Original Article

# Reversible Causes in Cardiovascular Collapse at the Emergency Department Using Ultrasonography (REVIVE-US)

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## Abstract

**Introduction: Ultrasonographic evaluation of patients in cardiac arrest is currently not protocolised in the advanced cardiac life support (ACLS) algorithm. Potentially reversible causes may be identified using bedside ultrasonography that is ubiquitous in most emergency departments (EDs). This study aimed to evaluate the incidence of sonographically detectable reversible causes of cardiac arrest by incorporating an ultrasonography protocol into the ACLS algorithm. Secondary objectives include rates of survival to hospital admission, hospital discharge, and 30-day mortality. Materials and Methods: We conducted a prospective study using bedside ultrasonography to evaluate for potentially reversible causes in patients with cardiac arrest at the ED of National University Hospital, Singapore, regardless of the initial electrocardiogram rhythm. A standardised ultrasonography protocol was performed during the 10-second pulse check window. Results: Between June 2015 and April 2016, 104 patients were recruited, corresponding to 65% of all out-of-hospital cardiac arrest patients conveyed to the ED. Median age was 71 years (interquartile range, 55 to 80) and 71 (68.3%) patients were male. The most common rhythm on arrival was asystole (45.2%). Four (3.8%) patients had ultrasonographic findings suggestive of massive pulmonary embolism while 1 received intravenous thrombolysis and survived until discharge. Pericardial effusion without tamponade was detected in 4 (3.8%) patients and 6 (5.8%) patients had intra-abdominal free fluid. Twenty (19.2%) patients survived until admission, 2 of whom (1.9%) survived to discharge and beyond 30 days. Conclusion: Bedside ultrasonography can be safely incorporated into the ACLS protocol. Detection of any reversible causes may alter management and improve survival in selected patients.**

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**Key words: Advanced cardiac life support, Heart arrest, Hospital**

## Introduction

Cardiac arrest, the sudden cessation of heart contractility and effective cardiac output, carries a very high mortality rate regardless of an out-of-hospital or in-hospital setting. There are more than 350,000 patients who suffer an out-of-hospital cardiac arrest (OHCA) annually in the United States alone,[1] while the incidence in Singapore is around 1500 cases per year.[2] The rate of in-hospital cardiac arrest ranges from 0.17 to 0.26 events per bed-year, with higher event rates occurring in hospitals with fewer beds.[3] Survival to discharge in OHCA varies from 2% to 11% depending on the continent, with Asia having the lowest survival rate of only 2%.[4] In Singapore, the survival rate to discharge is 3.9%.[5] In a Japanese study, survival with neurologically favourable outcomes is even lower at 2.2%.[6]

The use of bedside echocardiography by non-cardiologists first gained clinical interest more than 20 years ago.[7] Since then, it has garnered increasing use and attention among novice sonographers in the evaluation of the critically ill. From the year 2001, bedside point-of-care ultrasonography has evolved to include systematic sonographic evaluation for other abnormalities such as abdominal aortic aneurysm and intra-abdominal free fluid in the haemodynamically unstable patient.[8] Subsequently, more well established protocols such as Rapid Ultrasound in SHock (RUSH),[9] Bedside Lung Ultrasound in Emergency (BLUE)[10] and

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Extended Focused Assessment using Sonography in Trauma (EFAST)[11] have been widely used for the evaluation of hypotensive, dypsnoeic and trauma patients, respectively. Such protocols utilise point-of-care bedside ultrasonography to guide management.

Potentially reversible causes of cardiac arrest such as massive pulmonary embolism, cardiac tamponade and tension pneumothorax can be readily detected and images accurately interpreted by non-experts using ultrasonography.[12,13] The main concern about bedside ultrasonography, especially of the thorax, is the increase in no-flow interruptions (in order to obtain images) while a patient is undergoing cardiopulmonary resuscitation (CPR). Therefore, a critical challenge would be to devise a well defined ultrasound protocol that not only is able to acquire interpretable images comprehensively but also minimises pauses in chest compressions. This would enable better coordination with ongoing resuscitative efforts and identifying causes of the cardiac arrest that may be amenable to emergent interventions, thus improving the chances of survival.

Most previous studies focused on the use of echocardiography alone in resuscitation,[12,14-16] while ultrasonographic evaluation of the abdomen during resuscitation was mainly studied in traumatic arrest.[17] Hernandez et al derived an algorithm to incorporate both echocardiography and lung views for evaluation in cardiac arrest but its applicability was not evaluated in clinical practice.[18] The objective of our study entitled "REVersible causes In cardioVascular collapse at the Emergency department using UltraSonography (REVIVE-US)" was to evaluate the incidence of reversible causes by incorporating an all-encompassing bedside ultrasonography protocol into the advanced cardiac life support (ACLS) algorithm with no interruptions to cardiac compressions. Secondary objectives were to evaluate the rates of survival to hospital admission, hospital discharge and 30-day mortality.

## Materials and Methods

### *Study Design and Setting*

This prospective study was conducted from June 2015 to April 2016 in the Emergency Department (ED) of National University Hospital, Singapore. The ED is situated in a 1100-bed tertiary academic medical centre that receives over 110,000 attendances annually, of which about 47% of the cases require urgent (42.5%) or immediate (4.5%) care. Ethics approval was obtained from the local ethics review board for waiver of consent followed by delayed informed consent from the patient (after recovery) or their legally acceptable representative.

OHCAs were managed by emergency medical services as per ACLS protocols that included early defibrillation using automated external defibrillators, chest compressions with LUCAS$^{TM}$ 2 (a mechanical chest compression device), ventilation using laryngeal mask airways and intravenous or intraosseous administration of adrenaline prior to arrival in the ED.

### *Selection Criteria*

Inclusion criteria were patients aged at least 21 years who arrived in the ED in cardiac arrest regardless of initial electrocardiographic rhythm. Exclusion criteria were pregnant women and terminally ill patients where resuscitation efforts were deemed to be inappropriate or futile by the attending physician.

### *Ultrasonography Training*

A structured training programme for credentialing in bedside ultrasonography was formulated for emergency medicine specialists and residents beginning from their junior residency year. Every participant had to go through a lecture followed by hands-on training sessions on simulated and real patients. At the end of their training, all participants were required to pass a multiple choice question test to ensure their understanding of anatomy, image interpretation and decision-making skills. Competency was achieved after the participants had completed the training programme, passed the test and performed 25 scans for each organ system (for example, cardiac, lung and aorta), 5 of which were done under direct observation (Direct Observation of Procedural Skills) by the ultrasound programme director.[19] This was to ensure good probe handling techniques, accurate image acquisition and interpretation skills.

The bedside ultrasonography protocol in this study was subsequently only performed by senior residents and above who had completed the training programme.

### *Ultrasonography Protocol*

The protocol for bedside ultrasonographic evaluation during resuscitation of patients in cardiac arrest is shown in Figure 1. The protocol included the evaluation for presence or absence of cardiac wall motion, pericardial effusion with or without tamponade, pneumothorax, free fluid in the abdomen, aortic dissection or aneurysm, femoral deep vein thrombosis (DVT) and regional wall motion abnormalities and ventricular sizes, if return of spontaneous circulation (ROSC) was achieved. The presence of ultrasonographic signs of right heart strain (i.e. dilated right ventricle and straightened interventricular septum) would suggest that massive pulmonary embolism could be a possible cause for the cardiac arrest. The protocol was implemented using the SonoSite Edge II (Fujifilm SonoSite, Inc., Bothell, WA) and Terason (Teratech Corporation, Burlington, MA) ultrasound scanners.

The evaluation of inferior vena cava (IVC) size and collapsibility or distensability was not included in the protocol as evidence had shown that assessment of the IVC in an intubated patient with ongoing chest compressions is likely to be fraught with misinterpretation.[20] Detection of free fluid in the abdomen was performed using the right hypochondrium, left hypochondrium and suprapubic views. Abdominal ultrasonography with evaluation of the abdominal aorta and presence or absence of intra-abdominal free fluid, lung sliding and femoral DVT were performed during ongoing chest compressions (Fig. 1).

Ultrasonographic assessments of the heart and lung were performed only during pulse checks and limited to less than 10 seconds to avoid unnecessary interruptions to chest compressions, which is in congruence with guidelines recommended by the ACLS committee.[21] Evaluation of the aorta and intra-abdominal free fluid was done with ongoing chest compressions to avoid disruptions. As part of the department's resuscitation protocol, a scribe nurse was designated to be in charge of time-keeping and documentation. An emergency physician who was not part of the study team led the resuscitation. Once the resuscitation leader assessed that further resuscitation efforts were to be continued (for instance, defibrillation was required for a shockable rhythm or chest compressions were to be continued for those in asystole) or if the 10-second limit was reached, whichever occurred earlier, bedside ultrasonographic assessment would cease.

The scanning physician reviewed the ultrasound images and conveyed the findings to the managing team. Subsequent treatment rendered was based on the clinical evaluation and decision of the resuscitation team.

*Data Collection*

Data was collected using a standardised data collection form. Variables including age, gender, ethnicity, initial rhythms at scene and in ED, ultrasound findings and survival to admission were entered into the data collection form by the scanning physician. Patients who survived to admission were followed up for discharge outcome and survival at 30 days after informed consent was obtained.

*Statistical Analysis*

The primary outcome measure is the incidence of reversible causes detected on ultrasonography. Secondary outcomes include survival to hospital admission, survival to hospital discharge and 30-day mortality. Categorical data are reported in frequency and percentages, while continuous data were reported as mean (standard deviation [SD]) or median (interquartile range [IQR]) as appropriate. Parametric variables were analysed using Student's t-test and non-parametric variables were analysed using Mann-Whitney U test. Statistical significance was set at $P$ <0.05. Binary logistic regression was used to obtain odds ratio estimates with 95% confidence intervals (CI). Data analyses were performed with Stata 14 (StataCorp LP, College Station, TX).

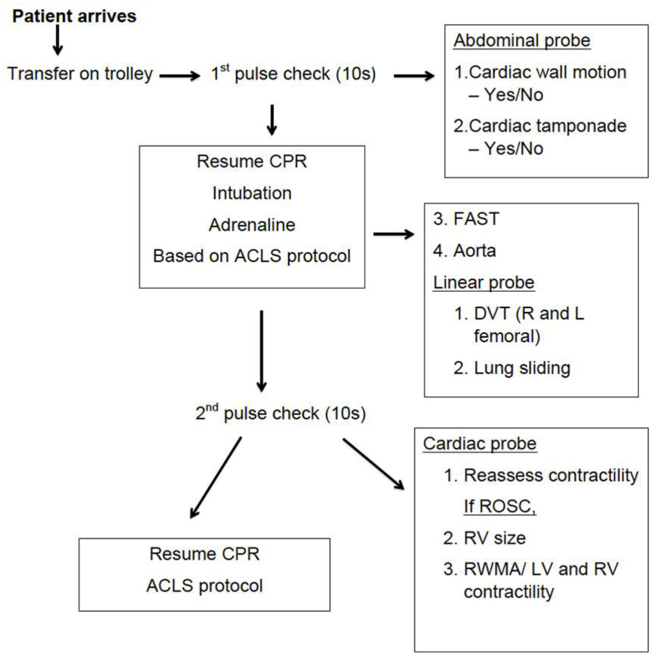


Fig. 1. Ultrasonography protocol. ACLS: Advanced cardiac life support; AP4: Apical 4 chamber; CPR: Cardiopulmonary resuscitation; DVT: Deep venous thrombosis; FAST: Focused assessment using sonography in trauma (views include hepatorenal, splenorenal and suprapubic views for intra-abdominal free fluid); PSL: Parasternal long; PSS: Parasternal short; ROSC: Return of spontaneous circulation; RV: Right ventricle; RWMA: Regional wall motion abnormality; LV: Left ventricle.

## Results

A total of 104 patients were recruited over a period of 10 months between June 2015 and April 2016, corresponding to 65% of out-of-hospital cardiac arrest patients seen in our ED who were eligible for inclusion into this study during the corresponding period (Fig. 2). Patients were predominantly male (68.3%) with a median age of 71 (IQR: 55 to 80) years. The majority (45.2%) of patients were found to be in asystole by paramedics at scene and in the ED (Table 1).

*Ultrasound Findings*

The incidence of potentially reversible causes (composite

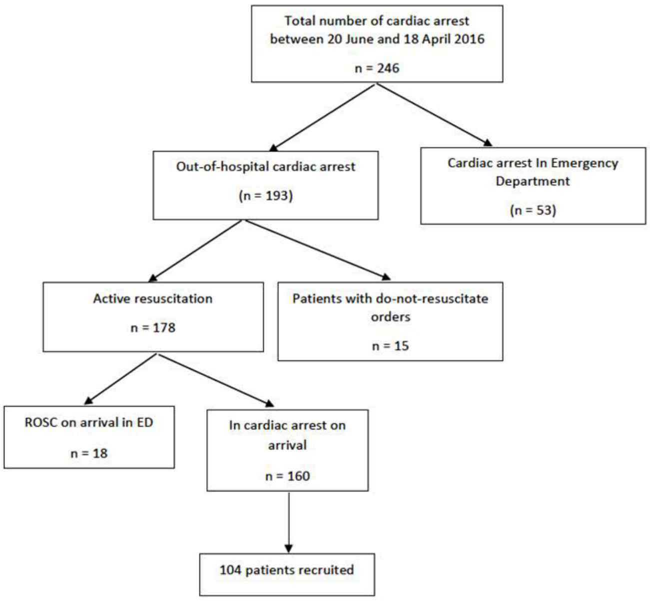


Fig. 2. Recruitment flowchart.

of pericardial effusion and pulmonary embolism) was 7.7% (n = 8).

Straightening of interventricular septum ('D' sign) in the presence of a dilated right ventricle suggestive of massive pulmonary embolism as the cause of cardiac arrest was found on ultrasonography in 4 out of 35 (11.4%) patients with ROSC (Table 2). One of these patients received intravenous thrombolysis with alteplase and survived to discharge from hospital. The same patient also had a positive DVT scan of the right femoral vein.

Four (3.8%) patients had pericardial effusion without tamponade detected on ultrasonography (Table 2). However, no intervention was carried out by the resuscitation team after clinical considerations and feasibility.

Presence of cardiac wall motion was detected in 26 (25.0%) patients on initial ultrasonographic assessment (Table 2). This was significantly associated with survival to hospital admission (Table 3). Patients with asystole and pulseless electrical activity (PEA) as initial rhythms in the ED with presence of wall motion seen on ultrasonography were more likely to survive until hospital admission (Table 4).

Intra-abdominal free fluid was present in 6 (5.8%) patients, all of whom experienced non-traumatic cardiac arrest and had underlying medical conditions such as ascites or renal failure. One patient had an aneurysmal abdominal aorta but without accompanying free fluid in the abdomen to suggest an aneurysmal rupture as the cause of the cardiac arrest.

There were 20 (19.2%) patients who survived to hospital admission but only 2 (1.9%) survived until discharge from hospital and beyond 30 days. The overall survival rate was 1.9% (2/103; 1 patient's next-of-kin declined consent for follow-up of discharge outcomes). The initial cardiac rhythm at scene and on arrival to the ED did not predict survival to hospital admission (Table 3).

Table 1. Characteristics of Patients

| Characteristics | Number of Patients, n (%) |
|---|---|
| Gender | |
| Male | 71 (68.3) |
| Female | 33 (31.7) |
| Ethnicity | |
| Chinese | 71 (68.3) |
| Malay | 16 (15.4) |
| Indian | 9 (8.7) |
| Others | 8 (7.7) |
| Ventilation via LMA (pre-hospital) | |
| No | 21 (20.2) |
| Yes | 81 (77.9) |
| Unknown | 2 (1.9) |
| Initial rhythm at scene | |
| VF | 17 (16.4) |
| Asystole | 47 (45.2) |
| PEA | 33 (31.7) |
| Other rhythms | 7 (6.7) |
| Initial rhythm on arrival in ED | |
| VF | 10 (9.6) |
| Asystole | 57 (54.8) |
| PEA | 32 (30.8) |
| Other rhythms | 5 (4.8) |

ED: Emergency department; LMA: Laryngeal mask airway; PEA: Pulseless electrical activity; VF: Ventricular fibrillation

## Discussion

Although ultrasonography has been recommended for the detection of reversible causes of cardiac arrest during resuscitation in the 2015 ACLS guidelines, concerns remain on whether its use would delay and compromise the quality of chest compressions given the lack of a structured protocol.[22] In our REVIVE-US study, we successfully devised and implemented a bedside ultrasonography protocol in keeping with the acceptable 10-second pauses for pulse checks during CPR. Potentially reversible causes of massive PE and pericardial effusion constituted 7.7% of the study population from more than 90% of interpretable images.

Since no gold standard diagnostic tests are available for some of the reversible causes of cardiac arrest, ultrasonography is a useful modality and easily available diagnostic tool in time-sensitive situations. Laboratory tests,

Table 2. Ultrasound Findings

| Ultrasound Findings | Number of Patients, n (%) |
|---|---|
| Wall motion present | |
| Yes | 26 (25.0) |
| No | 75 (72.1) |
| Unable to assess | 3 (2.9) |
| Pericardial effusion | |
| Yes | 4 (3.8) |
| No | 98 (94.2) |
| Unable to assess | 2 (1.9) |
| Cardiac tamponade | |
| Yes | 0 |
| No | 103 (99.0) |
| Unable to assess | 1 (1.0) |
| Presence of intra-abdominal free fluid | |
| Yes | 6 (5.8) |
| No | 97 (93.3) |
| Unable to assess | 1 (1.0) |
| Aorta | |
| Normal | 94 (90.4) |
| Aneurysmal | 1 (1.0) |
| Unable to assess | 9 (8.7) |
| Pneumothorax | |
| Yes | 0 |
| No | 99 (95.2) |
| Unable to assess | 5 (4.8) |
| DVT | |
| No DVT/femoral veins compressible | 94 (90.4) |
| DVT/femoral veins not compressible | 1 (1.0) |
| Unable to assess | 9 (8.6) |
| RV size (for patients with ROSC) (n = 35) | |
| Dilated RV with straightened IVS | 4 (11.4) |
| Normal RV size | 28 (80.0) |
| Unable to assess | 3 (8.6) |

DVT: Deep vein thrombosis; IVS: Interventricular septum; ROSC: Return of spontaneous circulation; RV: Right ventricle

Table 3. Survival to Admission

| | Survived Until Admission, n (%) | Odds Ratio (95% CI) | *P* Value |
|---|---|---|---|
| Initial cardiac rhythm at scene | | | 0.387 |
| VF | 5 (25.0) | 1.00 | |
| Asystole | 6 (30.0) | 0.35 (0.09 to 1.35) | |
| PEA | 8 (40.0) | 0.77 (0.21 to 2.85) | |
| Others* | 1 (5.0) | 0.40 (0.15 to 1.18) | |
| Initial cardiac rhythm in ED | | | 0.627 |
| VF | 2 (10.0) | 1.00 | |
| Asystole | 9 (45.0) | 0.75 (0.14 to 4.13) | |
| PEA | 7 (35.0) | 1.12 (0.19 to 6.52) | |
| Others* | 2 (10.0) | 2.67 (0.25 to 28.4) | |
| Presence of wall motion on US | | | <0.001 |
| Yes | 13 (72.2) | 14.0 (4.26 to 46.0) | |
| No | 5 (27.8) | 1.00 | |

ED: Emergency department; PEA: Pulseless electrical activity; US: Ultrasound; VF: Ventricular fibrillation
*Other rhythms include unknown, sinus or idioventricular rhythms for patients who had cardiac arrest en route to ED during ambulance transfer.

Table 4. Presence of Wall Motion in Patients with PEA and Asystole

| Initial Rhythm in ED | Wall Motion Present | Survived until Admission | *P* Value |
|---|---|---|---|
| Asystole (n = 57) | Yes (n = 13, 22.8%) | 6/13 (46.2%) | 0.003 |
| | No (n = 44, 77.2%) | 3/44 (6.8%) | |
| PEA (n = 30) | Yes (n = 7, 23.3%) | 4/7 (57.1%) | 0.01 |
| | No (n = 23,76.7%) | 2/23 (8.7%) | |

ED: Emergency department; PEA: Pulseless electrical activity

such as D-dimer, are non-specific for pulmonary embolism and have an unacceptable turnaround time to results in resuscitation situations. A patient in extremis would be too unstable for transport to undergo definitive imaging such as computed tomography of the pulmonary vessels or a ventilation-perfusion scan.[23] Clinical assessment with history and physical examination is also limited either due to lack of corroborative history or absence of signs when there is circulatory shutdown. For example, findings of muffled heart sounds and distended neck veins in pericardial effusion or unilateral decreased breath sounds in pneumothorax are difficult to be detected in the absence of spontaneous circulation and respiration. Emergency physicians who are non-experts in ultrasonography can be adequately trained to obtain interpretable images.[12,16] With appropriate training, emergency physicians can obtain ACLS-based echocardiographic images to identify pathology within 5 seconds and pneumothorax images within 3 seconds.[13]

Our study results demonstrated that the presence of cardiac wall motion was associated with higher odds of survival; this is in congruence with results from other studies.[24-27] However, the incidence of reversible causes detected in our study population was low. Nonetheless, in view of a low survival to discharge rate of 3.9% in the local population,[5] detection of any reversible cause with prompt treatment would make a significant difference to each patient's chances of survival. Timely administration of intravenous thrombolysis in patients with PEA due to massive PE has also been shown to achieve high rates of ROSC and survival with good neurological recovery.[28]

That being said, the intervention rate for detectable causes in our study cohort was marginal. For instance, the resuscitation team did not undertake any aggressive intervention for the 4 patients with pericardial effusion. As echocardiographic features of cardiac tamponade may not always be present during arrest states, the presence of a pericardial effusion should prompt consideration for pericardial drainage.[29] There is a generally low risk of complications associated with ultrasound-guided pericardiocentesis.[29] Further training of emergency physicians in ultrasound-guided pericardiocentesis should be considered. Familiarisation with this procedure may increase the confidence of clinicians and likelihood of intervention. Pericardiocentesis in the presence of pericardial effusion during cardiac arrest has been shown to increase survival rate to hospital discharge from a baseline of 1.3% to 15.4% among this group of patients in a large study in the United States by Gaspari et al.[24]

Our study has several limitations. First, there is currently no gold standard for interpretation of ultrasound images during cardiac arrest. Radiologists trained in ultrasound interpretation may not be adept in evaluating images obtained during cardiac arrest states. It is also impractical to station a radiologist in the ED for the purpose of interpretating and performing ultrasound images on cardiac arrest patients. There have been multiple previous studies to show that novice sonographers can be trained in as short as 1 day to obtain images of diagnostic quality.[13,30] Second, the images were not reviewed independently due to practical limitations. The scanning physicians may not have time to save images in a standardised format during resuscitation for subsequent evaluation. However, the scanning physicians in this study were senior staff who had completed the structured training programme for credentialing in bedside ultrasonography. Furthermore, as this was a pragmatic study mimicking real world scenarios, accredited scanning physicians were expected to obtain, interpret and act on the images as they would have during their daily practice. Due to lack of confirmatory tests and post-mortem reports for all patients, we could not exclude missed pathology or false-positive findings.

Third, the setting of the study in a single tertiary centre may limit generalisability worldwide. The emergency medicine community in Singapore does have regular ultrasonography training programmes conducted annually. By collaborating across hospitals through our ultrasound programme director, the protocol utilised in this study may be incorporated into the training curriculum and in other institutions, thus enabling applicability to all institutions locally. Future prospective multicentre studies can be explored to further characterise the incidence of reversible causes of cardiac arrest nationally and internationally.

Fourth, we were not able to ascertain the true incidence of reversible causes of cardiac arrest as 35% of eligible patients (56/160) were not recruited. Although we were unable to ascertain the underlying reasons, we postulate that the lack of available credentialed staff in the midst of a busy shift during the resuscitation and lenient enforcement of the study protocol may have led to this less than desirable result. Nevertheless, audit data from departmental statistics of OHCA cases during the corresponding period reported a 1.6% (26/160) survival rate, which was not significantly different from our study cohort of 1.9%. Hence, recruitment of the rest of the arrest patients was unlikely to increase the positive detectable conditions significantly. As all the cases were out-of-hospital cardiac arrest cases, those excluded are unlikely to differ significantly in terms of prognostic factors in the incidence of reversible causes. In our personal communications with the department's OHCA and mortality auditor (unpublished data from departmental clinical audit on OHCA cases in Emergency Medicine Department, National University Hospital, Singapore), there were no final diagnoses of pulmonary embolism or pericardial effusion for the other 56 cases that were not recruited during the study period.

Lastly, as this was designed to be an observational study, we did not mandate the interventions to be performed for any positive reversible cause detected. All interventions were based on the clinical judgment of the managing team. As such, the intervention rate was dismal. However, as a result of this study's findings, we were able to identify areas of deficiency where further training could be carried out.

The strengths of our study included the use of a protocol that incorporated evaluation of all possible reversible causes that could be diagnosed by ultrasonography. By integrating this into the ACLS protocol for resuscitation, the evaluation of the cardiac arrest patient would be more thorough and exhaustive, potentially allowing for timely detection of treatable causes. More importantly, by restricting the time of image acquisition to less than 10 seconds during pulse checks, it does not compromise the quality of chest compressions. With ease of training and widespread availability of ultrasonography, evaluation of arrest patients with ultrasound should be part of the resuscitation management algorithm and can be extended to both OHCA and in-hospital cardiac arrest patients. In addition, we have since established a regular simulation training programme for pericardiocentesis with the help of cardiologists to address this need. All senior staff have been accredited with capabilities to perform ultrasound-guided pericardiocentesis.

## Conclusion

Bedside ultrasound assessment during CPR in cardiac arrest is feasible and can be safely incorporated into the ACLS protocol with no interruptions to chest compressions. Detection of any reversible causes can potentially alter clinical management and greatly benefit the patient in extremis with increase in chances of survival.

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