



STRUCTURED EVIDENCE-BASED MEDICINE REVIEW

Bedside Focused Echocardiography as Predictor of Survival in Cardiac Arrest Patients: A Systematic Review

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Abstract

Objectives: The objective was to determine if focused transthoracic echocardiography (echo) can be used during resuscitation to predict the outcome of cardiac arrest.

Methods: A literature search of diagnostic accuracy studies was conducted using MEDLINE via PubMed, EMBASE, CINAHL, and Cochrane Library databases. A hand search of references was performed and experts in the field were contacted. Studies were included for further appraisal and analysis only if the selection criteria and reference standards were met. The eligible studies were appraised and scored by two independent reviewers using a modified quality assessment tool for diagnostic accuracy studies (QUADAS) to select the papers included in the meta-analysis.

Results: The initial search returned 2,538 unique papers, 11 of which were determined to be relevant after screening criteria were applied by two independent researchers. One additional study was identified after the initial search, totaling 12 studies to be included in our final analysis. The total number of patients in these studies was 568, all of whom had echo during resuscitation efforts to determine the presence or absence of kinetic cardiac activity and were followed up to determine return of spontaneous circulation (ROSC). Meta-analysis of the data showed that as a predictor of ROSC during cardiac arrest, echo had a pooled sensitivity of 91.6% (95% confidence interval [CI] = 84.6% to 96.1%), and specificity was 80.0% (95% CI = 76.1% to 83.6%). The positive likelihood ratio for ROSC was 4.26 (95% CI = 2.63 to 6.92), and negative likelihood ratio was 0.18 (95% CI = 0.10 to 0.31). Heterogeneity of the results (sensitivity) was nonsignificant (Cochran's Q: $\chi^2 = 10.63$, $p = 0.16$, and $I^2 = 34.1\%$).

Conclusions: Echocardiography performed during cardiac arrest that demonstrates an absence of cardiac activity harbors a significantly lower (but not zero) likelihood that a patient will experience ROSC. In selected patients with a higher likelihood of survival from cardiac arrest at presentation, based on established predictors of survival, echo should not be the sole basis for the decision to cease resuscitative efforts. Echo should continue to be used only as an adjunct to clinical assessment in predicting the outcome of resuscitation for cardiac arrest.

ACADEMIC EMERGENCY MEDICINE 2012; 19:000-000 © 2012 by the Society for Academic Emergency Medicine

According to the Heart and Stroke Foundation of Canada, approximately 45,000 cardiac arrests occur in Canada annually, which means there is one cardiac arrest every 12 minutes.¹ It has been estimated that 90% of Canadians have at least

one risk factor for heart disease or stroke.¹ Cardiac arrest is an extreme medical emergency and prognosis is generally poor with less than 5% survival rate for those who have cardiac arrest out of hospital. However, occasionally, cardiac arrest is caused by an

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Received February 28, 2012; revision received May 3, 2012; accepted June 21, 2012.

The authors have no relevant financial information or potential conflicts of interest to disclose.

Supervising Editor: Shahriar Zehtabchi, MD.

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underlying condition that is reversible if quickly identified and treated.¹ Early reliable identification of patients who are more likely to survive has been elusive and currently no strong recommendations for when to stop or continue resuscitative efforts exist. Although studies have not yet been done to examine the relationship between the use of echocardiography and survival rates, there is growing evidence describing the value of echocardiography as a predictive tool of outcome during cardiac arrest.²

The use of point of care ultrasound (US) in emergency settings has developed over the past 10 to 20 years. It has been studied and is used extensively in trauma, gynecologic, procedural, cardiac, and vascular clinical presentations.² US has also become a vital diagnostic tool in the emergency department (ED) for managing patients with hypotension.³ In the cardiac arrest patient, immediate bedside US to visualize the heart may help guide further interventions and management. Limited transthoracic echocardiography (echo) during a cardiac arrest or periarrest setting is a core skill recognized by many national professional organizations,^{2,4,5} and the use of echo in life support has become integrated in the everyday practice of many EDs.

The presence or absence of cardiac activity visualized by echo during cardiac arrest is one indicator that has been investigated to determine its value as a predictor of outcome.^{6,7} The absence of cardiac kinetic activity has been promoted as a way to confirm poor prognosis and to back up the decision to terminate cardiopulmonary resuscitative efforts. Alternatively, the presence of kinetic activity may encourage a more aggressive treatment approach.⁶⁻⁸ Although several studies have suggested that the absence of any cardiac activity predicts a poor prognosis despite ongoing resuscitative efforts, and even excludes the possibility of a functional recovery, most of these studies have had small numbers of patients. As such we wish to systematically review the literature and perform a meta-analysis to determine if this hypothesis is valid.

The clinical question addressed in this systematic review was the following: does detection of cardiac contractility on bedside echocardiography predict return of spontaneous circulation (ROSC) during cardiac arrest?

METHODS

Study Design

A systematic review protocol was created to specifically address the question and was reviewed and agreed upon by all co-investigators a priori (see Data Supplement S1, available as supporting information in the online version of this paper). The preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement⁹ was followed for the purpose of reporting this systematic review.

Search Strategy

Four databases were identified for searching: MEDLINE via PubMed, EMBASE, CINAHL, and the Cochrane Library. No limits were used in any database search, except the terms were searched in title and abstract

only in EMBASE. Copies of the search strategies for each database are included in Data Supplement S1. The search was completed on February 23, 2011, and repeated on January 29, 2012. Searches were not limited by date. The references of relevant papers were also scanned for any missed papers. Exact duplicates were removed by the duplicates function of RefWorks (ProQuest, LLC, Ann Arbor, MI). Close duplicates were examined individually and only deleted if citation information matched perfectly or strongly were suspected of representing the same data source.

Study Selection

To ensure that all relevant articles were identified by the literature search and that those returned were unbiased and relevant, we developed strict inclusion and exclusion criteria. Studies were accepted for further evaluation if a clinician performed transthoracic echo on an adult in cardiac arrest during cardiopulmonary resuscitation and the outcome was reported. Case reports were excluded, as well as studies in which transesophageal echo was performed instead of transthoracic echo.

Two reviewers (LB, PA) independently selected papers relevant to the research topic, based on title and abstract review of the initial search results. Reviewers then compared selected articles, and discrepancies in article selection were discussed. A consensus was reached through discussion as to which articles should be included for further analysis, without the need for an arbiter.

Quality Assessment

To ensure that the articles included in our meta-analysis were of good quality and should be included, two independent reviewers conducted a critical appraisal using a modified version of the quality assessment tool for diagnostic accuracy studies (QUADAS) tool.¹⁰ The original QUADAS tool has 14 criteria, but the authors felt that only eight were pertinent to this study. The modified QUADAS tool applied to the papers included in the meta-analysis is shown in Table 1.

Data Analysis

Statistical analysis was performed by using software (Meta-DiSc 1.4, Hospital Universitario Ramón y Cajal, Madrid, Spain) to calculate pooled estimates of likelihood ratios, specificity and sensitivity with 95% confidence intervals (CI), and a summary receiver operator curve (ROC). These were calculated against a criterion standard of death or failure to establish ROSC. Heterogeneity was determined using the I-squared statistic with the decision to pool all outcomes of interest and if need be advise cautious interpretation for I-squared results exceeding 50%. A random-effects model was employed in conducting the pooled analysis.

RESULTS

Figure 1 shows the results of the search and article selection. The relevance screen of 2,539 titles identified in the MEDLINE, EMBASE, CINAHL, and Cochrane Library databases showed good agreement between

Table 1
Modified QUADAS Scores for Included Papers

QUADAS question	Aichinger (2012) ⁶	Blaivas (2001) ⁷	Breitkreutz (2010) ¹¹	Hayhurst (2011) ¹²	Salen (2001) ¹³	Salen (2005) ¹⁴	Schuster (2009) ¹⁵	Tayal (2003) ¹⁶
Representative spectrum?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Selection criteria described?	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes
Quality reference standard?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Blinding of index test?	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Blinding of reference test?	Yes	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes
Did everyone receive the same reference standard?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Uninterpretable results reported?	Yes	Yes	Yes	Yes	Yes	Yes/unclear	Yes	No
Withdrawals from study explained?	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	No

QUADAS = quality assessment tool for diagnostic accuracy studies.

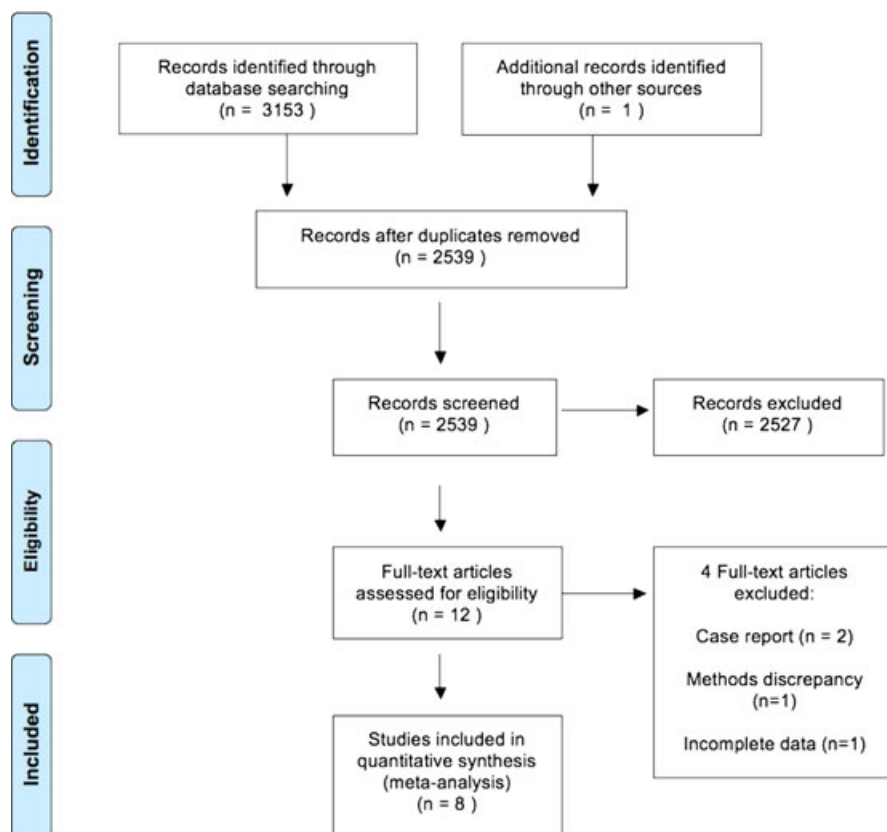


Figure 1. Results of the search strategy.

the two reviewers. Expert contact and relevance screening of grey literature and conference proceedings yielded two additional potentially relevant articles. After adjudication of the relevance search, a complete article review was completed on the remaining 12 articles. Upon review, four studies did not meet our inclusion criteria for various reasons as described in Figure 1. If it was unclear whether inclusion criteria were met, authors were contacted for clarification. Eight articles were included in the final analysis.^{6,7,11–16} These eight studies provided a sample of 568 patients, all of whom had echo performed during cardiac arrest and received the criterion reference standard care to

determine the presence or absence of kinetic cardiac activity and were followed up to determine ROSC (Table 2). The positive and negative likelihood ratios for each study are presented in Figures 2 and 3. Of the 568 patients, 107 (18.8%) achieved ROSC. Of the 378 patients with no detectable cardiac contractility on echo, only nine (2.4%) achieved ROSC (see Table 3).

Quality Assessment

The strict inclusion criteria required that all eight studies be rated “yes” for having a representative patient spectrum and acceptable reference standard (see Table 1). All eight studies adequately described their

Table 2
Summary of Study Details

Study	Outcome Measure(s)	Population	US Methods
Blaivas (2001) ⁷	Survival to hospital admission	<i>n</i> = 169 Convenience sample Nontraumatic arrests	Performed by US-trained residents Aloka 2000, 2.5-MHz curved-array and phased-array transducer
Salen (2001) ¹³	Survival to hospital admission	<i>n</i> = 102 Nonconsecutive convenience sample	EPs, residents, and attending physicians had a minimum 4-hour trauma US course Pie Medical Scanner 200 GE RT 3200 Advantage II
Tayal (2003) ¹⁶	ROSC	<i>n</i> = 20 Nontraumatic arrests	Both used a 3.5-MHz curvilinear transducer EPs were trained with a 20-hour US course
Salen (2005) ¹⁴	Survival to hospital discharge ROSC Survival to ED discharge Survival to hospital discharge	<i>n</i> = 70 Traumatic and nontraumatic All patients presenting in or progressing to PEA	Shimadzu SDU-400 gray-scale, 3.5-MHz probe EP ultrasonographers 3.5-MHz curvilinear or sector probes
Schuster (2009) ¹⁵	Survival to ED discharge Survival to hospital discharge	<i>n</i> = 27 Traumatic and nontraumatic All patients presenting in or progressing to PEA	US-trained residents performed US under supervision of credentialed EP or trauma surgeon Phillips EnVisor, 5-MHz curvilinear probe for subxiphoid images or phased array for parasternal views
Breitkreutz (2009) ¹¹	Survival to hospital admission	<i>n</i> = 88	Emergency physician trained in periresuscitation echo Modified hand-held US device with 3.5-MHz probe
Hayhurst (2010) ¹²	ROSC Survival to ED discharge Survival to hospital discharge	<i>n</i> = 50 Traumatic and nontraumatic arrests Convenience sample	SonoSite i-Look 15 with a curved array probe ED physicians and specialist trainees who already held Level 1 competency in emergency US Primary view obtained was xiphoid using a curvilinear probe with the option to proceed to another window using either a curvilinear or a phased array probe
Aichinger (2012) ⁶	ROSC in the field Arrival to ED with spontaneous circulation Survival to hospital discharge	<i>n</i> = 42 Nontraumatic arrests Nonconsecutive sample	EPs underwent a 2-hour introduction and training session

echo = echocardiography; EP = emergency physician; PEA = pulseless electrical activity; ROSC = return of spontaneous resuscitation; US = ultrasound.

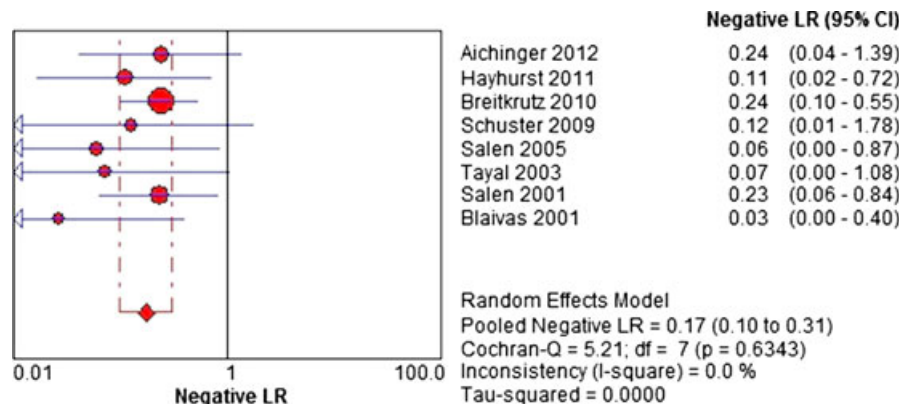


Figure 2. Summary and Forest plot of individual and pooled negative LRs. LR = likelihood ratio.

selection criteria. In all studies, resuscitation was continued, regardless of the echo findings.

Meta Analysis

The random-effects pooled results for sensitivity and specificity of echo as a predictor of ROSC were 91.6% (95% CI = 84.6% to 96.1%) and 80.0% (95% CI = 76.1%

to 83.6%), respectively. Test characteristics for individual studies are outlined in Table 4. According to these summary estimates, the positive likelihood ratio is 4.26 (95% CI = 2.63 to 6.92) and negative likelihood ratio is 0.18 (95% CI = 0.10 to 0.31). The pooled area under the curve is 0.93, with 95% CIs as shown on the summary ROC curve presented in Figure 4.

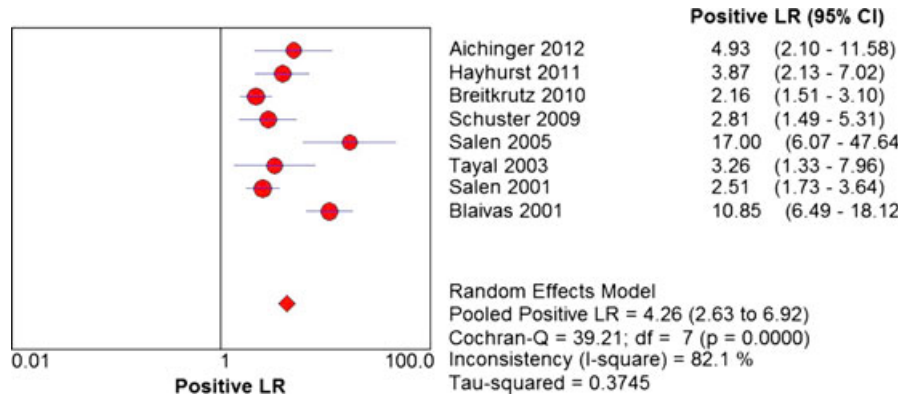


Figure 3. Summary and Forest plot of individual and pooled positive LRs. LR = likelihood ratio.

Table 3
Two-by-Two Table Showing Summary of Pooled Results

	ROSC (Positive Outcome)	No ROSC (Negative Outcome)
Cardiac contractility seen on echo (positive test)	98	92
No cardiac contractility seen on echo (negative test)	9	369

Heterogeneity of the results was low for negative likelihood ratio (LR) ($I^2 = 0.0$), but higher for positive LR ($I^2 = 82.1\%$), and is shown along with Cochran Q analysis in Figures 2 and 3. The small size and number of studies precluded any meaningful subgroup analysis. An attempt was made to analyze outcome based on survival to hospital discharge, but this was not possible as echo findings in those patients were not clearly reported in some studies.

DISCUSSION

This meta-analysis has shed important light on the accuracy of focused echo as a prognostic tool during cardiac arrest. The homogeneous and strong results with regard to predicting a failure of ROSC, based on a

pooled negative LR of 0.18 (95% CI = 0.10 to 0.31), suggest that focused transthoracic echo is a fairly effective (although not definitive) test for predicting death if no cardiac activity is noted during resuscitation. This, after all, is the most common situation in which echo is used by the resuscitation team. While absence of ventricular wall motion (VWM) on echo is a strong predictor for failure of ROSC, in circumstances where the prior probability of survival is high (e.g., witnessed arrest, early CPR, short down time), a negative echo should not be relied on to predict eventual death. Not surprisingly, and with less than consistent findings across the evidence base, and with a positive likelihood ratio of 4.26 (95% CI = 2.63 to 6.92), echo is a weak predictor of ROSC, never mind survival. There is a growing literature demonstrating that transthoracic cardiac US is a useful diagnostic tool in identifying underlying causes of cardiac arrest and also that it is feasible to incorporate echo into resuscitation guidelines without compromising patient care.^{12,17,18}

Based on the results of this meta-analysis, only 2.4% of patients without VWM detected on echo will go on to achieve ROSC. However, it is interesting to note that of all the included studies, Breitkreutz et al.¹¹ reported the most false-negatives, with five of 37 (13.5%) participants demonstrating cardiac standstill on echo subsequently achieving ROSC. False-negatives from the remaining studies, when pooled, totaled four of 332 patients (or 1.2%). It is unlikely that the study by Breitkreutz et al. would have such a disproportionate number

Table 4
Individual Study Results with Sensitivity and Specificity

Study	TP	FP	TN	FN	n	Sensitivity (95% CI)	Specificity (95% CI)
Aichinger (2012) ⁶	4	6	1	31	42	0.800 (0.284–0.995)	0.838 (0.680–0.938)
Hayhurst (2011) ¹²	11	9	1	29	50	0.917 (0.615–0.998)	0.763 (0.598–0.886)
Breitkreutz (2010) ¹¹	30	21	5	32	88	0.857 (0.697–0.952)	0.604 (0.460–0.735)
Schuster (2009) ¹⁵	5	7	0	15	27	1.000 (0.478–1.000)	0.682 (0.451–0.861)
Salen (2005) ¹⁴	8	3	0	59	70	1.000 (0.631–1.000)	0.952 (0.865–0.990)
Tayal (2003) ¹⁶	9	3	0	8	20	1.000 (0.664–1.000)	0.727 (0.390–0.940)
Salen (2001) ¹³	11	30	2	59	102	0.846 (0.546–0.981)	0.663 (0.555–0.760)
Blaivas (2001) ⁷	20	13	0	136	169	1.000 (0.832–1.000)	0.913 (0.855–0.953)
Pooled					568	0.916 (0.846–0.961)	0.800 (0.761–0.836)

FN = false-negative; FP = false-positive; n = number of subjects; TN = true negative; TP = true-positive.

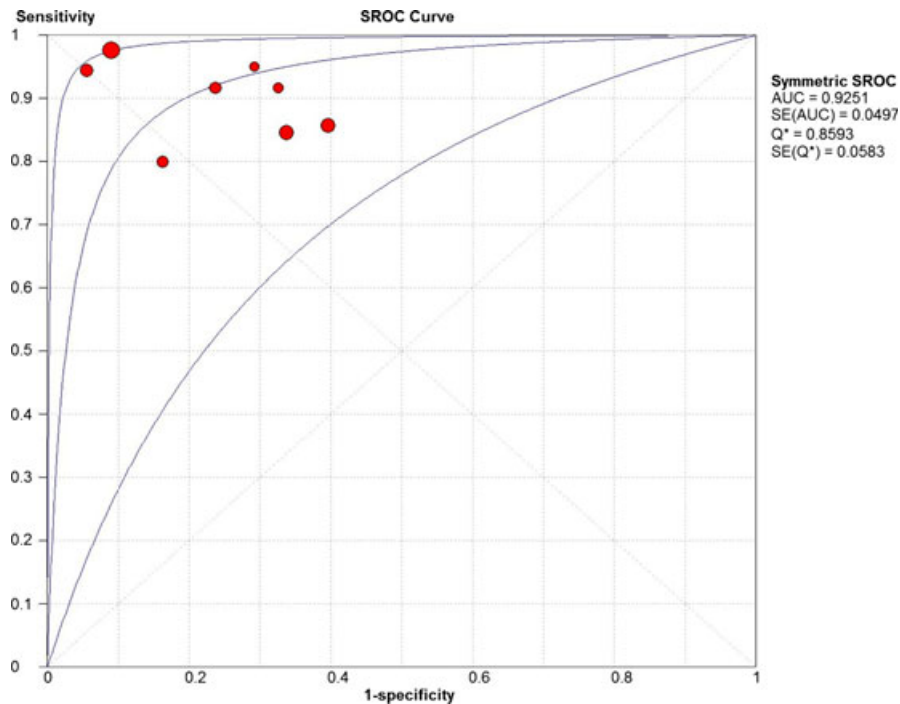


Figure 4. SROC curve. This summarizes test characteristics of focused echocardiography as a predictor of ROSC during cardiac arrest. Circles represent individual studies. The upper and lower curves represent the 95% CIs. AUC = area under the curve; ROSC = return of spontaneous circulation; SROC = summary receiver operator characteristics.

of false-negatives by chance alone, which would lead one to question whether this outlier could be as a result of different population samples (e.g., traumatic vs. non-traumatic), underreporting of VWM as a result of ultrasonographer error, or another difference in study methods that precipitated a higher number of false-negatives. Regardless of the outlying study, only a very small percentage of patients with cardiac standstill on echo proceeded to ROSC.

Although echo performed less well as a predictor of survival, of the 190 patients in whom VWM was detected, 98 had ROSC. Compared to patients in whom no VWM was identified, the likelihood of survival increased substantially from 2.4% to 51.6% if VWM was identified. However, despite the fact that ROSC is more likely in patients with VWM seen on echo, it is clear that echo is not a reliable independent prognostic tool for survival.

While there is insufficient evidence to support using echo in isolation to decide whether or not to continue with cardiopulmonary resuscitations, the presence or absence of VWM in the context of the pretest survival likelihood can provide emergency personnel with further information to assist making that difficult decision whether to stop cardiopulmonary resuscitation with more confidence. An elderly patient with an unwitnessed cardiac arrest already has very poor odds for survival. Confirmation of asystole on echo lowers those pretest odds by a factor of 5.6 and therefore might lead to termination of resuscitation. However, in the case of a 50-year-old rescued from drowning, detection of cardiac contractility on echo would increase his already fair odds of survival by a factor of 4.3, prompting continued aggressive resuscitation.

LIMITATIONS

While the authors sought to include studies that had the same outcome measurements, not all studies reported patient outcomes past ROSC, limiting evaluation of transthoracic echo as a long-term prognostic indicator. Although all studies included data pertinent to our research question, not all studies were designed specifically for the purpose of evaluating the prognostic capability of US. Some studies also examined diagnostic accuracy, thus changing management and potentially patient outcomes. Readers should consider that ROSC is not a patient-oriented outcome, in that achieving ROSC does not necessarily translate to patient survival to ED or hospital discharge. Due to unclear data from the studies that followed patient outcomes to hospital discharge, data could not be analyzed to better appreciate the use of echo in the context of a patient-oriented outcome. It is important to realize that many factors contribute to mortality after successful resuscitation, such as comorbid conditions, medications, and treatments, making it impossible to establish a direct relationship between echo findings during resuscitation and the cause of death.

Studies also varied in patient population, as one study had traumatic arrests participants only, two included only nontraumatic, two had a combination of traumatic and nontraumatic, and two studies did not specify. Although combining data from traumatic and nontraumatic patients could affect the results of this study, as they have differing etiologies and prognoses, they could not be analyzed separately due to different outcome measures between studies and the small number of specified traumatic versus nontraumatic participants.

It should also be noted that while all sonographers had some training in performing and interpreting US, some may have had a higher level of training, potentially reducing interpreting error compared to those studies in which the sonographer had less training. Not all studies reported the number of times echo was performed on a patient and if the findings differed over the course of resuscitation. Echo findings were not often recorded for confirmation of findings by another qualified practitioner. Likewise, there is variability between trials as to what constitutes cardiac activity. Some are very specific: Aichinger et al.⁶ used “any detected motion of the myocardium, ranging from visible ventricular fibrillation to coordinated ventricular contraction,” whereas some are very broad, Breikreutz et al.¹¹ using “cardiac motion.” In addition to the variation in the classification of ventricular contractility, Salen et al.¹⁴ indicated that valvular motion alone was considered to represent cardiac activity. There is clearly no standard in widespread use, at least in these studies. This is particularly relevant as the level of cardiac activity may independently be a predictor of viable myocardium or the likelihood of ROSC. It is therefore possible that the recording of isolated flickers of mitral valve motion as cardiac activity would confound the results. It should be noted, however, that this would have a greater effect on the predictive value of positive echo findings, rather than the validity of cardiac standstill as a predictor of death. It should be noted that in terms of analysis of the data, this variability in recording could by itself be a source of significant heterogeneity. Overall, limited research has been conducted in this area as it is an emerging intervention and has only recently been incorporated into Advanced Cardiac Life Support guidelines.¹

CONCLUSIONS

To our knowledge, this is the first systematic review and meta-analysis of the medical literature on the topic of point-of-care ultrasound for predicting survival in cardiac arrest. When performed during cardiac arrest, the absence of cardiac activity harbors a significantly lower but not zero likelihood that a patient will experience return of spontaneous circulation. In selected patients with a higher likelihood of survival from cardiac arrest at presentation, based on established predictors of survival, point-of-care ultrasound should not be the sole basis for the decision to cease resuscitative efforts. Presence of cardiac activity on ultrasound is a weak predictor of return of spontaneous circulation.

We are aware of a large multicenter prospective study currently examining the same question as we have attempted to answer. It is hoped that the REASON study will answer definitively which components of cardiac activity seen on echo during cardiac arrest might predict outcome including return of spontaneous circulation and survival to hospital discharge.¹⁹ Currently, focused transthoracic echocardiography should continue to be used only as an adjunct to clinical assessment in predicting the outcome of resuscitation for cardiac arrest.

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Supporting Information

The following supporting information is available in the online version of this paper:

Data Supplement S1. Search strategy.

The document is in PDF format.

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