Do Out-of-Hospital Cardiac Arrest Patients Have Increased Chances of Survival When Transported to a Cardiac Resuscitation Center? A Systematic Review and Meta-Analysis

Demis Lipe, MD, MSc; Al Giwa, MD, MBA; Nicholas D. Caputo, MD, MSc; Nachiketa Gupta, MD, PhD; Joseph Addison, BS, NRAEMT; Alexis Cournoyer, MD

***Background*—**Patients suffering from an out-of-hospital cardiac arrest are often transported to the closest hospital. Although it has been suggested that these patients be transported to cardiac resuscitation centers, few jurisdictions have acted on this recommendation. To better evaluate the evidence on this subject, a systematic review and meta-analysis of the currently available literature evaluating the association between the destination hospital's capability (cardiac resuscitation center or not) and resuscitation outcomes for adult patients suffering from an out-of-hospital cardiac arrest was performed.

***Methods and Results*—**PubMed, EMBASE, and the Cochrane Library databases were first searched using a specifically designed search strategy. Both original randomized controlled trials and observational studies were considered for inclusion. Cardiac resuscitation centers were defined as having on-site percutaneous coronary intervention and targeted temperature management capability at all times. The primary outcome measure was survival. Twelve nonrandomized observational studies were retained in this review. A total of 61 240 patients were included in the 10 studies that could be included in the meta-analysis regarding the survival outcome. Being transported to a cardiac resuscitation center was associated with an increase in survival (odds ratio=1.95 [95% confidence interval 1.47-2.59], P<0.001).

***Conclusions*—**Adult patients suffering from an out-of-hospital cardiac arrest transported to cardiac resuscitation centers have better outcomes than their counterparts. When possible, it is reasonable to transport these patients directly to cardiac resuscitation centers (class IIa, level of evidence B, nonrandomized).

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Key Words: cardiac arrest • emergency medical services • percutaneous coronary intervention • resuscitation • sudden cardiac arrest

Out-of-hospital cardiac arrest (OHCA) is one of the leading causes of death in the United States, and it is a serious public health burden.[1] Despite an improvement in prehospital resuscitation practices, including an increased access to early cardiopulmonary resuscitation and defibrillation, mortality rates remain high, with only 10% of patients surviving to hospital discharge.[1-5] To further decrease the mortality from OHCA, the establishment of a regionalized approach for the treatment of OHCA, including direct transport to specialized cardiac resuscitation centers, such as in the case of an ST-segment–elevation myocardial infarction, has been proposed (class IIb, level of evidence C-limited data).[5-7] For a hospital to be considered a cardiac resuscitation center, it must be able to provide diagnostic angiography and percutaneous coronary intervention (PCI) on site at all times as well as targeted temperature

From the Department of Emergency Medicine, MD Anderson Cancer Center, Houston, TX (D.L.); Icahn School of Medicine at Mount Sinai, New York, NY (A.G., N.G.); Department of Emergency Medicine, Mount Sinai Hospital, New York, NY (A.G., N.G.); Department of Emergency Medicine, Lincoln Medical Center, New York, NY (N.D.C.); Columbus State University, Columbus, GA (J.A.); Université de Montréal, Montréal, Québec, Canada (A.C.); Department of Emergency Medicine, Hôpital du Sacré-Cœur de Montréal, Montréal, Québec, Canada (A.C.); Institut de Cardiologie de Montréal, Montréal, Québec, Canada (A.C.).

Accompanying Data S1 and Tables S1, S2 are available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.118.011079

Correspondence to: Alexis Cournoyer, MD, Hôpital du Sacré-Cœur, 5400 Gouin Ouest, Montréal, Québec, Canada H4J 1C5. E-mail: alexis.cournoyer@umontreal.ca

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Clinical Perspective

What Is New?

- This is the first systematic review to evaluate the association between destination hospital characteristics and resuscitation outcomes following an out-of-hospital cardiac arrest.
- Direct transport to a cardiac resuscitation center is associated with improved survival and survival with a good neurologic outcomes for these patients.
- This association was stronger among patients not having experienced a prehospital return of spontaneous circulation.

What Are the Clinical Implications?

- When possible, it is reasonable to transport patients suffering from an out-of-hospital cardiac arrest directly to a cardiac resuscitation center.
- A bypass delay of up to 15 minutes for patients not having experienced prehospital return of spontaneous circulation and of 30 minutes for patients having experienced prehospital return of spontaneous circulation is probably safe. This should be further tested in a prospective study.

management (TTM).[5] Indeed, most nontraumatic OHCA results from an acute coronary syndrome, and PCI is the preferred therapeutic procedure for that pathology.[8-12] Patients remaining comatose following an OHCA also strongly benefit from some form of TTM.[10,13,14]

Despite these recommendations made by the American Heart Association, few jurisdictions have implemented a regionalized approach for OHCA patients with designated receiving centers. As a result, there remains significant variation with regard to treatment standards for these patients.[15,16] However, since these guidelines were published, multiple new studies have emerged, and their results could influence the decisions made for patients suffering from an OHCA.

To better evaluate the evidence on this subject, a systematic review and meta-analysis of the currently available literature evaluating the association between the destination hospital capability (cardiac resuscitation center or not) and resuscitation outcomes (survival and survival with a good neurologic outcome) for patients suffering from an OHCA were performed.

Methods

This review was registered (Prospero CRD42018086608) before its initiation. Its results are presented as per the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[17] Its main objective was to evaluate the association between the transport to a cardiac resuscitation center (defined as having on-site PCI and TTM capability at all times) and resuscitation outcomes (survival and survival with a good neurologic outcome) for adult patients suffering from an OHCA. The data that support the findings of this study are available from the corresponding author on reasonable request. Because of its nature, this study did not need to be reviewed by an institutional review board.

Search Strategy

The search strategy aimed to find both published and unpublished studies. PubMed, EMBASE, and the Cochrane Library databases were first queried using a specifically designed search strategy. This search strategy included terms such as heart arrest, cardiac arrest, out-of-hospital cardiac arrest, cardiopulmonary arrest, ventricular fibrillation, pulseless electrical activity, hospital characteristics, critical care center, high-volume hospital, regionalization of care, and high-volume centers (Data S1). The search was limited to humans and English-language publications. Gray literature was searched using Web of Science and Google Scholar. The references of all identified articles and main review articles were also searched for additional relevant studies. The search was performed initially on February 4, 2018 and repeated on July 24, 2018 to ensure that no new literature had been published in the interim.

Article Selection

Following the automatic removal of duplicates, remaining citations were screened by 2 independent reviewers (D.L., A.G.) for potentially pertinent publications using the Covidence online software (Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia). Potentially eligible citations were then fully evaluated. Discrepancies regarding the selection of articles were resolved by consensus with a third reviewer (N.C.).

Original randomized controlled trials and observational studies were both considered for inclusion. Case series describing only 1 population were excluded. Studies published before 2008 were excluded because the evolution in treatment standard might make these results no longer applicable by today's standards.[18] To be included, studies had to include adults suffering from a nontraumatic OHCA who were transported to the hospital. Studies reporting on traumatic OHCA or in-hospital cardiac arrest were excluded. Included studies also had to report outcome data on patients being transported to a cardiac resuscitation center and those who were transported to a hospital that was not a cardiac resuscitation center. To be considered a cardiac center, a hospital was required to have both PCI capability and TTM capability as defined by the American Heart Association.[5] If that information was not available, it was decided to exclude these studies from the review to limit the risk of bias.

Quality Assessment

The quality assessment of all retained articles was performed by 2 independent reviewers (D.L., A.C.). The risk of bias was evaluated using the Newcastle-Ottawa scale (Table S1).[19] Disagreements were resolved by consensus.

Data Abstraction

Data for the outcomes of interest were independently extracted from the included articles by 3 reviewers (N.C., N.G., and J.A.). In addition, the study design, population characteristics, sample sizes, and outcomes were also extracted. A standard template was created for the purpose of data extraction (Table S2).

Outcome Measures

The primary outcome measure was survival. The preferred timing of measurement was at hospital discharge. If that information was not available, survival at 30 or 90 days was used. The secondary outcome measure was survival with a good neurologic outcome (defined as a Cerebral Performance Category of 1 or 2).[20] The preferred timings of measurement were the same as for the primary outcome.

Analyses

Adjusted odds ratio (OR) was the effect measure used whenever available. If these were not provided, unadjusted ORs were used or calculated from the available data instead.

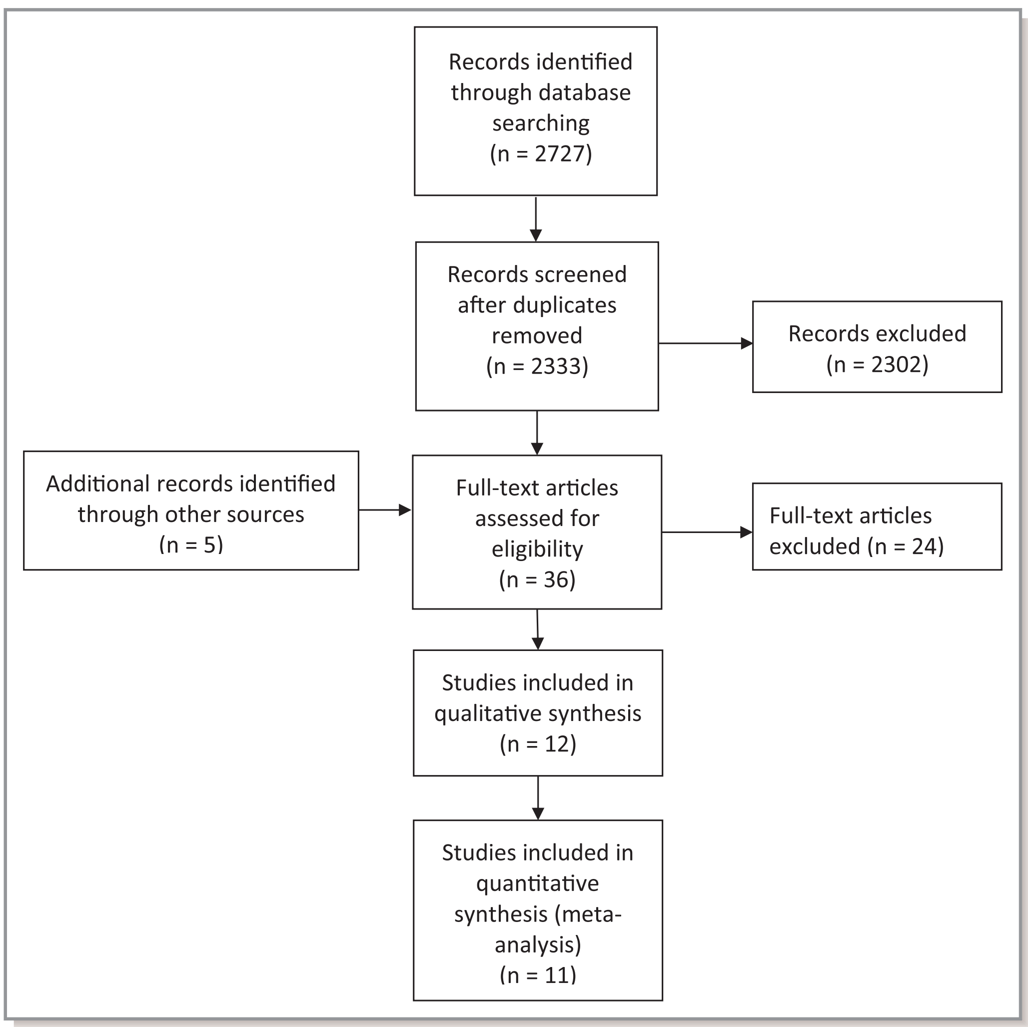

Figure 1. Flow diagram of the systematic search.

For outcomes reported in multiple studies, results were pooled in a meta-analysis using Revman (Version 5.3. The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark, 2014) if appropriate.

Heterogeneity was assessed statistically using I^2. Random effect models were preferred to better account for the differences in selection criteria and design among the included studies, but fixed-effect models were also presented as supplementary analyses. All results are presented with their 95% confidence interval (CI).

For each meta-analysis of more than 10 articles, a funnel plot was constructed to assess for a publication bias.[21] When fewer than 10 articles were available, the reporting bias was assessed qualitatively.

Three sets of sensitivity analyses were performed to explore the heterogeneity, 1 excluding articles with some risk of bias (Newcastle-Ottawa Scale ≤8), 1 including only patients having experienced prehospital return of spontaneous circulation (ROSC), and 1 including only those who did not. The same outcome measures (survival and survival with a good neurologic outcomes) were used for each set of sensitivity analyses.

Results

Search and Article Selection

The initial electronic search yielded 2727 references (Figure 1). A title and abstract screening left 31 potentially

Table. Characteristics of Included Studies

Study	Level of Risk of Bias/NOS	Specific Inclusion/Exclusion Criteria	Number of Eligible Patients	Average Age (y)	Percentage of Initial Shockable Rhythm	Percentage of Prehospital ROSC	Outcomes of Interest Presented
Kajino 2010[22]	Low/9	None	10 383	73	17%	8%	Survival at 30 d and survival with a good neurologic outcome at 30 d
Stub 2011[23]	Low/8	Included only patients with prehospital ROSC	2706	67	57%	100%	Survival to hospital discharge
Wnent 2012[24]	Low/9	None	889	69	26%	N/A	Survival to hospital discharge
Soholm 2013[25]	Low/9	None	1020	65	45%	N/A	Survival at 30 d
Hunter 2016[26]	Low/8	Included only patients with prehospital ROSC	1024	61	27%	100%	Survival to hospital discharge
Kragholm 2017[27]	Low/8	Included only patients with prehospital ROSC	1507	65	39%	100%	Survival to hospital discharge
Matsuyama 2017[28]	Low/8	Excluded patients with paramedic-witnessed arrest	39 965	75	8%	6%	Survival with a good neurologic outcome at 30 d
Tranberg 2017[29]*	Low/9	None	41 186	70	21%	N/A	···
Tsai 2017[30]	Low/8	Included only patients with an initial shockable rhythm without a prehospital ROSC	546	62	100%	0%	Survival to hospital discharge and survival with a good neurologic outcome at hospital discharge
Casey 2018[31]	Low/8	Included only patients who survived to hospital admission	38 163	67	29%	N/A	Survival to hospital discharge and survival with a good neurologic outcome at hospital discharge
Cournoyer 2018[32]	Low/9	None	4922	67	35%	34%	Survival to hospital discharge
McKenzie 2018[33]	Low/8	Included only patients who survived to hospital admission	535	62	62%	86%	Survival to hospital discharge

N/A indicates not applicable; NOS, Newcastle-Ottawa Scale; ROSC, return of spontaneous circulation.
*Only included in the qualitative synthesis.

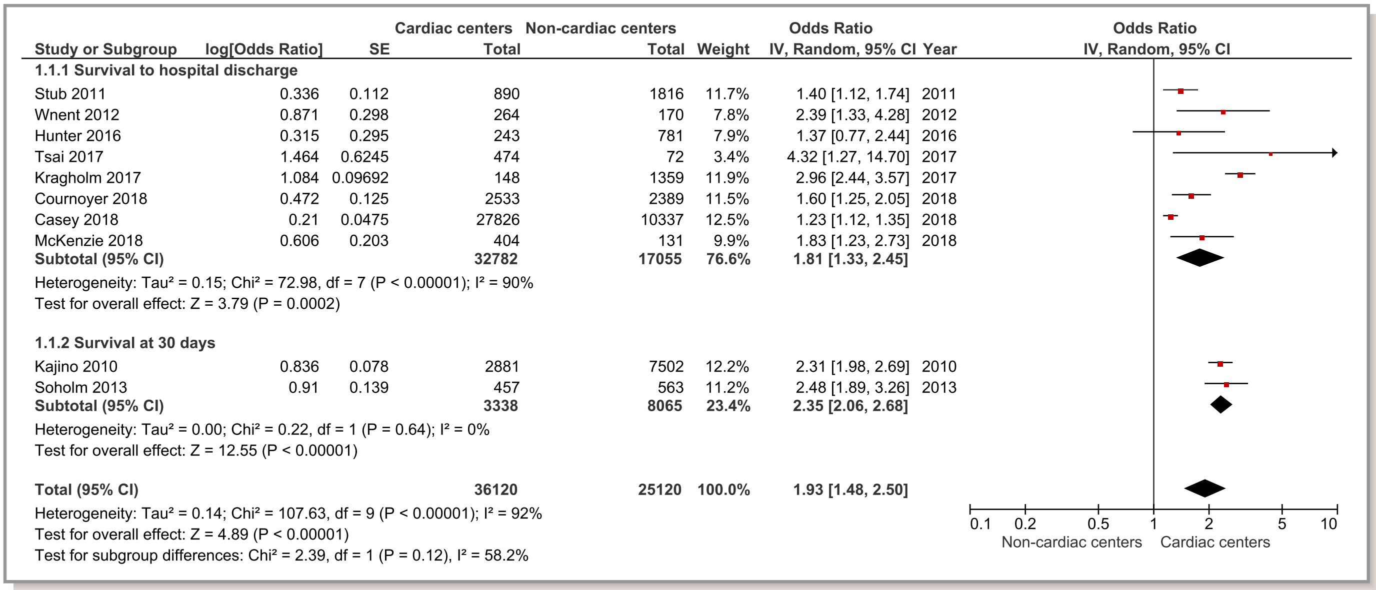

Figure 2. Meta-analysis evaluating the association between transport to a cardiac resuscitation center and survival, performed using a random-effect model.[22-27,30-33] CI indicates confidence interval; IV, inverse variance; SE, standard error.

eligible citations. The search of gray literature, the second electronic search, and communications with authors of potentially eligible articles yielded an additional 5 citations for a total of 36 included for the full-text review. Among these articles, a total of 24 were excluded for the following reasons: absence of comparison between cardiac centers and noncardiac centers (17), unknown availability of TTM (2), only abstract published (2), review article (1), availability of more recently published data from the same cohort (1), and included in-hospital cardiac arrest (1). A total of 12 studies were included in the narrative review and 11 in the meta-analysis.

Included Studies

All included articles were nonrandomized observational studies (Table).[22-33] It was possible to extract data regarding survival for 10 studies and regarding neurologic outcomes for

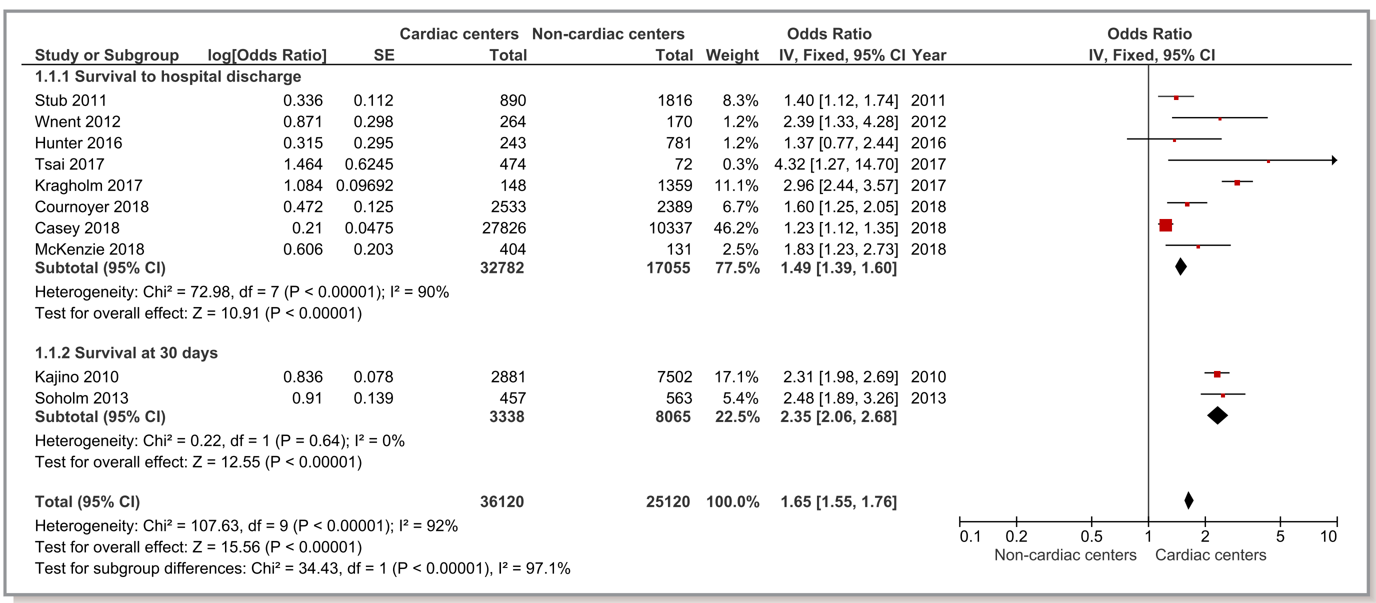

Figure 3. Meta-analysis evaluating the association between transport to a cardiac resuscitation center and survival, performed using a fixed-effect model.[22-27,30-33] CI indicates confidence interval; IV, inverse variance; SE, standard error.

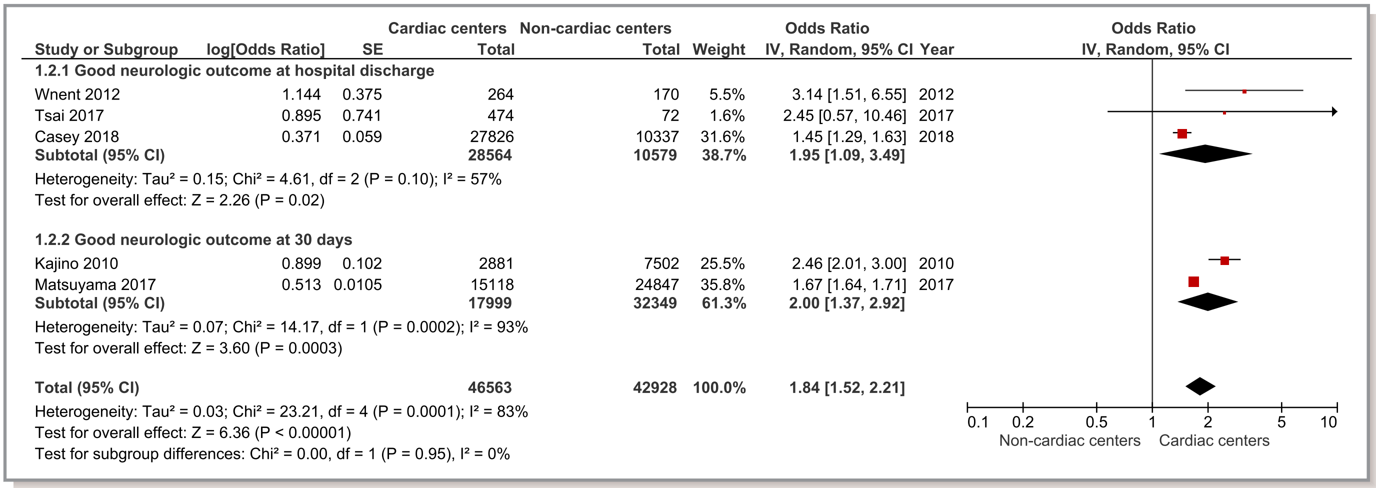

Figure 4. Meta-analysis evaluating the association between transport to a cardiac resuscitation center and survival with a good neurologic outcome, performed using a random-effect model.[22,24,28,30,31] CI indicates confidence interval; IV, inverse variance; SE, standard error.

5 studies. One study only provided hazard ratios, which prevented its inclusion in the meta-analysis.[29] Despite some adjusted results being available for all included studies, unadjusted results needed to be used in some analyses or sensitivity analyses for 2 studies because they were not provided for all the outcomes or populations pertaining to the present study.[22,33]

Quality Assessment

All included studies were considered at low risk of bias (Table). Seven studies lost a point regarding the representativeness of their cohort because it was composed of a selected subpopulation of nontraumatic OHCA transported to the hospital.[23,26-28,30,31,33]

Main Results

Survival

A total of 61 240 patients were included in the 10 studies that were part of this meta-analysis.[22-27,30-33] Eight studies presented results regarding survival to hospital discharge, and the other 2 studies reported on survival at 30 days. This resulted in 2 independent subgroups.

Being transported to cardiac resuscitation centers was associated with an increase in survival (OR=1.93, 95% CI 1.48-2.50, $P<0.001$) (Figures 2 and 3). There was no significant difference between the 2 subgroups (hospital discharge OR=1.81, 95% CI 1.33-2.45, $P<0.001$; 30 days OR=2.35, 95% CI 2.06-2.68, $P<0.001$; test for subgroup differences $P=0.12$).

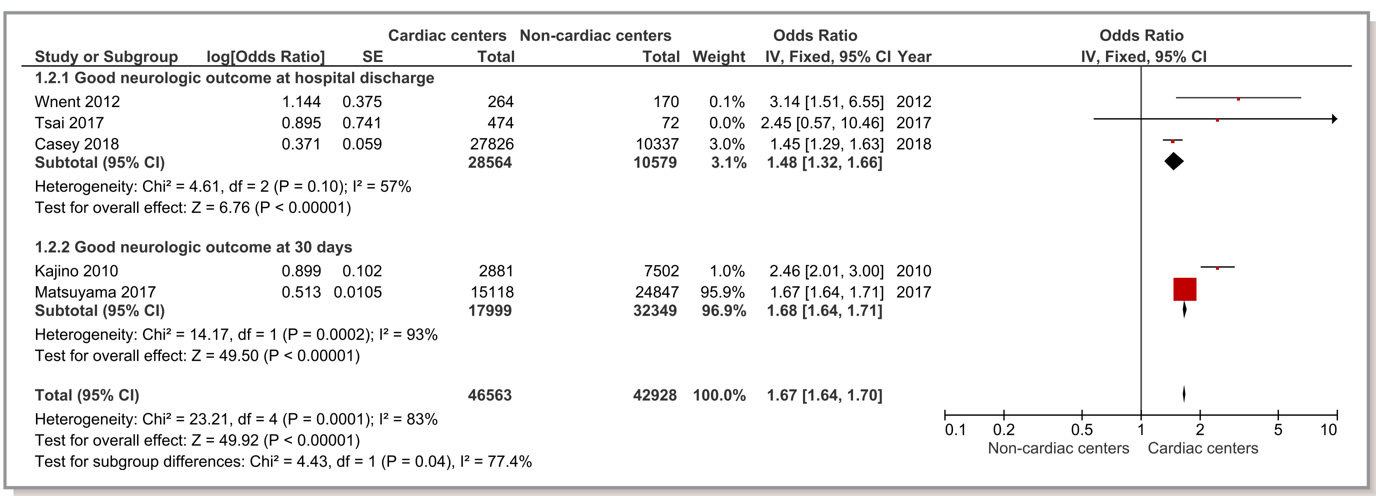

Figure 5. Meta-analysis evaluating the association between transport to a cardiac resuscitation center and survival with a good neurologic outcome, performed using a fixed-effect model.[22,24,28,30,31] CI indicates confidence interval; IV, inverse variance; SE, standard error.

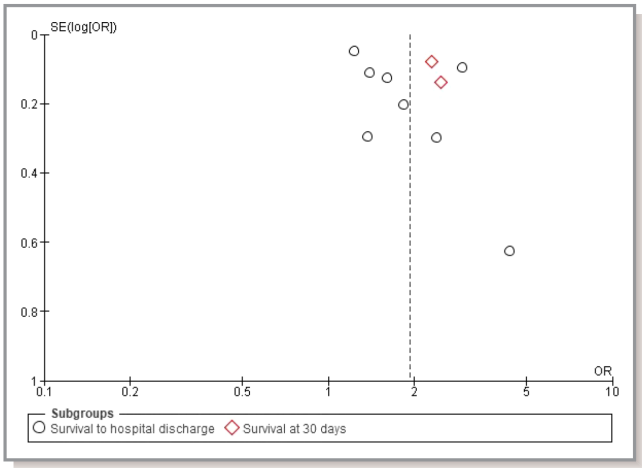

Figure 6. Funnel plot for the evaluation of publication bias for the survival outcome.

The heterogeneity was high across this analysis and was hence explored using sensitivity analyses.

In addition, for the study that presented hazard ratios, which could not be mathematically included in this meta-analysis, being transported to a cardiac resuscitation centers was also independently associated with better survival (adjusted hazard ratio 1.10, 95% CI 1.08-1.12, *P*<0.001).[29]

Survival With a Good Neurologic Outcome

Five studies, including a total of 89 491 patients, reported rates of survival with good neurologic outcomes.[22,24,28,30,31] Three of these studies presented results regarding survival with a good neurologic outcome at discharge, and the other 2 presented results regarding survival with a good neurologic outcome at 30 days, resulting in 2 independent subgroups.

Being transported to a cardiac resuscitation centers was associated with an increase in survival with a good neurologic outcome (OR=1.84, 95% CI 1.52-2.21, *P*<0.001) (Figures 4 and 5). There was no significant difference between the 2 subgroups (hospital discharge OR=1.95, 95% CI 1.09-3.49, *P*=0.02; 30 days OR=2.00, 95% CI 1.37-2.92, *P*<0.001; test for subgroup differences *P*=0.95).

The heterogeneity was also high across this analysis. This was again explored using sensitivity analyses.

Publication Bias

There was no clear asymmetry in the funnel plot used to evaluate publication bias in the 10 studies addressing the survival outcome (Figure 6). It remains possible that some smaller studies with negative results might not have been published. For survival with a good neurologic outcome, after inspection of the results and nature of the studies, no evidence of a publication bias was observed.

Sensitivity Analyses

In the first set of sensitivity analyses, articles with some risk of bias were excluded. The results of these analyses did not differ from the ones presented in the main results (survival OR=2.13, 95% CI 1.73-2.63, *P*<0.001; survival with a good neurologic outcome OR=2.50, 95% CI 2.06-3.03, *P*<0.001) (Figures 7 through 10). However, the exclusion of these articles lowered the heterogeneity (survival I^2 from

Study or Subgroup	log[Odds Ratio]	SE	Cardiac centers Total	Non-cardiac centers Total	Weight	Odds Ratio IV, Random, 95% CI	Year
1.1.1 Survival to hospital discharge							
Stub 2011	0.336	0.112	890	1816	0.0%	1.40 [1.12, 1.74]	2011
Wnent 2012	0.871	0.298	264	170	10.1%	2.39 [1.33, 4.28]	2012
Hunter 2016	0.315	0.295	243	781	0.0%	1.37 [0.77, 2.44]	2016
Tsai 2017	1.464	0.6245	474	72	0.0%	4.32 [1.27, 14.70]	2017
Kragholm 2017	1.084	0.09692	148	1359	0.0%	2.96 [2.44, 3.57]	2017
Cournoyer 2018	0.472	0.125	2533	2389	27.9%	1.60 [1.25, 2.05]	2018
Casey 2018	0.21	0.0475	27826	10337	0.0%	1.23 [1.12, 1.35]	2018
McKenzie 2018	0.606	0.203	404	131	0.0%	1.83 [1.23, 2.73]	2018
Subtotal (95% CI)			**2797**	**2559**	**38.1%**	**1.79 [1.26, 2.53]**	
Heterogeneity: Tau² = 0.03; Chi² = 1.52, df = 1 (P = 0.22); I² = 34%							
Test for overall effect: Z = 3.27 (P = 0.001)							
1.1.2 Survival at 30 days							
Kajino 2010	0.836	0.078	2881	7502	36.3%	2.31 [1.98, 2.69]	2010
Soholm 2013	0.91	0.139	457	563	25.7%	2.48 [1.89, 3.26]	2013
Subtotal (95% CI)			**3338**	**8065**	**61.9%**	**2.35 [2.06, 2.68]**	
Heterogeneity: Tau² = 0.00; Chi² = 0.22, df = 1 (P = 0.64); I² = 0%							
Test for overall effect: Z = 12.55 (P < 0.00001)							
Total (95% CI)			**6135**	**10624**	**100.0%**	**2.13 [1.73, 2.63]**	
Heterogeneity: Tau² = 0.03; Chi² = 7.53, df = 3 (P = 0.06); I² = 60%							
Test for overall effect: Z = 7.03 (P < 0.00001)							
Test for subgroup differences: Chi² = 2.08, df = 1 (P = 0.15), I² = 52.0%							

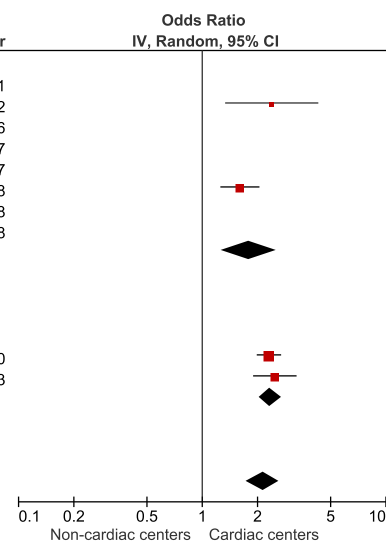

Figure 7. Meta-analysis evaluating the association between transport to a cardiac resuscitation center and survival, excluding studies with some risk of bias, performed using a random-effect model.[22-27,30-33] CI indicates confidence interval; IV, inverse variance; SE, standard error.

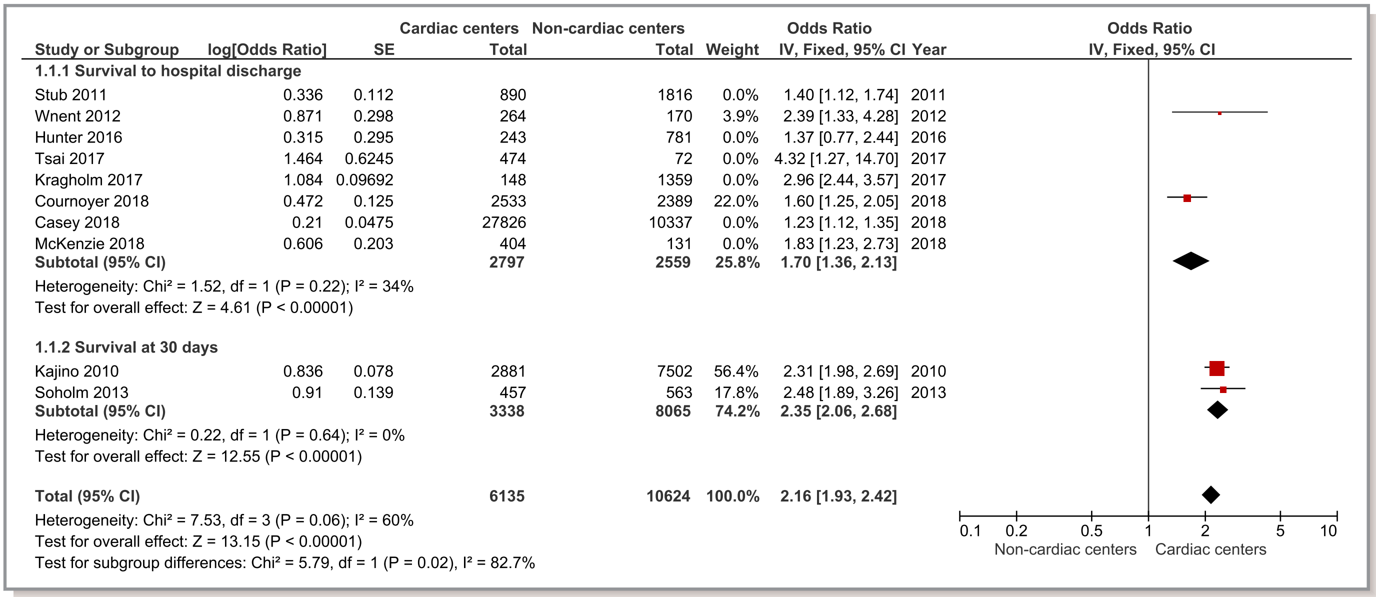

Figure 8. Meta-analysis evaluating the association between transport to a cardiac resuscitation center and survival, excluding studies with some risk of bias, performed using a fixed-effect model.[22-27,30-33] CI indicates confidence interval; IV, inverse variance; SE, standard error.

91% to 60%; survival with a good neurologic outcome I^2 from 88% to 0%).

In the other 2 sets of sensitivity analyses, the association between the transport to cardiac resuscitation centers and both resuscitation outcomes seemed stronger among patients not having experienced prehospital ROSC than in those who did (survival OR 2.54, 95% CI 2.05-3.15, $P<0.001$ versus OR 1.56, 95% CI 1.03-2.36, $P=0.04$; survival with a good neurologic outcome OR=2.74, 95% CI 1.71-4.38, $P<0.001$ versus OR=1.32, 95% CI 0.94-1.86, $P=0.11$) (Figures 11 through 18). The number of articles that could be included in these sensitivity analyses was, however, limited.

Discussion

The present systematic review and meta-analysis sought to evaluate the association between the direct transport to cardiac resuscitation centers and resuscitation outcomes for patients suffering from an OHCA. Direct transport to a cardiac resuscitation center is associated with improved resuscitation outcomes for these patients. Interestingly, this association

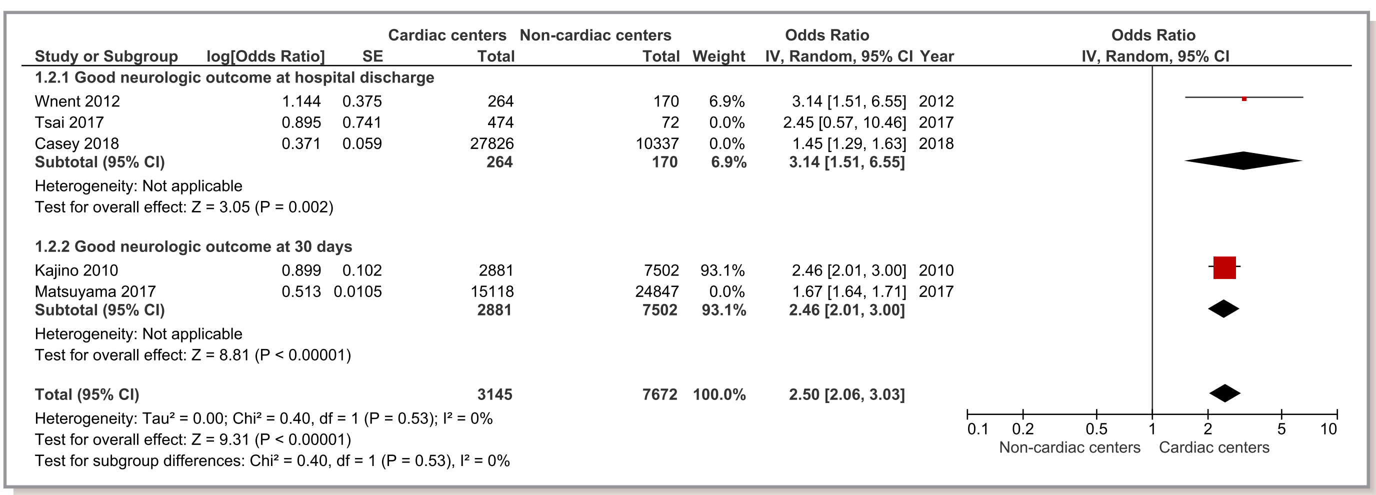

Figure 9. Meta-analysis evaluating the association between transport to a cardiac resuscitation center and survival with a good neurologic outcome, excluding studies with some risk of bias, performed using a random-effect model.[22,24,28,30,31] CI indicates confidence interval; IV, inverse variance; SE, standard error.

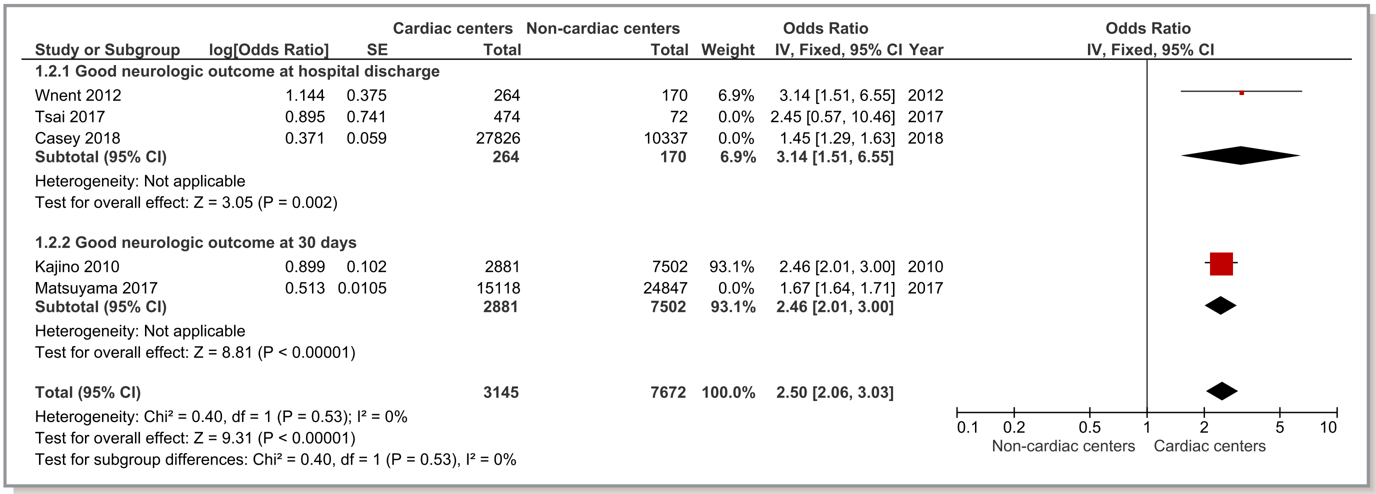

Figure 10. Meta-analysis evaluating the association between transport to a cardiac resuscitation center and survival with a good neurologic outcome, excluding studies with some risk of bias, performed using a fixed-effect model.[22,24,28,30,31] CI indicates confidence interval; IV, inverse variance; SE, standard error.

was stronger among patients without prehospital ROSC than among those who had experienced prehospital ROSC. Given the broad review performed, the presented results can now serve as the benchmark on this topic.

Despite the observational nature of the included articles, the quality of the evidence from which the present review's conclusions can be drawn is moderate.[34] Indeed, all included articles were considered at low risk of bias and provided consistent results for 2 patient-oriented outcomes. Despite some studies including only a selected subpopulation of OHCA, the global population assessed likely represents the population of interest. Given the large cohorts included, the obtained results were relatively precise for the main analyses. Although the observed association was significant, it did not reach the threshold required for it to be considered large.[35] However, a dose-response effect was observed, which upgrades the quality of the evidence.[34] Because the vast majority of the included studies provided results adjusted for the Utstein criteria, which have been shown to predict most of the survival variability following OHCA, it is unlikely that any

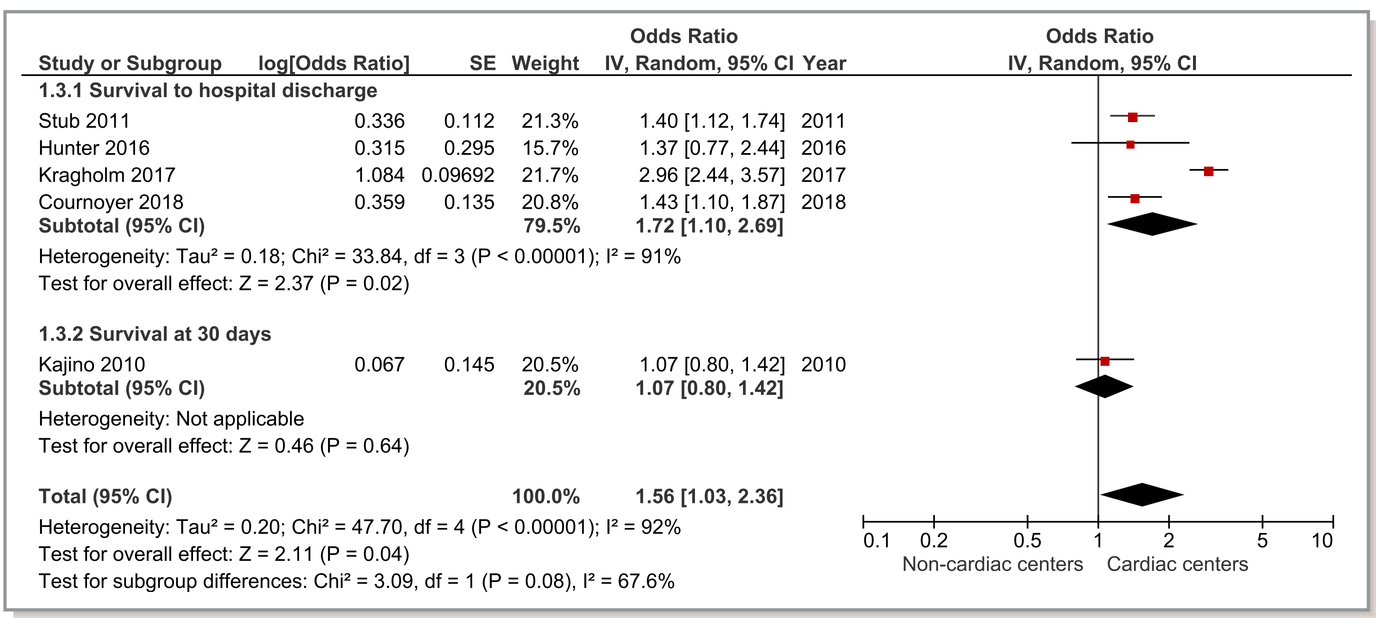

Figure 11. Meta-analysis evaluating the association between transport to a cardiac resuscitation center and survival, including only patients who experienced prehospital return of spontaneous circulation, performed using a random-effect model.[22,23,26,27,32] CI indicates confidence interval; IV, inverse variance; SE, standard error.

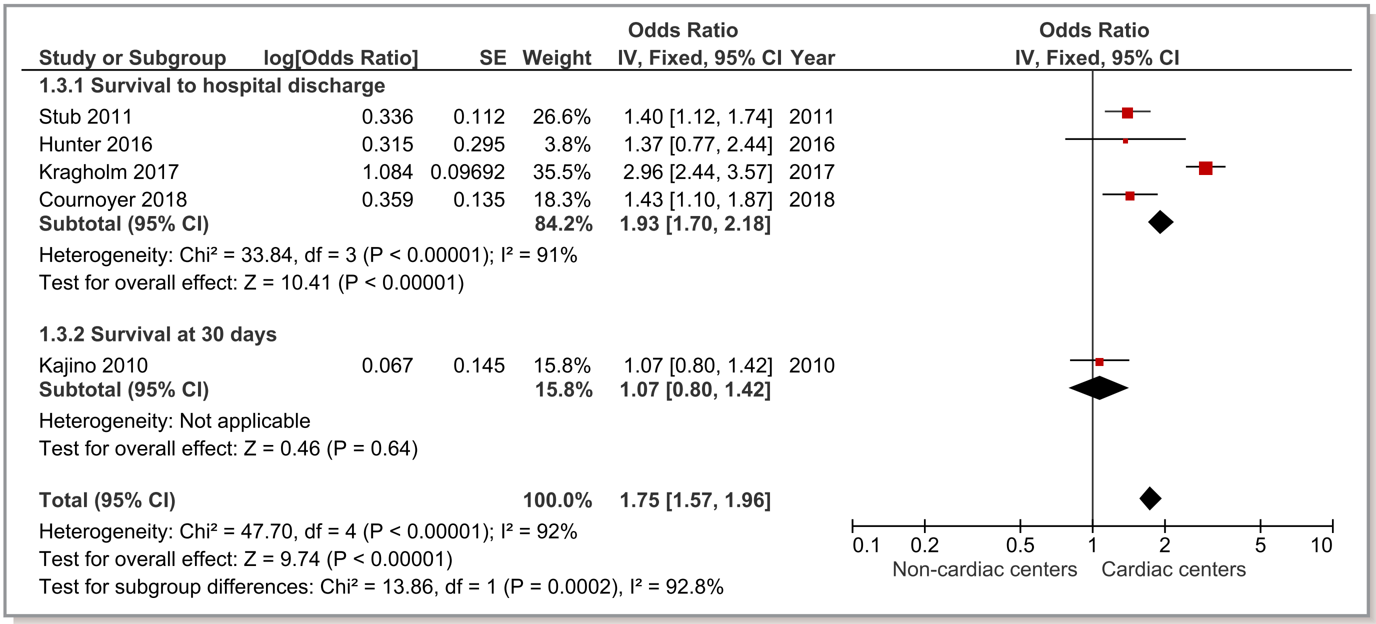

Figure 12. Meta-analysis evaluating the association between transport to a cardiac resuscitation center and survival, including only patients who experienced prehospital return of spontaneous circulation, performed using a fixed-effect model.[22,23,26,27,32] CI indicates confidence interval; IV, inverse variance; SE, standard error.

residual confounding would have significantly affected the main analyses.[36] Finally, it is also unlikely that a publication bias would have altered significantly the presented results, given the consistency of the observed results and the absence of evidence of such a bias.

The potential benefits of being transported to a cardiac resuscitation center probably derive from the additional capabilities and experience that these centers have at treating patients suffering from an OHCA. Of note, acute coronary syndrome is the most common cause of OHCA, and its treatment of choice is PCI.[1,9,37] Further, the timing of PCI also seems to be important for these patients because earlier treatment has been associated with better outcomes, even in the absence of an ST-segment–elevation myocardial infarction on the initial ECG.[38-40] Having on-site access to this treatment all of the time increases the odds of providing this emergent intervention to patients.[31] A similar argument can be made about TTM, which has been shown to increase survival among

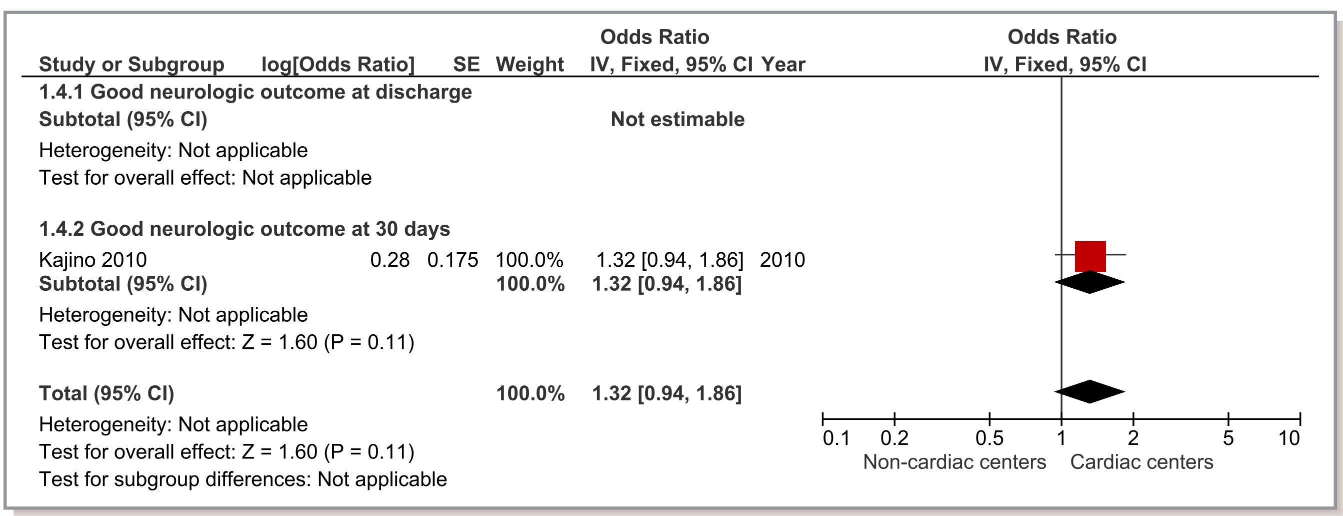

Figure 13. Meta-analysis evaluating the association between transport to a cardiac resuscitation center and survival with a good neurologic outcome, including only patients who experienced prehospital return of spontaneous circulation, performed using a random-effect model.[22] CI indicates confidence interval; IV, inverse variance; SE, standard error.

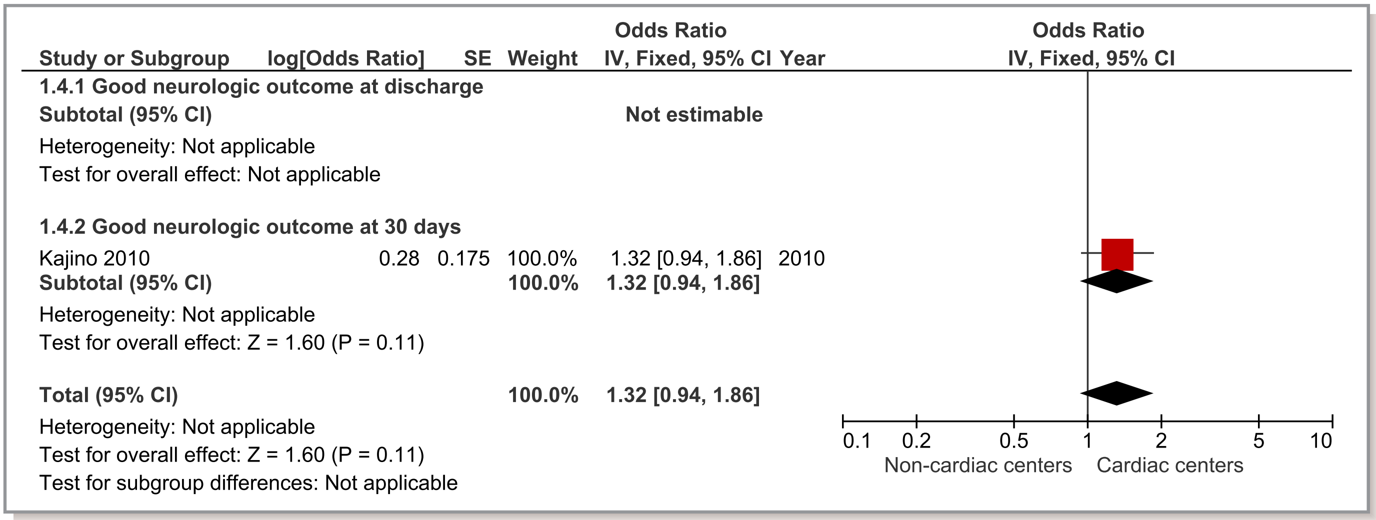

Figure 14. Meta-analysis evaluating the association between transport to a cardiac resuscitation center and survival with a good neurologic outcome, including only patients who experienced prehospital return of spontaneous circulation, performed using a fixed-effect model.[22] CI indicates confidence interval; IV, inverse variance; SE, standard error.

OHCA patients.[10,13,14] In addition, many cardiac resuscitation centers are large, academic, tertiary or quaternary medical centers with increased exposure to and experience with patients suffering from severe disease. These characteristics have been associated less consistently with better outcomes for patients suffering from an OHCA, but it remains plausible that having more experienced professionals could be beneficial to these patients.[26,31,41]

The observation that the association between improved outcomes and direct transport to a cardiac resuscitation center is stronger among patients not having experienced prehospital ROSC had previously been made in 2 of the included studies.[22,32] Indeed, it is plausible that patients having the poorest prognosis are the ones who can benefit the most from the treatments available at cardiac resuscitation centers. However, this is based on a relative measure of effect. Given the observed difference in survival between patients having experienced prehospital ROSC and those who did not (≈50% versus ≈2%), it remains possible that patients having experienced prehospital ROSC could benefit the most in absolute terms from a direct transfer to cardiac resuscitation centers.[22,32]

In light of the presented results, the remaining challenge is the operationalization of such a change in paradigm (transport to a

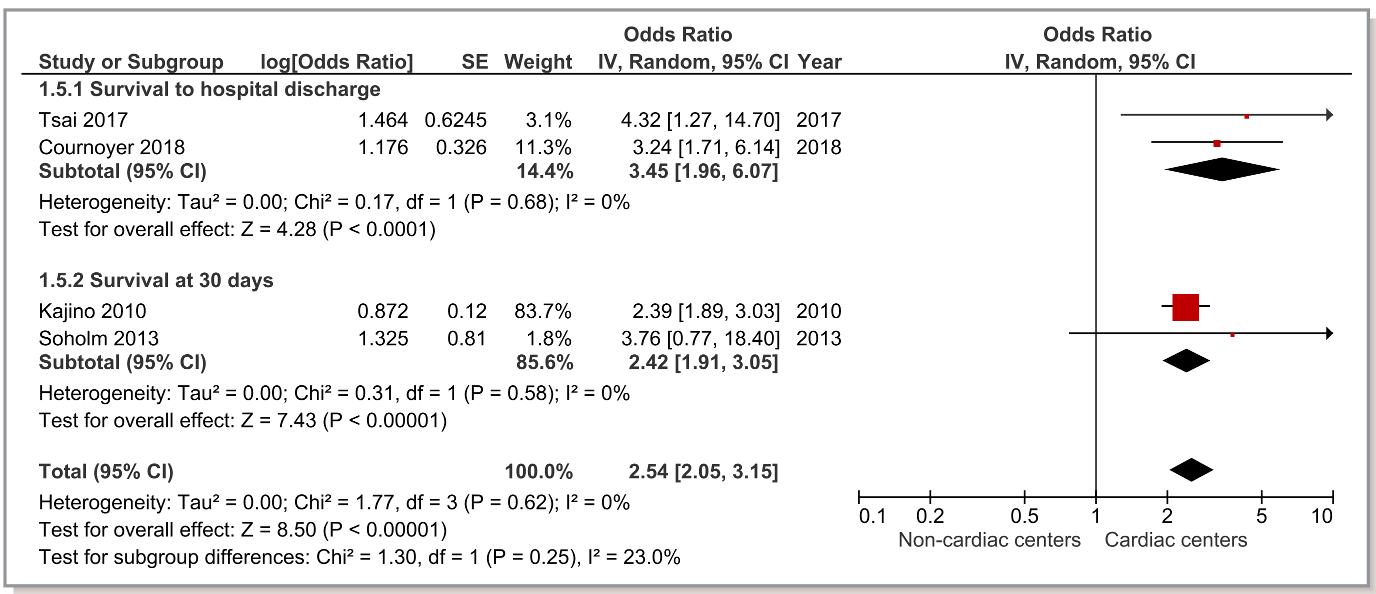

Figure 15. Meta-analysis evaluating the association between transport to a cardiac resuscitation center and survival, including only patients who did not experience prehospital return of spontaneous circulation, performed using a random-effect model.[22,25,30,32] CI indicates confidence interval; IV, inverse variance; SE, standard error.

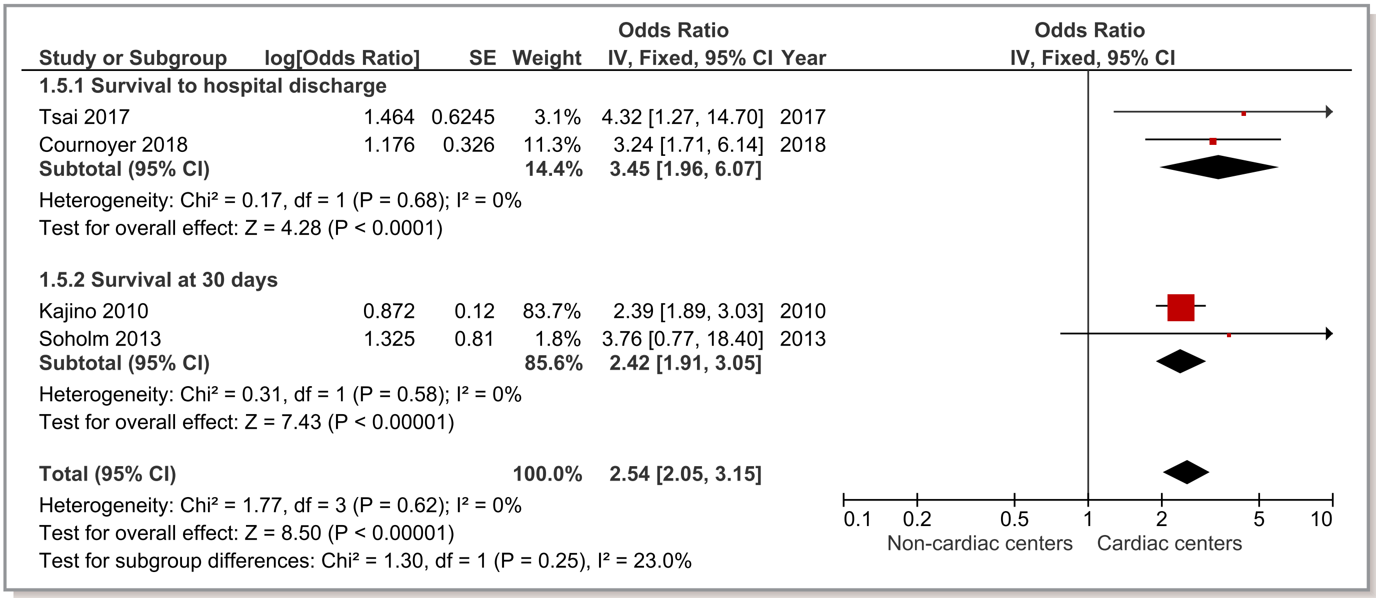

Figure 16. Meta-analysis evaluating the association between transport to a cardiac resuscitation center and survival, including only patients who did not experience prehospital return of spontaneous circulation, performed using a fixed-effect model.[22,25,30,32] CI indicates confidence interval; IV, inverse variance; SE, standard error.

cardiac resuscitation centers versus transport to the closest hospital) for emergency medical services. Multiple studies have concluded that there is no harm in prolonging the transport time of patients suffering from an OHCA, especially for patients having experienced prehospital ROSC.[27,29,42,43] The maximum tolerable bypass time for these patients remains uncertain, but delays of more than 30 minutes were still associated with improvements in survival for patients having experienced prehospital ROSC in 1 study.[27] For patients not having experienced prehospital ROSC, this remains uncertain. In 1 study, a maximum bypass time of 14 minutes was proposed for a population consisting mostly of patients not having prehospital ROSC.[32] The harm caused by prolonged transport for these patients was thought to be due to poor quality of the resuscitation during transport. However, 1 study observed that the quality of cardiopulmonary resuscitation did not decrease during transport.[44] Because the observed benefit of direct transport to a cardiac resuscitation center in the study that proposed the maximum bypass time of 15 minutes was lower than what was observed in the meta-analysis results, it is probably safe to tolerate a bypass time of 15 minutes for patients with ongoing resuscitation. This strategy should be tested in future prospective trials.

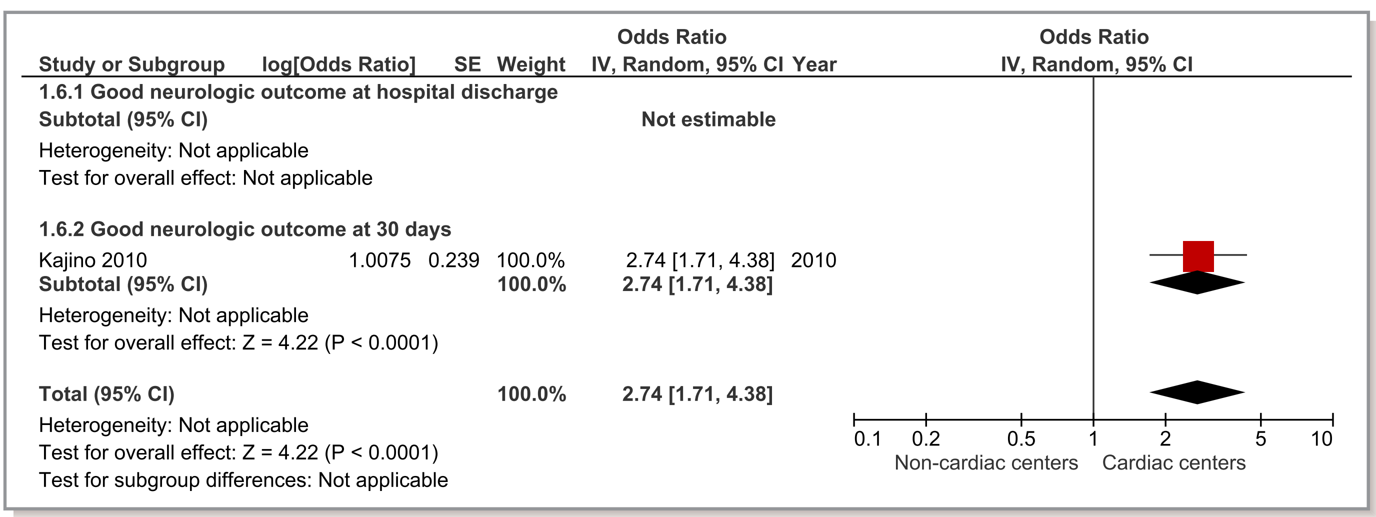

Figure 17. Meta-analysis evaluating the association between transport to a cardiac resuscitation center and survival with a good neurologic outcome, including only patients who did not experience prehospital return of spontaneous circulation, performed using a random-effect model.[22] CI indicates confidence interval; IV, inverse variance; SE, standard error.

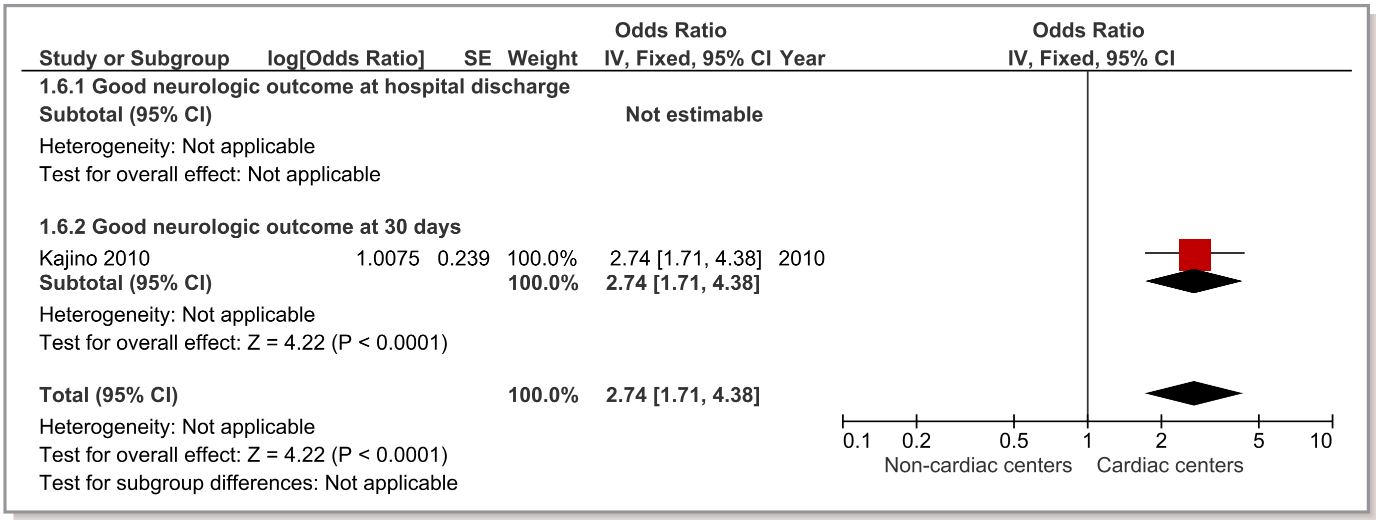

Figure 18. Meta-analysis evaluating the association between transport to a cardiac resuscitation center and survival with a good neurologic outcome, including only patients who did not experience prehospital return of spontaneous circulation, performed using a fixed-effect model.[22] CI indicates confidence interval; IV, inverse variance; SE, standard error.

Limitations

The main limitation of this review is the observational nature of the articles it retained. In addition, although most of the literature is published in English, it is possible that a pertinent article was missed by the initial search. However, given the consistency of the observed results, this may still be unlikely to affect the overall conclusion. A minority of articles provided data for patients having and not having experienced prehospital ROSC. Albeit to a lesser extent, this is also true regarding survival with a good neurologic outcome. All of these analyses provided significant results, but the generalization of their results should still be made with caution. Some articles provided results while adjusting for other hospital characteristics in addition to being a cardiac resuscitation centers. Given the generally positive relationships between these other characteristics and resuscitation outcomes, this could have lowered the differences observed between the 2 groups in the present analysis.

Conclusions

Adult patients suffering from an OHCA transported to cardiac resuscitation centers seem to have better outcomes than their counterparts. It is reasonable to transport these patients directly to cardiac resuscitation centers (class IIa, level of evidence B-nonrandomized). Future studies should further clarify how long a bypass time is tolerable for these patients, especially for the subpopulation of patients not having experienced prehospital ROSC.

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Disclosures

None.

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SUPPLEMENTAL MATERIAL

Data S1. Search strategies.

<u>Web of Science: 1,097</u>

#7	1,097	#6 OR #5 Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI, CCR-EXPANDED, IC Timespan=2008-2018
#6	542	#4 AND #2 AND #1
#5	585	#3 AND #2 AND #1
#4	329,005	(TI=("transport time*" OR "transport interval*" OR "transportation time*" OR "transportation interval*" OR "transportation delay*" OR "transport delay" OR "Transport to hospital" OR "transport to ED" OR "transport to emergency department" OR "time to hospital" OR "distance to hospital" OR "ems transport" OR "transport to ER" OR "transportation of patients" OR "time factors" OR "emergency medical services" OR "transport to ER" OR "time to ED" OR "time to ER" OR "time to emergency department" OR "time to emergency room" OR "transport to center" OR "time" OR "transport to ER" OR "distance to hospital" OR "distance to ER" OR "distance to ED" OR "distance to emergency room" OR "distance to emergency department")) *AND* **LANGUAGE:** (English)
#3	40,010	(TS=("hospital characteristic*" OR "high volume hospital" OR "high-volume hospital" OR "high-volume center" OR "teaching hospital" OR "Cardiac hospital" OR "cardiac center" OR "regionalization of care" OR "Regionalisation of care" OR "tertiary care center" OR "critical care center" OR "high volume center" OR "PCI capable hospital" OR PCI or "PCI center" or "percutaneous coronary intervention center")) *AND* **LANGUAGE:** (English)
#2	1,832,413	(TS=("outcome*" OR "survival" OR "survival to hospital discharge" OR "survival to discharge" OR "Cerebral performance category" OR "CPC" OR "mortality" OR "mortality

rate*" OR "survival rate" OR "disease free survival" OR "neurologic outcome" OR "improved mortality")) *AND* **LANGUAGE:** (English)

# 1	60,321	(TS=("heart arrest" OR "Cardiac arrest" OR "resuscitation" OR "out-of-hospital cardiac arrest" OR "out of hospital cardiac arrest" OR "cardiovascular arrest" OR "cardiopulmonary arrest" OR "ventricular fibrillation" OR "cardiopulmonary resuscitation" OR "asystole" OR "PEA" OR "pulseless electrical activity" OR "CPR" OR "ACLS" OR "advanced cardiac life support" OR "return of spontaneous circulation" OR "without return of spontaneous circulation" OR "ROSC" OR "without ROSC")) *AND* **LANGUAGE:** (English)

PubMed: 701

(((((("heart arrest" or "Cardiac arrest" or "out-of-hospital cardiac arrest" or "out of hospital cardiac arrest" or "cardiovascular arrest" or "cardiopulmonary arrest" or "ventricular fibrillation" or "cardiopulmonary resuscitation" or "asystole" or "PEA" or "pulseless electrical activity" or "CPR" or "ACLS" or "advanced cardiac life support" or "return of spontaneous circulation" or "without return of spontaneous circulation" or "ROSC" or "without ROSC") and ("outcome*" or "survival" or "survival to hospital discharge" or "Cerebral performance category" or "mortality" or "mortality rate*")))) AND (("hospital characteristic*" or "high volume hospital" or "teaching hospital" or "Cardiac hospital" or "regionalization of care" or "Regionalisation of care" or "tertiary care center" or "critical care center" or "high volume center" or "cath lab" or "catherization laboratory" or "PCI capable hospital" or PCI)))) AND ((((("heart arrest" or "Cardiac arrest" or "out-of-hospital cardiac arrest" or "out of hospital cardiac arrest" or "cardiovascular arrest" or "cardiopulmonary arrest" or "ventricular fibrillation" or "cardiopulmonary resuscitation" or "asystole" or "PEA" or "pulseless electrical activity" or "CPR" or "ACLS" or "advanced cardiac life support" or "return of spontaneous circulation" or "without return of spontaneous circulation" or "ROSC" or "without ROSC") and ("outcome*" or "survival" or "survival to hospital discharge" or "Cerebral performance category" or "mortality" or "mortality rate*")))) AND (("transport time*" or "transport interval*" or "transportation time*" or "transportation interval*" or "transportation delay*" or "Transport to hospital" or "transport to ED" or "transport to emergency department" or "time to hospital" or "distance to hospital" or "ems transport" or "transport to ER" or "transportation of patients" or "time factors" or "emergency medical services" or "time" or "treatment outcomes" or "transport to ER" or "distance to hospital"))) AND "last 10 years"[PDat] AND Humans[Mesh] AND English[lang] AND "last 10 years"[PDat] AND Humans[Mesh]

Cochrane Library: 195

ID Search Hits

#1 (("heart arrest" or "Cardiac arrest" or "out-of-hospital cardiac arrest" or "out of hospital cardiac arrest" or "cardiovascular arrest" or "cardiopulmonary arrest" or "ventricular fibrillation" or "cardiopulmonary resuscitation" or "asystole" or "PEA" or "pulseless electrical activity" or "CPR" or "ACLS" or "advanced cardiac life support" or "return of spontaneous circulation" or "without return of spontaneous circulation" or "ROSC" or "without ROSC") and ("outcome*" or "survival" or "survival to hospital discharge" or "Cerebral performance category" or "mortality" or "mortality rate*")) 3920

#2 ("hospital characteristic*" or "high volume hospital" or "teaching hospital" or "Cardiac hospital" or "regionalization of care" or "Regionalisation of care" or "tertiary care center" or "critical care center" or "high volume center" or "cath lab" or "catherization laboratory" or "PCI capable hospital" or PCI) 12102

#3 ("transport time*" or "transport interval*" or "transportation time*" or "transportation interval*" or "transportation delay*" or "Transport to hospital" or "transport to ED" or "transport to emergency department" or "time to hospital" or "distance to hospital" or "ems transport" or "transport to ER" or "transportation of patients" or "transport to ER" or "distance to hospital") 409

#4 #1 and #2 176

#5 #1 and #3 20

#6 #4 or #5 195

<u>EMBASE: 536</u>

1 exp heart arrest/ or exp cardiopulmonary arrest/ or exp "out of hospital cardiac arrest"/ or exp sudden cardiac death/ or exp heart ventricle fibrillation/ or exp asystole/ or exp "return of spontaneous circulation"/ (103276)

2 (OOHCA or OHCA or 'without return of spontaneous circulation' or 'without ROSC' or ROSC).ti,ab. (6580)

3 exp patient transport/ (24023)

4 ('transport time' or 'transportation time' or 'transport to emergency department' or 'transportation to emergency department' or 'time to hospital' or 'transportation delay' or 'transportation time' or 'transport of patient' or 'transportation of patient' or 'distance to hospital' or 'distance to emergency department' or 'distance to ED' or 'distance to ER' or 'transport interval' or 'transportation interval').ab,ti. (9427)

5 exp time to treatment/ (9918)

6 exp emergency treatment/ or exp treatment outcome/ or exp disease free survival/ or survival/ or exp survival rate/ or exp long term survival/ or exp median survival time/ or exp overall survival/ (2104836)

7 ('survival to hospital discharge' or 'survival to discharge' or CPC or 'cerebral performance category').ab,ti. (11226)

8 exp heart center/ (360)

9 ('hospital characteristics' or 'high volume hospital' or 'high volume center' or 'Cardiac center' or 'specialized hospital' or 'regionalization of care' or 'regionalisation of care' or 'teaching hospital' or 'tertiary care center' or 'PCI center' or 'critical care center' or 'PCI hospital').ab,ti. (63248)

10 1 or 2 (103648)

11 3 or 4 or 5 (42625)

12 6 or 7 (2110407)

13 8 or 9 (63552)

14 10 and 11 and 12 (1053)

15 10 and 12 and 13 (536)

16 14 or 15 (1558)

17 limit 16 to english (1481)

18 limit 17 to humans (1404)

19 limit 18 to yr="2008 -Current" (1101)

20 limit 19 to (editorial or letter) (88)

21 case report/ (2290727)

22 19 not (20 or 21) (873)

23 limit 22 to embase (548)

24 remove duplicates from 23 (536)

****

Table S1. NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE FOR COHORT STUDIES

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability

Selection

1) Representativeness of the exposed cohort

   a) truly representative of the average out-of-hospital cardiac arrest in the community ✵

   b) somewhat representative of the average out-of-hospital cardiac arrest in the community ✵

   c) selected group of users eg nurses, volunteers

   d) no description of the derivation of the cohort

2) Selection of the non exposed cohort

   a) drawn from the same community as the exposed cohort ✵

   b) drawn from a different source

   c) no description of the derivation of the non exposed cohort

3) Ascertainment of exposure

   a) secure record (eg surgical records) ✵

   b) structured interview ✵

   c) written self report

   d) no description

4) Demonstration that outcome of interest was not present at start of study

   a) yes ✵

   b) no

Comparability

1) Comparability of cohorts on the basis of the design or analysis

   a) study controls for the initial rhythm ✵

   b) study controls for any additional factor ✵

Outcome

1) Assessment of outcome

a) independent blind assessment ✸

b) record linkage ✸

c) self report

d) no description

2) Was follow-up long enough for outcomes to occur (at least until discharge)

a) yes ✸

b) no

3) Adequacy of follow up of cohorts

a) complete follow up - all subjects accounted for ✸

b) subjects lost to follow up unlikely to introduce bias - small number lost - > 90 % follow up, or description provided of those lost) ✸

c) follow up rate < 90 % and no description of those lost

d) no statement

Table S2. Template for data extraction.

Study	N	Age (mean std dev)	Male (%)	Witnessed (%)	Byst CPR (%)	VT/VF (%)	Prehospital ROSC	D/Cd alive	CPC 1/2

Study	Year	Journal	Study Design	LOE	N	Cardiac	Non-cardiac	Mortality, Cardiac	% (95% CI)	Mortality, Non-cardiac	% (95% CI)	AOR / OR