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Pulseless electrical activity cardiac arrest: time to amend the mnemonic “4H&4T”?

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Summary

BACKGROUND: Pulseless electrical activity (PEA) cardiac arrest is characterised by a residual organised electrical activity. PEA is frequently induced by reversible conditions. The mnemonic “4H&4T” was proposed as a reminder to assess for Hypoxia, Hypovolaemia, Hypo/Hyperkalaemia, Hypothermia, Thrombosis, cardiac Tamponade, Toxins, and Tension pneumothorax. Other potential aetiologies have been identified, but their respective probability and frequencies are unclear. The aim of this study was to analyse the aetiologies of PEA out-of-hospital cardiac arrests and to evaluate their relative frequencies.
METHODS: This was a retrospective study based on data routinely and prospectively collected. All adult patients with PEA as the first recorded rhythm and admitted between 2002 and 2012 to the emergency department (ED) after return of spontaneous circulation or under resuscitation were included.
RESULTS: A total of 1,866 out-of-hospital cardiac arrests were included. PEA was the first recorded rhythm in 232 adult patients (12.4%) and 144 of these were admitted to the ED. The mean age was 63.8 ± 20.0 years, 58.3% were men. The survival rate at 48 hours was 29%. Hypoxia (23.6%), acute coronary syndrome (12.5%) and trauma (12.5%) were the most frequent causes. We were unable to identify a specific cause in 17.4%. Pulmonary embolism, hypovolaemia, intoxication and hypo/hyperkalaemia occurred in fewer than 10% of the cases. Nonischaemic cardiac disorders and intracranial haemorrhage occurred in 8.3% and 6.9%, respectively.
CONCLUSIONS: Intracranial haemorrhage and nonischaemic cardiac disorders represent significant causes of PEA, with a prevalence equalling or exceeding the frequency of classical 4H&4T aetiologies. These conditions are potentially accessible to simple diagnostic procedures (computed tomography or echocardiography).

Key words: *cardiac arrest; pulseless electrical activity; aetiologies; nonischaemic cardiomyopathy; intracranial haemorrhage; ACLS; advanced coronary life support*

Abbreviations

CPR: cardiopulmonary resuscitation
ED: emergency department
OCC: other (nonischaemic) cardiac causes
OHCA: out-of-hospital cardiac arrest
PEA: pulseless electrical activity
PEMS: prehospital emergency medical service

Introduction

Pulseless electrical activity (PEA) cardiac arrests present with residual organised electrical activity on the electrocardiogram that would normally be associated with a palpable pulse. The absence of mechanical contractions and palpable pulse are due to either the absence of synchronous myocyte depolarisation, vascular failure or alterations of cardiac function [1, 2]. Some patients present with residual mechanical myocardial contractions, but these are too weak to produce a detectable pulse or blood flow [3].
In past decades, the relative incidence of PEA has regularly increased compared with ventricular fibrillation or pulseless ventricular tachycardia, and is now reported to be between 19%–29% [4, 5]. Patients suffering out-of-hospital cardiac arrests (OHCAs) presenting initially with PEA have a poor prognosis, with a survival rate to the hospital discharge estimated as between 2%–5% [6, 7].
Out-of-hospital management of PEA is mainly based on cardiopulmonary resuscitation (CPR) and on early epinephrine administration. Simultaneously to these measures, identification of potential causes is warranted [3, 8]. The mnemonic “4 (or 5) Hs and Ts”, first described by Kloeck et al. in 1995 [9], is proposed as a reminder to assess for Hypoxia, Hypovolaemia, Hypo-/Hyperkalaemia, Hypothermia, Thrombosis (cardiac or pulmonary), cardiac Tamponade, Toxins, and Tension pneumothorax. These causes are potentially reversible during the out-of-hospital period or shortly after admission in the emergency department (ED), thereby promoting the concept of “reversible causes” [3, 8]. Nevertheless, no study has been published that prospectively evaluates the aetiologies of PEA OHCA and their relative prevalence. These causes are not comprehensive and other pathologies have been identified as potential aetiologies, including intracranial haemorrhage [10, 11], severe sepsis [12], nonischaemic myocardial dysfunc-

tion, or primary cardiac arrhythmia [13]. The respective frequencies of these aetiologies are unclear. Until now, they are not included into the resuscitation guidelines, with the risk that they will not be suspected in OHCA, and that a significant number of critical, but potentially reversible conditions, could be missed. The aim of this study was to analyse the aetiologies of PEA OHCA, in order to evaluate the relative frequencies of each cause.

Materials and methods

Setting and design

This retrospective study took place at the Lausanne University Hospital (CHUV). The CHUV is a 1,000-bed university hospital located in western Switzerland and covers a population of 300,000 persons. The prehospital emergency medical service (PEMS) has a unique emergency dispatch centre (EDC), using a specific keyword-based dispatch protocol including dispatcher-assisted CPR. Trained paramedics or emergency medical technicians constitute the initial response on site. Emergency physicians may be dispatched on scene in the case of cardiac arrest, major trauma, respiratory distress,, or other life-threatening emergencies, or secondarily at the request of the paramedics on site.

The advanced cardiac life support algorithm used by the EMS included cardiopulmonary resuscitation, intravenous or intraosseous access, epinephrine and amiodarone administration, defibrillation in the case of a shockable rhythm, endotracheal intubation with end-tidal CO_2 monitoring. In accordance with previous guidelines, atropine had been used systematically until the end of 2011 [3, 8].

No mechanical chest compression device was available during the study. In the case of return of spontaneous circulation or successful resuscitation, the patient is transported to the hospital. PEA without return of spontaneous circulation could be transported to the hospital, particularly if pulmonary embolism, hypothermia, drug intoxication or cardiac tamponade are suspected. The decision was left to the discretion of on-scene EMS personal.

Data collection

This study was based on data routinely and prospectively collected in a registry for each PEMS intervention. Ambulance reports comprise EDC data, evaluation of the patient on site (vital signs, severity, life-saving measures), and actions undertaken (e.g. hospital transport, death on site). Emergency physician reports contain clinical conditions, life-saving measures, treatments and procedures on site, and immediate outcome of the patient at time of hospital admission. Hospital diagnosis, specific interventions (surgical procedure, percutaneous coronary angioplasty) and outcomes are systematically collected after 48 hours. The recorded data are in agreement with the Utstein recommendations for uniform reporting of OHCA [14].

Classification of pulseless electrical activity aetiologies

The description of the PEA aetiologies was retrospective and based on the patient's data, including the prehospital report, the hospital therapeutic and diagnostic data, the final diagnosis and the 48-hour survival rate. The aetiologies of PEA cardiac arrest were classified into subgroups, based on the classical H and T classification, supplemented by four other subgroups: trauma, intracranial haemorrhage, other cardiac causes (OCC) and undetermined cause (table 1).

Population

All adult patients treated from 1st January 2002 to 31st December 2012 by the PEMS for out-of-hospital cardiac arrest, with PEA as the first recorded rhythm, and admitted to the ED of the Lausanne University Hospital were included.

Patients were excluded if they either (1) presented with cardiac arrest initially due to pulseless ventricular tachycardia, ventricular fibrillation or asystole as first recorded rhythm; (2) were declared dead on scene or during transport; (3) suffered from an in-hospital cardiac arrest; (4) were aged less than 16 years; or (5) if the medical record was missing.

Statistical analysis

All individual data were anonymised and entered into an anonymous computerised database. Categorical data are presented as counts and percentage frequencies. Continuous variables are shown as means ± standard deviations. Statistical analyses were performed using Stata Statistical Software Release 12.0 (Stata Corporation, College Station, TX).

Ethical aspect

The study protocol was agreed by the Ethics Committee of the University, as well as by the healthcare authorities of the state.

Results

During the study period, there were 1,866 OHCAs treated by the PEMS. PEA was the first recorded rhythm in 232 adult patients (13.8%). We excluded 96 patients: 76 were declared dead on scene, 4 were less than 16 years old, 3 died during transport, 3 were in-hospital cardiac arrests and for 2 patients the medical records were missing. Finally, 144 patients with a PEA cardiac arrest admitted to the ED were included in the analysis (appendix). The mean age was 63.8 ± 20.0 years, 58.3% were men and the survival rate at 48 hours was 29%. The survival rate at hospital discharge was 13.4% (n = 20) for the patients admitted in the ED and 8.6% of the 232 PEA cardiac arrests. Eight patients (40%) who survived to hospital discharge presented with primary hypoxia, mainly related to upper airways obstruction, but this result was statistically nonsignificant ($p > 0.05$).

During the first 48 hours after admission in the ED, 46 patients (31.9%) benefited from an echocardiographic investigation, 20 (13.9%) from a head or "total body" CT-scan and 14 (10%) from a percutaneous coronary angioplasty. We found 32 different causes of OHCA PEA for 119 patients, which we have classified into four groups (nine subgroups). For 25 patients (17.4%), we were unable to attribute a specific cause for the PEA cardiac arrest and the patients were thus classified as undetermined causes (table 2).

Hypoxia (23.6%), acute coronary syndrome (12.5%) and trauma (12.5%) were the three most frequent causes. Pulmonary embolism, hypovoalaemia, intoxication and hypo/hyperkalaemia occured in fewer than 10% of the cases (7.6%, 5.6%, 3.5% and 2.1%, respectively). Nonischaemic cardiac causes (other cardiac causes) and intracranial haemorrhage occurred in 8.3% and 6.9%, respectively. We had no case of isolated tension pneumothorax, cardiac tamponade or hypothermia in our population as the main cause of PEA cardiac arrest. Patients with trauma-related conditions were younger (mean 52.9 ± 20.3 vs 65.0 ± 19.6, $p <0.05$), received more frequently dispatcher-assisted CPR (76% vs 41%, $p <0.05$), were less frequently administered epinephrine (67 % vs 87%, $p <0.05$) or defibrillation (17% vs 33 %, $p <0.05$), and presented a worse survival rate at 48 hours (22% vs 30%, $p <0.05$).

Discussion

The main result of our study was the important variety of PEA causes and the relatively low proportion of mnemonic-classical Hs and Ts. According to our results, the classical mnemonic Hs&Ts represent only 54.9% of the aetiologies. Other aetiologies were suspected in 27.8% of the cases (n = 40), and mainly involved trauma (12.5%), other cardiac causes (8.3%), and intracranial haemorrhage (6.9%).

Hypoxia and cardiac pathologies represent the main causes of PEA in our study. These results are in accordance with previous studies, which usually showed that hypoxia and cardiac ischaemic pathologies are the main causes of PEA OHCA [6, 15, 16]. The distribution of our cases nevertheless revealed a high prevalence of other cardiac causes, these conditions being heterogeneous by nature and their management requiring a specific diagnosis. However, it is important to consider the possibility of nonischaemic cardiac causes in the differential diagnosis of PEA OHCA. In the ED, bedside echocardiography may be of major interest in these cases [17].

Traumatic pathologies deserve a particular commentary. Trauma-related cardiac arrest is a rare condition, involving mainly young patients with asystole as initial rhythm. Despite resuscitation attempts they are associated with a highly limited survival rate. Trauma is not a specific cause of PEA as it may induce several types of injuries (severe bone fractures, haemo/pneumothorax, cardiac tamponade, flail chest, brain injury, spinal cord trauma, penetrating trauma, haemorrhage or visceral injuries). It is therefore often not

Table 1: Classification of pulseless electrical activity cardiac arrest according to aetiology.

Groups	Subgroups	Related aetiologies
H	Hypoxaemia	Acute pulmonary oedema
		Hanging
		Drowning
		Pneumonia
		Massive haemoptysis
		Upper airways obstruction
		Respiratory failure
		Pulmonary aspiration
	Hypovolaemia	Traumatic haemorrhage
		Ruptured aortic aneurysm
		Upper gastrointestinal bleeding
	Hyper/hypokalaemia	Hyper/hypokalaemia
T	Toxic	Carbon monoxide
		Methadone
		Benzodiazepine
		Opioid
	Acute coronary syndrome	STEMI
		Non-STEMI
	Pulmonary embolism	Massive pulmonary embolism
		Non-massive pulmonary embolism
O	Trauma:	Motor vehicle accident
		Fall
		Traumatic brain injury
	Intracranial haemorrhage	Subarachnoid haemorrhage
		Intracerebral haemorrhage
	Other cardiac causes	Long QT
		Malignant arrhythmia
		Pacemaker dysfunction
		Valvular disease
		Graft rejection
		Congenital heart disease
U	Undetermined	Missing data
		Diagnostic uncertainty

H and T = the classical 4Hs and 4Ts; O = other; U = undetermined; STEMI = ST elevation myocardial infarction possible to identify a unique traumatic cause of CA and this category is frequently excluded from analysis of cardiac arrests, or investigated separately [18, 19].

Finally, we found a high prevalence of intracranial haemorrhage in our study (6.9%). Intracranial haemorrhage is a recognised potential cause of cardiac arrest and PEA, with a postulated mechanism involving catecholamine increase [10, 20]. It is a potentially reversible cause and could be easily diagnosed with a local CT scan in the ED [10]. We therefore propose a new mnemonic, including intracranial haemorrhage and OCC and based on a “6H&4T” systematic approach (table 3).

Limitations

PEA was the first rhythm in 13.8% of our patients. This relatively low proportion of PEA may be related to specific local conditions, to the patients (age, comorbidities and aetiologies) or to the PEMS system (response time, bystander cardiopulmonary resuscitation, procedures at the site) [4, 6]. The limited amount of information for patients declared dead before arrival in the ED is a noticeable limitation. We included only patients suffering from PEA OHCA and admitted alive into the ED. These cases may represent a particular sample of the PEA population with a potential selection bias. The limited number of patients precludes any further multivariate statistics of factors related to survival or mortality. The retrospective method warrants exhaustive evaluation of the cases, limiting the information in some cases and reducing the diagnostic accuracy. A previous study demonstrated that there might be differences between clinical diagnosis and autopsy findings, especially in the case of vascular ruptures or pulmonary embolism [14]. Similarly, our higher rate of intracranial haemorrhage may be explained by a higher rate of CT scans performed, compared with other previous studies. Finally, the specific context of this study restrains the extrapolation of the results to other EMS systems.

Conclusion

In our patients, intracranial haemorrhage and OCC represent notable causes of PEA in OHCA, with a prevalence equalling or exceeding the frequency of classical 4H&4T aetiologies. Even pulmonary embolism, which is often described as a frequent and classic cause of PEA, occurred only in 7.6% of our cases [21, 22]. Intracranial haemorrhage and nonischaemic cardiac disease are potentially accessible to simple diagnostic procedures and should be included in a 6H&4T mnemonic.

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Table 2: Distribution of the aetiologies of pulseless electrical activity out-of-hospital cardiac arrest.

	No.	**%**
Hypoxia	34	23.6
Undetermined	25	17.4
Acute coronary syndrome	18	12.5
Trauma-related conditions	18	12.5
Other cardiac causes*	12	8.3
Acute pulmonary embolism	11	7.6
Intracranial haemorrhage†	10	6.9
Hypovolaemia	8	5.6
Intoxication	5	3.5
Hypo/hyperkalaemia	3	2.1
Total	**144**	
Classical 4Hs	45	31.3
Classical 4Ts	34	23.6
Other conditions	40	27.8
Undetermined	25	17.4

* Malignant arrhythmia (long QT syndrome, ventricular tachycardia, familial sudden cardiac death, n = 8), pacemaker or implantable defibrillator dysfunction (n = 2), acute valvular disease (n = 1), cardiac allograft rejection (n = 1).
† Intracranial haemorrhage: subarachnoid haemorrhage (n = 8), subdural haematoma (n = 1), intracerebral haemorrhage (n = 1)

Table 3: New mnemonic with 6H&4T.

Hypoxaemia	**T**oxic
Hypovolaemia	**T**hrombosis (cardiac, pulmonary)
Hypo/hyperkalaemia/acidosis	Cardiac **t**amponade
Hypothermia	**T**ension pneumothorax
Haemorrhage – intracerebral	
Heart disease – other	

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Appendix

Study flowchart