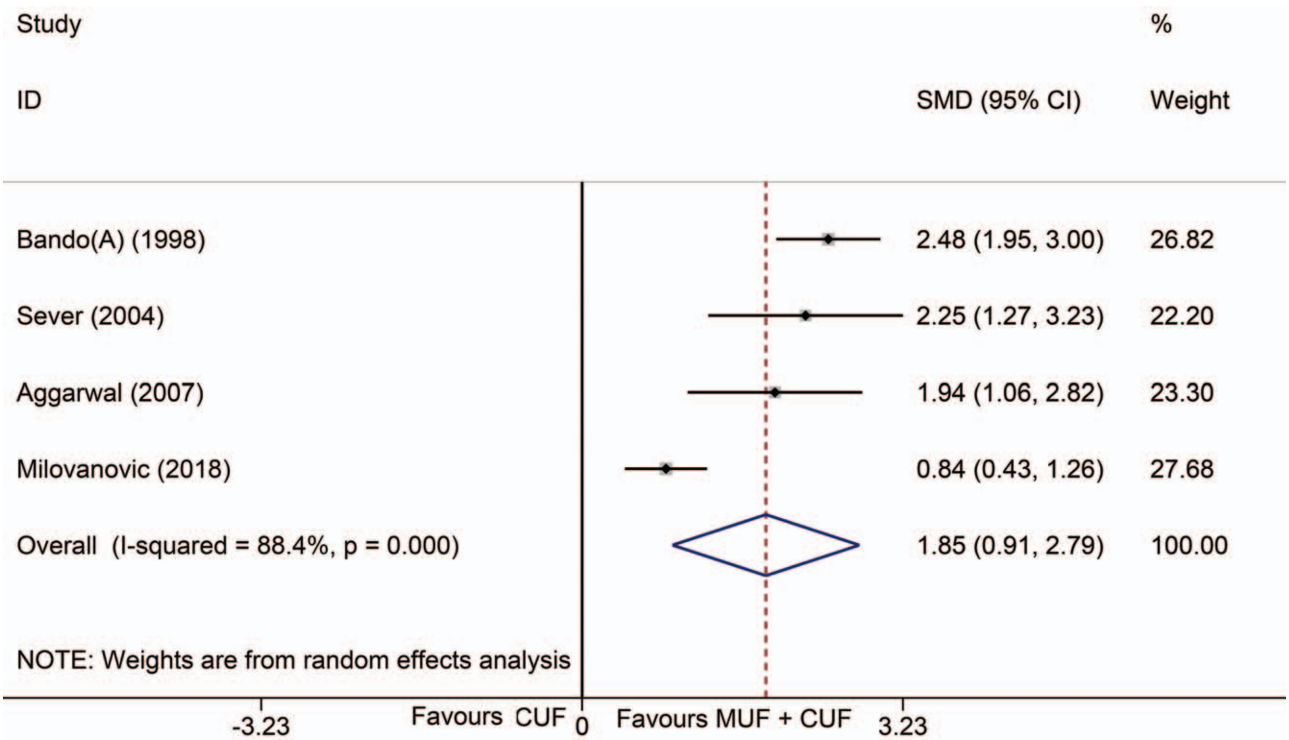

Figure 3. Forest plot of post-cardiopulmonary bypass hematocrit between MUF plus CUF and CUF alone in pediatric cardiac surgery. Bando (A): published in *Ann Thorac Surg* by Bando. CI, confidence interval, CUF=conventional ultrafiltration, MUF=modified ultrafiltration, SMD, standard mean difference.

operation. Unfortunately, the hemodynamic data did not report in all the trials included. Only 2 trials[16,19] reported the postoperative MAP. There was significant heterogeneity basing on the available MAP data (I^2=73.2%, P=.054), and the pooled result under random model suggested that MUF increased the postoperative MAP (SMD=1.270, 95% CI 0.082–2.468, P=.036) comparing CUF alone. However, this conclusion did not stand true when the trial of Sever et al[16] was removed from the analysis (SMD=0.684, 95% CI −0.14 to 1.51). Further evidence may be required to reach a clear conclusion concerning the effects of MUF on postoperative hemodynamic changes.

3.6. Postoperative blood requirement and chest tube drainage

Blood requirement was reported in 4 trials.[16,17,19,20] The pooled result under the random model (I^2=93.5%, P<.001) demonstrated that MUF did not reduce the perioperative blood requirement (SMD=−0.81, 95% CI −1.95 to 0.33, P=.165, Fig. 5A). But this conclusion reversed when the trial of Milovanovic et al[20] was removed from the analysis because all the 95% CIs were below zero (SMD=−1.32, 95% CI −2.51 to −0.13). A further clinical trial may be required to draw a clear conclusion concerning perioperative blood requirements.

The volumes of chest tube drainage weighted by body weight 48 hours after operation were examined in 5 trials.[1,16,17,19,20] Random model was selected because of the significant heterogeneity (I^2=76.5%, P=.002). Combined result showed that MUF plus CUF did not influence the postoperative chest tube drainage volume (SMD=−0.53, 95% CI −1.07 to 0.02, P=.128, Fig. 5B). This conclusion reversed when the trial of Milovanovic et al[20] was removed by sensitivity analysis (SMD=0.73,95% CI −1.43 to −0.04).

3.7. Duration of postoperative ventilation support, ICU stay, and hospital stay

Results of the postoperative ventilation support duration between MUF plus CUF and CUF alone were reported in 8 trials,[1,14–20] using a random effect model (I^2=87.0%, P<.001) showed that there was no significant difference in postoperative ventilation support duration between MUF plus CUF and CUF alone (SMD=−0.52, 95% CI −1.12 to 0.07, P=.084, Fig. 6A). When the trial of Williams et al[1,14–20] was removed from the pooled trials, the result suggests that MUF plus CUF got a shorter postoperative ventilation support duration than CUF alone (SMD=−0.71, 95% CI −1.29 to −0.14). Further pieces of evidence may be required to reach a clear conclusion concerning postoperative ventilation support duration because of the unstable sensitivity analysis result.

Postoperative ICU stay duration was examined in 7 trials.[1,14–18,20] Pooled result under random model (I^2=62.2%, P=.014) indicated that MUF plus CUF shorted the ICU stay duration (SMD=−0.38, 95% CI −0.73 to −0.04, P=.031, Fig. 6B). However, when the trials of Bando (A),[17] Sever (2004),[16] Aggarwal (2007),[1] or Ziyaeifard (2016)[18] were removed from all the including trials, the value of zero was included in the 95% CIs (SMD=−0.32, 95% CI −0.71 to 0.07; SMD=−0.32, 95% CI −0.68 to 0.04, SMD=−0.39, 95% CI −0.78 to 0.01, and SMD=−0.30, 95% CI −0.67 to 0.60, respectively). So, more clinical evidences were required to clarify the postoperative ICU stay duration in these infants.

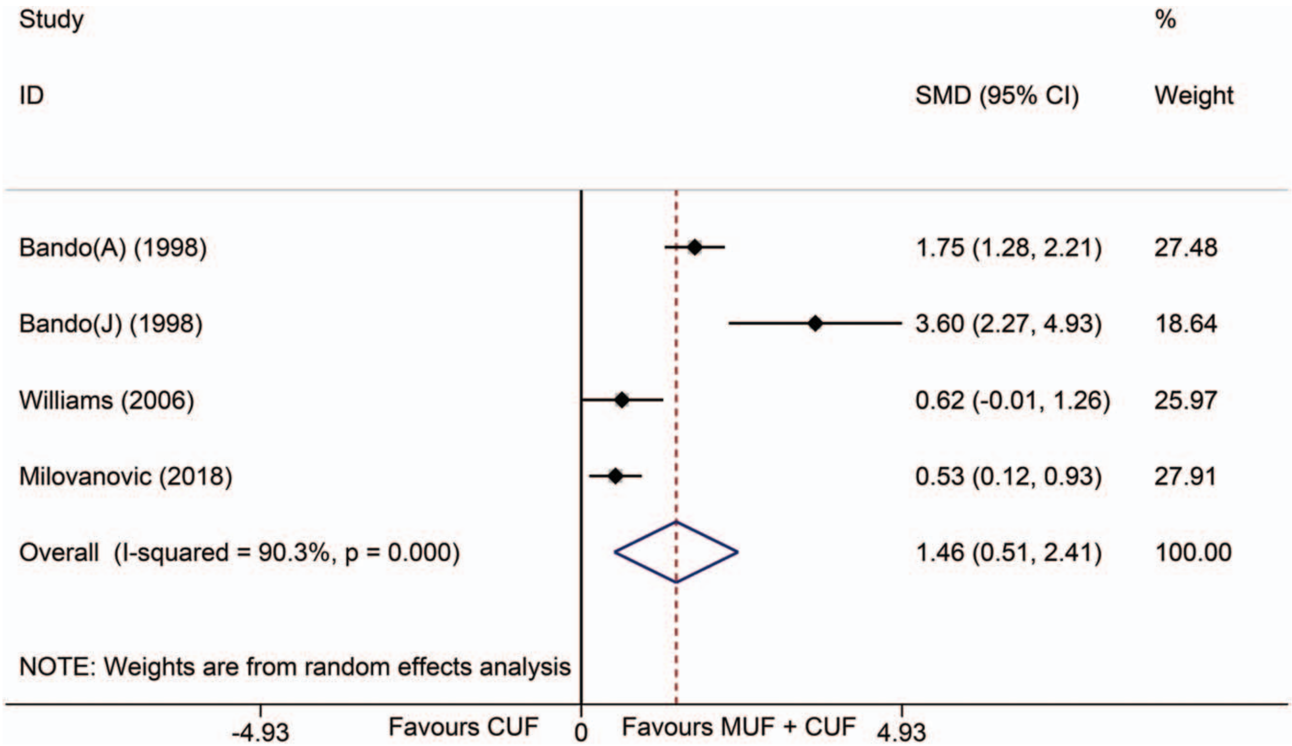

Figure 4. Forest plot of ultrafiltration volume between MUF plus CUF and CUF alone in pediatric cardiac surgery. CI = confidence interval, CUF = conventional ultrafiltration, MUF = modified ultrafiltration, SMD = standard mean difference.

Days of hospital stay after operation were reported in 4 trials,[14,15,18,20] and the heterogeneity test indicated that there was no significant heterogeneity ($I^2=15.3\%$, $P=.315$). The pooled results using a fixed model showed that there was no significant difference in the hospital stay days after operation between MUF+CUF and CUF alone (SMD = −0.003, 95% CI −0.27 to 0.26, $P=.883$, Fig. 6C). The sensitivity analysis concerning ICU stay and hospital stay duration did not change the conclusion.

4. Discussion

On the basis of currently available clinical trials regarding combination MUF and CUF versus alone CUF for pediatric cardiac surgery, this meta-analysis showed MUF plus CUF increase post-CPB hematocrit and ultrafiltration volume when compared with CUF alone for pediatric cardiac surgery. Meanwhile, MUF plus CUF did not significantly influence postoperative hospital stay duration, CPB and AO duration. Further study will be necessary to clarify the effect of MUF plus CUF on the prime volume, postoperative hemodynamic changes, blood requirement, the postoperative chest tube drainage volume, mechanical ventilation duration, and ICU duration.

The effect of priming-related hemodilution is significant in pediatric patients, including an increased capillary permeability with tissue edema, which is followed by multiple organ dysfunctions, principally in the lungs, heart, and brain. Nowadays, both MUF and CUF are widely used in pediatric cardiac surgery. MUF was a very effective technique to stabilize pediatric patients after CPB in the past decades, and reported benefits of MUF include raising the hematocrit, decreasing blood product transfusion, intubation duration, and postoperative chest tube drainage.[8] The main reason is that the CPB circuits and priming volumes were very large compared with today.[8] In our analysis, pooled results suggested that MUF plus CUF can increase post-CPB hematocrit and ultrafiltration volume when compared with CUF alone. Unfortunately, the effect of MUF and CUF combination on postoperative hematocrit and prime volume still unclear because of the clinical outcome deficiency. This result suggested that MUF and CUF combination has a higher efficiency of hemoconcentration compared with CUF alone. Excess water removal and blood salvage by MUF result in higher hematocrit levels after CPB. Meanwhile, the hematocrit was increased because of the elimination of body water. A meta-analysis in 2011 revealed that MUF resulted in significantly higher post-CPB hematocrit levels in pediatrics.[21]

Technical advances in reducing the size of CPB circuitry have decreased prime volumes significantly in the current era, CPB circuits are smaller, and prime volumes are less than in past decades.[8,22] 2007 STS/SCA guideline on perioperative blood transfusion and blood conservation in cardiac surgery reported that MUF considerably attenuated the dilutional coagulopathy that occurs during CPB in children by improving hematocrit.[23] Some experts insisted that much lesser reported but very significant complications the possibility of is no longer a risk by eliminating MUF, which including the potential risk for cerebral artery steal and air entrainment into the oxygenator, cannula obstruction, hypothermia during MUF.[24] Additionally, MUF can be ineffective if the patient is bleeding excessively, making this another common cause of MUF-associated hemodynamic instability after separation from CPB.[25]

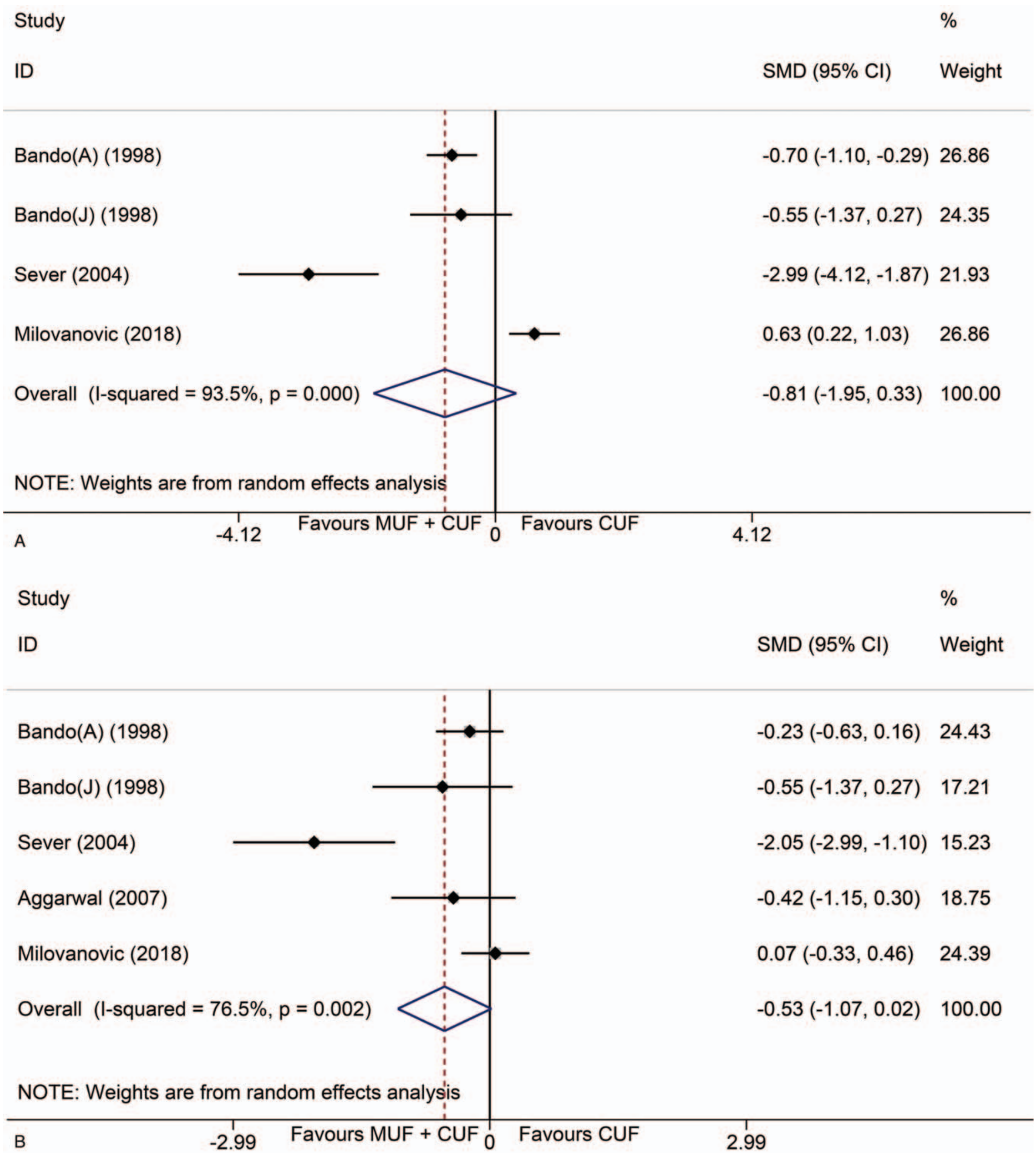

Figure 5. Forest plot of postoperative blood requirement and chest tube drainage between MUF plus CUF and CUF alone in pediatric cardiac surgery. (A) Forest plot of postoperative blood requirement between MUF plus CUF and CUF alone. (B) Forest plot of chest tube drainage between MUF plus CUF and CUF alone. Bando (A): published in *Ann Thorac Surg* by Bando; Bando (J): published in *J Thorac Cardiovasc Surg* by Bando. CI=confidence interval, CUF=conventional ultrafiltration, MUF=modified ultrafiltration, SMD=standard mean difference.

Our current analysis could not get a reliable result concerning the effect of MUF combined CUF on postoperative hemodynamic changes because of the limitation of hemodynamics clinical data, so more trials are essential to make a clear conclusion with high reliability. Better infants' hemodynamic changes were seen after MUF in most clinical trials. A meta-analysis in 2011 found a significant improvement in systemic blood pressure favoring the MUF group infants.[21] Numerous factors may involve in the hemodynamic improvements after MUF. The cardiac function improvement may contribute to these improvements.[26,27] Another important mechanism that accounts for the improvements in hemodynamic by MUF may be MUF-induced

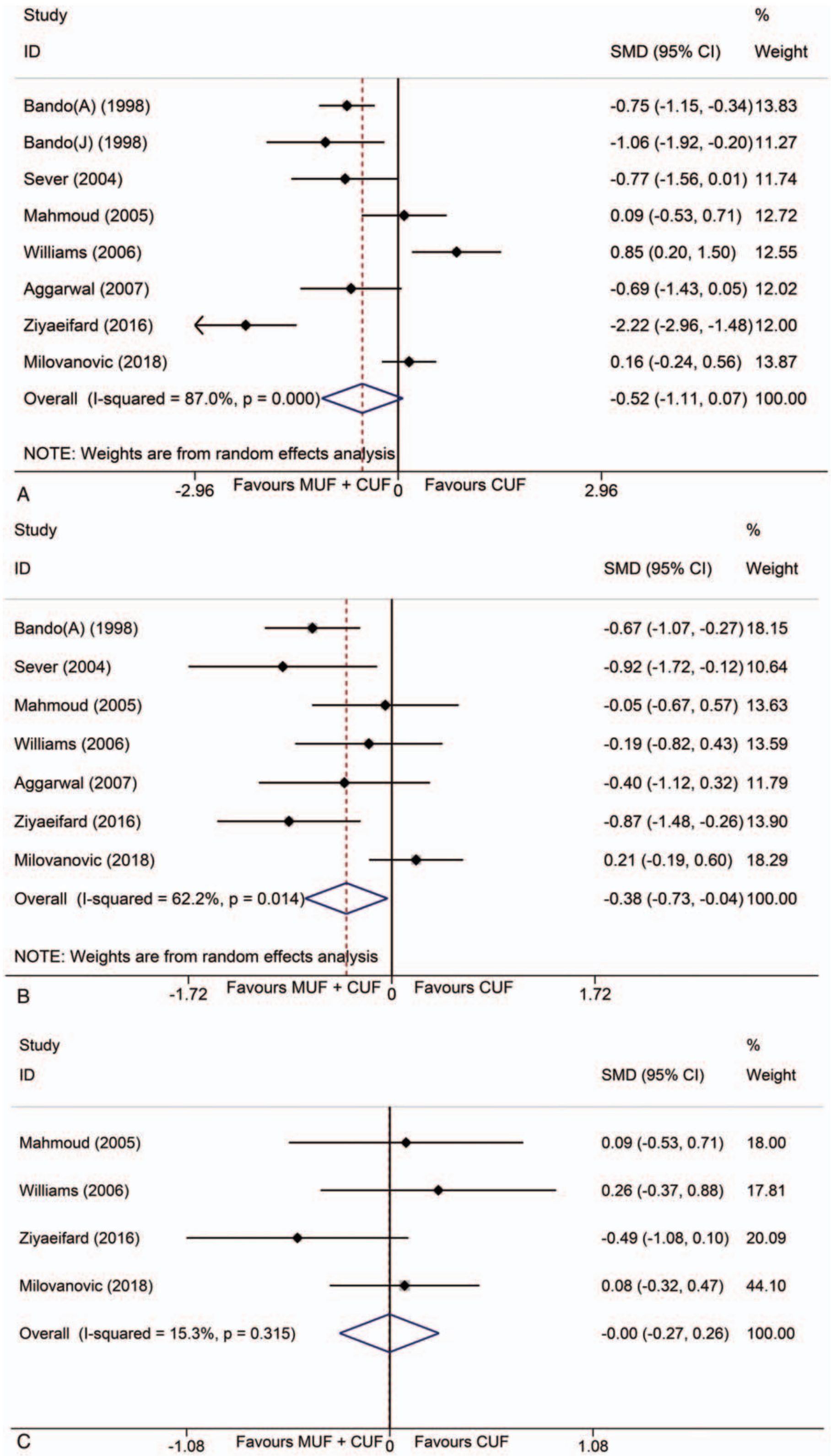

Figure 6. Forest plot of duration of postoperative ventilation support, ICU stay, and hospital stay between MUF plus CUF and CUF alone. (A) Forest plot of postoperative ventilation support between MUF plus CUF and CUF alone. (B) Forest plot of ICU stay between MUF plus CUF and CUF alone. (C) Forest plot of hospital stay duration between MUF plus CUF and CUF alone. Bando (A): published in *Ann Thorac Surg* by Bando; Bando (J): published in *J Thorac Cardiovasc Surg* by Bando. CI=confidence interval, CUF=conventional ultrafiltration, MUF=modified ultrafiltration, SMD=standard mean difference.

hemoconcentration and reduction of myocardial edema. Meanwhile, our meta-analysis indicated that CUF combined MUF did not get reliable pooled results concerning postoperative chest tube drainage volumes, blood requirements. The previous meta-analysis regarding the effects of MUF on pediatric cardiac surgery failed to identify a statistically significant difference in postoperative chest tube drainage between MUF and CUF.[26,27] Bleeding and blood requirement in the postoperative period have multiple factors, such as hemodilution, fibrinolysis disorder, and platelet activation.[23,28] Trials suggested that MUF considerably attenuated the coagulopathy after CPB in children,[29,30] and found that MUF was associated with considerable rises in platelet count, hematocrit, plasma protein, prothrombin, factor VII, and fibrinogen levels.[23,31]

In our meta-analysis, CUF and MUF combination did not influence the postoperative hospital stay duration and did not prolong the CPB and AO duration. Meanwhile, it failed to make a clear conclusion concerning postoperative ventilation support and ICU stay duration. Pulmonary compliance after CPB as common compliance in pediatric may result in a delay in the ICU and hospital stay duration. The main reasons for CPB-induced lung injury include increased interstitial lung water, lung ischemia, and inflammatory reaction.[32] MUF reported can eliminate excess water and ameliorate inflammatory reactions,[27,32,33] which may influence the duration of mechanical ventilation, ICU stays, and total hospitalization after the operation.[15,34] The previous meta-analysis regarding the effects of MUF on pediatric cardiac surgery indicated that there was no difference in the postoperative duration of ventilation support and ICU stay between MUF alone and CUF alone.[15,34] The synthesized results in our meta-analysis suggest that MUF plus CUF failed to make clear conclusions concerning postoperative ventilation and ICU stay, and had no effect on the postoperative hospital stay duration. It is noteworthy that these clinical outcomes including duration of ventilation, length of ICU stay, and length of hospital stay were significantly affected by criteria for extubation, ICU discharge, and hospitalization, which may differ from study to study.

Our meta-analysis has some limitations to note. First, the clinical outcomes such as inotropic drug usage, removal of extracellular water, cardiac function, pulmonary function and coagulation function, inflammatory response after MUF were not analyzed because of the original data missing. Second, some outcomes such as postoperative hemodynamic changes, hematocrit after operation, and tube drainage were only reported in very few trials, so the evidence strength of these pooled outcomes may not be so reliable. Third, some important clinical outcomes, such as surgical outcome, reduction of perioperative morbidity and mortality, adverse events, cost analysis did not analyze, because these outcomes did not mention in the including trials. Last, some outcomes in our meta-analysis had significant heterogeneity by the I^2 test, and pooled results under a random model may reduce the persuasion of these outcomes based on currently available randomized controlled trials. The types of cardiac surgeries, age distribution, very small numbers of patients, and included trials may contribute to the significant heterogeneity of these outcomes, and may influence the confidence of the merged results. More trials are required to evaluate the contribution of these factors on the clinical results, to optimize individual CPB management.

In conclusion, based on current clinical trials concerning MUF plus CUF versus CUF alone for pediatric cardiac surgery, this meta-analysis showed that MUF plus CUF increase post-CPB hematocrit and ultrafiltration volume when compared with CUF alone. Meanwhile, MUF did not significantly influence the postoperative hospital stay, CPB, and AO duration.

Author contributions

Conceptualization: Chengliang Zhang.
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Project administration: Jianqin Yan.
Software: Xuliang Chen, Junjie Zhang, Chengliang Zhang.
Supervision: Chengliang Zhang.
Writing – original draft: Jiajia Hu, Xuliang Chen.
Writing – review & editing: Chengliang Zhang.

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