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Transesophageal Echocardiography During CPR in Patients With Out-of-Hospital Cardiac Arrest
The EXECT-CPR Randomized Clinical Trial

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IMPORTANCE Cardiopulmonary resuscitation (CPR) guidelines recommend chest compressions at the lower half of the sternum. This may lead to aortic valve compression, which is associated with poor outcomes, while compressions over the left ventricle are seldom achieved.

OBJECTIVE To test the hypothesis that transesophageal echocardiography (TEE) guidance during CPR to avoid aortic valve compression and target the left ventricle would improve outcomes in patients with nontraumatic out-of-hospital cardiac arrest compared with conventional CPR.

DESIGN, SETTING, AND PARTICIPANTS This cluster-randomized clinical trial (the EXECT-CPR study) was conducted from June 26 to November 19, 2023, at 1 tertiary medical center in Taiwan. Participants were adults who consecutively presented to the emergency department (ED) with nontraumatic out-of-hospital cardiac arrest. Exclusion criteria were prehospital return of spontaneous circulation, extracorporeal CPR, contraindications to TEE, prior do-not-resuscitate orders, and obvious signs of death. Complete blinding was not feasible; the allocation schedule was disclosed only to the principal investigator.

INTERVENTION Post–ED arrival CPR at TEE-guided (avoid aortic-valve compression and target the left ventricle) or guideline-recommended (the lower half of the sternum) site.

MAIN OUTCOMES AND MEASURES The primary outcome was a sustained return of spontaneous circulation (≥20 minutes). Secondary outcomes were any return of spontaneous circulation, survival to intensive care unit admission, survival to hospital discharge, cerebral performance category of 2 or lower at discharge, and intra-CPR end-tidal carbon dioxide levels.

RESULTS A total of 132 patients underwent randomization (66 in each group; median [IQR] age, 68 [55-74] years; 87 [66%] male). The primary outcome was similar between groups (TEE-guided group, 29 [44%]; conventional group, 26 [39%]; cluster-adjusted odds ratio, 1.21; 95% CI, 0.64-2.29). The secondary outcomes also did not significantly differ, except for higher intra-CPR end-tidal carbon dioxide levels in the TEE-guided group during the 11th to 20th minutes after arrival. Adverse event rates related to TEE and CPR were comparable.

CONCLUSIONS AND RELEVANCE In this randomized clinical trial among adults transported to the emergency department with ongoing CPR for nontraumatic out-of-hospital cardiac arrest, TEE-guided CPR with an adjusted compression site after arrival did not significantly improve clinical outcomes compared with conventional CPR, although it produced potential hemodynamic benefits without increasing adverse events. Given that the trial was underpowered due to optimistic effect size assumptions, these neutral findings should be interpreted with caution.

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According to cardiopulmonary resuscitation (CPR) guidelines, chest compressions are recommended at the center of the chest or the lower half of the sternum. However, this recommendation is not strongly supported by clinical evidence,[1] and concerns have been raised.[2-7] Teran et al[7] reported that approximately half of patients experience deformity of the aortic valve (AV) and peri-AV structures during such compressions. Chu et al[6] used transesophageal echocardiography (TEE) to further demonstrate that AV compression was associated with poorer prognosis and reduced diastolic and mean arterial pressures during CPR.

Theoretically, direct compression over the left ventricle (LV) is more advantageous. Animal studies have shown that LV-targeted compressions produce superior hemodynamic effects, including higher end-tidal carbon dioxide ($ETCO_2$) levels, arterial pressure, coronary perfusion pressure, and cerebral perfusion.[8,9] Human observational studies further demonstrate a strong correlation between ventricular deformity during compressions and $ETCO_2$ levels.[10,11] These findings suggest that avoiding AV compression and targeting the LV may improve CPR quality.

TEE enables real-time identification of the area of maximal compression (AMC) without interrupting chest compressions, unlike transthoracic ultrasonography, which may require CPR pauses or chest contact.[12] The aim of this study was to compare TEE-guided CPR, avoiding the AV and targeting the LV, with conventional, guideline-directed CPR in patients with out-of-hospital cardiac arrest (OHCA). We hypothesized that TEE-guided CPR would improve return of spontaneous circulation (ROSC) through enhanced hemodynamic effects and lead to better survival and neurological outcomes.

Key Points

Question Does transesophageal echocardiography (TEE)–guided cardiopulmonary resuscitation (CPR) to target the left ventricle while avoiding the aortic valve improve clinical outcomes in adults with nontraumatic out-of-hospital cardiac arrest?

Findings In this cluster-randomized clinical trial involving 132 adults, TEE guidance yielded no significant differences in return of spontaneous circulation, survival, or neurological outcomes compared with conventional CPR. However, the TEE-guided group demonstrated significantly higher postintervention end-tidal carbon dioxide levels without increased adverse events.

Meaning In this study, emergency department–based TEE guidance for compression site adjustment did not significantly improve clinical outcomes but appeared to enhance hemodynamic efficacy without increasing harm.

Methods

Study Design and Setting

The EXECT-CPR (Executing TEE During CPR) trial was a cluster-randomized clinical trial with periodic crossover, conducted from June 26 to November 19, 2023, at the emergency department (ED) of Far Eastern Memorial Hospital, a tertiary center in Taipei. It compared TEE-guided CPR—targeting the LV while avoiding AV compression—with guideline-directed CPR in adults with nontraumatic OHCA. Cluster randomization was implemented via operator scheduling to accommodate specialized training requirements. The study was approved by the hospital's institutional review board with a waiver of informed consent because the time-critical nature of cardiac arrest resuscitation made prospective consent impossible to obtain. The trial protocol appears in Supplement 1, and it was conducted in accordance with the Declaration of Helsinki.[13] We followed the Consolidated Standards of Reporting Trials (CONSORT) reporting guideline for cluster randomized trials.

Patients

We included adults aged 20 years and older who experienced nontraumatic OHCA. Exclusion criteria were as follows: (1) obvious signs of death; (2) resuscitation explicitly refused by family members or a documented advanced do-not-resuscitate (DNR) decision; (3) contraindications to TEE[14]; (4) extracorporeal CPR (ECPR); and (5) ROSC having been achieved prior to ED arrival.

Resuscitation Protocol

On receipt of an OHCA call, dispatchers alerted the hospital, and paramedics or emergency medical technicians initiated on-scene resuscitation according to the New Taipei City Fire Department (NTFD) protocol (eFigure 1 in Supplement 2). Chest compressions were initiated manually and transitioned to mechanical CPR for transport using the LUCAS device (Stryker Medical), secured to the transport sheet to prevent displacement (eFigure 2 in Supplement 2). Advanced airway management (endotracheal intubation [ETI] or supraglottic airway), defibrillation, and resuscitative medications were provided as indicated. Resuscitation was withheld only in patients with a valid DNR order or those meeting NTFD termination criteria (eFigure 3 in Supplement 2); all others were transported to the hospital.

In the ED, CPR was continued according to guidelines[1] using the same mechanical device to maintain consistent compression rate and depth; manual compressions were used only if the device was not feasible. ETI and standardized mechanical ventilation were performed as needed. In the TEE-guided group, TEE was performed after intubation to guide compression-site adjustment by avoiding AV compression and targeting the LV; TEE operators were not permitted to lead the resuscitation or interrupt CPR. In the conventional group, compressions were directed to the lower half of the sternum, with repositioning performed if displacement occurred using pretrained techniques (eFigure 4 in Supplement 2). Point-of-care ultrasonography was permitted except for chest scanning and AMC assessment. CPR quality was monitored using $ETCO_2$, and the cardiovascular team remained on standby for extracorporeal membrane oxygenation (ECMO). Patients achieving ROSC were admitted to the intensive care unit, whereas resuscitation was terminated if ROSC was not achieved within 1 hour.

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Randomization and Allocation

A time-based, cluster-randomized design was used, with a total of 26 predefined 2-week blocks (ie, clusters) planned based on the expectation that enrollment would be completed within approximately 1 year. These blocks were randomized 1:1 using a computer-generated sequence (eTable 1 in Supplement 2). No more than 6 consecutive weeks were assigned to the same intervention to reduce temporal bias. Patients were enrolled according to ED presentation period. During TEE-guided periods, trained personnel were on standby in the ED. Although complete blinding was not feasible, the allocation schedule was disclosed only to the principal investigator, and TEE-trained personnel were present during both intervention and control periods to limit predictability.

Upon notification of an incoming patient with OHCA, the resuscitation and research teams were alerted. Eligibility was assessed at ED arrival, and the assigned intervention was communicated to the resuscitation team. The research team collected all study data. After study completion, the intraclass correlation coefficient (ICC) was calculated using generalized estimating equations (GEEs) to assess intracluster correlation.

Intervention

In the TEE-guided group, TEE was initiated after intubation following a published protocol (eFigure 5 in Supplement 2)[15] to identify the AMC using a predefined algorithm (eFigure 6 in Supplement 2).[16] Both long- and short-axis views at the mid-esophageal or transgastric levels were used to confirm AV opening and LV compression. AMC was continuously monitored until ROSC or termination. If AMC was not over the LV, immediate adjustment was performed with team leader approval using a pretrained technique (eFigures 4 and 7 in Supplement 2) and secured to the transport sheet. All TEE operators completed structured simulation-based training and supervised clinical cases and demonstrated independent competency before participation. All images were recorded and reviewed by a blinded expert to validate AMC and assess interrater reliability. In the conventional group, TEE was prohibited, and the compression site was consistently secured at the lower half of the sternum, with prompt correction of any displacement.

Study Outcomes

The primary outcome was sustained ROSC (≥20 minutes). Secondary outcomes included any ROSC (≥1 minute), survival to ICU admission, survival to hospital discharge, and discharge with favorable neurological outcome (cerebral performance category [CPC] 1 or 2). $ETCO_2$ was assessed during in-hospital CPR, with achievement of $ETCO_2$ greater than 20 mm Hg[1] at any time point used as a representative physiological indicator.

Data Collection and Variable Definitions

Data were collected using Utstein-style definitions,[17,18] including demographic characteristics, arrest characteristics, prehospital and in-hospital resuscitation details, complications, and outcomes. Compression-site distances were recorded relative to the lower half of the sternum. Key time intervals included prehospital times, ED arrival to first TEE image, adjustment duration, and total CPR duration. $ETCO_2$ was recorded every minute during in-hospital resuscitation. TEE images and videos were archived for postevent review. Detailed variable definitions are provided in Supplement 1.

Sample Size Determination

Sample size was based on sustained ROSC, assuming rates of 53.8% in the intervention group (from our prior AV-uncompressed cohort[6]) and 25.6% in the control group (from Taipei OHCA registry[19]). With $\alpha = .05$ and 80% power, 46 patients per arm were required. After adjusting for clustering (ICC, 0.03; cluster size, 6) and 25% attrition, the final target was 66 patients per arm (132 total), corresponding to approximately 26 clusters over 1 year.

Statistical Analysis

Normality was evaluated using the Shapiro-Wilk test. Data are presented as mean with SD, median with IQR, or frequency with percentage. Continuous variables were compared using 2-tailed *t* tests or Mann-Whitney *U* tests; categorical data were compared using χ^2 or Fisher exact tests. Primary and secondary outcomes were analyzed using logistic regression with GEE to account for clustering. Cluster-level outcomes were further assessed using unweighted and cluster size–weighted analyses. Sensitivity analyses included complier average causal effect analysis for noncompliance and time-based GEEs with alternative clustering. Subgroups were analyzed via logistic regression, and temporal $ETCO_2$ differences via GEE. Cohen κ quantified interrater reliability. Missing data were handled by complete-case exclusion, with multiple imputation for the $ETCO_2$ greater than 20 mm Hg sensitivity analysis.

Exploratory analyses examined associations of AV and LV compression with outcomes and $ETCO_2$, specifically comparing initial AV vs non-AV compression, initial LV vs non-LV effects, and specific adjustment vectors (AV to LV vs other to LV). We also assessed repositioning attempts and adjustment direction. Analyses were independently performed by the Statistical Consulting Unit at National Taiwan University Hospital using SPSS version 29.0 (IBM Corp) or SAS version 9.3 (SAS Institute). Significance was set at 2-sided $P < .05$.

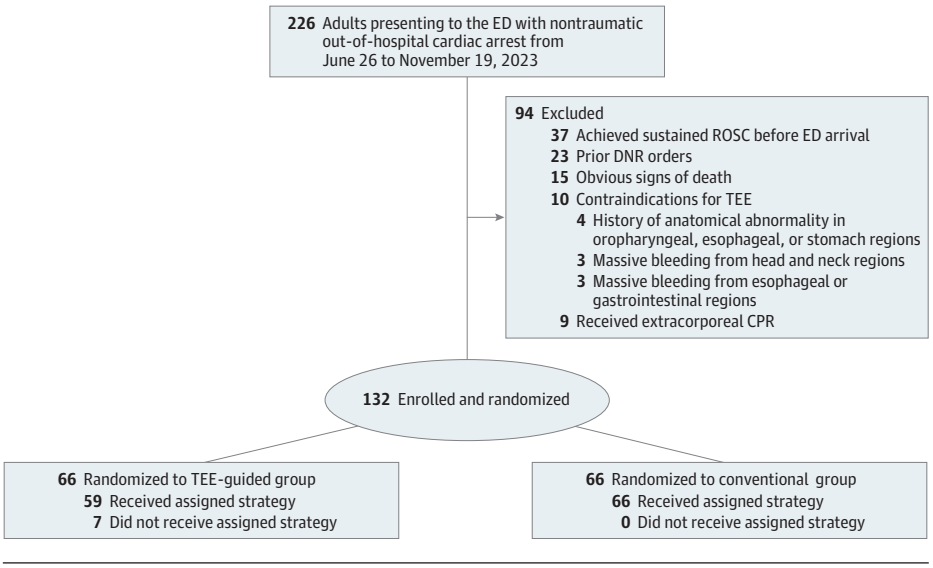
Results

Patient Characteristics

From June 26 to November 19, 2023, 132 patients were enrolled (66 per group; median [IQR] age, 68 [55-74] years; 87 [66%] male) (**Figure 1**). No interim analysis was conducted because the study reached its target sample size ahead of schedule. A total of 11 clusters were randomized, with cluster sizes ranging from 3 to 22 patients (eTable 2 in Supplement 2); no significant cluster effects were observed (GEE $\alpha = -0.010$; 95% CI = −0.042 to 0.134). Baseline characteristics were balanced (**Table 1**). There were no missing data for the primary outcome; however, $ETCO_2$ data were unavailable in 59 patients (45%) due to clinical factors (eg, early ROSC) or technical issues.

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Figure 1. Study Flowchart



CPR indicates cardiopulmonary resuscitation; DNR, do not resuscitate; ED, emergency department; ROSC, return of spontaneous circulation; TEE, transesophageal echocardiography.

Implementation of TEE-Guided CPR

In the TEE-guided group (n = 66), 7 did not receive TEE (4 probe disinfection; 3 ETI difficulty). Images were obtained before ROSC in 52 patients (median [IQR] time, 5.3 [3.2-6.5] minutes from ED arrival; 34.9 [31.4-40.7] minutes from call), with mechanical CPR continuing in 48 patients (73%). The AMC was identified in 45 patients: 9 (20%) were over the LV, while 36 required adjustment (24 [53%] near AV; 12 [27%] over other sites). Operator interpretation matched expert validation (κ = 0.888; SE, 0.054) (eTables 3-5 in Supplement 2).

Of the 36 patients who required adjustment, 33 (92%) had successful relocation (2 [6%] misidentified LV outflow tract as LV, 1 [3%] had ROSC during adjustment). Adjustment required a median (IQR) of 3 (3-5) repositionings over a median (IQR) of 23 (12-92) seconds, completed at a median (IQR) 8.5 (5.4-9.9) minutes from ED arrival (mean [SD], 38.1 [6.7] minutes from call). The site shifted a mean (SD) 4.9 (2.6) cm downward and 2.8 (2.3) cm leftward, and mean $ETCO_2$ increased from 23.5 (18.8) to 28.3 (22.0) mm Hg ($P < .001$). No cases required further adjustment thereafter. In total, 42 patients had compressions secured over the LV (eFigure 8-9 in Supplement 2; **Video**). In the conventional group, no TEE or near-field transthoracic cardiac scanning was performed, and only 3 patients received compression-site adjustment using a pretrained technique for cephalad displacement upon ED arrival.

Clinical Outcomes and Subgroup Analysis

Cluster-level outcomes are detailed in eTables 2, 6, and 7 in Supplement 2. In the primary intention-to-treat analysis (**Table 2**), sustained ROSC occurred in 29 patients (44%) in the TEE-guided group vs 26 patients (39%) in the conventional CPR group (cluster-adjusted odds ratio [OR], 1.21; 95% CI, 0.64-2.29; complier average causal effect, 7.1%). Secondary outcomes were similar between the TEE-guided and conventional CPR groups, including any ROSC (33 [50%] vs 33 [50%]) and survival to ICU admission (20 [30%] vs 20 [30%]). No patient in the TEE-guided group survived to discharge (all care withdrawn); 5 patients (8%) in the conventional CPR group were discharged with poor neurological outcomes (all CPC = 4). Per-protocol, as-treated, and time-based GEE sensitivity analyses were consistent (eTables 8-9 in Supplement 2). Subgroup analyses showed no significant differences (**Figure 2**).

$ETCO_2$

$ETCO_2$ data were missing in 59 patients (45%) (likely randomly distributed) (eTable 10 in Supplement 2). The proportion achieving $ETCO_2$ greater than 20 mm Hg did not differ statistically between the TEE-guided and conventional CPR groups (26 of 37 [70%] vs 23 of 36 [64%]; cluster-adjusted OR, 1.54; 95% CI, 0.45-5.25), a finding confirmed by multiple imputation (imputed OR, 1.22; 95% CI, 0.44-3.39). However, temporal analysis revealed that $ETCO_2$ values were significantly higher in the TEE-guided group specifically during the 11- to 20-minute interval after ED arrival, with an estimated mean difference of 8.61 (95% CI, 0.40-16.81) mm Hg (**Figure 3**A; eTable 11 and eFigure 10 in Supplement 2). Furthermore, securing compression over the LV yielded the highest $ETCO_2$ levels compared with incomplete protocols or conventional placement (Figure 3B).

Safety

Chest compression fraction (CCF) and resuscitation-related complications did not differ (eg, median [IQR] CCF, TEE-guided group vs conventional group: 94.6% [92.5%-96.5%] vs 95.9% [92.6%-97.6%]) (Table 1; eTable 12 in Supplement 2). According to post-ROSC imaging (43 computed tomography scans and 9 radiographs), rib fractures were similarly distributed, with 1 trivial pneumothorax in the TEE-guided group requiring no intervention; no hemothorax or gastrointestinal perforation occurred. One patient in the TEE-guided group developed upper gastrointestinal bleeding requiring treatment.

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Table 1. Baseline Characteristics and Resuscitation Parameters of Patients

Variables	Patients, No. (%)			*P* value
	All (N = 132)	TEE-guided CPR (n = 66)	Conventional CPR (n = 66)	
Patients' baseline characteristics				
Age, median (IQR), y[a]	68 (55-74)	68 (52-75)	69 (57-74)	.85
Sex				
Female	35 (34)	24 (36)	21 (32)	.58
Male	87 (66)	42 (64)	45 (68)	
Charlson Comorbidity Index, median (IQR)[a]	4 (2-6)	4 (2-6)	4 (2-6)	.65
Height, mean (SD), cm	163.6 (8.71)	163.4 (8.52)	163.9 (8.95)	.74
Weight, median (IQR), kg[a]	65.0 (55.1-80.0)	65.0 (55.0-80.0)	67.5 (59.1-80.0)	.71
Body mass index, median (IQR)[a,b]	24.4 (20.9-27.5)	23.4 (20.8-27.8)	24.9 (21.4-27.2)	.44
Chronic disease				
Chronic heart disease	27 (20)	15 (23)	12 (18)	.52
Chronic lung disease	14 (11)	9 (14)	5 (8)	.26
Chronic kidney disease[c]	14 (11)	4 (6)	10 (15)	.16
Chronic liver disease[c]	5 (4)	2 (3)	3 (5)	>.99
Total dependence in ADL	14 (11)	7 (11)	7 (11)	>.99
Arrest location				
Home	88 (67)	42 (64)	46 (70)	.39
Public	29 (22)	14 (21)	15 (23)	
Ambulance	9 (7)	5 (8)	4 (6)	
Health care facility	6 (5)	5 (8)	1 (2)	
Prehospital resuscitation				
Arrest witnessed	58 (44)	26 (39)	32 (49)	.29
Bystander CPR	75 (57)	39 (59)	36 (55)	.60
Bystander AED	15 (11)	8 (12)	7 (11)	.78
Initial shockable rhythm	27 (20)	13 (20)	14 (21)	.83
Prehospital defibrillations, median (IQR), No.[a]	3 (1-4)	3 (1-5)	2.5 (1-4)	.69
Airway management				
ETI	20 (15)	8 (12)	12 (18)	.33
SGA device	105 (80)	54 (82)	51 (77)	.52
Bag-valve-mask[c]	7 (5)	4 (6)	3 (5)	>.99
Received epinephrine preadmission	90 (68)	45 (68)	45 (68)	>.99
Prehospital epinephrine doses, median (IQR), No.[a]	3 (2-4)	3 (3-5)	3 (2-4)	.32
Prehospital encounter time, median (IQR), min				
Total[a]	30 (25-35)	30 (26-36)	30 (25-34)	.64
Response time[a]	5 (4-6)	5 (4-6)	5 (4-7)	.49
Scene time[a]	17 (13-21)	18 (13-22)	17 (14-20)	.28
Transport time[a]	7 (5-9)	7 (5-9)	7 (5-9)	.40
Mechanical CPR during transport[c]	116 (88)	56 (85)	60 (91)	.43
In-hospital resuscitation				
Mechanical CPR[c]	126 (95)	62 (94)	64 (97)	.68
Resuscitative TEE[c]	59 (45)	59 (89)	0	<.001
Chest compression site adjusted[c]	37 (28)	34 (52)[d]	3 (5)[e]	<.001

(continued)

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Table 1. Baseline Characteristics and Resuscitation Parameters of Patients (continued)

Variables	Patients, No. (%)			*P* value
	All (N = 132)	TEE-guided CPR (n = 66)	Conventional CPR (n = 66)	
Hand repositionings per adjustment, median (IQR), No.[a]	3 (3-4.5)	3 (3-5)	1 (1-1)	<.001
Epinephrine doses in ED, median (IQR), No.[a]	8 (5-10)	8 (5-8)	8 (5-10)	.06
Shockable rhythm on ED arrival	27 (20)	14 (21)	13 (20)	.83
Defibrillations in ED, median (IQR), No.[a]	2 (1-4)	2 (1-5)	2 (1-4)	.79
Total ED CPR time, median (IQR), min[a]	31 (15-36)	31 (15-36)	31 (14-35)	.91
Total CPR time, mean (SD), min	55.20 (16.47)	55.53 (13.50)	54.88 (19.05)	.82
Total CPR pause time, mean (SD), s	84 (61)	86 (47)	82 (71)	.36
Chest compression fraction, median (IQR), %[a]	95.5 (92.5-97.3)	94.6 (92.5-96.5)	95.9 (92.6-97.6)	.20
Initial pH level upon ED arrival, mean (SD)	6.85 (0.21)	6.83 (0.22)	6.88 (0.21)	.23
Pco_2, mean (SD)	90.2 (41.77)	90.98 (40.87)	89.47 (42.95)	.84
HCO_3, median (IQR)[a]	14.6 (10.9-18.3)	14.9 (10.9-17.6)	14.2 (12.2-18.8)	.41
Base excess, mean (SD)	−19.49 (8.21)	−20.42 (7.91)	−18.57 (8.51)	.20
ECMO after ROSC[c]	3 (2)	2 (3)	1 (2)	>.99
Coronary angiography or PCI	11 (8)	6 (9)	5 (8)	.75
TTM	22 (17)	14 (21)	8 (12)	.16
Withdrawal of life-sustaining treatment in ICU	17 (13)	12 (18)	5 (8)	.18
Cause of cardiac arrest				
Cardiogenic	60 (45)	28 (42)	32 (48)	
Acute aortic syndrome	7 (5)	4 (6)	3 (5)	
Pulmonary embolism	3 (2)	1 (2)	2 (3)	
Asphyxia or respiratory failure	26 (20)	16 (24)	10 (15)	.64
Massive nontraumatic hemorrhage	1 (1)	0	1 (2)	
Stroke or nontraumatic ICH	1 (1)	1 (2)	0	
Inconclusive or other medical causes	34 (26)	16 (24)	18 (27)	

Abbreviations: ADL, activities of daily living; AED, automated external defibrillator; CPR, cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation; ED, emergency department; ETI, endotracheal intubation; HCO_3, bicarbonate; ICH, intracranial hemorrhage; ICU, intensive care unit; PCI, percutaneous coronary intervention; Pco_2, partial pressure of carbon dioxide; ROSC, return of spontaneous circulation; SGA, supraglottic airway; TEE, transesophageal echocardiography; TTM, targeted temperature management.

[a] These variables were analyzed using the 2-tailed Mann-Whitney *U* test owing to their nonnormal distribution, as indicated by the Shapiro-Wilk test.

[b] Body mass index is calculated as weight in kilograms divided by height in meters squared.

[c] These variables were analyzed using Fisher exact test given their small sample size.

[d] All chest compression site adjustments were guided by TEE.

[e] No chest compression site adjustments were guided by TEE.

Table 2. Primary and Secondary Outcomes in the Intention-to-Treat Analysis

Outcome	Patients, No. (%)			OR (95% CI)	
	Total (N = 132)	TEE-guided CPR group (n = 66)	Conventional CPR group (n = 66)	Crude	Cluster adjusted[a]
Primary outcome					
Sustained ROSC	55 (42)	29 (44)	26 (39)	1.21 (0.60-2.41)	1.21 (0.64-2.29)
Secondary outcome					
Any ROSC	66 (50)	33 (50)	33 (50)	1.00 (0.51-1.98)	1.00 (0.62-1.62)
Survival to ICU admission	40 (30)	20 (30)	20 (30)	1.00 (0.48-2.10)	1.00 (0.45-2.21)
Survival to hospital discharge[b]	5 (4)	0	5 (8)	NA	NA
Discharged with CPC score ≤2	0	0	0	NA	NA
Achieving $ETCO_2$ >20 mm Hg at any time point during CPR in the ED, No./total No. (%)	49/73 (67)	26/37 (70)	23/36 (64)	1.34 (0.50-3.56)	1.54 (0.45-5.25)

Abbreviations: CPC, cerebral performance category; CPR, cardiopulmonary resuscitation; ED, emergency department; $ETCO_2$, end-tidal carbon dioxide; ICU, intensive care unit; NA, not applicable; OR, odds ratio; TEE, transesophageal echocardiogram; ROSC, return of spontaneous circulation.

[a] Cluster-adjusted OR estimated using a generalized estimating equation logistic model with an exchangeable working correlation and robust (sandwich) standard errors.

[b] All patients who survived to discharge had a CPC score of 4.

Additional Analyses

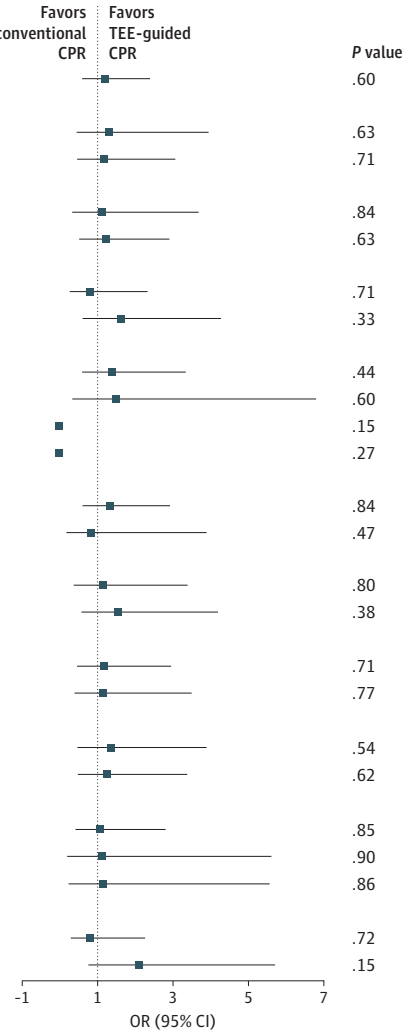
At ED presentation, absence of AV compression was associated with higher rates of ROSC and $ETCO_2$ greater than 20 mm Hg (eTable 13 in Supplement 2). Among these patients with an uncompressed AV, however, clinical outcomes did not differ significantly based on whether the LV was initially com-

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Figure 2. Dot Plot of Subgroup Analysis Results for Sustained Return of Spontaneous Circulation

Variable	Patients, No./total No. (%)		OR (95% CI)	P value
	TEE-guided CPR	Conventional CPR		
All enrolled patients	29/66 (43.9)	26/66 (39.4)	1.21 (0.60-2.41)	.60
Age, y				
<68	10/32 (31.2)	8/31 (25.8)	1.31 (0.44-3.92)	.63
≥68	19/34 (55.9)	18/35 (51.4)	1.20 (0.46-3.09)	.71
Sex				
Male	11/24 (45.8)	9/21 (42.9)	1.13 (0.35-3.67)	.84
Female	18/42 (42.9)	17/45 (37.8)	1.24 (0.52-2.91)	.63
CCI score				
<4	9/32 (28.1)	11/34 (32.4)	0.82 (0.29-2.35)	.71
≥4	20/34 (58.8)	15/32 (46.9)	1.62 (0.61-4.29)	.33
Location				
Home	18/42 (42.9)	16/46 (34.8)	1.41 (0.59-3.33)	.44
Public	6/14 (42.9)	5/15 (33.3)	1.50 (0.33-6.77)	.60
Ambulance	3/5 (60.0)	4/4 (100.0)	0 (0-NA)	.15
Health facility	2/5 (40.0)	1/1 (100.0)	0 (0-NA)	.27
Prehospital rhythm				
Nonshockable	23/53 (43.4)	19/52 (36.5)	1.33 (0.61-2.92)	.84
Shockable	6/13 (46.2)	7/14 (50.0)	0.86 (0.19-3.89)	.47
Witnessed cardiac arrest				
Yes	15/25 (60.0)	17/30 (56.7)	1.15 (0.39-3.37)	.80
No	14/41 (34.1)	9/36 (25.0)	1.56 (0.58-4.20)	.38
Bystander CPR				
Yes	19/39 (48.7)	16/36 (44.4)	1.19 (0.48-2.95)	.71
No	10/27 (37.0)	10/30 (33.3)	1.18 (0.40-3.50)	.77
pH				
<6.87	13/35 (37.1)	9/30 (30.0)	1.38 (0.49-3.90)	.54
≥6.87	16/30 (53.3)	17/36 (47.2)	1.28 (0.48-3.37)	.62
Etiology				
Cardiogenic	15/33 (45.5)	16/37 (43.2)	1.09 (0.43-2.81)	.85
Respiratory	10/16 (62.5)	6/10 (60.0)	1.11 (0.22-5.62)	.90
Other	4/17 (23.5)	4/19 (21.1)	1.15 (0.24-5.56)	.86
Total prehospital time, min				
<30	13/32 (40.6)	14/31 (45.2)	0.83 (0.31-2.26)	.72
≥30	16/32 (50.0)	11/34 (32.4)	2.09 (0.77-5.67)	.15



CCI indicates Charlson Comorbidity Index; CPR, cardiopulmonary resuscitation; NA, not applicable; OR, odds ratio; TEE, transesophageal echocardiography.

pressed (eTable 14 in Supplement 2). Physiological improvement was driven primarily by adjustments shifting the AMC from the AV to the LV (mean [SD] increase, 5.1 [5.0] mm Hg; $P = .002$), whereas adjustments from other sites to the LV yielded smaller, nonsignificant increases (eTable 15 in Supplement 2). Neither the number of repositioning attempts nor anatomical stratification was associated with clinical outcomes or demographic characteristics (eTables 16-19 in Supplement 2).

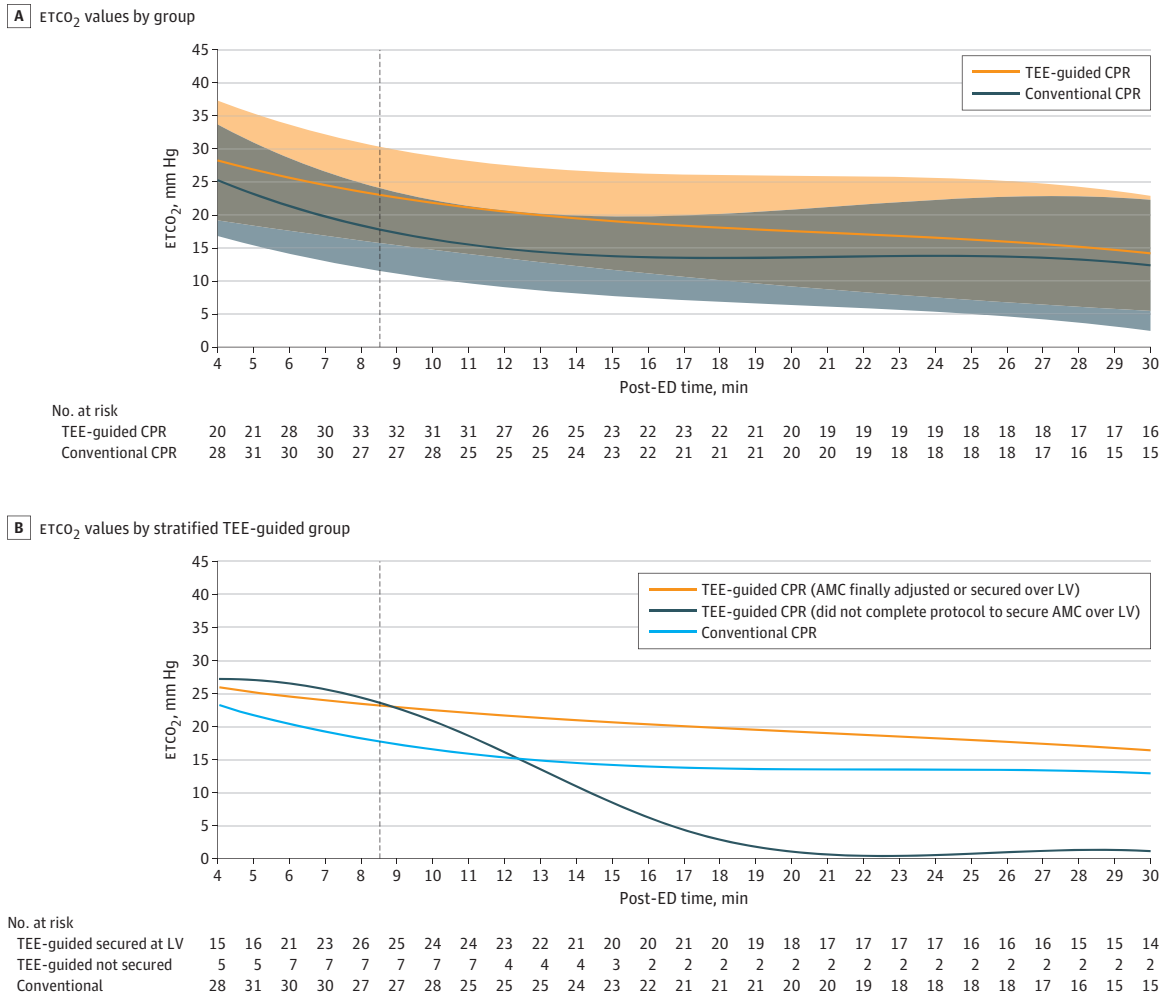
Discussion

To our knowledge, this is the first randomized clinical trial comparing TEE-guided CPR with conventional CPR in patients with OHCA. TEE-guided CPR in the ED did not significantly improve ROSC, survival, or neurological outcomes but was associated with higher postintervention $ETCO_2$ levels, without differences in CCF or adverse events.

A key explanatory factor for the discrepancy between the observed hemodynamic benefit and the absence of survival improvement in our trial is likely the late timing of the intervention. Prior swine models of simulated OHCA demonstrated higher survival rates and $ETCO_2$ levels with LV compression compared with AV compression.[8,9] Although a similar $ETCO_2$ advantage was observed in our study, it did not persist beyond 20 minutes after ED arrival. This attenuation is likely attributable to the prolonged arrest duration, as patients had already undergone approximately 30 minutes of prehospital CPR, such that by 20 minutes in the ED, more than 50 minutes had elapsed since collapse. At this stage, patients with favorable physiology may already have achieved ROSC, leaving a refractory cohort less responsive to further hemodynamic augmentation. Consistently, unlike the animal studies, no survival benefit was observed with LV compression in our trial, in which the mean time from arrest to LV-targeted compression exceeded 38 minutes, compared with only 2 to 10 min-

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Figure 3. Line Graph of End-Tidal Carbon Dioxide ($ETCO_2$) Trends During Resuscitation Following Emergency Department (ED) Arrival



A smoothing spline was applied using the splrep function (SciPy) to visualize overall trends. The vertical dashed line at 8.5 minutes indicates the median time of completion of transesophageal echocardiography (TEE)–guided compression site adjustment. AMC indicates area of maximal compression; CPR, cardiopulmonary resuscitation; LV, left ventricle.

utes in animal models. This substantial delay likely blunted any potential survival benefit, even if our in-hospital execution was already highly optimized. Consequently, TEE-guided CPR may be more suitable for in-hospital cardiac arrest. For OHCA, a more effective strategy may be to integrate TEE into the prehospital setting to allow TEE-guided CPR as early as possible after collapse. Further research is needed to explore the feasibility and clinical impact of these two scenarios.

TEE-guided CPR involves 2 key components: avoiding AV compression and targeting the LV. The exploratory analyses suggest that the primary benefit may lie more in avoiding AV compression than in targeting the LV (eTables 13-15 in Supplement 2). Patients without AV compression were more likely to achieve ROSC and to maintain $ETCO_2$ greater than 20 mm Hg, with physiological improvements driven largely by shifting specifically away from the AV. In contrast, when the AV was already uncompressed, direct LV targeting showed no clear clinical association, and adjustments from non-AV sites to the LV yielded only modest physiological gains. Taken together, these findings suggest that ensuring AV opening with forward flow may represent the dominant physiological benefit of TEE-guided CPR. Whether this forward flow is primarily driven by direct LV compression (cardiac pump theory) or by global changes in intrathoracic pressure (thoracic pump theory) may be of secondary importance in this context.

Anatomical landmarks remain the primary method for selecting the chest compression site; however, concerns persist regarding this approach. In this cohort, standard compression sites overlaid the AV in more than 50% of patients, whereas the LV was beneath this landmark in only 20%. No clear associations were observed between cardiac position and sex, body habitus, or chronic heart disease to further refine these landmarks. Although chronic lung disease appeared more prevalent among patients whose AV was not beneath the lower sternum, the subgroup size was too small for definitive conclusions. Larger TEE-based studies are needed to better char-

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acterize dynamic anatomic variability and guide individualized compression strategies.

In this study, chest compressions were primarily delivered using the LUCAS device to standardize compression quality. However, LUCAS is not universally used, and lateral repositioning can be technically challenging, especially in patients with larger body size. Brief manual compressions were required during adjustment to localize the optimal site before resecuring the device, increasing training demands. In contrast, manual compressions allow faster and more flexible repositioning, real-time modulation of compression depth, and fewer body habitus constraints, potentially improving the practicality of TEE-guided CPR.

Limitations

This study has several limitations. First, to evaluate ED-based TEE-guided CPR, patients with prehospital ROSC or ECPR were excluded, resulting in a population with prolonged CPR and likely contributing to the very low survival rate (4%) and absence of favorable neurological outcomes compared with the overall hospital OHCA cohort (15% and 6%) (eTable 20 in Supplement 2). Future studies of prehospital TEE-guided CPR may allow evaluation of a broader and earlier-stage population. Second, the study was underpowered owing to overly optimistic assumptions regarding the anticipated difference in sustained ROSC rates between groups. A post hoc sample size calculation based on the observed difference (44% vs 39%) suggests that more than 4000 patients would be required to detect a statistically significant effect. However, enrolling such a large sample in a TEE-guided clinical trial is unlikely to be feasible. Third, 11% of patients in the TEE group did not receive TEE, and LV-targeted compression was achieved in only 64%. Although this may dilute the treatment effect, it reflects the challenges of a pragmatic trial and provides a conservative estimate of effectiveness. Fourth, contamination in the conventional CPR group cannot be fully excluded, particularly as outcome differences narrowed in later clusters (eTable 21 in Supplement 2). However, record reviews confirmed no intentional deviation from standard compression, suggesting any contamination was inadvertent and minimal. Fifth, despite the potential for a Hawthorne effect, we minimized this by implementing protocol safeguards and involving less senior operators in more than 60% of cases. Sixth, interpretation of the $ETCO_2$ findings should be approached with caution due to substantial missing data, even though baseline characteristics were comparable between patients with and without missing values and the direction of association remained unchanged after imputation. Additionally, although this study focused on compression-site guidance, TEE also enables real-time diagnostics and procedural guidance such as ECMO, which warrant further investigation.

Conclusions

In adults with nontraumatic OHCA transported to the ED with ongoing resuscitation, ED-based TEE guidance targeting the LV and avoiding the AV did not significantly improve clinical outcomes compared with conventional CPR, although it produced favorable hemodynamic effects without evidence of harm. Given the study's limited power due to optimistic effect-size assumptions, these neutral clinical findings should be interpreted with caution. Larger, adequately powered trials will be necessary to determine the true clinical impact of TEE-guided compressions.

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