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## Review

# Chest-compression-only versus conventional cardiopulmonary resuscitation by bystanders for children with out-of-hospital cardiac arrest: A systematic review and meta-analysis



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### Abstract

**Background:** For children with out-of-hospital cardiac arrest, previous observational studies regarding chest-compression-only CPR (CC-CPR) versus conventional CPR yielded inconsistent results. We aimed to summarize the current evidence and compare the outcomes after CC-CPR with those after conventional CPR by bystanders in children with out-of-hospital cardiac arrest.

**Methods:** Observational studies that compared CC-CPR to conventional CPR for children with out-of-hospital cardiac arrest were identified through systematic searches of three databases (PubMed, EMBASE, and the Cochrane Library). The primary outcome was 30-day survival after hospital discharge. STATA 11.0 was used for data analysis.

**Results:** Five studies with 14,427 participants were included. Pooled results indicated that children who received conventional CPR had a higher 30-day survival than those who received CC-CPR (odds ratio, 1.49; 95% confidence interval [CI], 1.27–1.74). Moreover, conventional CPR led to a higher 30-day neurologically intact survival compared to CC-CPR (odds ratio, 1.63; 95%CI, 1.30–2.04). Subgroup analyses showed that the higher survival associated with conventional CPR was only significant in children who had cardiac arrest with non-cardiac causes (odds ratio, 1.77; 95% CI, 1.30–2.40).

**Conclusions:** Children who receive conventional CPR for out-of-hospital cardiac arrest may have better outcomes than those who receive CC-CPR. Due to the limited number of studies and lack of randomized trials included in this meta-analysis, more evidence is needed to confirm our findings.

**Keywords:** Out-of-hospital cardiac arrest, Cardiopulmonary resuscitation, Children, Meta-analysis

### Introduction

According to a study in 2012, more than 5000 children experience out-of-hospital cardiac arrests (OHCA) every year in the United States<sup>1</sup>. Children with cardiac arrest have poor clinical outcomes with a mortality

rate of more than 90%<sup>2,3</sup>. The role of early bystander cardiopulmonary resuscitation (CPR) for OHCA is significant in the chain of survival<sup>4,5</sup>. However, only about one-third of children receive bystander CPR immediately after the cardiac arrest<sup>2,6</sup>. To increase the rate of timely initiation of bystander CPR, the American Heart Association (AHA) recommended chest-compression-only CPR (CC-CPR) for adults with

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OHCA<sup>7</sup>. Several studies have confirmed that the CC-CPR is equivalent to conventional CPR in adults<sup>8–11</sup>. However, CC-CPR for cardiac arrest does not apply to patients with non-cardiac origin, unwitnessed arrest, or children<sup>12</sup>.

Recently, the use of CC-CPR for children with OHCA remains controversial. According to some studies, the procedure of rescue breathing should not be discarded because of the prevalence of respiratory etiologies over cardiac etiologies in children with cardiac arrest<sup>13,14</sup>. Large-scale observational studies from Japan indicated that conventional CPR is the preferable approach for children who have OHCA, particularly when the etiology is non-cardiac<sup>6,15</sup>. On the other hand, some studies have indicated that conventional CPR was not associated with superior neurologically favorable survival compared to 15 16CC-CPR<sup>16,17</sup>. In view of these inconsistencies, we therefore conducted a meta-analysis to evaluate whether bystander CC-CPR compared to conventional CPR improves outcomes in children with OHCA.

## Materials and methods

This systematic review was conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement<sup>18</sup>. The protocol was registered at <http://www.crd.york.ac.uk/PROSPERO/> (registration number: CRD42018087569).

### Data sources and search strategy

We searched PubMed, EMBASE, and Cochrane CENTRAL Library with different combinations of MeSH terms and keywords tailored to each database, through January 2018: (Pediatric\*) OR "Pediatrics" [Mesh] OR "Child" [Mesh] OR children) AND (((Out-of-Hospital) OR "Out-of-Hospital Cardiac Arrest" [Mesh]) AND ((CPR) OR cpr) OR chest next compression) OR cardiac next massage) OR heart next massage) OR resuscitat\*) OR sudden near/3 death) OR cardiopulmonary next arrest) OR heart next arrest) OR cardiac next arrest) OR "Heart Massage"[Mesh] OR "Cardiopulmonary Resuscitation"[Mesh] OR "Death, Sudden" [Mesh] OR "Heart Arrest"[Mesh])). We also used subject terms and truncation symbols in our search strategy. We searched the potential grey studies through Google Scholar.

### Study selection

All studies identified by our search strategies were reviewed by two independent reviewers (XM Zhang and WW Zhang) who evaluated the title and abstract of each record. Any disagreement on inclusion or exclusion of the studies was solved by discussion and consensus with a third reviewer.

### Inclusion and exclusion criteria

The inclusion criteria were as follows:

- (1) study design: observational studies that compared the effects of CC-CPR with conventional CPR by bystanders for children with OHCA;
- (2) participants: children suffering from OHCA due to any cause;
- (3) comparisons: CC-CPR vs. conventional CPR procedures;
- (4) outcomes: survival rate and neurologic outcome data.
- (5) neurologically favorable outcomes at 30 days: cerebral performance category 1 (good cerebral performance) or 2 (moderate

cerebral disability). The other categories—3 (severe cerebral disability), 4 (coma or vegetative state), and 5 (death)—were considered as unfavourable neurological outcomes<sup>19</sup>.

Exclusion criteria were as follows:

- (1) insufficient data;
- (2) conference abstracts or review articles;
- (3) involvement of any other intervention (e.g., public education plan);
- (4) adult or geriatric patients rather than children.

### Data extraction

Two authors (XM Zhang, WW Zhang) independently extracted the following data from the included studies into a standardized Microsoft Excel spreadsheet: year of publication, country, demographic characteristics of participants, and outcome measures. All the data were cross-checked by the reviewers. Any disagreement was resolved by discussion and consensus.

### Patient and public involvement

Our meta-analysis was based on secondary data; therefore, ethical approval, patient consent or Public Involvement was not necessary.

### Assessment of risk bias

Assessment of risk of bias was performed by two independent reviewers (XM Zhang and WW Zhang) according to the Newcastle Ottawa Scale(NOS)<sup>20</sup>, which evaluated the quality of cohort studies via the following aspects: (1) representativeness of the exposed cohort, (2) comparability of the groups, (3) blinding of investigators who measured outcomes, (4) the time and completeness of follow-up, (5) contamination bias, and (6) other potential sources of bias. A higher score indicated better quality.

### Statistical analysis

STATA version 11.0 (Stata Corp, College Station, TX, USA) was used for data analyses. Odds ratios (ORs) and their 95% confidence intervals (Cis) were calculated for 30-day survival and favorable neurological outcomes. Subgroup analyses according to the Etiology of OHCA and age of the children were implemented. The statistical heterogeneity among the included studies was examined with Cochran's Q statistic using chi-square and I<sup>2</sup> Statistics, with cut-off values of 25%, 50%, and 75% representing low, moderate, and high heterogeneity, respectively<sup>21</sup>. If heterogeneity  $\geq 50\%$ , a random-effects model was used. Otherwise, a fixed-effects model was used. Moreover, we performed sensitivity analyses to assess the effect of a single study on the overall estimate. Publication bias was assessed by a funnel plot with Begg's test to plot the logOR against its standard error.

## Results

### Selection processes

A total of 891 articles were initially identified by the literature search. After removal of 32 duplicates, 859 articles were screened for potential eligibility. After title and abstract screening, non-related articles were

removed, and 12 studies remained. After removal of seven review articles or duplicated reports of the same cohorts, five studies were finally included in the meta-analysis. The flow diagram in Fig. 1 depicts the article search and selection.

### Included studies

Table 1 presents the characteristics of the five included cohort studies. They were published from year 2010 to 2018, and these investigations included a total of 14,427 patients. One study was conducted in the USA<sup>16</sup>, and four studies were conducted in Japan<sup>6,12,15,17</sup>.

### Quality assessment

The methodological quality evaluation using NOS is shown in Table 2. The quality of these studies was moderate to high with scores ranging from 8 to 9.

### Meta-analysis of studies

#### 30-day survival

As shown in Fig. 2, the pooled results showed that the OR for 30-day survival in children who received conventional CPR versus those who received CC-CPR was 1.49 (95%CI, 1.27–1.74), suggesting conventional CPR was associated with a higher 30-day survival than

CC-CPR. No significant heterogeneity was detected from these studies (Q-value = 9.49, degree of freedom = 6,  $I^2 = 36.8%$ ,  $p = 0.148$ ).

#### Subgroup analysis for 30-day survival

For 30-day survival, subgroup analysis was conducted based on etiology for cardiac arrest. For children who had arrests of non-cardiac causes, conventional CPR resulted in a significantly higher 30-day survival than CC-CPR (OR = 1.77; 95% CI, 1.30–2.40). However, for those who had arrests of cardiac causes, the improvement in 30-day survival with conventional CPR was not significant (OR = 1.12; 95% CI, 0.77–1.62; Fig. 3).

#### Neurologically favorable 30-day survival

As shown in Fig. 4, the pooled results showed that the OR of 30-day neurologically intact survival in patients who received conventional CPR versus those who received CC-CPR was 1.63 (95%CI, 1.30–2.04), which suggests conventional CPR may be superior to CC-CPR in terms of neurologically intact survival. No significant heterogeneity was detected from these studies (Q-value = 9.32, degree of freedom = 7,  $I^2 = 24.9%$ ,  $p = 0.230$ ).

#### Subgroup analysis for neurologically favorable 30-day survival

In subgroup analyses based on cardiac arrest etiology, in children who had arrests of non-cardiac causes, conventional CPR resulted in a significantly higher neurologically favorable 30-day survival than

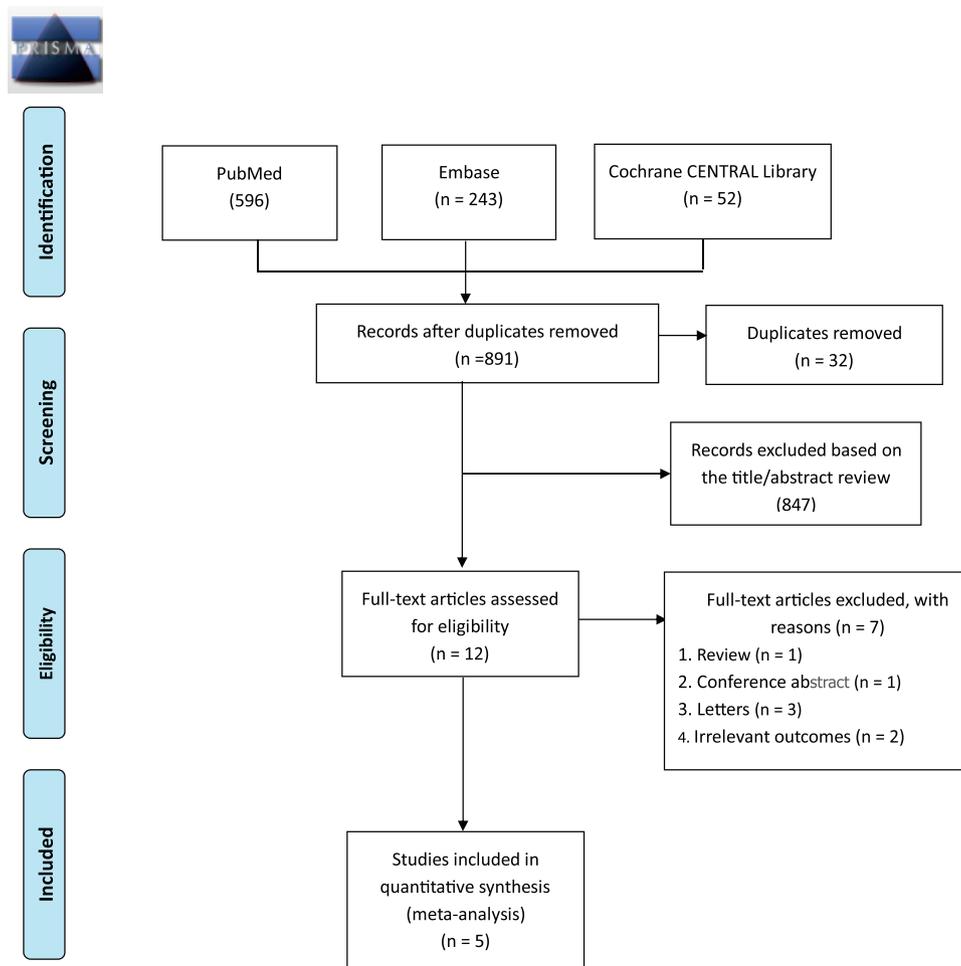


Fig. 1 – Flow diagram of study selection.

**Table 1 – Summary of included studies.**

Study first author	Year	Patient age, years	Male, %	Country	Compression –only CPR, n	Conventional CPR, n	30-day survival	Favorable neurologic outcome	Adjusted OR
Kitamura T	2010	≤ 18	61.1%	Japan	888	1551	84/888	193/1551	4
Fukuda T	2016	≤ 18	36.1%	Japan	733	417	129/733	142/417	*2
Goto Y	2018	≤ 18	60.2%	Japan	4123	2887	412/4123	405/2687	*1
Naim MY	2017	≤ 18	39.8%	USA	714	697	101/714	119/697	5
Goto Y	2014	≤ 18	60.6%	Japan	1402	1215	Not available	Not available	3

\*Propensity score matching.

- (1) geographic Japanese regions, age, male, etiology of cardiac arrest initial cardiac rhythm, bystander witnessed status, dispatcher CPR instruction, use of public access AED by bystander CPR by emergency responder.
- (2) sex, age, bystander witness, PAD use, first documented rhythm, etiology of cardiac arrest, and time from call to contact with patient.
- (3) age, sex, presumed cardiac etiology, shockable initial rhythm, witnessed by a family member, and call-to-response time.
- (4) sex, age, cause of arrest, witness status, first documented rhythm, time from call to CPR by emergency medical service, and time from call to hospital arrival.
- (5) age, sex, arrest witness status, location of the arrest, rhythm type, and AED use.

CC-CPR (OR = 1.94; 95% CI, 1.27–2.96). However, the superiority of conventional CPR was not significant for those who had arrests of cardiac causes (OR = 1.31; 95% CI, 0.88–1.95; Fig. 5). In addition, subgroup analysis based on age indicated that patients aged 1–7 years who received conventional CPR had a higher 30-day neurologically intact survival than those who received CC-CPR (OR = 2.13; 95% CI, 1.23–3.68). However, for those aged 8–17 years, there was no significant difference between the two groups (OR = 1.33; 95% CI, 0.96–1.86; Fig. 6).

**Publication bias assessment**

When the outcome was 30-day survival, the low I<sup>2</sup> = 36.8% showed that there may be no publication bias in our study; plus, the result of Begg's test (p = 0.548) confirmed our conclusion. In addition, when the outcome was neurologically favorable 30-day survival, we also obtained similar results with a low I<sup>2</sup> = 7.1% and Begg's test (p = 0.244), as shown in Supplemental File 1.

**Sensitivity analysis of 30-day survival and neurologically favourable 1-month survival**

We conducted a sensitivity analysis of Neurologically favourable 1-month survival and 30-day survival by omitting one study each time and pooling the others to find which study influenced the main effect. No statistically significant changes were found, as shown in Supplemental File 2.

**Discussion**

In this meta-analysis, children with OHCA who received conventional CPR had significantly more favorable neurological outcomes and a higher 30-day survival than those who received CC-CPR. In addition, subgroup analysis indicated that the improvement was only significant in patients with arrests of non-cardiac causes. On the other hand, for those with cardiac causes, these two CPR methods showed no significant difference in terms of survival or neurological outcomes.

To our knowledge, this is the first meta-analysis to compare the survival outcomes after CC-CPR versus conventional CPR in pediatric OHCA. We found that conventional CPR was associated with a higher neurologically favorable 30-day survival and 30-day overall survival compared with CC-CPR. Yao et al.<sup>22</sup>, performed an updated systematic review and meta-analysis of CC-CPR versus standard CPR in 2014. However, they focused on adult patients and concluded that CC-CPR resulted in the similar survival rate as standard CPR in the cardiac etiology subgroup. It is unclear which of the CPR techniques is best for patients with noncardiac cause of arrest or with long periods of untreated arrest. Most recently, Zhan et al.<sup>23</sup>, conducted a systematic review and meta-analysis regarding continuous chest compression versus interrupted chest compression for CPR of non-asphyxial out-of-hospital cardiac arrest. In their study, bystander-administered CC-CPR, supported by telephone instruction, increased the proportion of people who survived to hospital discharge compared with conventional interrupted chest compression CPR plus rescue breathing. This meta-analysis showed a higher level of evidence than the previous one because only randomized controlled trials were included. However, the patient population still included only adults.

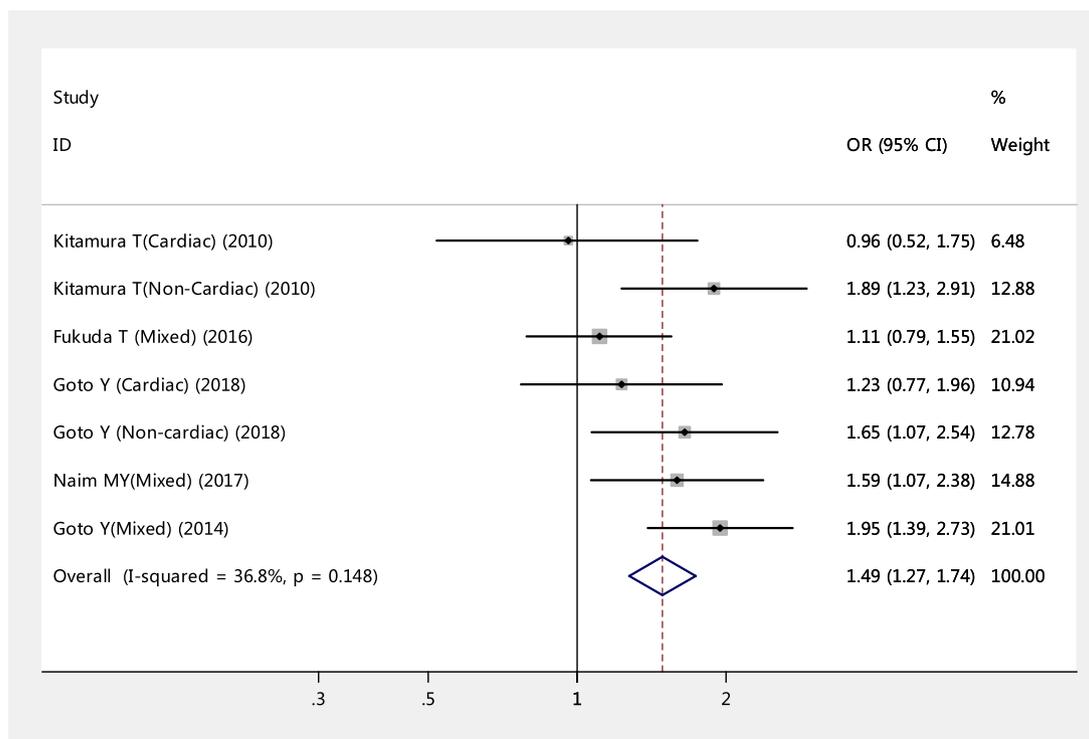
**Table 2 – Result of the Newcastle-Ottawa scale quality assessment.**

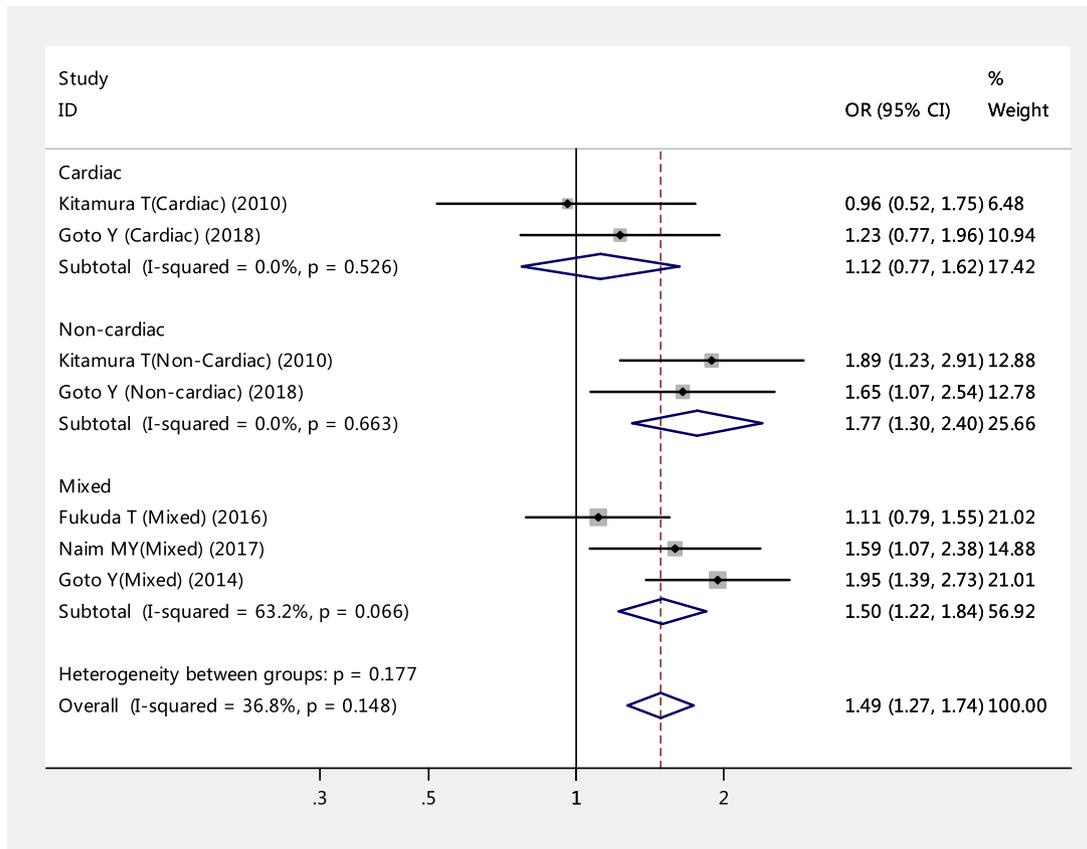
Newcastle-Ottawa scale		Kitamura T 2010	Fukuda T 2016	Goto Y 2018	Naim MY 2017	Goto Y 2014
Selection (4)	Representativeness of the exposed cohort	1	1	1	1	1
	Selection of the non-exposed cohort	1	1	1	1	1
	Ascertainment of exposure	1	1	1	1	1
	Demonstration that outcome of interest was not present at start of study	1	1	1	1	1
Comparability (2)	Comparability of cohorts on the basis of the design or analysis	2	2	2	1	2
Outcome (3)	Assessment of outcome	1	1	1	1	1
	Was follow-up long enough for outcome to occur	0	0	1	0	0
	Adequacy of follow up of cohorts	1	1	1	1	1
Quality (9)	Total	8	8	9	8	8

There are several possible explanations for our results. First, our study focused on pediatric OHCA, which is different from that in adults. The etiological causes for children and adults are quite different. Physiological and epidemiological backgrounds with predominantly respiratory factors account for most pediatric OHCA cases<sup>14</sup>. According to Law's study<sup>24</sup>, the most common cause of OHCA in children is respiratory illness, followed by environmental hazards, such as drowning, poisoning, and trauma. However, cardiac factors are the main cause for adult OHCA<sup>25</sup>. A study of the OHCA Outcomes Project in England reported that 80% of adult OHCA cases were due to a cardiac cause<sup>26</sup>. In animal experiments, conventional CPR was shown to be as effective as CC-CPR after a ventricular fibrillation cardiac arrest<sup>27–29</sup>. In contrast, for cardiac arrest caused by acute asphyxia, standard CPR is obviously more important than CC-compressions<sup>30</sup>. Not surprisingly, for children with heart arrest caused by acute respiratory syndrome, trauma, drowning, and drug poisoning,

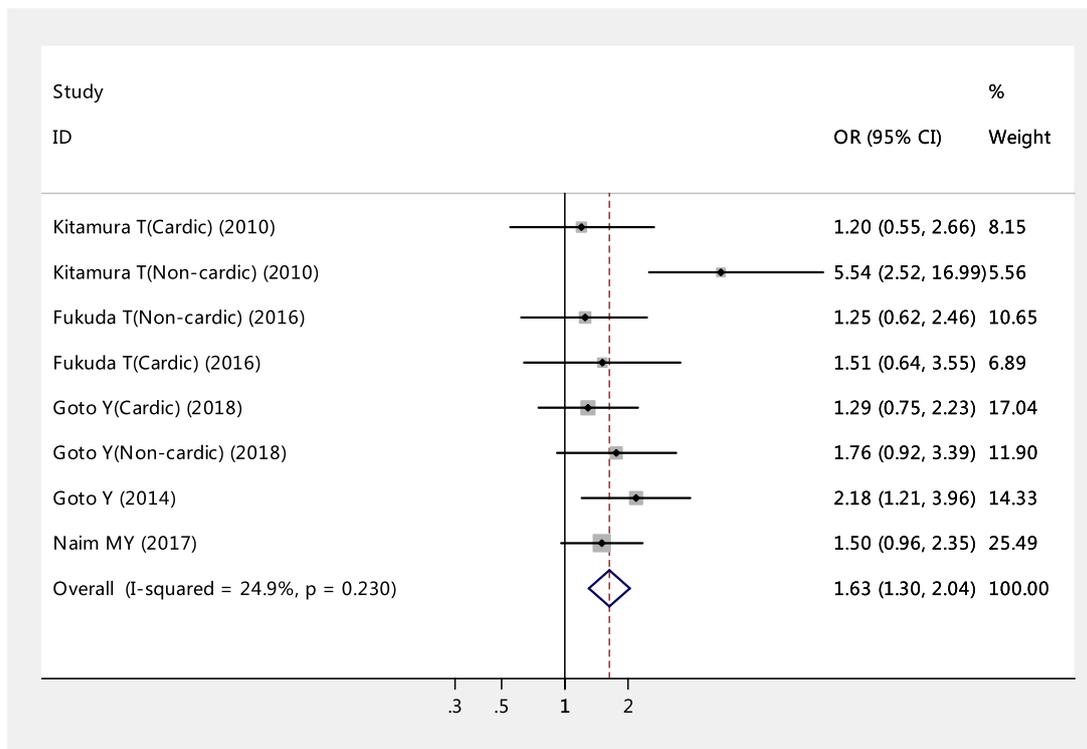
conventional CPR technique with both chest compressions and rescue breathing is of great importance. In fact, these clinical scenarios account for about 70% of pediatric cases. As a result, great emphasis has been placed on rescue breathing in bystander CPR. Rescue breathing provides more oxygen supply than CC-CPR<sup>31</sup>, which may improve neurological outcomes in children.

Subgroup analysis indicated that CC-CPR resulted in similar neurologically favorable 30-day and 30-day survival compared with conventional CPR in children who have arrests with cardiac cause. A recent study suggested that bystander CPR was associated with good neurologically favorable survival and overall survival compared with no bystander CPR<sup>32</sup>. In addition, CC-CPR is easier to teach, learn, and do for people than the fairly complex standard CPR, which could improve the feasibility of CPR by a bystander<sup>33</sup>. These results also address the importance of the chest compression procedure in the resuscitation of children with cardiac etiology arrest, which is consistent with the 2017

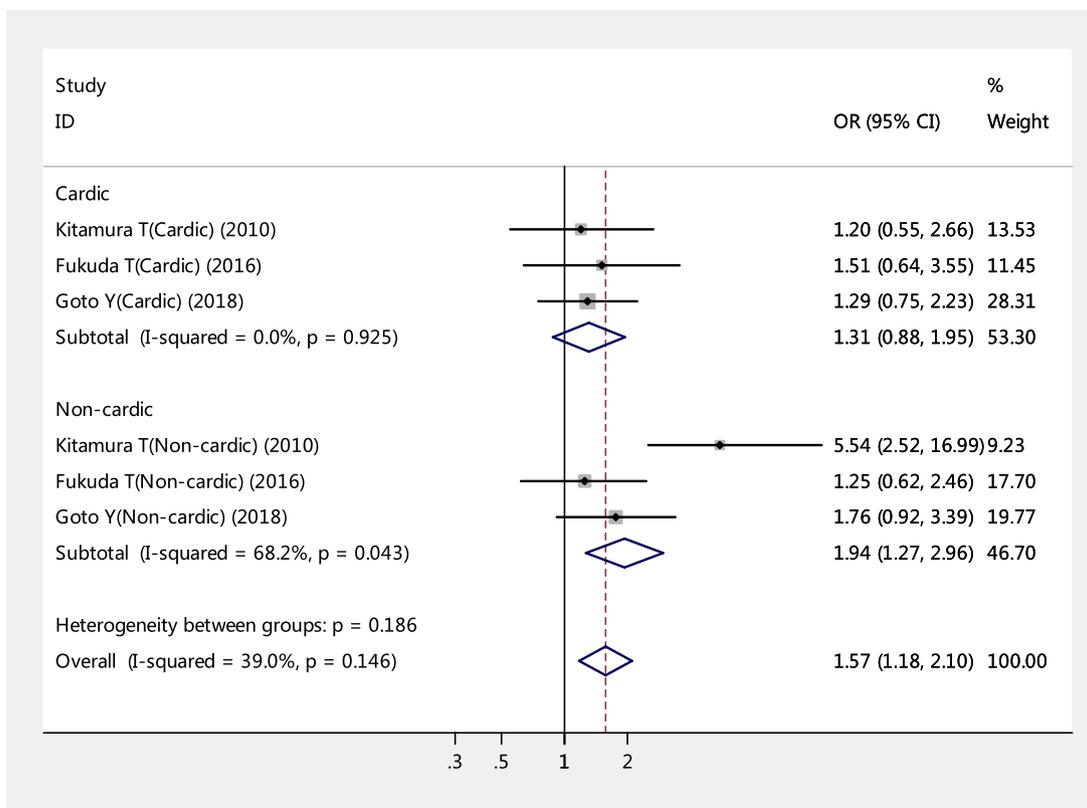
**Fig. 2 – Forest plot for the comparison of 30-day survival between the two CPR techniques.**



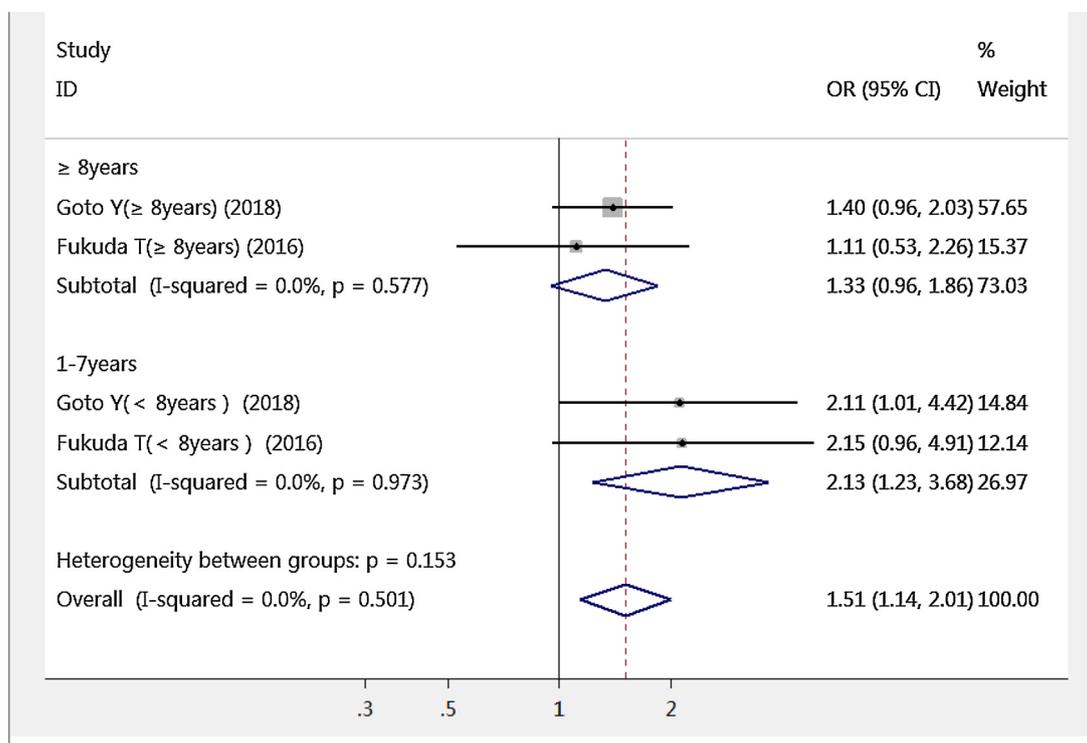
**Fig. 3 – Subgroup analysis for the comparison of 30-day survival between the two CPR techniques.**



**Fig. 4 – Forest plot for the comparison of neurologically favorable 30-day survival between the two CPR techniques.**



**Fig. 5 – Subgroup analysis for the comparison of neurologically favorable 30-day survival between two CPR techniques according to etiology of cardiac arrest.**



**Fig. 6 – Subgroup analysis for the comparison of neurologically favorable 30-day survival between two CPR techniques according to age of children.**

International Liaison Committee on Resuscitation summary statement<sup>34</sup> and the 2017 American Heart Association guidelines update<sup>35</sup>. On the other hand, we found that for children who had arrests of non-cardiac causes, conventional CPR was associated with better 1-month neurologically intact survival and 30-day survival compared to CC-CPR. Our results indicate that compressions plus rescue ventilations produced better clinical outcomes for non-cardiac arrest. In the study by Kitamura et al.<sup>36</sup>, they also showed that conventional CPR is effective for adult OHCA of non-cardiac origin.

Subgroup analysis based on age showed that the patients aged 1–7 years who received conventional CPR had a higher 30-day neurologically intact survival than those who received CC-CPR, whereas in children aged 8–17 years, the two CPR methods showed no significant difference. Generally, infants with OHCA have poor outcomes. Studies have shown that patients with sudden infant death syndrome<sup>37,38</sup> usually die within a couple of hours before emergency medical staff arrive. Of note, no benefits of CC-CPR without ventilation for infants have been reported, which is different from results in older children. Due to the low survival rate of infants OHCA<sup>39</sup> and the emphasis of provision of chest compression over ventilation by public health campaigns (a more difficult technique)<sup>40</sup>, more attention should be given to the prevention of OHCA in infants.

There are some strengths and limitations in our systematic review and meta-analysis. One of the strengths is that we performed an extensive search process in electronic data-bases, evaluated the quality of each study, and tested heterogeneity, sensitivity analysis and publication bias among the including studies. Second, all the included studies have high quality scores. The primary limitation of this study is the limited number of cohort studies included and the lack of randomized controlled trials in this topic. Next, other associated factors may have introduced bias. Fukuda et al.<sup>17</sup> and Goto et al.<sup>12</sup> did propensity matching to alleviate this concern, and the other three studies (Goto et al.<sup>15</sup>, Kitamura et al.<sup>6</sup> and Naim et al.<sup>16</sup>) used regression models to adjust for confounding factors, including sex, age, cause of arrest, witness status, first documented rhythm, time from call to CPR by emergency medical service, and time from call to hospital arrival. Despite the above methods, some confounding factors still need to be considered (e.g., comorbid diseases, location of arrest, CPR quality, and in-hospital medication). Of note, patients who received CC + rescue breathing had better CPR outcomes in general, and this may reflect a population of rescuers who were better trained. According to CPR guidelines published by the American Heart Association, high-quality CPR improves survival and neurological outcomes<sup>41</sup>. Third, rescue breathing was a crucial procedure to improve the outcomes of children with OHCA, especially for non-cardiac OHCA. According to the study of Nagata et al.<sup>42</sup>, for children who have OHCA from non-cardiac origin, bystander rescue breathing is mandatory to achieve cerebral performance category (CPC) 1 or 2. Besides, in the Goto et al. 2014 study, patients who received rescue breathing alone also did better with a 1-month CPC of 1–2 (OR:3.04, 95%CI: 1.18–6.78) than those who received conventional CPR (OR: 2.30, 95%: 1.56–3.41), which may reflect a different population of patients/rescuers. Last, data from four of the included studies were extracted from the National Japanese Cardiac arrest registry. It is possible that there was some overlap of included patients from the studies based on the Japan FDMA data, which may have resulted in potential bias. Taken together, based on the current findings, we call

for well-designed randomized controlled trials on this topic in the near future.

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## Conclusion

This meta-analysis suggests that children with OHCA who receive conventional CPR may have better outcomes than those who receive CC-CPR. Due to the limited number of studies included in this meta-analysis, more evidence is needed to compare the two resuscitation methods in pediatric OHCA. Specifically, randomized controlled trials are urgently needed to verify the current results.

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## Conflict of interest

None of the authors have any conflict of interest to declare.

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## Contributors

XiaoMing Zhang was responsible for producing the initial draft of the manuscript.

WenWu Zhang was responsible for data extraction and for producing the initial draft of the manuscript.

CongHua Wang was responsible for data extraction.

WuYuan Tao was responsible for screening the papers and quality assessment.

YunZhi Yang was responsible for screening the papers.

QingLi Dou was responsible for quality assessment, statistical analysis and revision of the manuscript.

All the authors approved the final version of the manuscript

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## Data sharing statements

All the data can be found in the electronic databases (PubMed, EMBASE, and the Cochrane Library).

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## Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.resuscitation.2018.10.032>.

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