Pulseless Electrical Activity: Detection of Underlying Causes in a Prehospital Setting

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Significance of the Study

- Clinical and anamnestic signs remain vital and should be linked to 4H's and 4T's.
- Ultrasonography should be used to detect underlying causes of cardiac arrest.
- Cerebral oximetry could become an important tool in prognostication.
- Detection of cardiac movement by ultrasonography has important prognostic implications.

Keywords

Pulseless electrical activity · Out-of-hospital cardiac arrests · Clinical decision-making

Abstract

The proportion of out-of-hospital cardiac arrests (OHCA) with pulseless electrical activity (PEA) as initial rhythm is increasing. PEA should be managed by identifying the underlying cause of the arrest and treating it accordingly. This often poses a challenge in the chaotic prehospital environment with only limited resources available. The aim of this study was to review the diagnostic tools available in a pre-hospital setting, and their interpretation during cardiac arrest (CA) with PEA as initial rhythm. A systematic literature search of the PubMed database was performed. Articles were assessed for eligibility by title, abstract, and full text. Ultrasonography has become a great asset in detecting underlying causes, and a variety of protocols have been pro-

posed. There are currently no studies comparing these protocols regarding their feasibility and their effect on patient survival. Further research concerning the relationship between electrocardiogram characteristics and underlying causes is required. Limited evidence suggests a role for point-of-care testing in detecting hyperkalemia and a role for capnography in the diagnosis of asphyxia CA. Multiple studies describe a prognostic potential. Although evidence about the prognostic potential of cerebral oximetry in OHCA is accumulating, its diagnostic potential is still unknown. In the management of OHCA, anamnestic and clinical information remains the initial source of information in search for an underlying cause. Ultrasonographic evaluation should be performed subsequently, both for detecting an underlying cause and discriminating between true PEA and pseudo PEA. Comparative studies are required to identify the best ultrasonographic protocol, which can be included in resuscitation guidelines.

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Introduction

Sudden cardiac arrest (CA) is a leading cause of death in the Western world. In Europe, annual incidences up to 119 per 100,000 adults have been reported [1]. Despite considerable efforts to improve the various links in the chain of survival, out-of-hospital cardiac arrest (OHCA) remains associated with an exceptionally poor prognosis [2–6]. As the proportion of CAs with pulseless electrical activity (PEA) as initial rhythm is increasing, this particular subtype is the main subject of this review [4].

PEA is defined as the absence of a palpable pulse, even though the electrocardiogram (ECG) demonstrates a synchronized electrical rhythm [7, 8]. In true PEA, no cardiac movement can be detected. The heart is at a complete standstill despite a normal electrical rhythm. This should however be differentiated from pseudo PEA in which some cardiac movement is still present although not powerful enough to produce adequate circulation. This is often caused by a severe shock state (such as hypovolemia or obstruction of cardiac output) [9]. If the underlying cause is not reversed, the heart continues to pump despite an ongoing depletion of oxygen and metabolic supplies. Eventually, with ongoing depletion and deterioration, myocardial contractions disappear completely, resulting in true PEA [7, 9]. True PEA can thus be regarded as the final common pathway of pseudo PEA.

Even though prognosis has increased over the years, PEA still has an estimated 1-month survival of merely 4.9–6.8% [4, 10, 11]. In contrast to arrhythmogenic CAs, where the main treatment strategy consists of shock delivery, PEA is managed by diagnosis and treatment of the underlying cause [12, 13]. The most frequent reversible causes of PEA are hypoxia, hypovolemia, hypo-/hyperkalemia, hypo-/hyperthermia, cardiac tamponade, tension pneumothorax, thrombosis (both coronary and pulmonary), and toxins [12].

Early identification of these reversible etiologies during resuscitation is key, as it allows health care professionals to optimize treatment, and thus increase chances of survival. However, the limited availability of diagnostic equipment in prehospital care poses a challenge in the identification of the cause of the arrest, as emergency physicians can often only rely on the patient's medical history and clinical examination.

Over the last few years, technology has improved and an increasing number of diagnostic tools have become available for use in a prehospital CA setting. Not only are these tools helpful in detecting an underlying cause, they can also assist emergency physicians in clinical decision-

making by determining the expected prognosis [2, 14–24]. Several studies have been published investigating the usefulness of QRS characteristics on ECG to discriminate between groups of causal mechanisms [25, 26]. Another tool that has been used extensively to monitor OHCA is capnography. A magnitude of studies have been conducted on its usefulness and its ability to predict return of spontaneous circulation (ROSC) [14, 27]. Ultrasonography has the potential to become an important asset in CA settings as well, even more so since the development of wireless, handheld devices. Finally, portable cerebral oxygenation monitoring devices have become a hot topic in research on OHCA. This study reviews the current literature regarding the available diagnostic tools in a prehospital setting and their application and interpretation during a CA with pulseless electric activity as initial rhythm.

Search Strategy

A systematic literature search of the PubMed database was performed (Fig. 1). The database was searched from inception until October 2019. All titles and abstracts were screened for their relevance. After this initial screening, full-text articles were assessed for eligibility. Case reports and non-English articles were not included. The search strategy combined Medical Search Headings and Subheadings (MeSH) terms (in PubMed), with Boolean operators “AND” and “OR” to capture all relevant article suggestions. Table 1 shows the search terms for each topic. Abstracts without full-text articles were excluded. The references of the identified articles were screened for additional eligible articles. The search strategy resulted in 926 hits in total. After initial screening, 44 full-text articles were assessed for eligibility, of which 37 articles were included in this review. Of these 37 articles, 3 were found concerning ECG. Seven articles were found on the subject of capnography. A total of 17 articles were used to review ultrasonography. Six articles concerning cerebral oximetry were included. Another 6 articles were identified describing point-of-care testing (POCT).

4H's and 4T's

The current approach to PEA consists of unveiling and treating the underlying cause using anamnestic information and clinical signs. The most frequent reversible causes of CA with PEA as the initial rhythm are commonly referred to as the 4H's and 4T's: hypoxia, hypovo-

Fig. 1. Search methodology. **a** Search methodology for ECG. **b** Search methodology for capnography. **c** Search methodology for ultrasonography. **d** Search methodology for FEEL. **e** Search methodology for cerebral oximetry. **f** Search methodology for POCT. FEEL, Focused Echocardiographic Evaluation in Life support; POCT, point-of-care testing.

Table 1. Search terms

Subject	Search term
ECG	((("Electrocardiography"[MeSH]) AND ("Heart Arrest/etiology"[MeSH] OR "Out-of-Hospital Cardiac Arrest/etiology"[MeSH])) AND "Cardiopulmonary Resuscitation"[MeSH])
Capnography	((("Prognosis"[MeSH]) OR "Outcome Assessment (Health Care)"[MeSH]) AND "Capnography"[MeSH]) AND ((("Heart Arrest"[MeSH]) OR "Out-of-Hospital Cardiac Arrest"[MeSH]) AND "Cardiopulmonary Resuscitation"[MeSH])
Ultrasonography	((("Heart Arrest/etiology"[MeSH]) AND "Cardiopulmonary Resuscitation"[MeSH]) AND ("Echocardiography"[MeSH] OR "Ultrasonography"[MeSH])
FEEL	Focused echocardiographic evaluation in life support
Cerebral oximetry	("Oximetry"[MeSH]) AND "Out-of-Hospital Cardiac Arrest"[MeSH]
POCT	(((((Point of care testing[MeSH terms]) OR (point of care system[MeSH terms])) OR (point of care systems[MeSH terms])) OR (analysis, blood gas[MeSH terms])) AND ((cardiac arrest, out of hospital[MeSH terms]) OR (heart arrest[MeSH terms]))

ECG, electrocardiogram; MeSH, Medical Search Headings and Subheadings; FEEL, Focused Echocardiographic Evaluation in Life support; POCT, point-of-care testing.

lemia, hypo/hyperkalemia, hypo/hyperthermia, cardiac tamponade, tension pneumothorax, thrombosis (both coronary and pulmonary), and toxins [12]. However, in the case of potassium disorders, it appears that especially hyperkalemia results in PEA [28].

Treatment of the 4H's and 4T's is described extensively in the 2015 ERC Guidelines [12]. Hypoxia is treated by providing adequate oxygen delivery to the lungs. Hypovolemia requires adequate hemostasis and administration of IV fluids. Hyperkalemia should be managed by administering calcium, glucose/insulin, and sodium bicarbonate. In the case of hypothermia CA, patients should be rewarmed, while in contrast, hyperthermic patients should be cooled. Resuscitative thoracotomy or pericardiocentesis can be lifesaving in the case of cardiac tamponade. In the presence of a tension pneumothorax, needle decompression can be performed but should be followed by thoracotomy. In patients suffering from CA caused by pulmonary embolism, fibrinolytic therapy can be administered. Finally, the treatment of toxic CA depends on the causal toxic agent [12].

Instruments

Electrocardiogram

ECG is an important instrument in CA settings. It can be used to differentiate between initial rhythms. Furthermore, it has been suggested that ECG could help to diag-

nose the underlying cause of PEA. Littmann et al. [25] stated on a theoretical basis that a small-complex PEA on ECG signifies a mechanical cause while a wide-complex PEA indicates a metabolic cause. However, a study by Bergum et al. [26] could not demonstrate a correlation between ECG patterns and the causal mechanism of PEA. They suggested that the aberrant depolarization resulting from metabolic deterioration of myocardial fibers during CA can cause widened ECG patterns.

Even though Bergum et al. [26] stated that ECG cannot help to determine the causal mechanism of PEA, it appears to be able to predict ROSC. Skjeflo et al. [29] discovered that 3–6 min prior to ROSC the heart rate on ECG during CPR starts to increase while QRS width appears to decrease. The heart rate of patients who did not achieve ROSC remained constant or decreased, and QRS width increased or remained unchanged [29].

Capnography

In end-tidal capnography, expiratory CO₂ levels reflect tissue metabolism, tissue and lung perfusion, and alveolar ventilation [27]. Detection of CO₂ can thus be used to verify the correct placement of the endotracheal tube and to monitor the effectiveness of chest compressions [8]. An end-tidal CO₂ (ETCO₂) value below 10–15 mm Hg indicates an insufficient quality of chest compressions [14]. A sudden ETCO₂ increase to >40 mm Hg during CPR is indicative for ROSC [14]. Furthermore, Pokorná et al. [27] discovered that a sudden ETCO₂ increase of at

least 10 mm Hg during advanced life support (ALS) can also indicate ROSC.

Not only can capnography be used to detect ROSC, it can also predict the likeliness of ROSC. Poon et al. [14] found that an ETCO_2 level >10 mm Hg 3 min after intubation can predict ROSC with odds ratio 18.16. In a study by Grmec et al. [17], all patients suffering from a CA with shockable rhythm that achieved ROSC had an initial $\text{ETCO}_2 >10$ mm Hg as well. Pearce et al. [18] confirmed that higher initial levels of ETCO_2 were indeed associated with ROSC but not with survival to discharge. Although ETCO_2 levels appeared to be higher in survivors to discharge compared to non-survivors, the difference was not statistically significant [18]. The same trend was observed by Salen et al. [19] where median ETCO_2 levels were higher in the ROSC group (35 mm Hg) compared to the non-survivor group (13.7 mm Hg). There were no survivors with ETCO_2 levels below 16 mm Hg [19].

Grmec et al. [17] also found that CA patients who suffered from asphyxia (initial rhythm PEA or asystole) had higher ETCO_2 levels than those with an initial shockable rhythm. Mean ETCO_2 values were 66.4 ± 17 and 16.5 ± 9.2 mm Hg for asphyxial and primary CA, respectively. This was explained by accumulation of CO_2 in the lungs. Cessation of breathing results in cessation of alveolar washout of CO_2 . However, circulatory CO_2 delivery to the lungs is initially preserved, which causes the CO_2 to accumulate and results in initial high ETCO_2 values [17, 30, 31]. This also explains why no significant difference in initial ETCO_2 could be demonstrated between patients achieving and not achieving ROSC in asphyxia CA [17].

Ultrasonography

Evidence is accumulating regarding the benefits of ultrasonography use during CPR. First, detection of cardiac contractions with ultrasonography makes differentiation between true and pseudo PEA possible [2, 8]. This has important implications as pseudo PEA has a much better prognosis than true PEA [2, 9, 20]. The rate of survival to hospital admission in PEA with cardiac movement is 55%, while in PEA without cardiac movement it is only 8% [2, 20]. Pseudo PEA should also potentially be managed differently as it was shown that administration of 20 IU vasopressin during a prolonged cessation of chest compressions of 15 s could significantly improve its outcome [32]. Since this treatment strategy was however investigated in a relatively small study population, further research is required to confirm these findings.

Second, detection of spontaneous cardiac movement by ultrasonography could be predictive of ROSC (note:

reference identified by manual PubMed search using a different search term) [33]. Finally, some of the underlying causes of PEA that are difficult to detect clinically can easily be detected by ultrasonography [34]. Echocardiographic signs of cardiac tamponade include presence of pericardial effusion, right atrial or ventricular diastolic collapse, and non-collapsible inferior vena cava. These signs can easily be detected using a subxiphoidal or parasternal view [35, 36]. Hypovolemia can also be diagnosed by detecting an underfilled right or left ventricle or a collapsed inferior vena cava [35–37]. Sonographical signs of tension pneumothorax include absence of lung sliding when positioning a probe at the midclavicular line at the second intercostal space. The absence of lung sliding is a sign of high sensitivity (92.3%) and specificity (99.6%) and allows a diagnosis to be made within 30 s [35]. However, parietal emphysema can hide a pneumothorax by mimicking pleural motion. This is why bilateral examination and comparison should be performed [13].

Emboli can rarely be visualized directly [38]. Pulmonary embolism should be suspected when echocardiography shows a dilated right ventricle and a flattened left ventricle or when normal wall function at the apex combined with right ventricle dysfunction at the mid-free wall is seen [13, 35, 39, 40]. The latter is known as the McConnell sign. These sonographic signs have low sensitivity (and thus have limited value as a screening tool), but high specificity, making it very useful in therapeutic decision-making [35, 40–44].

Several studies have concluded that ultrasonography during resuscitation is indeed feasible and does not interfere with the management of ALS [38, 45, 46]. A variety of sonographic protocols have been suggested for use during CPR. The most notable sonographic protocols are mentioned in Table 2.

One widely used protocol is Focused Echocardiographic Evaluation in Life support (FEEL) which was developed to detect underlying etiologies during CPR. In this protocol, a subxiphoidal probe position is used to obtain imaging of the heart within a 10 s time frame, during a pulse check between two cycles of ALS [34]. This probe position is preferred as it leads to better imaging quality than other views [20] and should be brought in position while chest compressions are being delivered. A full 4-chamber view should be obtained and analyzed while chest compressions resume. If the subxiphoidal position fails to adequately visualize the heart, other probe positions should be used; the parasternal window, long-axis, short-axis, or finally the apical 4-chamber view. The FEEL protocol allows diagnosis of hypovolemia, cardiac tam-

Table 2. Summary of ultrasonographic protocols

	FEEL	CAUSE	PEA	SHOC
Probe positioning	Subxiphoidal	Subxiphoidal (parasternal, apical) Second intercostal space on midclavicular line	Epigastric (apical) Parasternal at second or third intercostal space Left parasternal at third and fourth intercostal space Abdomen Lower limbs	Subxiphoidal (parasternal) Anterior and lateral chest Abdomen Proximal lower limbs Anterior neck
Detectable causes	Hypovolemia Cardiac tamponade Pulmonary embolism	Hypovolemia Cardiac tamponade Pulmonary embolism Tension pneumothorax	Cardiac tamponade Pulmonary embolism Tension pneumothorax Hypovolemia Hyperkalemia Acute coronary syndrome	Cardiac tamponade Tension pneumothorax Hypovolemia Pulmonary embolism
Time frame	Pulse check (max. 10 s)	Cardiac examination: pulse check (max. 10 s) Lung examination: 30 s	Unspecified	Cardiac examination: pulse check (max. 10 s)
FEEL, Focused Echocardiographic Evaluation in Life support; CAUSE, Cardiac Arrest Ultra Sound Examination; PEA, pulseless electrical activity.				

ponade, and pulmonary embolism [34]. Although additional research on its effect on patient outcome is recommended, the feasibility of the FEEL protocol was demonstrated in a prehospital setting. Implementation of sonographic evaluation using FEEL resulted in a change in therapy in 89% of patients undergoing CPR [20].

The Cardiac Arrest Ultra Sound Examination (CAUSE) protocol aims to diagnose the most common and easily reversible underlying causes of non-arrhythmogenic CA: hypovolemia, cardiac tamponade, pulmonary embolism, and tension pneumothorax. In this protocol, two sonographic perspectives of the thorax are used: a cardiac 4-chamber view and a view of the lung and pleura. The latter view is obtained by placing the probe at the second intercostal space on the midclavicular line. The cardiac and pericardial 4 chamber view can be obtained using a subcostal, parasternal, or apical probe position. The CAUSE protocol states that a cardiac view should be obtained first, moving on to the lung and pleural view if a cardiac cause could not be detected. This is because the cardiac view takes the least amount of time to complete, does not interfere with chest compressions and can detect three possible causes at once [35].

Testa et al. [36] proposed the P.E.A. protocol yet another sonographic protocol for PEA which is an acronym for the proposed probe positions, parasternal, epigastric, and abdominal. With the parasternal probe position, pneumothorax, pleural effusion, and wet or dry lungs can be detected. The epigastric position can demonstrate pericardial effusion, inferior vena cava filling and filling

status of the left and right ventricle, and their wall motion. The abdominal probe position is used to detect the presence of an abdominal aneurysm or dissection, peritoneal effusion, bowel occlusion or perforation, and deep venous thrombosis. Cardiac evaluation should be performed first. The second probe position depends on the findings of the cardiac examination. If hypovolemia is suspected on cardiac evaluation (collapsed IVC), an abdominal scan should be performed next. If cardiac tamponade is found, parasternal views should be obtained to detect aortic dissection. If an enlarged, hypokinetic right ventricle is detected, pulmonary embolism is suspected and a compression sonography of the lower limbs should be carried out. If a hypokinetic, distended left ventricle is detected, the lungs should be checked for pleural effusion or signs of a wet lung [36]. Testa et al. [36] state that the P.E.A. protocol can easily be applied during ALS and cite other studies [34, 46] to demonstrate that ultrasonography does not delay CPR.

In 2017, The International Federation for Emergency Medicine (IFEM) Ultrasound Special Interest Group (USIG) published another sonographic protocol for hypotension and CA, the SHoC protocol. This protocol consists of core, supplementary, and additional views. The sonographic views in the “core” category should be performed routinely in all patients. In a CA setting, the core category consists of a subxiphoid view or a parasternal cardiac view if the former could not obtain adequate images. These views can both be performed during the pauses used for rhythm checks and thus cause only mini-

Table 3. Summary of clinical and anamnestic clues linked to 4H's and 4T's

Hypoxia (asphyxia)	Hypokalemia	Hyperkalemia	Hypothermia	Hypovolemia	Tension pneumothorax	Cardiac tamponade	Pulmonary embolism	Toxins
Airway obstruction (e.g., aspiration)	Prolonged diarrhea	Renal failure	Exposure to cold	Excessive blood loss	Subcutaneous emphysema	Distended jugular veins	Sudden onset dyspnea	History of drug/toxin ingestion
Hanging	Diabetes insipidus	Diabetes mellitus	Trunk appearing cold on palpation	Clinical signs of anaphylaxis	Absence of vesicular breath sounds	Laceration/bruising of chest wall	Chest pain	Pupil abnormality
Drowning	Cushing's syndrome	Addison's disease	Decreased core temperature	Tracheal deviation	Tracheal deviation	Cough	Needle marks	
	Dialysis			Distended jugular veins		Hemoptysis	Oropharyngeal corrosion	
						Clinical signs of DVT	Odors/smoke	
						Prolonged period of inactivity		
						Active cancer		
						Former DVT		
DVT, deep venous thrombosis.								

mal interruption of chest compressions. Supplementary views should be obtained in all patients where this could lead to additional information without delaying CPR. These consist of inferior vena cava and lung views. Additional views should only be performed when clinically indicated. The SHoC protocol recommends the 4-F's approach for interpreting the obtained sonographic images, fluid, form, function, and filling. For cardiac views, this means checking for pericardial effusion (fluid), interpreting the cardiac dimensions (form), and judging the contractility and valve functioning (function). For inferior vena cava, this means assessing whether the vessel is dilated and non-collapsing or small and collapsing, while the lungs should be checked for B-lines and pleural effusion, indicating congestive heart failure (filling). The lung views can also detect pneumothorax by noticing an absence of the lung sliding sign. Additional views can, for example, consist of checking the lower limbs for DVT when pulmonary embolus is suspected, or checking the abdomen for rupture of an aortic aneurysm or another cause of blood loss when hypovolemia is detected [37].

Cerebral Oximetry

Evidence is accumulating for monitoring the patient's status during CPR by cerebral oximetry using near infrared spectroscopy. A monitor with a light source is placed on the forehead of the patient undergoing CPR. This takes on average 15 s, without interrupting CPR. The light emitted by the light source travels through the skin, skull, and brain tissue of the patient. The device measures the difference in light absorption between oxygenated and non-oxygenated hemoglobin and calculates the tissue oxygenation based on the amount of light arriving at the detectors. In brain tissue, normal oxygenation values range from 60 to 80% [47].

Prosen et al. [22] investigated the cerebral oxygen saturation (rSO₂) level and its change during CPR for ROSC and no-ROSC patients. The initial rSO₂ levels on arrival of the emergency medical services were undetectable (<15%) in 52% of patients achieving ROSC and 59% of patients not achieving ROSC. During CPR, rSO₂ levels rose in all cases. However, a significantly higher rise is seen in patients achieving ROSC (median rise of 22% in ROSC vs. 14% in no-ROSC). Furthermore, minutes before ROSC a significant and rapid rise in rSO₂ levels is seen. In this study, the mean rSO₂ value at ROSC was 47%, while the mean peak rSO₂ level in no-ROSC patients was only 31%, indicating that ROSC might be predicted by a significant rise in rSO₂ prior to occurrence. On the contrary, persistently low rSO₂ levels during CPR pre-

dicted poor neurological outcomes [22]. A systematic review and meta-analysis by Sanfilippo et al. [23] also concluded that both higher initial rSO₂ levels and higher average rSO₂ levels are associated with greater chances of achieving ROSC after CA. Singer et al. [24] also observed a correlation between higher mean rSO₂ levels and ROSC after CA. Their study also showed that ROSC was rarely achieved when rSO₂ remained below 30% [24]. A study by Fukuda et al. [15] found that an initial rSO₂ level of 26% or less could predict no-ROSC with a sensitivity of 89%, a specificity of 56%, a positive predictive value of 87%, and a negative predictive value of 60%.

Not only do rSO₂ levels predict ROSC, they can also predict neurological outcome. Nishiyama et al. [48] investigated the relationship between rSO₂ levels at hospital arrival after OHCA and neurological outcome after 90 days. They found that with increasing lower rSO₂ values, the percentage of patients with good 90-day neurological outcome increased proportionally, irrespective of the ROSC status upon arrival at the hospital [48]. In a previous study, they found an optimal cutoff rSO₂ value for good neurological outcome of >42% [49].

Point-of-Care Testing

Due to its ability to provide pO₂-, pCO₂-, lactate-, and potassium values in just a few minutes, POCT using a blood gas analyzer promises to be useful during CA. However, evidence regarding the role of POCT in OHCA is limited. Ahn et al. [50] discovered that POCT was able to detect life-threatening hyperkalemia during CPR with 85% sensitivity and 97% specificity. Furthermore, the potassium values measured by POCT were sufficiently similar to values measured in the central laboratory [50]. These results indicate that prehospital POCT could be useful in detecting hyperkalemia during OHCA.

In addition to venous and arterial samples, intraosseous (IO) samples can be used for POCT as well [51–53]. IO samples can be a good alternative as arterial and venous samples can be difficult to obtain in a prehospital setting. Lactate, pH, sodium, and calcium values are similar in arterial, venous, and IO samples [51]. However, IO potassium values should be interpreted with caution, as they are higher than in arterial or venous blood samples [51, 52]. Also, potassium levels during CPR are on average 2.8–4.4 mmol/L higher than pre-arrest potassium levels in all types of samples. This is why hyperkalemia may be falsely diagnosed in IO samples but can be reliably ruled out [51].

The remaining available literature predominantly describes a prognostic rather than a diagnostic potential.

Table 4. Summary of diagnostic tools and their applicability

	CC quality	Diagnostic value	ROSC prediction	Long term
4H's and 4T's	–	+	–	–
ECG	–	–	+	–
Capnography	+	–	+	–
Ultrasonography	+	+	+	–
Cerebral oximetry	–	–	+	+
POCT	–	+	+	+

CC Quality, ability to monitor chest compression quality; Diagnostic value, ability to detect underlying causes of CA; ROSC, return of spontaneous circulation; ROSC prediction, ability to predict ROSC; Long term, ability to predict long-term outcome; ECG, electrocardiogram; POCT, point-of-care testing.

Kim et al. [16] found that pCO₂ values on blood samples taken within the first 4 min of CPR were independently predictive for ROSC. More specifically, patients with an initial pCO₂ value <75 mm Hg were 3.3 times more likely to achieve ROSC than patients with higher pCO₂ values [16]. In a study by Shin et al. [54], a relationship between pH and potassium values and survival to hospital discharge was demonstrated, as well as an association between pH and neurological outcome. Higher pH levels were associated with a higher percentage of patients surviving to discharge, while increment of potassium levels beyond 3.5 mEq/L on the other hand resulted in a decreased survival to discharge ratio. Good neurological outcome could be observed if pH levels were ≥6.8, with the probability of this outcome increasing with increasing pH levels [54].

According to the ALS protocol, an OHCA with PEA as initial rhythm, should be managed by determining and treating the underlying cause of the arrest. This poses a challenge in a prehospital setting, which is often characterized by a chaotic environment and limited availability of diagnostic equipment. In this setting, the first line of information comes from clinical examination of the patient and questioning bystanders about the current event and the patient's medical history. This information is then linked to the 4H's and 4T's (Table 3) [12]. However, since clinical and anamnestic information is often limited or absent, other instruments are required to diagnose underlying causes. The available tools and their applicability are summarized in Table 4.

ECG is generally accepted, and has been widely implemented, as an indispensable instrument in CA settings as

it can discriminate between the various initial rhythms of CA and is able to monitor CPR progression. In addition, ECG appears to be able to predict ROSC by detecting an increase in heart rate and a decrease in QRS width [29]. Its diagnostic potential however is still unclear since there is only limited and conflicting evidence. Further research is required to determine the diagnostic value of ECG.

As with ECG, capnography has the ability to predict ROSC during ALS by detecting increasing ET CO_2 values [14, 27]. Its diagnostic potential is also rather limited since only one study describes its ability to indicate the cause of CA by detecting high initial ET CO_2 values in case of asphyxia [17]. In contrast to ECG, however, capnography can be used for prognosis. Patients with ET CO_2 values >10 mm Hg are more likely to achieve ROSC than patients with lower values [14, 17–19]. Furthermore, capnography can be used to monitor quality of chest compressions, while ECG cannot [8, 14].

Of all instruments available in a prehospital setting, ultrasonography appears to be the most promising in detecting the underlying cause of a CA. It is the only instrument in this review that is able to detect multiple potential underlying causes [34–37]. Like capnography and ECG, ultrasonography is able to predict ROSC by detecting spontaneous cardiac movement, and like capnography (but not ECG), ultrasonography can indicate the expected prognosis by differentiating pseudo PEA and true PEA [2, 20, 21]. Furthermore, ultrasonography appears to be able to monitor chest compression quality much like capnography [55] because ultrasonography is able to directly visualize the area of compression so that hand positioning can be adjusted, resulting in optimal compression of the left ventricle [55].

Currently, there is no literature available on the diagnostic possibilities of cerebral oximetry. Multiple studies have however investigated its prognostic value. Like capnography and ultrasonography, cerebral oximetry has the potential to determine the short-term prognosis [15, 22–24]. Moreover, like ECG, capnography, and ultrasonography, cerebral oximetry is able to predict ROSC as well [22]. However, unlike other instruments, it can also determine the expected long-term prognosis and neurological outcome [49, 56]. Because of this additional ability, cerebral oximetry could become an important asset for prognostication and can assist physicians in determining whether or not resuscitative efforts should be discontinued.

POCT appears to be a promising instrument as well. Like capnography, cerebral oximetry, and ultrasonography, POCT can be used to determine the expected prog-

nosis and predict ROSC [16]. In addition, like cerebral oximetry, POCT allows the prediction of long-term and neurological outcome [54]. An additional advantage of POCT is the ability to rule out and diagnose hyperkalemia, which cannot be done with any other diagnostic tool described in this review [50, 51].

A literature search based on a predefined search strategy was performed. There may be a risk of studies not appearing due to missing relevant key terms in the search. Moreover, publication bias is possible as unpublished studies were not searched.

Conclusion

We propose the following approach to OHCA with PEA as the initial rhythm. First, emergency physicians should look for clinical signs and anamnestic information and link this to the 4H's and 4T's. Secondly, a portable handheld ultrasonography device should be used to check for myocardial contractions (thereby discriminating between true PEA and pseudo PEA), and to screen for underlying treatable causes. Ultrasonography allows physicians to detect or exclude a variety of underlying causes in an efficient manner, with minimal CPR interruptions. Future studies should compare the various ultrasonographic protocols in terms of their feasibility and their effect on patient survival.

Evidence concerning other diagnostic tools is limited. However, further research is required since their use appears promising.

Conflict of Interest Statement

The authors have no conflict of interest to declare.

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Author Contributions

All authors contributed to the conception and design of the work. Acquisition, analysis, and interpretation of data and drafting of the manuscript was done by Van den Bempt S., with input from and critical revision by Wauters L. and Dewolf Ph. Dewolf Ph. supervised, edited, and finalized the manuscript. All authors gave final approval of the manuscript.

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