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Original Article

Quantifying the Effect of Cardiopulmonary Resuscitation Quality on Cardiac Arrest Outcome

A Systematic Review and Meta-Analysis

Sarah K. Wallace, AB; Benjamin S. Abella, MD, MPhil; Lance B. Becker, MD

Background—Evidence has accrued that cardiopulmonary resuscitation quality affects cardiac arrest outcome. However, the relative contributions of chest compression components (such as rate and depth) to successful resuscitation remain unclear.

Methods and Results—We sought to measure the effect of cardiopulmonary resuscitation quality on cardiac arrest outcome through systematic review and meta-analysis. We searched for any clinical study assessing cardiopulmonary resuscitation performance on adult cardiac arrest patients in which survival was a reported outcome, either return of spontaneous circulation or survival to admission or discharge. Of 603 identified abstracts, 10 studies met inclusion criteria. Effect sizes were reported as mean differences. Missing data were resolved by author contact. Estimates were segregated by cardiopulmonary resuscitation metric (chest compression rate, depth, no-flow fraction, and ventilation rate), and a random-effects model was applied to estimate an overall pooled effect. Arrest survivors were significantly more likely to have received deeper chest compressions than nonsurvivors (mean difference, 2.44 mm; 95% confidence interval, 1.19–3.69 [$P<0.001$]; n=6 studies; $I^2=0.0\%$; P for heterogeneity=0.9). Likewise, survivors were significantly more likely to have received chest compression rates closer to 85 to 100 compressions per minute (cpm) than nonsurvivors (absolute mean difference from 85 cpm, −4.81 cpm; 95% confidence interval, −8.19 to −1.43 [$P=0.005$]; from 100 cpm, −5.04 cpm; 95% confidence interval, −8.44 to −1.65 [$P=0.004$]; n=6 studies; $I^2<49\%$; P for heterogeneity >0.2). No significant difference in no-flow fraction (n=7 studies) or ventilation rate (n=4 studies) was detected between survivors and nonsurvivors.

Conclusions—Deeper chest compressions and rates closer to 85 to 100 cpm are significantly associated with improved survival from cardiac arrest. **(*Circ Cardiovasc Qual Outcomes*. 2013;6:148-156.)**

Key Words: cardiac arrest ■ cardiopulmonary resuscitation ■ heart arrest ■ meta-analysis ■ resuscitation

Prompt delivery of cardiopulmonary resuscitation (CPR) with an emphasis on high-quality chest compressions has long been considered an essential link in the chain of survival for cardiac arrest resuscitation.[1] As a result, the American Heart Association and the European Resuscitation Council have published guidelines that stipulate a consensus rate and depth of chest compressions to be delivered during CPR.[1,2] However, the quantitative impact of high-quality CPR on survival has never been prospectively assessed in a randomized trial, leading to lingering questions about the magnitude of its therapeutic benefit. Some have even suggested that CPR may have only the appearance of value.[3] Meanwhile, nonrandomized studies assessing the effect of CPR quality on clinical outcome have yielded conflicting results.

Editorial see p 135

The extent to which CPR quality affects survival from cardiac arrest remains poorly understood. A growing body of investigations has quantified CPR performance metrics and clinical outcomes from cardiac arrest, yet no study to date has rigorously analyzed the available evidence on CPR quality to determine a best estimate of its effect on survival. We sought to measure the relationship between key CPR quality parameters (chest compression rate, depth, no-flow fraction, and ventilation rate) and clinical outcomes using a formal approach of systematic review and meta-analysis.

Methods

Search Strategy

We compiled and assessed the available clinical literature on CPR quality following the consensus meta-analysis methodology of Stroup et al[4] in conjunction with Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines.[5] We searched for all cohort studies, case–control studies, and randomized trials assessing CPR performance by bystanders or health professionals on adult patients experiencing out-of-hospital cardiac arrest (OHCA) or in-hospital cardiac arrest (IHCA) in which survival was an explicit outcome. Acceptable survival measures included return of spontaneous circulation (ROSC) for IHCA or OHCA, survival to hospital admission for OHCA, and survival to hospital discharge for IHCA or OHCA. When >1 survival outcome was available for a single study, data on survival to hospital admission or discharge were

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WHAT IS KNOWN

- Prompt delivery of cardiopulmonary resuscitation with an emphasis on high-quality chest compressions improves survival from cardiac arrest.
- The relative contributions of cardiopulmonary resuscitation components (such as chest compression rate, depth, no-flow fraction, and ventilation rate) to successful resuscitation remain unclear.

WHAT THE STUDY ADDS

- We measured the relationship between key cardiopulmonary resuscitation quality parameters and clinical outcomes using a formal approach of systematic review and meta-analysis.
- Deeper chest compressions and chest compression rates closer to the range of 85 to 100 compressions per minute were significantly associated with improved survival from cardiac arrest.
- There were no significant differences in ventilation rate and no-flow fraction between survivors and nonsurvivors.

included in the meta-analysis preferentially because they provide a better estimate of long-term clinical outcomes. Additionally, studies were eligible for inclusion only if at least 1 metric of CPR quality (eg, chest compression depth, rate, no-flow fraction, or ventilation rate) and its independent effect on survival were evaluated. These criteria were established to allow testing of individual components of CPR quality and their association with clinical outcome.

A comprehensive search of the published and unpublished literature was performed with the use of PubMed Plus, MEDLINE (Ovid), the Cochrane Library, www.ClinicalTrials.gov, Grey literature sources (OpenGrey, CAB Abstracts), related articles, hand searching of reference lists, and direct author contact. Key words used in these searches were cardiopulmonary resuscitation, quality, heart arrest, and cardiac arrest. The time period searched ranged from the earliest available online indexing year for each database through June 2012. We limited our search to those studies published in the English language and conducted on humans.

We a priori excluded studies comparing manual with mechanical CPR and those comparing different approaches to CPR (eg, minimally interrupted cardiac resuscitation versus traditional CPR) because direct comparisons of CPR quality between these investigations would be significantly confounded. Studies were also excluded if they were cross-sectional or ecological, commentaries, general reviews, or case reports. If multiple investigations were published from the same cohort, we included the study with the greatest number of patients preferentially.

Selection of Articles

Of 603 identified articles, 545 were excluded after review of the title and abstract (Figure 1). Full texts of the 58 remaining articles were assessed for potential inclusion by 2 investigators independently (S.K.W. and B.S.A.). Group consultation among authors was used to resolve uncertainties. Forty-two studies were excluded for representing reviews (n=2), not assessing CPR quality metrics individually (n=22), comparing mechanical with manual CPR (n=2), reporting simulation data on manikins (n=1), including diseases other than cardiac arrest in the study population (n=2), not meeting outcome criteria (n=5), and representing overlapping publications from the same patient cohorts (n=8).

Six additional studies assessed a categorical overall quality metric (eg, good CPR versus bad CPR) concomitant with associated survival to hospital discharge.[6–11] Five of the 6 studies were conducted before 1995.[7–11] All but 1 study[6] relied on subjective assessments of CPR quality by an observer who was not blinded to the outcome of the resuscitation, making recall bias a significant concern. Meta-analysis of these studies revealed that categorically defined higher-quality CPR was significantly associated with survival to discharge (odds ratio, 10.4; 95% confidence interval [CI], 6.45–14.2). However, high heterogeneity was present among included studies (I^2=98.9%; P<0.001), suggesting that they are not comparable. Therefore, these 6 articles were excluded from our primary analysis because of concerns about bias and quality.

Data Extraction

We identified 10 studies evaluating the effect of CPR quality metrics on survival after cardiac arrest. Three studies represented data from the Resuscitation Outcomes Consortium Epistry. However, they did not include overlapping patients at the level of our planned meta-analyses because 1 study evaluated rate and depth,[12] 1 study evaluated chest compression fraction in ventricular fibrillation/ventricular tachycardia OHCA only,[13] and 1 study evaluated chest compression fraction in non–ventricular fibrillation/ventricular tachycardia OHCA only.[14] Data were extracted in an open-ended fashion by 1 investigator (S.K.W.) and were reviewed twice to minimize data-entry errors. Variables included study design, location, dates over which the study was performed, sample size, whether the CPR quality assessment was a prespecified aim, definition of CPR process variables and their assessment methods, definition of outcome variables and their assessment methods, effect estimates, and possible sources of bias.

Standardized quality scores for observational studies have not been established. Thus, quality assessment of the included studies was performed by evaluating and scoring 6 criteria on an integer scale (0 or 1, with 1 being better), including (1) study design, (2) multicenter or single-center designation, (3) assessment of CPR quality measures, (4) assessment of outcome, (5) evidence of bias, and (6) whether CPR quality assessment was a prespecified aim. Studies with a sum from 0 to 4 were considered low quality, whereas those with a sum of 5 or 6 were considered high quality. This system was adapted from quality scores used in other published meta-analyses of observational studies.[15,16]

For 7 of the 10 included studies, authors were directly contacted to request missing or additional data. Six study authors[12–14,17–19] were asked to provide summary statistics for continuous CPR quality variables stratified by survival outcome so that a mean difference could be computed. A seventh study[20] included both IHCA and OHCA events; the author was asked to provide separate estimates for each group to allow stratification by cardiac arrest location. This information was obtained from all authors as requested.

Statistical Analysis

All included studies were either prospective cohort studies or post hoc analyses of primary clinical trial cohorts. Effect sizes were reported as mean differences. Standard errors were calculated using group SD or 95% CI measures. Survival outcomes were categorized as ROSC, survival to admission, or survival to hospital discharge.

Estimates were segregated into groups by the specific CPR performance metric assessed (eg, depth, rate). The DerSimonian–Laird random-effects model was then applied to studies within each group to estimate an overall pooled effect. This model was chosen because it assumes random variability among studies beyond subject-level sampling error.[21] We constructed forest plots to visually display the data. We used the Begg adjusted-rank correlation test and constructed funnel plots to assess publication bias.[22]

Evidence for statistical heterogeneity between studies was tested by goodness of fit (χ^2). Heterogeneity was also quantified with the I^2 measure.[23] This measure, ranging from 0% to 100%, represents the degree of inconsistency across studies included in the meta-analysis. Low, moderate, and high heterogeneity correspond to I^2 values of 25%, 50%, and 75%, respectively. Prespecified potential sources of heterogeneity explored in sensitivity analyses were as follows: cardiac arrest location (OHCA versus IHCA), study design (prospective cohort or post hoc clinical trial analysis), study region (North

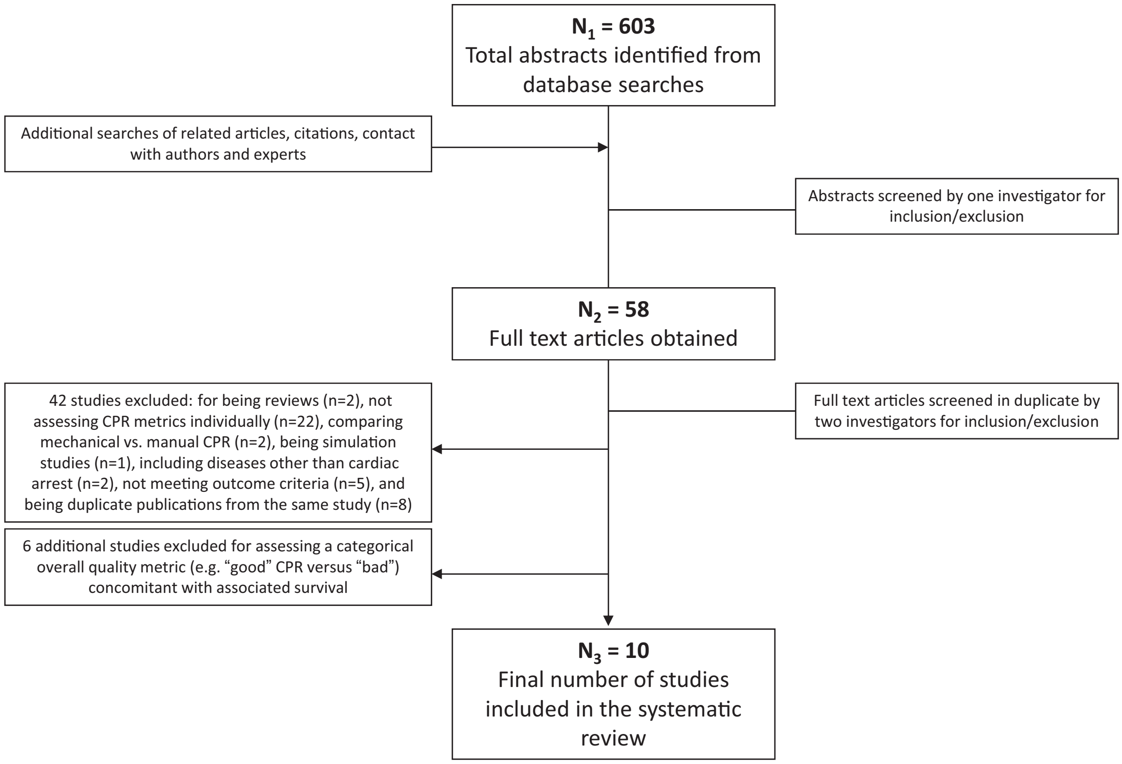

Figure 1. Screening and selection process for studies of cardiopulmonary resuscitation (CPR) quality and survival outcomes.

America or Europe), type of person performing the measured CPR (bystanders versus health professionals), outcome (ROSC versus survival to hospital admission or discharge), investigation quality score (high versus low), and whether the analysis was a prespecified aim or conducted post hoc (to address publication bias of positive findings). Analyses were performed with a statistical software package (STATA 11; StataCorp, College Station, TX) with α set at 0.05.

Results

Four variables of CPR quality were assessed among the 10 included studies: compression rate; compression depth; no-flow fraction (defined as the percent of resuscitation time during which compressions were not performed) or its inverse, compression fraction; and ventilation rate.

The 10 studies included 8 prospective cohort studies[12–14,18–20,24,25] and 2 post hoc analyses of clinical trials (the Table).[17,26] Seven studies were conducted in North America[12–14,18,20,24,25] and 3 in Europe.[17,19,26] Data on chest compression rate were available for 1641 patients (176 IHCA and 1465 OHCA); data on depth were available for 1892 patients (77 IHCA and 1815 OHCA); data on no-flow fraction were available for 3424 patients (79 IHCA and 3345 OHCA); and data on ventilation rate were available for 483 patients (71 IHCA and 412 OHCA). No randomized, controlled trials of manual CPR quality and survival were identified. For all included studies, survival outcomes were ascertained by the original study authors through prehospital and hospital records. Among included studies, mean age was 67.3 years; 65% of the cohort were male. The overall ROSC rate was 34.3%; survival to discharge rate was 5.9%.

Averaged across investigations, mean chest compression rate was 107 compressions per minute (cpm); mean chest compression depth was 39.9 mm; mean no-flow fraction was 39.3%; and mean ventilation rate was 13.6 breaths per minute. Most studies quantifying rate, depth, no-flow fraction, and ventilation rate[12–14,17–20,25,26] did so using an investigational monitor/defibrillator with accelerometer, force detector, and chest wall impedance detector; however, 1 investigation[24] used customized personal digital assistant software controlled by a research assistant to collect compression rate data. The total number of patients varied substantially between studies (n=49–2103). For all but 3 studies,[17,25,26] assessing the relationship of CPR quality and survival was a prespecified primary or secondary aim. CPR was performed by trained prehospital personnel such as emergency medical technicians and paramedics in 8 publications[12–14,18–20,26] and by trained in-hospital personnel such as nurses, physicians, and medical students in 3 publications.[20,24,25] Study quality was high in 6 investigations,[12–14,18,20,24] as defined by our scoring system described in Methods.

Chest Compression Depth

Six studies provided separate estimates for the relationship between chest compression depth and outcome.[12,17,18,20,25,26] In 4 investigations,[18,20,25,26] this outcome was ROSC; in 1 study,[12] it was survival to hospital discharge; and in 1 study,[17] it was survival to hospital admission. IHCA was assessed in 1 study,[25] OHCA was assessed in 4 studies,[12,17,18,26] and both IHCA and OHCA were assessed in 1 study (providing separate estimates for each).[20]

Cardiac arrest survivors were significantly more likely to receive deeper chest compressions than nonsurvivors, as shown in Figure 2 (mean difference, 2.44 mm; 95% CI, 1.19–3.69;

Table. Identified Studies Evaluating CPR Quality and Survival After Cardiac Arrest

First Author	Study Design	Region(s)	CPR Quality Measure(s)	Ascertainment of Quality Measure(s)	Who Performed the CPR?	Outcome	Population	Sample Size, n	Prespecified Analysis	Quality Score
Abella et al[24]	Prospective cohort	US	Rate	Counting by an observer	Nurses, physicians, medical students	ROSC	IHCA	97	Yes (primary)	5 (High)
Abella et al[25]	Prospective cohort	US	Rate, depth, no-flow fraction, ventilation rate	Investigational monitor/ defibrillator	Nurses, physicians, medical students	ROSC	IHCA	60	No	4 (Low)
Babbs et al[18]	Prospective cohort	North America	Depth	Investigational monitor/ defibrillator	EMS providers	ROSC	OHCA	172	Yes (secondary)	5 (High)
Bohn et al[26]	Post hoc analysis of a clinical trial	Germany	Depth, no-flow fraction	Investigational monitor/ defibrillator	EMTs, physicians	ROSC	OHCA	300	No	3 (Low)
Edelson et al[20]	Prospective cohort	USA, Norway	Rate, depth, no-flow fraction, ventilation rate	Investigational monitor/ defibrillator	Nurses, physicians, medical students, paramedics	ROSC	IHCA and OHCA	49	Yes (primary)	6 (High)
Kramer-Johansen et al[17]	Post hoc analysis of a clinical trial	UK, Sweden, Norway	Rate, depth, no-flow fraction, ventilation rate	Investigational monitor/ defibrillator	Paramedics, nurses	Survival to admission	OHCA	284	No	4 (Low)
Stiell et al[12]	Prospective cohort	US, Canada (ROC)	Rate, depth	Investigational monitor/ defibrillator	EMS providers	Survival to discharge	OHCA	1029	Yes (primary)	6 (High)
Stecher et al[19]	Prospective cohort	Norway	Rate, no-flow fraction, ventilation rate	Investigational monitor/ defibrillator	EMS providers	ROSC	OHCA	122	Yes (secondary)	4 (Low)
Christenson et al[13]	Prospective cohort	US, Canada (ROC)	No-flow fraction	Investigational monitor/ defibrillator	EMS providers	Survival to discharge	OHCA (VF/ VT)	506	Yes (primary)	6 (High)
Vaillancourt et al[14]	Prospective cohort	US, Canada (ROC)	No-flow fraction	Investigational monitor/ defibrillator	EMS providers	Survival to discharge	OHCA (non-VF/ VT)	2103	Yes (primary)	6 (High)

CPR indicates cardiopulmonary resuscitation; EMS, emergency medical services; EMT, emergency medical technician; IHCA, in-hospital cardiac arrest; OHCA, out-of-hospital cardiac arrest; ROC, Resuscitation Outcomes Consortium; ROSC, return of spontaneous circulation; and VF/VT, ventricular fibrillation/ventricular tachycardia.

$P<0.001$). No heterogeneity was detected among included studies ($I^2=0.0\%$; $P=0.90$). Findings were similar in analyses restricted to the 5 studies examining OHCA/where emergency medical service providers performed the CPR[12,17,18,20,26] (mean difference, 2.44 mm; 95% CI, 1.16–3.72); the 3 studies with highest quality scores/where the assessment was prespecified[12,18,20] (mean difference, 2.62 mm; 95% CI, 0.18–5.06); the 4 studies that were conducted in North America/had a prospective cohort design[12,18,20,26] (mean difference, 2.41 mm; 95% CI, 0.13–4.69); and the 2 studies where the outcome was survival to hospital admission or discharge[12,17] (mean difference, 3.06 mm; 95% CI, 1.22–4.90).

We assessed these results for possible publication bias by visually inspecting the funnel plot and calculating its statistical analog, the Begg test.[22] These methods suggested no significant publication bias (Begg test, $P=0.88$).

Chest Compression Rate

Six studies provided separate estimates for the relationship between chest compression rate and outcome.[12,17,19,20,24,25] In 4 investigations,[19,20,24,25] the outcome was ROSC; in 1 study,[12] it was survival to hospital discharge; and in 1 study,[17] it was survival to hospital admission. IHCA was assessed in 2 studies,[24,25] OHCA was assessed in 3 studies,[12,17,19] and both IHCA and OHCA were assessed in 1 study (providing separate estimates for each).[20] One publication[17] represented a post hoc analysis of a primary clinical trial cohort; the rest of the included studies had a prospective cohort design. Notably, the rate estimate by Bohn et al[26] was considered to be methodologically heterogeneous to the others because of the use of an acoustic metronome prompting a compression rate of 100 cpm in resuscitation events; it was therefore excluded a priori from the present meta-analysis.

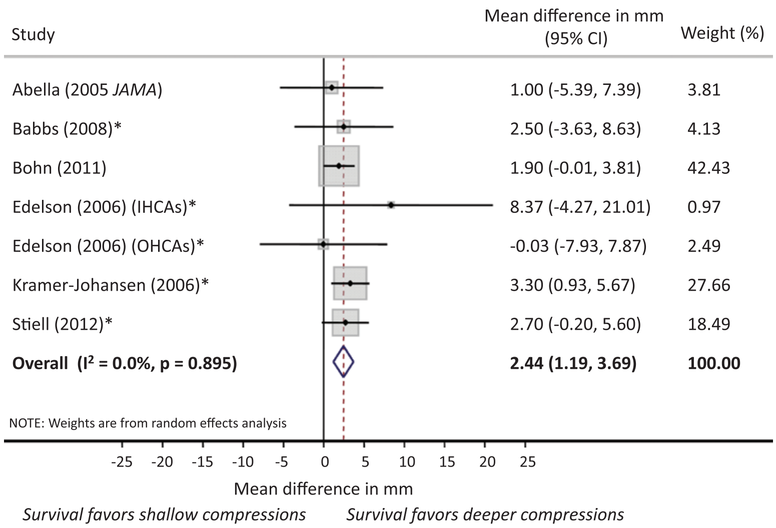

Figure 2. Random-effects meta-analysis of mean differences in chest compression depth (mm), survivors vs nonsurvivors. Includes 4 cohort studies and 2 post hoc analyses of clinical trials, representing 77 in-hospital cardiac arrest (IHCA) and 1815 out-of-hospital cardiac arrest (OHCA) events. Positive values indicate that survival favors deeper chest compressions. Tests for heterogeneity were not significant. The size of the data marker corresponds to the weight of that study. Error bars represent 95% confidence intervals (CIs). *Estimates that were derived from new data requested from authors.

There was no overall difference in mean chest compression rate between survivors and nonsurvivors (data not shown). We conducted a second analysis to determine whether proximity to a particular rate maximized survival (ie, that very high-compression rates were as detrimental as low rates). This was achieved by calculating the absolute difference between rates recorded among the 2 survival groups and a series of compression rate set points. For each such set point, the mean compression rate difference between survivors and nonsurvivors was assessed. For example, in a scenario in which survivors received a mean chest compression rate of 110 cpm and nonsurvivors received 90 cpm, both groups would yield an absolute difference of 10 cpm at a set point of 100 cpm (|100–90|=10, |100–110|=10); thus, the overall mean difference between these 2 groups would be 0 cpm (10 minus 10 cpm). However, at a set point of 105 cpm, the overall mean difference between the 2 would be −10 cpm (|105–110|=5 for survivors minus |90–105|=15 for nonsurvivors). Set points were established in increments of 5 cpm within the range of 80 to 120 cpm. Meta-analyses were performed at each set point.

Survivors were significantly more likely to receive chest compression rates closer to the range of 85 to 100 cpm, as shown in Figure 3 (absolute mean difference from 85 cpm, −4.81 cpm; 95% CI, −8.19 to −1.43 [P=0.005]; from 90 cpm, −6.58 cpm; 95% CI, −10.4 to −2.72 [P=0.001]; from 95 cpm, −6.58 cpm; 95% CI, −10.4 to −2.72 [P=0.001]; from 100 cpm, −5.04 cpm; 95% CI, −8.44 to −1.65 [P=0.004]). Low to moderate, nonstatistically significant heterogeneity was detected among these associations (I^2<49.1%; P>0.07 for all analyses). At rates <85 cpm and >100 cpm, no significant association was found between survival and proximity to these rate set points (Figure 4).

Findings remained significant after stratification by cardiac arrest location, although the magnitude of the relationship was 2-fold greater for IHCA (at a set point of 95 cpm: overall mean difference for IHCA,[20,24,25] −10.4 cpm; 95% CI, −15.9 to −4.84; for OHCA,[12,17,19,20] −5.02 cpm; 95% CI, −9.61 to −0.43). Findings likewise remained significant when stratified by outcome (at a set point of 95 cpm: overall mean difference for studies reporting ROSC,[19,20,24,25] −6.54 cpm; 95% CI, −12.5 to −0.58; overall mean difference for studies reporting survival to admission or discharge,[12,17] −7.55 cpm; 95% CI, −11.6 to −3.49). Sensitivity analyses by type of CPR performer, study region, study design, quality score, and whether the analysis was a prespecified aim had no effect on the results (data not shown).

Visual inspection of the funnel plot and calculation of the Begg test suggested no significant publication bias among the results. Results from all set points (between 80 and 120 cpm) yielded a Begg test value of P>0.35.

No-Flow Fraction

Seven studies provided separate estimates for the relationship between no-flow fraction and outcome.[13,14,17,19,20,25,26] In 4 investigations,[19,20,25,26] this outcome was ROSC; in 2 studies,[13,14] it was survival to hospital discharge; and in 1 study,[17] it was survival to hospital admission. IHCA was assessed in 1 study,[25] OHCA was assessed in 5 studies,[13,14,17,19,26] and both IHCA and OHCA were assessed in 1 study (providing separate estimates for each).[20]

We found no significant difference in no-flow fraction between survivors and nonsurvivors overall (mean difference, 1.34%; 95% CI, −1.50 to 4.18; P=0.36; Figure I in the online-only Data Supplement). A low to moderate degree of nonsignificant heterogeneity was present among included studies (I^2=43.1%; P=0.09). Findings did not change when stratified by cardiac arrest location (IHCA versus OHCA), outcome measure, type of CPR performer, study region, study design, quality score, or whether the analysis was a prespecified aim (results not shown). Visual inspection of the funnel plot and calculation of the Begg test suggested no significant publication bias (Begg test, P=0.90).

Ventilation Rate

Four studies provided separate estimates for the relationship between ventilation rate and outcome.[17,19,20,25] In 3 studies,[19,20,25] this outcome was ROSC; in 1 study,[17] it was survival to hospital admission. IHCA was assessed in 1 study,[25] OHCA was assessed in 2 studies,[17,19] and both IHCA and OHCA were assessed in 1 study (providing separate estimates for each).[20]

We found no significant difference in ventilation rate between survivors and nonsurvivors overall (mean difference,

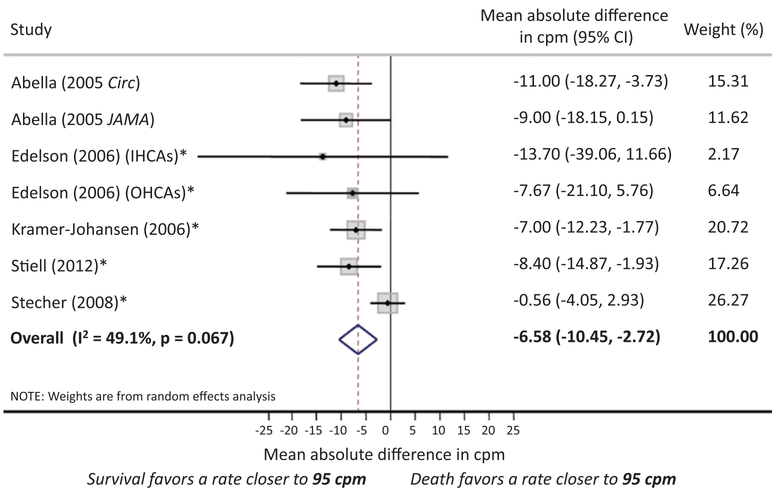

Figure 3. Random-effects meta-analysis of the mean absolute difference in chest compression rate (cpm) from a set point of 95 cpm, survivors vs nonsurvivors. Includes 5 cohort studies, 1 post hoc analysis of a clinical trial, 176 in-hospital cardiac arrests (IHCA), and 1465 out-of-hospital cardiac arrests (OHCA). Negative values indicate that survival favors proximity to the specified rate set point. Tests for heterogeneity were not significant. The size of the data marker corresponds to the weight of that study. Error bars represent 95% confidence intervals (CIs). A significant relationship with survival was also observed at set points of 85, 90, and 100 cpm (data not shown). *Estimates that were derived from new data requested from authors.

0.18 breaths per minute; 95% CI, −1.60 to 1.96; P=0.84; Figure II in the online-only Data Supplement). Moderate, significant heterogeneity was present among included studies (I^2=57.9%; P=0.05). This heterogeneity was not accounted for by any of our prespecified sources; however, sensitivity analyses were limited by the small number of studies.

The funnel plot suggested possible publication bias in the reporting of studies assessing ventilation rate and outcome; however, the Begg test did not achieve statistical significance in this case (P=0.50), and excluding the smallest study with the most unbalanced results on the funnel plot[20] had little effect on the results (mean difference, 0.34 breaths per minute; 95% CI, −1.71 to 2.38).

Discussion

Deeper chest compressions and compression rates closer to the range of 85 to 100 cpm were significantly associated with survival from cardiac arrest in this meta-analysis, consistent with current consensus guideline recommendations and the notion that survival from cardiac arrest is sensitive to CPR quality. This is the first systematic review and meta-analysis to evaluate such relationships including individual cardiac arrest events from an international and varied set of investigations. Our extensive search of multiple databases and direct contact with authors led to the identification of 10 relevant studies: 8 studies that evaluated prospective cohorts and 2 studies that represented post hoc analyses of clinical trials. Quality was high for 6 of the 10 included studies using an adapted metric based on study design, assessment methods for CPR quality and outcome, and evidence of bias. No randomized, controlled trials evaluating the effect of prespecified CPR quality on clinical outcomes were identified; this is perhaps not surprising given the ethical implications of such an approach and the limitations of nonblinding to intervention or outcome. In the present analysis, the best available evidence was derived from observational studies including both IHCA and OHCA.

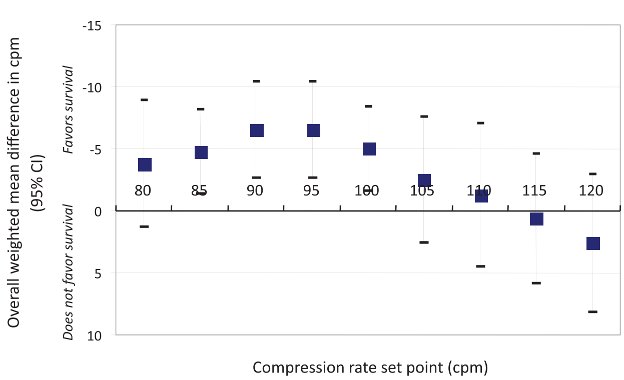

Figure 4. Overall mean absolute differences in chest compression rate (cpm), survivors versus nonsurvivors, plotted for rate set points between 80 cpm and 120 cpm. Each data marker represents the overall weighted result from a meta-analysis at that specific set point. Negative values indicate that survival favors proximity to the specified rate set point. Error bars represent 95% confidence intervals. Survival favored chest compression rates between 85 and 100 cpm. Survival did not significantly favor rates ≤80 cpm or ≥105 cpm.

Our results on the importance of chest compression depth are consistent with findings from previous laboratory studies such as a seminal investigation in dogs showing that cardiac output and blood flow were sensitive to compression depth.[27] Studies in porcine models have likewise found that deeper chest compressions predicted successful resuscitation more than prioritizing initial defibrillation[28] and that chest compressions delivered at a rate of 100±5 cpm and a depth of 50±1 mm were superior to those delivered at a rate of 80±5 cpm and a depth of 37±1 mm, resulting in higher rates of ROSC and neurologically intact survival.[29] Another porcine study found that depth of chest compressions was closely related to the likelihood of ROSC.[30]

In the present work, chest compression rates in the range of 85 to 100 cpm were significantly associated with survival from cardiac arrest; however, compression rates >105 cpm were not clearly associated with improved survival. These results are consistent with observations from animal studies that have suggested that blood flow in dogs receiving CPR was not increased[31] or even fell[32] at compression rates >120 cpm. It has been suggested that a reduction in diastolic perfusion time concomitant with very high chest compression rates may contribute to suboptimal coronary flow,[33] perhaps accounting for the findings in the present study.

Although chest compressions rates approaching 85 to 100 cpm were significantly associated with survival regardless of cardiac arrest location, we found that IHCA survival was more sensitive to chest compression rate than was OHCA survival. This may be explained by the inherent differences between the 2 conditions. In general, OHCA is more likely to present in shockable rhythms; 40% of all patients in 1 meta-analysis of 142 740 OHCA presented in ventricular fibrillation/ventricular tachycardia.[34] Time to defibrillation may therefore represent a relatively more important predictor of survival than compression rate in OHCA compared with IHCA. IHCA tends to present more frequently in pulseless electric activity or asystole and less often in ventricular fibrillation/ventricular tachycardia; just 23% of patients in 1 large cohort of 36 902 adult IHCA presented with shockable rhythms.[35] It is plausible that chest compression quality is more important during IHCA resuscitation in which defibrillation is less commonly required to achieve ROSC.

No-flow fraction was not associated with survival in this analysis. Data from laboratory studies have suggested that interruptions in CPR are detrimental to survival.[36,37] However, interruptions in chest compressions are common in the clinical setting[38,39] and occur for many reasons, including pauses for defibrillation. It is possible that the relative importance of no-flow fraction varies, depending on arrest characteristics not considered in this meta-analysis; for example, studies in the same population have revealed differing associations between chest compression fraction and survival, depending on initial rhythm.[12,13] Furthermore, the significant heterogeneity we detected between studies may be attributable in part to methodological differences in the measurement and assessment of no-flow fraction. Some authors of included articles measured no-flow fraction across the entire resuscitation,[26] whereas others only measured it during a 30-second fraction of time.[20] Some studies calculated chest compression fraction, the inverse of no-flow fraction[13]; others reported no-flow time, which we then converted to a percentage based on the length of the time period assessed.[20] This variability underscores the need for standardization of the definition and measurement of no-flow fraction in future studies.

We also found no significant difference in ventilation rate between survivors and nonsurvivors. Recent findings have suggested that assisted ventilation during OHCA is not necessarily beneficial to patients; in some cases, it may even contribute to worsened outcomes by interrupting chest compressions that drive perfusion to vital organs.[36,40,41] Excessive ventilation rate, volume, and duration may also lead to poor outcomes in IHCA or OHCA by elevating intrathoracic pressure, which has been shown to decrease cerebral perfusion pressure and blood flow in animals.[42,43] The exact role and timing of ventilation in the treatment of cardiac arrest victims are complex and uncertain. Ultimately, the relationships between no-flow fraction and ventilation rate and survival may be clinically relevant but more complex than a meta-analysis comparing means in overall populations of survivors and nonsurvivors can define.

Limitations

Potential limitations of this study should be considered. As with all meta-analyses, our assessments were restricted to available published and unpublished data. Studies from the Resuscitation Outcomes Consortium[12–14] were the only included studies to follow up patients to discharge, and they accounted for a large proportion of patients in the analysis. However, in the case of rate and depth, heterogeneity tests confirmed that smaller studies reported findings consistent with the Resuscitation Outcomes Consortium. Likewise, sensitivity analyses did not reveal differences by outcome type.

All of the included studies were observational; thus, confounding from patient-level differences (eg, body mass index, initial rhythm, and time to defibrillation) cannot be excluded, and our findings should be interpreted within that context. Multiple sensitivity analyses were performed to evaluate the extent to which our findings varied on the basis of cardiac arrest location, underlying study design, and other identified sources of heterogeneity. Generally, findings were consistent in each of these sensitivity analyses and consistent with the overall pooled results.

Publication bias was assessed for each relationship and was generally not found to be significant. The composite survival to discharge rate among included studies was low at 5.9%, which may reflect the fact that several of the studies were conducted before the release of the 2005 American Heart Association guidelines for CPR. It is possible that this may partly explain our lack of findings for no-flow fraction and ventilation rate. Some studies have observed an inverse association between chest compression rate and depth, which was not accounted for in our analysis.[12] However, this interaction has been poorly studied, and the clinical significance of a 2.44-mm difference is unclear.

Finally, although our findings are reported as means in this study, we were ultimately comparing distributions among survivors and nonsurvivors; therefore, the significant differences we found for rate and depth were dependent on the quality and distribution of CPR performed among the included studies. In the case of depth in particular, it is unclear how clinically significant a 2.44-mm difference may be. We speculate that a threshold effect exists at a certain depth, and what matters clinically is the extent of variability and distribution above and below that given threshold.

Although limitations of the individual studies should be considered, our work represents the most complete evidence to date on the relationship between CPR quality and survival from cardiac arrest.

Conclusions

The present analysis, based on a comprehensive search of both published and unpublished data, suggests that CPR is an effective treatment modality for cardiac arrest and that the quality of CPR delivery is associated with survival. Specifically, we found that deeper chest compressions were associated with higher survival rates and that proximity to an ideal chest compression rate of 85 to 100 cpm was associated with improved survival in an independent fashion. Our results stand in stark contrast to statements made in the literature that CPR makes people feel good but does little else.[3]

How CPR quality is measured remains an important consideration; future efforts should be made to standardize how CPR quality variables are ascertained and reported to improve comparability between studies. Hospital and EMS programs focused on quality assurance and patient safety should measure CPR quality in a systematic and objective manner, particularly the rate and depth of chest compressions. Our findings are particularly relevant for future updates to guidelines on cardiac arrest resuscitation; specifically, our work suggests that chest compression rates at or near 100 cpm should be encouraged and that an upper limit on the appropriate depth of chest compressions may not be defined by current data.

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Disclosures

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Original Article

Quantifying the Effect of Cardiopulmonary Resuscitation Quality on Cardiac Arrest Outcome

A Systematic Review and Meta-Analysis

Sarah K. Wallace, AB; Benjamin S. Abella, MD, MPhil; Lance B. Becker, MD AQ2

Background—Evidence has accrued that cardiopulmonary resuscitation quality affects cardiac arrest outcome. However, the relative contributions of chest compression components (such as rate and depth) to successful resuscitation remain unclear.

Methods and Results—We sought to measure the effect of cardiopulmonary resuscitation quality on cardiac arrest outcome through systematic review and meta-analysis. We searched for any clinical study assessing cardiopulmonary resuscitation performance on adult cardiac arrest patients in which survival was a reported outcome, either return of spontaneous circulation or survival to admission or discharge. Of 603 identified abstracts, 10 studies met inclusion criteria. Effect sizes were reported as mean differences. Missing data were resolved by author contact. Estimates were segregated by cardiopulmonary resuscitation metric (chest compression rate, depth, no-flow fraction, and ventilation rate), and a random-effects model was applied to estimate an overall pooled effect. Arrest survivors were significantly more likely to have received deeper chest compressions than nonsurvivors (mean difference, 2.44 mm; 95% confidence interval, 1.19–3.69 [P<0.001]; n=6 studies; I^2=0.0%; P for heterogeneity=0.9). Likewise, survivors were significantly more likely to have received chest compression rates closer to 85 to 100 compressions per minute (cpm) than nonsurvivors (absolute mean difference from 85 cpm, −4.81 cpm; 95% confidence interval, −8.19 to −1.43 [P=0.005]; from 100 cpm, −5.04 cpm; 95% confidence interval, −8.44 to −1.65 [P=0.004]; n=6 studies; I^2<49%; P for heterogeneity >0.2). No significant difference in no-flow fraction (n=7 studies) or ventilation rate (n=4 studies) was detected between survivors and nonsurvivors.

Conclusions—Deeper chest compressions and rates closer to 85 to 100 cpm are significantly associated with improved survival from cardiac arrest. **(*Circ Cardiovasc Qual Outcomes*. 2013;6:00-00.)**

Key Words: cardiac arrest ■ cardiopulmonary resuscitation ■ heart arrest ■ meta-analysis ■ resuscitation AQ4

Prompt delivery of cardiopulmonary resuscitation (CPR) with an emphasis on high-quality chest compressions has long been considered an essential link in the chain of survival for cardiac arrest resuscitation.[1] As a result, the American Heart Association and the European Resuscitation Council have published guidelines that stipulate a consensus rate and depth of chest compressions to be delivered during CPR.[1,2] However, the quantitative impact of high-quality CPR on survival has never been prospectively assessed in a randomized trial, leading to lingering questions about the magnitude of its therapeutic benefit. Some have even suggested that CPR may have only the appearance of value.[3] Meanwhile, nonrandomized studies assessing the effect of CPR quality on clinical outcome have yielded conflicting results. AQ5

The extent to which CPR quality affects survival from cardiac arrest remains poorly understood. A growing body of investigations has quantified CPR performance metrics and clinical outcomes from cardiac arrest, yet no study to date has rigorously analyzed the available evidence on CPR quality to determine a best estimate of its effect on survival. We sought to measure the relationship between key CPR quality parameters (chest compression rate, depth, no-flow fraction, and ventilation rate) and clinical outcomes using a formal approach of systematic review and meta-analysis.

Methods

Search Strategy

We compiled and assessed the available clinical literature on CPR quality following the consensus meta-analysis methodology of Stroup et al[4] in conjunction with Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines.[5] We searched for all cohort studies, case–control studies, and randomized trials assessing CPR performance by bystanders or health professionals on adult patients experiencing out-of-hospital cardiac arrest (OHCA) or in-hospital cardiac arrest (IHCA) in which survival was an explicit outcome. Acceptable survival measures included return of spontaneous circulation (ROSC) for IHCA or OHCA, survival to hospital admission for OHCA, and survival to hospital discharge for IHCA or OHCA. When >1 survival outcome was available for a single study, data on survival to hospital admission or discharge were included in the meta-analysis preferentially because they provide a better estimate of long-term clinical outcomes. Additionally, studies AQ6 AQ7

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The online-only Data Supplement is available at http://circoutcomes.ahajournals.org/lookup/suppl/doi:10.1161/CIRCOUTCOMES.111.000041/-/DC1.
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WHAT IS KNOWN

- Prompt delivery of cardiopulmonary resuscitation with an emphasis on high-quality chest compressions improves survival from cardiac arrest.
- The relative contributions of cardiopulmonary resuscitation components (such as chest compression rate, depth, no-flow fraction, and ventilation rate) to successful resuscitation remain unclear.

WHAT THE STUDY ADDS

- We measured the relationship between key cardiopulmonary resuscitation quality parameters and clinical outcomes using a formal approach of systematic review and meta-analysis.
- Deeper chest compressions and chest compression rates closer to the range of 85 to 100 compressions per minute were significantly associated with improved survival from cardiac arrest.
- There were no significant differences in ventilation rate and no-flow fraction between survivors and nonsurvivors.

were eligible for inclusion only if at least 1 metric of CPR quality (eg, chest compression depth, rate, no-flow fraction, or ventilation rate) and its independent effect on survival were evaluated. These criteria were established to allow testing of individual components of CPR quality and their association with clinical outcome.

A comprehensive search of the published and unpublished literature was performed with the use of PubMed Plus, MEDLINE (Ovid), the Cochrane Library, www.ClinicalTrials.gov, Grey literature sources (OpenGrey, CAB Abstracts), related articles, hand searching of reference lists, and direct author contact. Key words used in these searches were cardiopulmonary resuscitation, quality, heart arrest, and cardiac arrest. The time period searched ranged from the earliest available online indexing year for each database through June 2012. We limited our search to those studies published in the English language and conducted on humans.

We a priori excluded studies comparing manual with mechanical CPR and those comparing different approaches to CPR (eg, minimally interrupted cardiac resuscitation versus traditional CPR) because direct comparisons of CPR quality between these investigations would be significantly confounded. Studies were also excluded if they were cross-sectional or ecological, commentaries, general reviews, or case reports. If multiple investigations were published from the same cohort, we included the study with the greatest number of patients preferentially.

Selection of Articles

Of 603 identified articles, 545 were excluded after review of the title
F1 and abstract (Figure 1). Full texts of the 58 remaining articles were assessed for potential inclusion by 2 investigators independently (S.K.W. and B.S.A.). Group consultation among authors was used to resolve uncertainties. Forty-two studies were excluded for representing reviews (n=2), not assessing CPR quality metrics individually (n=22), comparing mechanical with manual CPR (n=2), reporting simulation data on manikins (n=1), including diseases other than cardiac arrest in the study population (n=2), not meeting outcome criteria (n=5), and representing overlapping publications from the same patient cohorts (n=8).

Six additional studies assessed a categorical overall quality metric (eg, good CPR versus bad CPR) concomitant with associated survival to hospital discharge.[6–11] Five of the 6 studies were conducted before 1995.[7–11] All but 1 study[6] relied on subjective assessments of CPR quality by an observer who was not blinded to the outcome of the resuscitation, making recall bias a significant concern. Meta-analysis of these studies revealed that categorically defined higher-quality CPR was significantly associated with survival to discharge (odds ratio, 10.4; 95% confidence interval [CI], 6.45–14.2). However, high heterogeneity was present among included studies (I^2=98.9%; P<0.001), suggesting that they are not comparable. Therefore, these 6 articles were excluded from our primary analysis because of concerns about bias and quality.

Data Extraction

We identified 10 studies evaluating the effect of CPR quality metrics on survival after cardiac arrest. Three studies represented data from the Resuscitation Outcomes Consortium Epistry. However, they did not include overlapping patients at the level of our planned meta-analyses because 1 study evaluated rate and depth,[12] 1 study evaluated chest compression fraction in ventricular fibrillation/ventricular tachycardia OHCA only,[13] and 1 study evaluated chest compression fraction in non–ventricular fibrillation/ventricular tachycardia OHCA only.[14] Data were extracted in an open-ended fashion by 1 investigator (S.K.W.) and were reviewed twice to minimize data-entry errors. Variables included study design, location, dates over which the study was performed, sample size, whether the CPR quality assessment was a prespecified aim, definition of CPR process variables and their assessment methods, definition of outcome variables and their assessment methods, effect estimates, and possible sources of bias.

Standardized quality scores for observational studies have not been established. Thus, quality assessment of the included studies was performed by evaluating and scoring 6 criteria on an integer scale (0 or 1, with 1 being better), including (1) study design, (2) multicenter or single-center designation, (3) assessment of CPR quality measures, (4) assessment of outcome, (5) evidence of bias, and (6) whether CPR quality assessment was a prespecified aim. Studies with a sum from 0 to 4 were considered low quality, whereas those with a sum of 5 or 6 were considered high quality. This system was adapted from quality scores used in other published meta-analyses of observational studies.[15,16]

For 7 of the 10 included studies, authors were directly contacted to request missing or additional data. Six study authors[12–14,17–19] were asked to provide summary statistics for continuous CPR quality variables stratified by survival outcome so that a mean difference could be computed. A seventh study[20] included both IHCA and OHCA events; the author was asked to provide separate estimates for each group to allow stratification by cardiac arrest location. This information was obtained from all authors as requested.

Statistical Analysis

All included studies were either prospective cohort studies or post hoc analyses of primary clinical trial cohorts. Effect sizes were reported as mean differences. Standard errors were calculated using group SD or 95% CI measures. Survival outcomes were categorized as ROSC, survival to admission, or survival to hospital discharge.

Estimates were segregated into groups by the specific CPR performance metric assessed (eg, depth, rate). The DerSimonian–Laird random-effects model was then applied to studies within each group to estimate an overall pooled effect. This model was chosen because it assumes random variability among studies beyond subject-level sampling error.[21] We constructed forest plots to visually display the data. We used the Begg adjusted-rank correlation test and constructed funnel plots to assess publication bias.[22]

Evidence for statistical heterogeneity between studies was tested by goodness of fit (χ^2). Heterogeneity was also quantified with the I^2 measure.[23] This measure, ranging from 0% to 100%, represents the degree of inconsistency across studies included in the meta-analysis. Low, moderate, and high heterogeneity correspond to I^2 values of 25%, 50%, and 75%, respectively. Prespecified potential sources of heterogeneity explored in sensitivity analyses were as follows: cardiac arrest location (OHCA versus IHCA), study design (prospective cohort or post hoc clinical trial analysis), study region (North

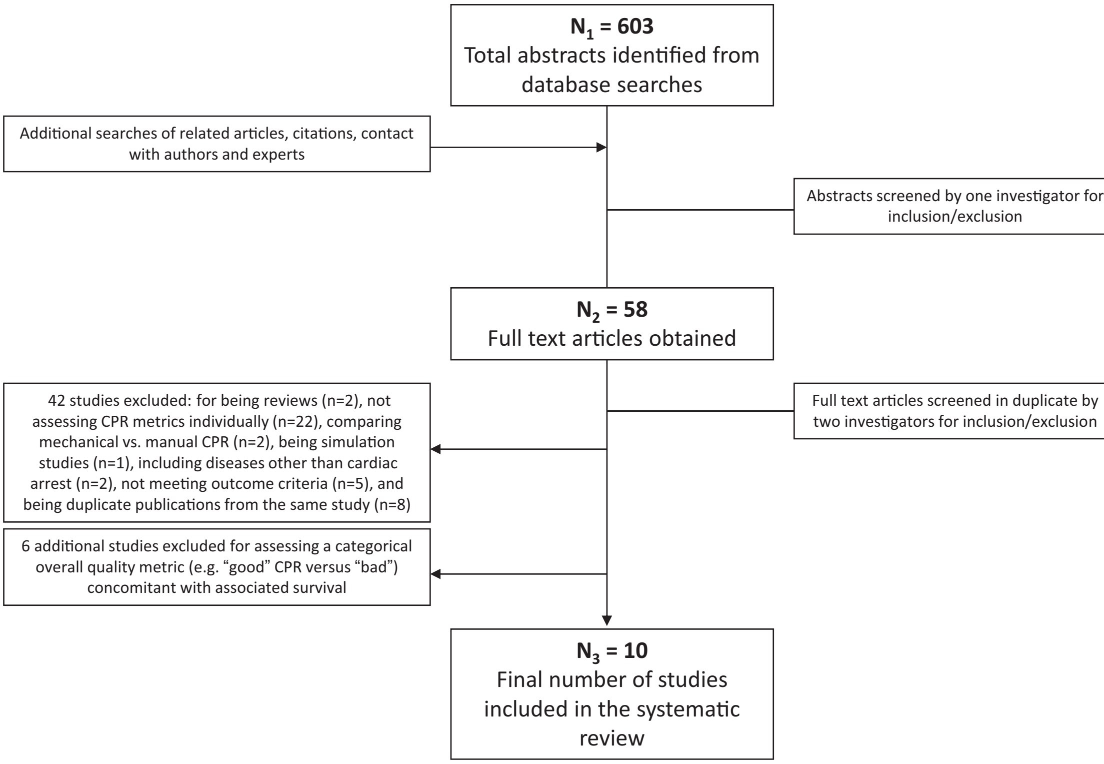

Figure 1. Screening and selection process for studies of cardiopulmonary resuscitation (CPR) quality and survival outcomes.

America or Europe), type of person performing the measured CPR (bystanders versus health professionals), outcome (ROSC versus survival to hospital admission or discharge), investigation quality score (high versus low), and whether the analysis was a prespecified aim or conducted post hoc (to address publication bias of positive findings). Analyses were performed with a statistical software package (STATA 11; StataCorp, College Station, TX) with α set at 0.05.

Results

Four variables of CPR quality were assessed among the 10 included studies: compression rate; compression depth; no-flow fraction (defined as the percent of resuscitation time during which compressions were not performed) or its inverse, compression fraction; and ventilation rate.

The 10 studies included 8 prospective cohort studies[12–14,18–20,24,25] and 2 post hoc analyses of clinical trials
T1 (the Table).[17,26] Seven studies were conducted in North America[12–14,18,20,24,25] and 3 in Europe.[17,19,26] Data on chest compression rate were available for 1641 patients (176 IHCA and 1465 OHCA); data on depth were available for 1892 patients (77 IHCA and 1815 OHCA); data on no-flow fraction were available for 3424 patients (79 IHCA and 3345 OHCA); and data on ventilation rate were available for 483 patients (71 IHCA and 412 OHCA). No randomized, controlled trials of manual CPR quality and survival were identified. For all included studies, survival outcomes were ascertained by the original study authors through prehospital and hospital records. Among included studies, mean age was 67.3 years; 65% of the cohort were male. The overall ROSC rate was 34.3%; survival to discharge rate was 5.9%.

Averaged across investigations, mean chest compression rate was 107 compressions per minute (cpm); mean chest compression depth was 39.9 mm; mean no-flow fraction was 39.3%; and mean ventilation rate was 13.6 breaths per minute. Most studies quantifying rate, depth, no-flow fraction, and ventilation rate[12–14,17–20,25,26] did so using an investigational monitor/defibrillator with accelerometer, force detector, and chest wall impedance detector; however, 1 investigation[24] used customized personal digital assistant software controlled by a research assistant to collect compression rate data. The total number of patients varied substantially between studies (n=49–2103). For all but 3 studies,[17,25,26] assessing the relationship of CPR quality and survival was a prespecified primary or secondary aim. CPR was performed by trained prehospital personnel such as emergency medical technicians and paramedics in 8 publications[12–14,18–20,26] and by trained in-hospital personnel such as nurses, physicians, and medical students in 3 publications.[20,24,25] Study quality was high in 6 investigations,[12–14,18,20,24] as defined by our scoring system described in Methods.

Chest Compression Depth

Six studies provided separate estimates for the relationship between chest compression depth and outcome.[12,17,18,20,25,26] In 4 investigations,[18,20,25,26] this outcome was ROSC; in 1 study,[12] it was survival to hospital discharge; and in 1 study,[17] it was survival to hospital admission. IHCA was assessed in 1 study,[25] OHCA was assessed in 4 studies,[12,17,18,26] and both IHCA and OHCA were assessed in 1 study (providing separate estimates for each).[20]

Cardiac arrest survivors were significantly more likely to receive deeper chest compressions than nonsurvivors, as shown in Figure 2 (mean difference, 2.44 mm; 95% CI, 1.19–3.69; F2

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Table. Identified Studies Evaluating CPR Quality and Survival After Cardiac Arrest AQ10

First Author	Study Design	Region(s)	CPR Quality Measure(s)	Ascertainment of Quality Measure(s)	Who Performed the CPR?	Outcome	Population	Sample Size, n	Prespecified Analysis	Quality Score
Abella et al[24]	Prospective cohort	US	Rate	Counting by an observer	Nurses, physicians, medical students	ROSC	IHCA	97	Yes (primary)	5 (High)
Abella et al[25]	Prospective cohort	US	Rate, depth, no-flow fraction, ventilation rate	Investigational monitor/ defibrillator	Nurses, physicians, medical students	ROSC	IHCA	60	No	4 (Low)
Babbs et al[18]	Prospective cohort	North America	Depth	Investigational monitor/ defibrillator	EMS providers	ROSC	OHCA	172	Yes (secondary)	5 (High)
Bohn et al[26]	Post hoc analysis of a clinical trial	Germany	Depth, no-flow fraction	Investigational monitor/ defibrillator	EMTs, physicians	ROSC	OHCA	300	No	3 (Low)
Edelson et al[20]	Prospective cohort	USA, Norway	Rate, depth, no-flow fraction, ventilation rate	Investigational monitor/ defibrillator	Nurses, physicians, medical students, paramedics	ROSC	IHCA and OHCA	49	Yes (primary)	6 (High)
Kramer-Johansen et al[17]	Post hoc analysis of a clinical trial	UK, Sweden, Norway	Rate, depth, no-flow fraction, ventilation rate	Investigational monitor/ defibrillator	Paramedics, nurses	Survival to admission	OHCA	284	No	4 (Low)
Stiell et al[12]	Prospective cohort	US, Canada (ROC)	Rate, depth	Investigational monitor/ defibrillator	EMS providers	Survival to discharge	OHCA	1029	Yes (primary)	6 (High)
Stecher et al[19]	Prospective cohort	Norway	Rate, no-flow fraction, ventilation rate	Investigational monitor/ defibrillator	EMS providers	ROSC	OHCA	122	Yes (secondary)	4 (Low)
Christenson et al[13]	Prospective cohort	US, Canada (ROC)	No-flow fraction	Investigational monitor/ defibrillator	EMS providers	Survival to discharge	OHCA (VF/ VT)	506	Yes (primary)	6 (High)
Vaillancourt et al[14]	Prospective cohort	US, Canada (ROC)	No-flow fraction	Investigational monitor/ defibrillator	EMS providers	Survival to discharge	OHCA (non-VF/ VT)	2103	Yes (primary)	6 (High)

CPR indicates cardiopulmonary resuscitation; EMS, emergency medical services; EMT, emergency medical technician; IHCA, in-hospital cardiac arrest; OHCA, out-of-hospital cardiac arrest; ROC, Resuscitation Outcomes Consortium; ROSC, return of spontaneous circulation; and VF/VT, ventricular fibrillation/ventricular tachycardia.

P<0.001). No heterogeneity was detected among included studies (I^2=0.0%; *P*=0.90). Findings were similar in analyses restricted to the 5 studies examining OHCA/where emergency AQ8 medical service providers performed the CPR[12,17,18,20,26] (mean difference, 2.44 mm; 95% CI, 1.16–3.72); the 3 studies with highest quality scores/where the assessment was prespecified[12,18,20] (mean difference, 2.62 mm; 95% CI, 0.18–5.06); the 4 studies that were conducted in North America/had a prospective cohort design[12,18,20,26] (mean difference, 2.41 mm; 95% CI, 0.13–4.69); and the 2 studies where the outcome was survival to hospital admission or discharge[12,17] (mean difference, 3.06 mm; 95% CI, 1.22–4.90).

We assessed these results for possible publication bias by visually inspecting the funnel plot and calculating its statistical analog, the Begg test.[22] These methods suggested no significant publication bias (Begg test, *P*=0.88).

Chest Compression Rate

Six studies provided separate estimates for the relationship between chest compression rate and outcome.[12,17,19,20,24,25] In 4 investigations,[19,20,24,25] the outcome was ROSC; in 1 study,[12] it was survival to hospital discharge; and in 1 study,[17] it was survival to hospital admission. IHCA was assessed in 2 studies,[24,25] OHCA was assessed in 3 studies,[12,17,19] and both IHCA and OHCA were assessed in 1 study (providing separate estimates for each).[20] One publication[17] represented a post hoc analysis of a primary clinical trial cohort; the rest of the included studies had a prospective cohort design. Notably, the rate estimate by Bohn et al[26] was considered to be methodologically heterogeneous to the others because of the use of an acoustic metronome prompting a compression rate of 100 cpm in resuscitation events; it was therefore excluded a priori from the present meta-analysis.

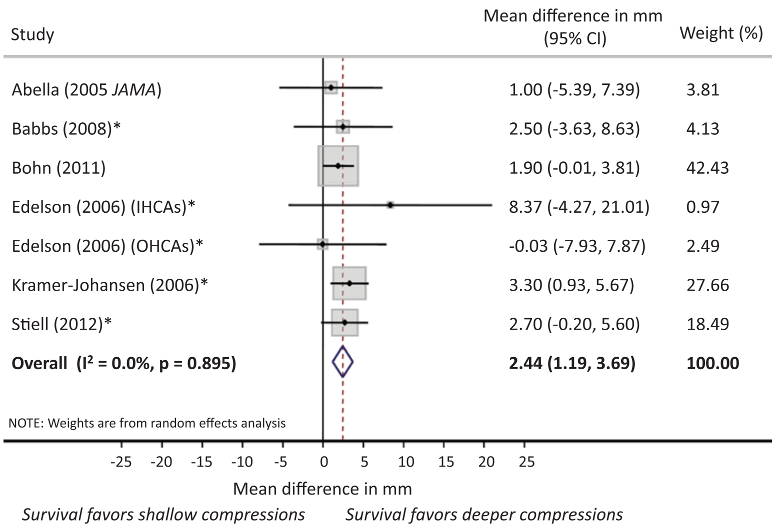

Figure 2. Random-effects meta-analysis of mean differences in chest compression depth (mm), survivors vs nonsurvivors. Includes 4 cohort studies and 2 post hoc analyses of clinical trials, representing 77 in-hospital cardiac arrest (IHCA) and 1815 out-of-hospital cardiac arrest (OHCA) events. Positive values indicate that survival favors deeper chest compressions. Tests for heterogeneity were not significant. The size of the data marker corresponds to the weight of that study. Error bars represent 95% confidence intervals (CIs). *Estimates that were derived from new data requested from authors.

There was no overall difference in mean chest compression rate between survivors and nonsurvivors (data not shown). We conducted a second analysis to determine whether proximity to a particular rate maximized survival (ie, that very high-compression rates were as detrimental as low rates). This was achieved by calculating the absolute difference between rates recorded among the 2 survival groups and a series of compression rate set points. For each such set point, the mean compression rate difference between survivors and nonsurvivors was assessed. For example, in a scenario in which survivors received a mean chest compression rate of 110 cpm and nonsurvivors received 90 cpm, both groups would yield an absolute difference of 10 cpm at a set point of 100 cpm (|100–90|=10, |100–110|=10); thus, the overall mean difference between these 2 groups would be 0 cpm (10 minus 10 cpm). However, at a set point of 105 cpm, the overall mean difference between the 2 would be −10 cpm (|105–110|=5 for survivors minus |90–105|=15 for nonsurvivors). Set points were established in increments of 5 cpm within the range of 80 to 120 cpm. Meta-analyses were performed at each set point.

Survivors were significantly more likely to receive chest compression rates closer to the range of 85 to 100 cpm, as
F3 shown in Figure 3 (absolute mean difference from 85 cpm, −4.81 cpm; 95% CI, −8.19 to −1.43 [P=0.005]; from 90 cpm, −6.58 cpm; 95% CI, −10.4 to −2.72 [P=0.001]; from 95 cpm, −6.58 cpm; 95% CI, −10.4 to −2.72 [P=0.001]; from 100 cpm, −5.04 cpm; 95% CI, −8.44 to −1.65 [P=0.004]). Low to moderate, nonstatistically significant heterogeneity was detected among these associations (I^2<49.1%; P>0.07 for all analyses). At rates <85 cpm and >100 cpm, no significant association was found between survival and proximity
F4 to these rate set points (Figure 4).

Findings remained significant after stratification by cardiac arrest location, although the magnitude of the relationship was 2-fold greater for IHCA (at a set point of 95 cpm: overall mean difference for IHCA,[20,24,25] −10.4 cpm; 95% CI, −15.9 to −4.84; for OHCA,[12,17,19,20] −5.02 cpm; 95% CI, −9.61 to −0.43). Findings likewise remained significant when stratified by outcome (at a set point of 95 cpm: overall mean difference for studies reporting ROSC,[19,20,24,25] −6.54 cpm; 95% CI, −12.5 to −0.58; overall mean difference for studies reporting survival to admission or discharge,[12,17] −7.55 cpm; 95% CI, −11.6 to −3.49). Sensitivity analyses by type of CPR performer, study region, study design, quality score, and whether the analysis was a prespecified aim had no effect on the results (data not shown).

Visual inspection of the funnel plot and calculation of the Begg test suggested no significant publication bias among the results. Results from all set points (between 80 and 120 cpm) yielded a Begg test value of P>0.35.

No-Flow Fraction

Seven studies provided separate estimates for the relationship between no-flow fraction and outcome.[13,14,17,19,20,25,26] In 4 investigations,[19,20,25,26] this outcome was ROSC; in 2 studies,[13,14] it was survival to hospital discharge; and in 1 study,[17] it was survival to hospital admission. IHCA was assessed in 1 study,[25] OHCA was assessed in 5 studies,[13,14,17,19,26] and both IHCA and OHCA were assessed in 1 study (providing separate estimates for each).[20]

We found no significant difference in no-flow fraction between survivors and nonsurvivors overall (mean difference, 1.34%; 95% CI, −1.50 to 4.18; P=0.36; Figure I in the online-only Data Supplement). A low to moderate degree of nonsignificant heterogeneity was present among included studies (I^2=43.1%; P=0.09). Findings did not change when stratified by cardiac arrest location (IHCA versus OHCA), outcome measure, type of CPR performer, study region, study design, quality score, or whether the analysis was a prespecified aim (results not shown). Visual inspection of the funnel plot and calculation of the Begg test suggested no significant publication bias (Begg test, P=0.90).

Ventilation Rate

Four studies provided separate estimates for the relationship between ventilation rate and outcome.[17,19,20,25] In 3 studies,[19,20,25] this outcome was ROSC; in 1 study,[17] it was survival to hospital admission. IHCA was assessed in 1 study,[25] OHCA was assessed in 2 studies,[17,19] and both IHCA and OHCA were assessed in 1 study (providing separate estimates for each).[20]

We found no significant difference in ventilation rate between survivors and nonsurvivors overall (mean difference,

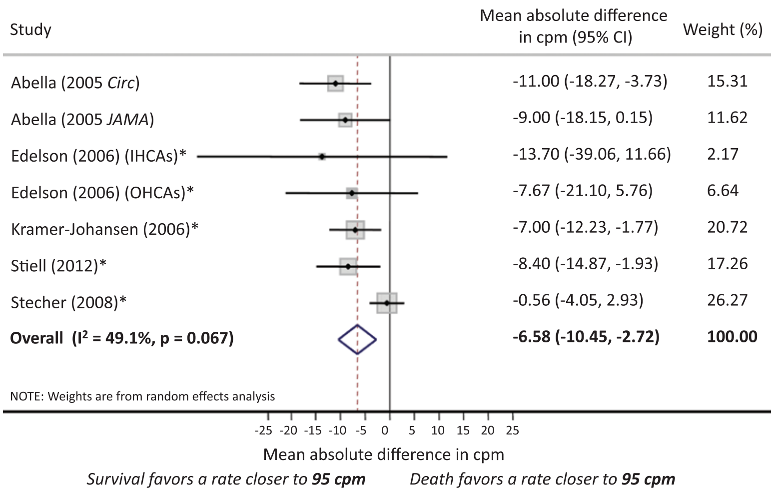

Figure 3. Random-effects meta-analysis of the mean absolute difference in chest compression rate (cpm) from a set point of 95 cpm, survivors vs nonsurvivors. Includes 5 cohort studies, 1 post hoc analysis of a clinical trial, 176 in-hospital cardiac arrests (IHCA), and 1465 out-of-hospital cardiac arrests (OHCA). Negative values indicate that survival favors proximity to the specified rate set point. Tests for heterogeneity were not significant. The size of the data marker corresponds to the weight of that study. Error bars represent 95% confidence intervals (CIs). A significant relationship with survival was also observed at set points of 85, 90, and 100 cpm (data not shown). *Estimates that were derived from new data requested from authors.

0.18 breaths per minute; 95% CI, −1.60 to 1.96; P=0.84; Figure II in the online-only Data Supplement). Moderate, significant heterogeneity was present among included studies (I^2=57.9%; P=0.05). This heterogeneity was not accounted for by any of our prespecified sources; however, sensitivity analyses were limited by the small number of studies.

The funnel plot suggested possible publication bias in the reporting of studies assessing ventilation rate and outcome; however, the Begg test did not achieve statistical significance in this case (P=0.50), and excluding the smallest study with the most unbalanced results on the funnel plot[20] had little effect on the results (mean difference, 0.34 breaths per minute; 95% CI, −1.71 to 2.38).

Discussion

Deeper chest compressions and compression rates closer to the range of 85 to 100 cpm were significantly associated with survival from cardiac arrest in this meta-analysis, consistent with current consensus guideline recommendations and the notion that survival from cardiac arrest is sensitive to CPR quality. This is the first systematic review and meta-analysis to evaluate such relationships including individual cardiac arrest events from an international and varied set of investigations. Our extensive search of multiple databases and direct contact with authors led to the identification of 10 relevant studies: 8 studies that evaluated prospective cohorts and 2 studies that represented post hoc analyses of clinical trials. Quality was high for 6 of the 10 included studies using an adapted metric based on study design, assessment methods for CPR quality and outcome, and evidence of bias. No randomized, controlled trials evaluating the effect of prespecified CPR quality on clinical outcomes were identified; this is perhaps not surprising given the ethical implications of such an approach and the limitations of nonblinding to intervention or outcome. In the present analysis, the best available evidence was derived from observational studies including both IHCA and OHCA.

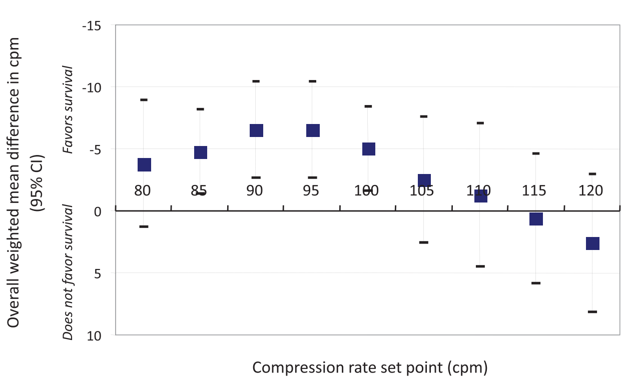

Figure 4. Overall mean absolute differences in chest compression rate (cpm), survivors versus nonsurvivors, plotted for rate set points between 80 cpm and 120 cpm. Each data marker represents the overall weighted result from a meta-analysis at that specific set point. Negative values indicate that survival favors proximity to the specified rate set point. Error bars represent 95% confidence intervals. Survival favored chest compression rates between 85 and 100 cpm. Survival did not significantly favor rates ≤80 cpm or ≥105 cpm.

Our results on the importance of chest compression depth are consistent with findings from previous laboratory studies such as a seminal investigation in dogs showing that cardiac output and blood flow were sensitive to compression depth.[27] Studies in porcine models have likewise found that deeper chest compressions predicted successful resuscitation more than prioritizing initial defibrillation[28] and that chest compressions delivered at a rate of 100±5 cpm and a depth of 50±1 mm were superior to those delivered at a rate of 80±5 cpm and a depth of 37±1 mm, resulting in higher rates of ROSC and neurologically intact survival.[29] Another porcine study found that depth of chest compressions was closely related to the likelihood of ROSC.[30]

In the present work, chest compression rates in the range of 85 to 100 cpm were significantly associated with survival from cardiac arrest; however, compression rates >105 cpm were not clearly associated with improved survival. These results are consistent with observations from animal studies that have suggested that blood flow in dogs receiving CPR was not increased[31] or even fell[32] at compression rates >120 cpm. It has been suggested that a reduction in diastolic perfusion time concomitant with very high chest compression rates may contribute to suboptimal coronary flow,[33] perhaps accounting for the findings in the present study.

Although chest compressions rates approaching 85 to 100 cpm were significantly associated with survival regardless of cardiac arrest location, we found that IHCA survival was more sensitive to chest compression rate than was OHCA survival. This may be explained by the inherent differences between the 2 conditions. In general, OHCA is more likely to present in shockable rhythms; 40% of all patients in 1 meta-analysis of 142 740 OHCA presented in ventricular fibrillation/ventricular tachycardia.[34] Time to defibrillation may therefore represent a relatively more important predictor of survival than compression rate in OHCA compared with IHCA. IHCA tends to present more frequently in pulseless electric activity or asystole and less often in ventricular fibrillation/ventricular tachycardia; just 23% of patients in 1 large cohort of 36 902 adult IHCA presented with shockable rhythms.[35] It is plausible that chest compression quality is more important during IHCA resuscitation in which defibrillation is less commonly required to achieve ROSC.

No-flow fraction was not associated with survival in this analysis. Data from laboratory studies have suggested that interruptions in CPR are detrimental to survival.[36,37] However, interruptions in chest compressions are common in the clinical setting[38,39] and occur for many reasons, including pauses for defibrillation. It is possible that the relative importance of no-flow fraction varies, depending on arrest characteristics not considered in this meta-analysis; for example, studies in the same population have revealed differing associations between chest compression fraction and survival, depending on initial rhythm.[12,13] Furthermore, the significant heterogeneity we detected between studies may be attributable in part to methodological differences in the measurement and assessment of no-flow fraction. Some authors of included articles measured no-flow fraction across the entire resuscitation,[26] whereas others only measured it during a 30-second fraction of time.[20] Some studies calculated chest compression fraction, the inverse of no-flow fraction[13]; others reported no-flow time, which we then converted to a percentage based on the length of the time period assessed.[20] This variability underscores the need for standardization of the definition and measurement of no-flow fraction in future studies.

We also found no significant difference in ventilation rate between survivors and nonsurvivors. Recent findings have suggested that assisted ventilation during OHCA is not necessarily beneficial to patients; in some cases, it may even contribute to worsened outcomes by interrupting chest compressions that drive perfusion to vital organs.[36,40,41] Excessive ventilation rate, volume, and duration may also lead to poor outcomes in IHCA or OHCA by elevating intrathoracic pressure, which has been shown to decrease cerebral perfusion pressure and blood flow in animals.[42,43] The exact role and timing of ventilation in the treatment of cardiac arrest victims are complex and uncertain. Ultimately, the relationships between no-flow fraction and ventilation rate and survival may be clinically relevant but more complex than a meta-analysis comparing means in overall populations of survivors and nonsurvivors can define.

Limitations

Potential limitations of this study should be considered. As with all meta-analyses, our assessments were restricted to available published and unpublished data. Studies from the Resuscitation Outcomes Consortium[12–14] were the only included studies to follow up patients to discharge, and they accounted for a large proportion of patients in the analysis. However, in the case of rate and depth, heterogeneity tests confirmed that smaller studies reported findings consistent with the Resuscitation Outcomes Consortium. Likewise, sensitivity analyses did not reveal differences by outcome type.

All of the included studies were observational; thus, confounding from patient-level differences (eg, body mass index, initial rhythm, and time to defibrillation) cannot be excluded, and our findings should be interpreted within that context. Multiple sensitivity analyses were performed to evaluate the extent to which our findings varied on the basis of cardiac arrest location, underlying study design, and other identified sources of heterogeneity. Generally, findings were consistent in each of these sensitivity analyses and consistent with the overall pooled results.

Publication bias was assessed for each relationship and was generally not found to be significant. The composite survival to discharge rate among included studies was low at 5.9%, which may reflect the fact that several of the studies were conducted before the release of the 2005 American Heart Association guidelines for CPR. It is possible that this may partly explain our lack of findings for no-flow fraction and ventilation rate. Some studies have observed an inverse association between chest compression rate and depth, which was not accounted for in our analysis.[12] However, this interaction has been poorly studied, and the clinical significance of a 2.44-mm difference is unclear.

Finally, although our findings are reported as means in this study, we were ultimately comparing distributions among survivors and nonsurvivors; therefore, the significant differences we found for rate and depth were dependent on the quality and distribution of CPR performed among the included studies. In the case of depth in particular, it is unclear how clinically significant a 2.44-mm difference may be. We speculate that a threshold effect exists at a certain depth, and what matters clinically is the extent of variability and distribution above and below that given threshold.

Although limitations of the individual studies should be considered, our work represents the most complete evidence to date on the relationship between CPR quality and survival from cardiac arrest.

Conclusions

The present analysis, based on a comprehensive search of both published and unpublished data, suggests that CPR is an effective treatment modality for cardiac arrest and that the quality of CPR delivery is associated with survival. Specifically, we found that deeper chest compressions were associated with higher survival rates and that proximity to an ideal chest compression rate of 85 to 100 cpm was associated with improved survival in an independent fashion. Our results stand in stark contrast to statements made in the literature that CPR makes people feel good but does little else.[3]

How CPR quality is measured remains an important consideration; future efforts should be made to standardize how CPR quality variables are ascertained and reported to improve comparability between studies. Hospital and EMS programs focused on quality assurance and patient safety should measure CPR quality in a systematic and objective manner, particularly the rate and depth of chest compressions. Our findings are particularly relevant for future updates to guidelines on cardiac arrest resuscitation; specifically, our work suggests that chest compression rates at or near 100 cpm should be encouraged and that an upper limit on the appropriate depth of chest compressions may not be defined by current data.

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Disclosures

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