The effect of the head-up position in cardiopulmonary resuscitation – A systematic review and meta-analysis

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Research

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Abstract

Objective

The pros and cons of the head-up position (HUP) in cardiopulmonary resuscitation (CPR) have been controversial in previous studies. This study aims to clarify the effect of HUP CPR compared to supine position (SUP) CPR.

Method

Three databases were comprehensively searched (PubMed, EMBASE and the Cochrane Library) for articles published from database inception to 10 May 2021. The primary outcome was cerebral perfusion pressure (CerPP). The secondary outcomes were mean intracranial pressure (ICP), mean artery pressure (MAP), coronary artery perfusion pressure (CoPP) and the return of spontaneous circulation (ROSC) rate.

Result

A total of 7 studies including 138 animals were included. We found that CerPP (SMD, 1.58; 95% CI, 0.98–2.19; $p < 0.01$; $I^2 = 51\%$) and ICP (SMD, -3.59; 95% CI, -5.16– -2.02; $p < 0.01$; $I^2 = 87\%$) were decreased significantly in the HUP group. HUP had a similar MAP (SMD, -0.54; 95% CI, -1.75–0.66; $p = 0.38$; $I^2 = 87\%$) and ROSC rate (RR, 0.9; 95% CI, 0.31–2.60; p = 0.84; I2 = 65%) to SUP. In addition, there was an increased CoPP trend in HUP, but the difference was not statistically significant (SMD, 0.92; 95% CI, -0.24–2.08; $p = 0.12$; $I^2 = 84\%$)

Conclusion

The HUP 30° in active compression-decompression CPR (ACD-CPR) with an impedance threshold device (ITD) can increase CerPP by significantly lowering ICP and maintaining MAP compared to SUP, and the effect is immediate and lasts the whole CPR duration. In addition, CoPP might also be increased compared to that with SUP.

Introduction

Cardiac arrest is the most critical challenge faced by every clinical physician because it has varied etiologies and a high mortality rate [1]. High-quality cardiopulmonary resuscitation (CPR) and improvement in emergency medical service (EMS) system has been proven to result in a higher return of spontaneous circulation (ROSC) rate in out-of-hospital cardiac arrest (OHCA) patients, and the survival rate has improved over time since 2006. However, less than 10% of patients survive to hospital discharge, and survival with good neurological outcomes is even lower [2, 27, 28].

Insufficient brain perfusion is a key factor in poor neurological outcome. Cerebral perfusion pressure (CerPP), which is calculated as the mean arterial pressure (MAP) minus the intracranial pressure (ICP), decreases dramatically during cardiac arrest for the following reasons. First, once cardiac arrest occurs, inflammatory systems are activated to respond to whole-body ischemia, resulting in increased membrane permeability [3]. In addition, the blood–brain barrier (BBB) breaks down because of intracellular acidosis, stopping oxidative phosphorylation and lactate accumulation [4]. Due to these two effects, serum proteins and water pass from blood to brain tissue, leading to neuronal, glial or axonal injuries [5] and increasing ICP. Second, chest compressions are performed to increase intrathoracic pressure, rather than direct compression of the heart, to create blood flow. Increased intrathoracic pressure increases ICP by elevating the pressure in non-valved veins (for example, the paravertebral venous plexus), which reduces the drainage of blood from the brain and thoracic cerebrospinal fluid (CSF) [6]. Finally, optimal CPR can provide approximately 20%~30% of pre-arrest cardiac output [7], and only 30% of it flows to the brain [4]. As a result, the rate of survival with good neurological outcomes is dismal.

In recent years, some studies have revealed that head-up position CPR could decrease ICP and improve CerPP [8], and that it may even improve coronary perfusion pressure (CoPP) [9] and increase the ROSC rate [10] in animal experiments. Compared to conventional CPR, in which the patient lies down at 0 degrees, elevating the head during CPR could accelerate brain venous return and the hydrostatic displacement of CSF from the cerebral ventricles to the spinal cavity [11]. Thus, ICP decreases and CerPP increases. In addition, facilitating venous return may increase CoPP, and a higher CoPP is associated with a higher ROSC rate [12]. However, Park YJ et al. demonstrated that head-up CPR could worsen the survival rate [13]. The outcome of head-up CPR seems inconclusive, so clarifying the effect of head-up CPR is important. Therefore, in this article, a comprehensive systematic review and meta-analysis was performed to evaluate the effect of head-up CPR in animal models and to draw conclusions to establish a new strategy for CPR in the future.

Method

We conducted this study according to the Cochrane Handbook for Systematic Reviews of Interventions guidelines [14], Hooijmans et al [15] and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statements [16].

Eligibility criteria:

Types of studies

All types of studies were eligible except for case reports, reviews, abstract publications and conference presentations because there is no detailed study design to assess quality or data to analyze.

Types of participants

We includes all kinds of animal studies. If different animal species were included, we analyzed and discussed them separately.

Types of interventions

Studies comparing head-up position (HUP) CPR at a fixed degree with supine position (SUP) CPR were included. There were no restrictions on the head-up degree, no-flow time, CPR device, CPR protocol, or CPR duration. The head-up degree is defined as the angle between the head-chest plane and the horizontal plane. A head-up degree of zero means the supine position. No-flow time was defined as the time from cardiac arrest to the start of CPR. CPR duration was defined as the time from the start of CPR to the stopping point of CPR regardless of whether ROSC was achieved.

Types of outcome measures

The primary outcome was the CerPP in both groups. The secondary outcomes were the mean ICP, MAP, CoPP and ROSC rates. If the studies presented outcomes such as systolic pressure, diastolic pressure and ICP during the compression/decompression phase, we estimated MAP as (systolic pressure + diastolic pressure)/2 and mean ICP as (ICP during compression + ICP during decompression)/2 because the compression time is approximately equal to the decompression time during CPR.

Search methods for the identification of studies

Studies were obtained by comprehensively searching 3 databases (PubMed, EMBASE and the Cochrane Library) from database inception to 10 May 2021 without language restriction. The following key words or medical subject heading (MeSH) terms were used: head-up position or head up or torso up or head elevation or tilt AND resuscitation or CPR. We also reviewed the references of the identified articles to avoid missing possible articles.

Data extraction and quality assessment

Two authors (C.K. Chen and Z.Y. Lin) searched articles from 3 databases and extracted the data independently. We collected the following information from each eligible study: authors, publication year, study design, study group, CPR protocol, CPR device, no-flow time, CPR duration, intervention/control details and outcome data. If the data were presented in a graph instead of as digits, we used GetData Graph Digitizer software, version 2.26 (http://getdata-graph-digitizer.com/download.php), to extract the data.

The Animal Research: Reporting of In Vivo Experiments (ARRIVE) guidelines 2.0 [17] were used to evaluate the quality of the included articles, as assessed by two authors (C.K. Chen and Z.Y. Lin) independently. There were 21 domains that were assessed for each study. Each domain was rated as “+” if it met the domain recommendation; otherwise, it was rated as “-”.

Finally, any disagreement that occurred during the article search, data extraction or quality assessment was resolved by a discussion between a third author (C.C. Huang) and the previously mentioned two authors to reach a consensus.

Statistical analysis

We use Review Manager (RevMan [Computer program], Version 5.4.1, The Cochrane Collaboration, 2020) to analyze all data. Because some of the included studies presented results as the standard error of the mean (SEM), we converted SEM to the standard deviation (SD) by the formula SEM = SD/√(sample size) [18]. We expressed continuous data as standardized mean differences (SMD) and dichotomous data as risk ratios (RR). In addition, 95% confidence intervals (CI) were calculated for all of the results.

We applied a random-effects model for all analyses and chi-square and I^2 tests to evaluate heterogeneity. Subgroup analysis was conducted based on the change in position in CPR and the CPR duration of fixed-position CPR. In addition, we performed a visual inspection of the funnel plot to assess publication bias, and a sensitivity analysis was conducted by repeating the analysis after removing one study at a time. Finally, the results were presented in forest plots.

Result

A total of 285 studies were retrieved initially from 3 databases (PubMed: 92, Embase: 143, Cochrane: 50). After removing duplicates (n = 62) and excluding 203 articles by screening titles and abstracts, 20 full-text articles were assessed for eligibility. Next, we excluded 13 articles because they were review articles, original studies, or posts/conference abstracts; studied human cadavers or sequential elevations; or lacked detailed data. Finally, 7 studies [8, 9, 13, 19–22], including 138 pigs, were included in the final meta-analysis (Fig. 1).

The head-up angle ranged from − 60° to 60°. Three studies [9, 13, 20] used the Trendelenburg position or reverse-Trendelenburg position, and the others [8, 19, 21, 22] elevated the head and shoulders at only 30°. Thus, we presented our outcomes by comparing the head-up position at 30° to the supine position. The no flow time ranged from 6 min to 15 min, and the CPR time ranged from 6 min to 26 min. All of the included studies used active compression-decompression (ACD) CPR with/without an impedance threshold device (ITD), and 2 of them [8, 19] also used conventional CPR (Table 1). However, we could not analyze the effect of HUP CPR in conventional CPR due to the lack of an experimental group in one study [8].

Table 1
The characteristics of the included studies

Study, year	Design	Species	Sample size	No-flow time	CPR method	Head-up angle	CPR time
Debaty et al. 2015 [9]	Non-RCT	Female Yorkshire farm pigs	22	6 min	ACD-CPR + ITD	-30°~50° [a]	22 min
Ryu et al. 2016 [19]	RCT	Female Yorkshire farm pigs	30	8 min	CCPR, ACD-CPR + ITD	0° and 30°	22 min
Kim et al. 2017 [20]	Non-RCT	Female pigs	12	6 min	ACD-CPR + ITD	-60°~60° [a]	18 min
Moore et al. 2017 [21]	RCT	Female Yorkshire farm pigs	18	8 min	ACD-CPR + ITD	0° and 30°	20 min
Putzer et al. 2018 [22]	RCT	Domestic pigs	20	8 min	ACD-CPR	0° and 30°	20 min
Moore et al. 2018 [8]	Non-RCT	Female Yorkshire farm pigs, pig cadaver, human cadaver	18 [b]	6 min	CCPR, ACD-CPR + ITD	0° and 30°	26 min
Park et al. 2019 [13]	RCT	Female Yorkshire farm pigs	18	15 min	ACD-CPR + ITD	0° and 30° [a]	6 min
RCT, randomized controlled trial; ACD, active compression-decompression; CPR, cardiopulmonary resuscitation; ITD, impedance threshold device; CCPR, conventional cardiopulmonary resuscitation							
a: A negative number represents the Trendelenburg position, and a positive number represents the reverse-Trendelenburg position.							
b: Includes 9 human cadavers							

Quality assessment

The quality assessments of our included studies are shown in Table 2. The average score was 16.86 ± 0.83 (mean ± SD), ranging from 15 to 18. A visual inspection of the funnel plot revealed symmetry, suggesting no publication bias (Additional file 1).

Table 2
Quality assessments according to the ARRIVE guidelines 2.0

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	Quality score
Debaty 2015	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	-	+	-	+	+	+	17
Ryu 2016	+	+	-	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	17
Kim 2017	+	+	-	+	+	+	+	-	+	+	+	+	+	+	-	-	+	+	+	+	+	17
Moore 2017	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+	18
Putzer 2018	+	+	-	+	-	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	17
Moore 2018	+	-	-	-	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	15
Park 2019	+	+	-	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	17

Quality items: (1) study design; (2) sample size; (3) inclusion and exclusion criteria; (4) randomization; (5) blinding; (6) outcome measures; (7) statistical methods; (8) experimental animals; (9) experimental procedures; (10) results; (11) abstract; (12) background; (13) objectives; (14) ethical statement; (15) housing and husbandry; (16) animal care and monitoring; (17) interpretation/scientific implications; (18) generalizability/translation; (19) protocol registration; (20) data access; and (21) declaration of interests.

Primary outcome

Seven studies including 131 participants were analyzed. The overall CerPP increased significantly in the HUP group compared to the SUP group (SMD, 1.58; 95% CI, 0.98–2.19; $p < 0.01$; $I^2 = 51\%$) (Fig. 2A).

Subgroup analysis of CerPP showed that regardless of whether the position was changed during CPR, CerPP was significantly increased in the HUP group (SMD, 2.47; 95% CI, 0.77–4.16; $p = 0.004$; $I^2 = 80\%$ and SMD, 1.29; 95% CI, 0.76–1.82; $p < 0.01$; $I^2 = 0\%$) (Fig. 2A).

In addition, in fixed-position CPR studies, we further evaluated whether the duration of CPR affected our primary outcome, and the results still showed a significant increase in CerPP in the HUP group regardless of whether the duration of CPR was < 10 min, 10–20 min, or > 20 min ($p < 0.01$ in all 3 subgroups) (Fig. 2B).

Secondary outcomes

ICP and MAP

The overall ICP was significantly lower in the HUP group than in the SUP group (SMD, -3.59; 95% CI, -5.16– -2.02; $p < 0.01$; $I^2 = 87\%$), regardless of whether the position was changed during CPR (SMD, -4.22; 95% CI, -7.37– -1.07; $p < 0.01$; $I^2 = 91\%$ and SMD, -3.47; 95% CI, -5.61 - -1.33; $p < 0.01$; $I^2 = 86\%$) (Fig. 3A) and the duration of CPR ($p < 0.01$ in all 3 subgroups) (Additional file 2). On the other hand, we did not find a significant difference in MAP between the HUP group and the SUP group (SMD, -0.54; 95% CI, -1.75–0.66; $p = 0.38$; $I^2 = 87\%$) regardless of whether the position was changed during CPR (SMD, -2.00; 95% CI, -4.48–0.48; $p = 0.11$; $I^2 = 91\%$ and SMD, 0.05; 95% CI, -1.50–1.61; $p = 0.95$; $I^2 = 87\%$) (Fig. 3B) and the duration of CPR (Additional file 3).

CoPP

There was an increased trend in CoPP in the HUP group, but it did not reach statistical significance (SMD, 0.92; 95% CI, -0.24–2.08; $p = 0.12$; $I^2 = 84\%$). However, the subgroup analysis revealed that CoPP was increased in the HUP group when the position during CPR was changed (SMD, 2.80; 95% CI, 0.15–5.45; $p = 0.04$; $I^2 = 90\%$) (Fig. 4A). We did not observe a difference between the groups according to the duration of CPR (Additional file 4).

ROSC rate

Only 3 studies [13, 19, 21] with 50 participants reported the ROSC rate. The ROSC rate was 50% (12/24) in the HUP group and 58% (15/26) in the SUP group. There was no significant difference between the groups (RR, 0.9; 95% CI, 0.31–2.60; $p = 0.84$; $I2 = 65\%$) (Fig. 4B).

Discussion

The most important result of our study is that the HUP at 30° during CPR can significantly increase CerPP, mainly by reducing ICP, compared to the SUP. CerPP, which is calculated by MAP minus ICP, could be increased by higher MAP and/or lower ICP. The reason for the lower ICP is that when elevating the head and body up to 30° during CPR, ICP will decrease by facilitating brain venous return and CSF movement into the spinal subarachnoid space, which is consistent with previous studies, even at different elevation angles ranging from 10° to 50° [9, 23]. In addition, the reduction in ICP also decreased the resistance to forward brain blood flow, which is generated by each chest compression. This effect could explain the findings of 2 of our included studies [9, 21], which demonstrate that brain blood flow increased significantly in HUP compared with SUP. Furthermore, due to the heterogeneous study protocols in our included studies, we analyzed the CerPP with regard to whether the position during CPR was changed or fixed, and in fix position CPR studies, we further evaluated the duration of CPR, which showed significantly increased CerPP in all HUP groups. Thus, HUP in CPR can reduce ICP, whenever the head is elevated during CPR, and the effect could last the whole CPR duration.

The other important result is that we did not find a significant difference in MAP between the HUP group and the SUP group, regardless of whether the position was changed during CPR and the duration of CPR. Maintaining a sufficient blood pressure by pumping upwards to the brain is important in CPR. From a physiological perspective, elevating the head and chest in CPR may reduce MAP because of the gravity effect. Each chest compression will pump more “uphill” than in the supine position. On the other hand, ACD-CPR with ITD could generate sustained aortic pressure, and the HUP may reduce the resistance of blood flow to the brain. Therefore, the net effect of MAP revealed no significant difference between the 2 groups in our study. The absolute MAP value was much lower in Putzer et al [22], who did not use ITD in ACD-CPR, and MAP along with CerPP decreased gradually over time. Debaty et al. [9] revealed that MAP showed a significant decrease immediately once ITD was removed in HUP CPR. These results could support our inferences. In addition, of our included studies, 2 [13, 20] showed decreased MAP in the HUP, while the others revealed no significant difference between the 2 groups. Both of them were in the reverse-Trendelenburg position, rather than elevated head and chest only. Because more blood deposits in the lower extremities, we speculate that ACD-CPR with ITD does not overcome the physiological effect of the reverse-Trendelenburg position, resulting in a decrease in MAP. Interestingly, pulmonary edema is a common complication of cardiac arrest [24]. Elevating the chest may have better blood-gas exchange caused by reduced lung congestion and pulmonary vascular resistance because of the gravity effect [19]. This potential benefit should be confirmed by more studies.

Although there were no differences found in CoPP between the 2 groups, there was an increasing trend of CoPP in the HUP, despite the lack of statistical significance. CoPP is calculated by diastolic aortic pressure minus right atrial pressure [25]. Theoretically, while the head and chest are elevated, right atrial pressure is also decreased by the gravity effect. As a result, CoPP could be increased under ACD-CPR with ITD to maintain sufficient diastolic aortic pressure. Kim et al. [20] revealed that CoPP increased gradually from the head-down position and supine position to the head-up position and reached the highest CoPP at 30°. On the other hand, two of the included studies [9, 21] directly measured heart flow and revealed no significant difference between the 2 groups. In our study, we did not observe an apparent increase in CoPP in the HUP, perhaps due to different study protocols and small study groups.

Only 3 included studies [13, 19, 21], including 50 Yorkshire farm pigs, reported the ROSC rate, and the results showed no difference between the two groups. In these 3 studies, Park et al. [13] revealed that the ROSC rate and survival rate were reduced significantly in the HUP group (ROSC rate: 1/8 in HUP vs. 6/8 in SUP, $p = 0.04$; survival rate: 0/8 in HUP vs. 6/8 in SUP), while the others showed no difference. Effective chest compression with sufficient CoPP is crucial for successful CPR. In a previous study on the relationship between CoPP and CPR, canines needed 20 mmHg, and humans needed at least 15 mmHg to achieve ROSC [26]. Although the minimal CoPP required to achieve ROSC is different between different species, the CoPP and MAP in Park et al. were much lower than those in the other included studies due to the use of the reverse-Trendelenburg position. In addition, the 15-min untreated ventricular fibrillation time was also far longer than the others. These 2 reasons could explain the dismal ROSC rate in the HUP.

To the best of our knowledge, this is the first meta-analysis comparing HUP to SUP CPR in animal models. The strength of this analysis includes further confirming the effect of HUP CPR. In addition, we performed subgroup analysis according to position changes and the duration of CPR due to heterogeneous study protocols. Moreover, two authors used the ARRIVE guidelines 2.0 to evaluate inclusion study quality. There were also some limitations. First, all of the included studies used healthy animals, and a ventricular fibrillation model was used to simulate cardiac arrest. However, cardiac arrest is caused by more complex reasons in human beings, and human CPR physiology is more dynamic. Thus, the results of our study may not be totally transferrable to humans. Second, an optimal CPR position is necessary to achieve ideal CerPP and CoPP. We compared only the head-up 30° position to the supine position. Thus, the best CPR position has not yet been found. Third, all of the included studies used calculated CerPP and CoPP. Only 2 studies further measured brain blood flow and heart blood flow directly by using microspheres. Although high perfusion pressure is associated with high blood flow, the evidence is indirect rather than direct. Finally, and most importantly, even though our study demonstrates strong evidence of increasing CerPP by lower ICP in HUP CPR, it is still unclear whether this benefit could equal an increased survival rate with good neurological outcome. Thus, further large-sample and standardized research is essential to confirm the optimal resuscitation position for humans as well as animals.

Conclusion

HUP 30° in ACD-CPR with ITD can increase CerPP by lowering ICP significantly and maintain MAP compared to SUP, and the effect is immediate and lasts for the whole CPR duration. In addition, CoPP might also increase compared to that with SUP. This study further confirms the benefit of HUP CPR in animal models, and further large-sample and standardized research is warranted to clarify the optimal resuscitation position for humans as well as animals.

Abbreviations

HUP
head-up position
SUP
supine position
CPR
cardiopulmonary resuscitation
CerPP
cerebral perfusion pressure
ICP
cerebral perfusion pressure
MAP
mean artery pressure
CoPP
coronary artery perfusion pressure
ROSC
return of spontaneous circulation
ACD-CPR
active compression-decompression cardiopulmonary resuscitation
ITD
impedance threshold device
EMS
emergency medical service
OHCA
out-of-hospital cardiac arrest
BBB
blood–brain barrier
CSF
cerebrospinal fluid
PRISMA
Preferred Reporting Items for Systematic Reviews and Meta-Analyses
MeSH
medical subject heading
ARRIVE

Animal Research:Reporting of In Vivo Experiments

SEM

standard error of the mean

SD

standard deviation

SMD

standardized mean differences

RR

risk ratios

CI

confidence intervals

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

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

Competing interests

The authors declare that they have no competing interests.

Funding

Not applicable.

Authors' contributions

YRL design this study. KCC and ZYL searched the articles, extracted the data and assessed the quality of the included articles. YHC and KTL collected data from graph by using GetData Graph Digitizer software. THL performed statistical analyses and interpreted the data under CCH supervision. The manuscript written by CCH mainly. WLC and CCC help with the revision of the manuscript. All authors read and approved the final manuscript.

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Figures

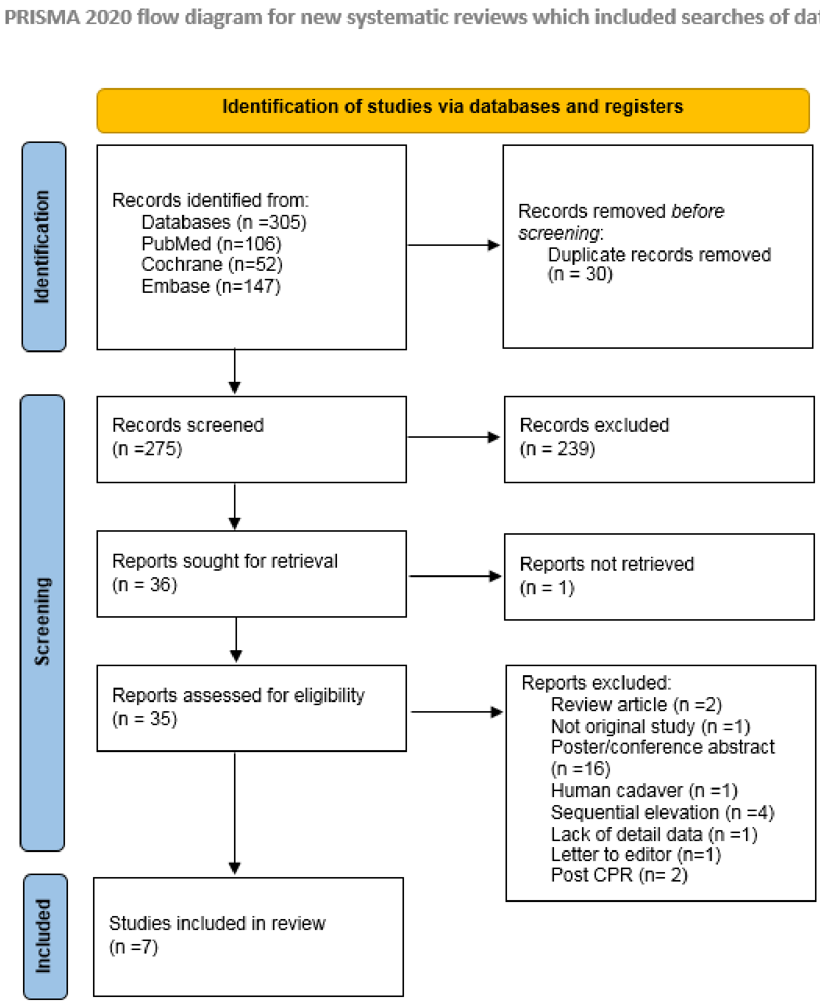


Figure 1

PRISMA flow diagram

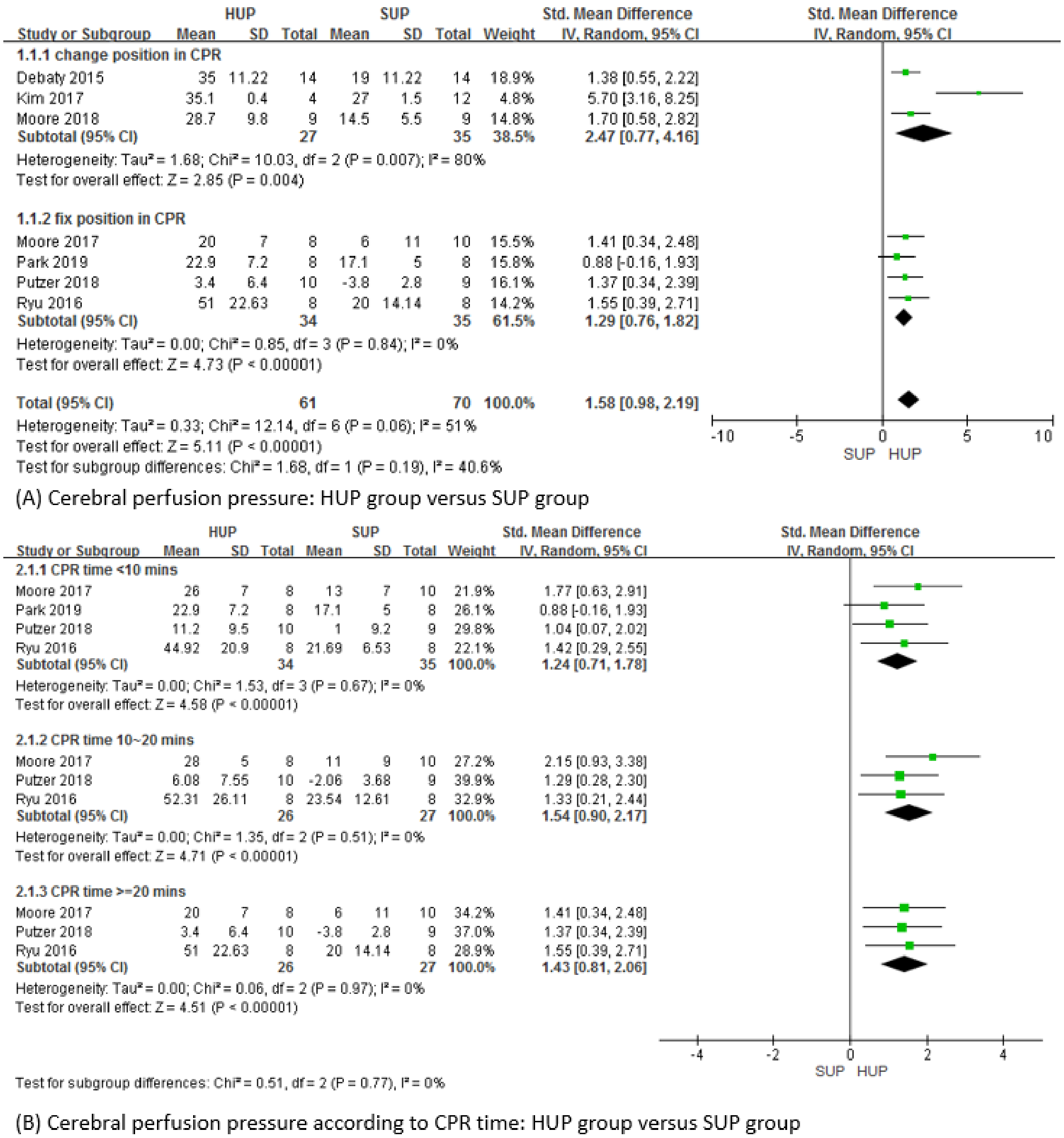
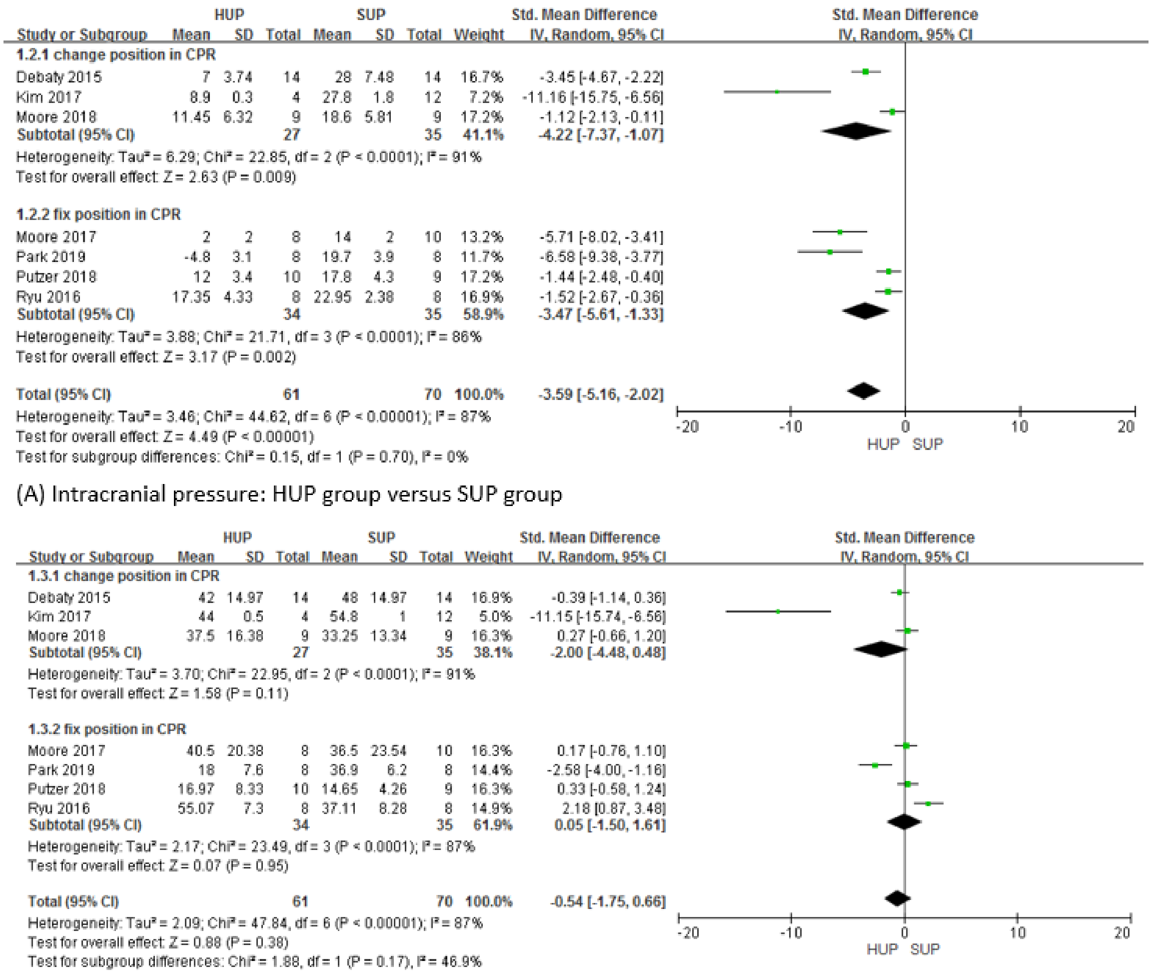


Figure 2

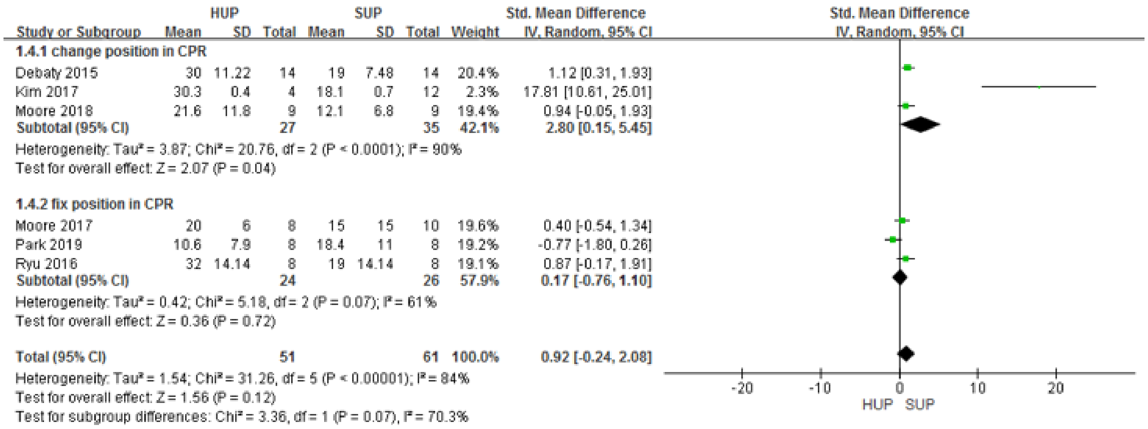
Cerebral perfusion pressure. (A) According to CPR position: HUP group versus SUP group. (B) According to CPR time: HUP group versus SUP group.



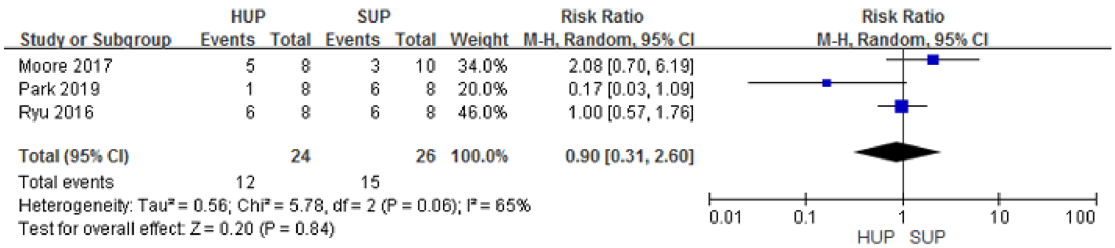
(B) Mean arterial pressure: HUP group versus SUP group

Figure 3

Intracranial pressure and mean arterial pressure. (A) Intracranial pressure: HUP group versus SUP group. (B) Mean arterial pressure: HUP group versus SUP group.



(A) Coronary artery pressure: HUP group versus SUP group



(B) ROSC rate: HUP group versus SUP group

Figure 4

Coronary artery pressure and ROSC rate. (A) Coronary artery pressure: HUP group versus SUP group. (B) ROSC rate: HUP group versus SUP group.