The Lazarus phenomenon

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Summary
The Lazarus phenomenon or the unassisted return of spontaneous circulation after cardiac arrest is a grossly underreported phenomenon in medical literature which essentially implies the ‘resurrection’ of an individual after cardiac arrest. Although there have been a handful of such cases reported, the clinical incidence and significance may be underestimated. Because of the presumed infrequency of this condition, there are no studies specifically researching Lazarus phenomenon in scientific literature. This review intends to systematically present current and past knowledge on this rare but definitive phenomenon. Research databases namely Google Scholar, Science Direct, Medline and PubMed were utilized. Only articles which identified cases where the return of spontaneous circulation occurred after cessation of Cardiopulmonary Resuscitation (CPR), and review articles on the entity were included. The mentioned databases were searched using the terms ‘Lazarus phenomenon’, ‘cardiopulmonary resuscitation’ and ‘return of spontaneous circulation’. A literature review was synthesised based on articles meeting the eligibility criteria to better understand the phenomenon of return of spontaneous circulation.

Keywords
Lazarus phenomenon, return of spontaneous circulation, CPR, resuscitation, cardiac arrest, myocardial infarction

Introduction
The term Lazarus phenomenon was first coined by Bray in 1983 because of its resemblance to the biblical story of Lazarus. Lazarus phenomenon is defined as the unassisted return of spontaneous circulation after cardiac arrest. Although a rare phenomenon, it is probably an under-reported one. The only logical explanation seems to attribute such an event to impaired venous return and auto-peak end expiratory pressure. With scientific explanations in literature being unsatisfactory, a proper review of the event is warranted to synthesise the available data into a meaningful presentation to aid in developing a better understanding of this entity.

Methods
Research databases namely Google Scholar, Science Direct, PubMed and Medline were searched using the search terms ‘Lazarus Phenomenon’, ‘cardiopulmonary resuscitation’ and ‘return of spontaneous circulation’.

Eligibility criteria
Only articles which identified cases where return of spontaneous circulation occurred after cessation of Cardiopulmonary Resuscitation (CPR) and review articles on the entity were included.

Information sources
Google Scholar, Science Direct, PubMed and Medline.

Search
The search terms ‘Lazarus phenomenon’, ‘cardiopulmonary resuscitation’ and ‘return of spontaneous circulation’ were utilized.

Study selection
Over 10,000 articles were screened to select the appropriate ones. All the articles were critically scrutinized to isolate the ones providing a review of the Lazarus phenomenon or ones which reported a return of spontaneous circulation after cessation of CPR.

So far, 38 cases of delayed return of spontaneous circulation have been published in medical literature.

The majority of the articles dealing with this phenomenon were published in journals of anaesthesia and resuscitation.

Incidence
Gerard et al. reported that almost 50% of French physicians have encountered autoresuscitation in
clinical practice. Dhanani et al. stated that 37% of Canadian intensivists have seen at least one case of autoresuscitation in their clinical practice.

Pre-disposing conditions

The cases of reported Lazarus phenomenon have had certain factors which were commonly present in conjunction or individually in patients who demonstrated this phenomenon. The following pre-disposing conditions have been noted (Table 1):

Aetiopathogenesis

A number of pathological mechanisms have been touted to be responsible for the occurrence of return of spontaneous circulation. It is imperative at this stage to clarify certain aspects of the Lazarus phenomenon. Scientific literature regarding this entity exists primarily in the form of case reports. It is crucial to understand that such reports have detailed the ‘resurrection’ of a patient based solely on a retrospective understanding of what might have happened. In the true sense of the term, one can term a patient ‘resurrected’ after having undergone no medical intervention. That would truly be a resurrection. However, in light of the data that the author assembled based on his literature review, the return of spontaneous circulation can be grossly attributed to the medical interventions which were instituted (including the withdrawal of resuscitative efforts). A possible way to categorise the mechanisms of the Lazarus phenomenon can be to group the aetiologies into those said to be explained post-true cardiorespiratory arrest and those in the absence of the same based on certain other factors such as overlooking minimal vital signs on the part of the physician.

Positive end expiratory pressure (PEEP)/hyperinflation (dynamic pulmonary hyperinflation)

Several authors cite auto-PEEP/hyperinflation as a cause for the return of spontaneous circulation. Hyperventilation is one of the most common aetiopathogenesis for the occurrence of a return of spontaneous circulation.

The link between mechanical ventilation of patients with obstructive ventilatory defects and circulatory failure was first demonstrated in 1982. Rapid manual ventilation without adequate time for exhalation during CPR leads to dynamic hyperinflation of lungs.

### Table 1. Pre-disposing conditions

| Condition                          | Accompanying factors                                      |
|------------------------------------|-----------------------------------------------------------|
| Acute myocardial infarction/ischaemia | Age > 60 years; dehydration; collateral circulation (chronic ischaemia) |
| Electromechanical dissociation/pulseless electrical activity (PEA) | Chronic obstructive pulmonary disease; asthma |
| Hyperkalaemia                      | Renal failure/metabolic disorder                         |
| Hypovolaemia                       | Bleeding                                                  |

### Table 2. Drugs and dosages reported by various authors in literature said to have precipitated the return of spontaneous circulation.

| Author                     | Drug          | Dose    |
|----------------------------|---------------|---------|
| Maeda et al.               | Atropine      | 2 mg    |
|                            | Adrenaline    | 1 mg    |
|                            | Noradrenaline | 5 mg    |
| De Salvia et al.           | Noradrenaline | 5 mg    |
| Adanali M et al.           | Adrenaline    | 11 mg   |
| Kämäräinen et al.          | Adrenaline    | 8 mg    |
|                            | Amiodarone    | 450 mg  |
| Cummings and Noviski       | Calcium bicarbonate | Not reported |
|                            | Sodium bicarbonate |          |

### Table 3. Role of true cardiopulmonary arrest in the aetiology of the Lazarus Phenomenon.

| Role                              | Aetiology                        |
|-----------------------------------|----------------------------------|
| True cardiopulmonary arrest       | PEEP                             |
|                                   | Myocardial reperfusion           |
|                                   | Myocardial stunning              |
|                                   | Alkalosis                        |
|                                   | Hypothermia                      |
|                                   | Hyperkalaemia                    |
|                                   | Q-T syndrome                     |
|                                   | Transient asystole               |
|                                   | Cardiomyopathy                   |
| Other factors (physician oversight/inexperience) | Minimal vital signs |
|                                   | Delayed action of drugs          |
Mechanism

Hyperinflation (resuscitative efforts) → elevated intrathoracic pressure → gas trapping → increased positive end-expiratory pressure (auto-PEEP) → delayed venous return to the heart → reduced cardiac output → cardiac arrest (in cases of obstructive pulmonary disease).

Recommendation

Intersperse chest compressions and ventilatory efforts during CPR with brief periods to allow the patient to exhale, hence, preventing gas trapping.

The beat of the popular Bee Gees song ‘Stayin’ Alive’ has been put forth by the American Heart Association to serve as a guide for physicians to base their resuscitative efforts on.8 However, another scenario where such a situation was emulated to the same result albeit as a result of readjustment of ventilator settings is interesting to note:

A patient with respiratory failure of asthmatic aetiology, the blood pressure in this patient was undetectable for 5 min after initiating artificial ventilation with tidal volume of 700 mL and respiratory rate of 25 breaths per minute. Even after inotrope administration, the systolic blood pressure was not in excess of 70 mm of Hg. The ventilator was subsequently adjusted to a respiratory rate of 6 breaths per minute and a tidal volume of 400 mL; after these adjustments were made, the blood pressure was noted to rise to 126/84 mm of Hg.5 This case, while not exactly following the aetiological mechanism described above, does in fact aid to recognise the fact that hyperventilation is a factor to reckon with in the aetiology of spontaneous return of circulation.

Myocardial reperfusion

Myocardial ischemia is caused by a deficiency or loss of adequate perfusion to the myocardium. Myocardial reperfusion as a consequence of return of spontaneous circulation can occur due to the spontaneous dislodging of embolised endovascular plaque from the coronary artery. This can occur as a consequence of resuscitative efforts in which external compressions applied, increase the intra-thoracic pressure, which coupled with adequate periods for exhalation can bring about a dislodgement of thrombus as described.4,6

Alkalosis

A normal body pH is 7.35–7.45. A pH below 7.35 places the patient in a state of acidosis. During severe acidosis, ventricular fibrillation and other types of arrhythmias are likely. The contractility of the musculature is depressed, there is hypotension and reduced hepatic blood flow. The administration of bicarbonates shifts the patient towards homeostasis, and there is exhalation of CO2 due to a shift in equilibrium towards alkalosis. However, bicarbonate administration has its pitfalls, it can reduce systemic vascular resistance and compromise CPR; it can result in hyperosmolarity (hypernatremia); can paradoxically cause intracellular acidosis; it can exacerbate central venous acidosis and subsequently inactivate catecholamines being administered; lastly, it may even cause extracellular alkalosis and inhibit oxygen release. The new American Heart Association guidelines revised after 2000 state that bicarbonate administration is to be done at the discretion of the physician.9

Delayed action of drugs

Return of spontaneous circulation can also be attributed to the delayed action of drugs,4 which were administered as part of and during resuscitative efforts, although this cannot be termed as a resurrection in the truest sense of the word. It does, however, point out the fact that a delayed drug action could lead physicians to believe that an actual resurrection did in fact occur. Such a misconception would obscure the understanding of this phenomenon, and it is important to clarify the validity of a ‘resurrection’ which might occur as a result of this mechanism. A suggested scenario is where drugs are administered via a peripheral line.1 As a result of impaired venous return, drugs administered through a peripheral line are unable to reach the heart and thus are incapable of exerting their desired effects. A contradiction to this is an alternate scenario in which drugs are administered via a central line and do indeed reach their target site. This mechanism, seemingly appropriate, is still difficult to completely accept.5 Drugs namely, inotropes such as atropine,10 adrenaline10,11 have been reported to be administered during resuscitative efforts. Latency of catecholamine action has also been proposed as a mechanism for the occurrence of return of spontaneous circulation (ROSC).

Catecholamines might facilitate self-defibrillation by their effects on ventricular fibrillation morphology and maintenance of cellular excitability.7

Mild hypothermia

Mild hypothermia has been reported to improve defibrillation success and resuscitation outcome.
from ventricular fibrillation. A reported case attributing the return of spontaneous circulation to mild hypothermia describes the resuscitative efforts to have been conducted on a windy, chilly day, outdoors which was incidentally where emergency medical personnel conducted their resuscitative efforts. The temperature of this patient was recorded to be 31.4°C.

After cessation of CPR, the patient was pronounced dead and placed in a body bag. It was when the bag was opened for recording details that the patient was found to be breathing spontaneously. The revival of the patient was attributed to the fact that placing the patient in the body bag provided the increase in energy necessary for revival.7

Hyperkalaemia

Hyperkalaemia is one of the most common causes for return of spontaneous circulation. Intra-cellular hyperkalaemia renders the myocardium refractile for extended periods of time. A case reported in literature describes a 68-year-old lady with cardiac arrest due to hyperkalaemia who did not respond to CPR and conventional treatment for up to 100 min, but later responded to dialysis and made a complete recovery.1,5

Q-T syndrome

Q-T syndrome can be of long or short variety, furthermore, long Q-T syndrome is a heterogeneous group of conditions that can have either a genetic origin or can be of an acquired nature. Spontaneous termination of ventricular fibrillation is an uncommon occurrence but has been found to be associated with the reperfusion of the myocardium, silent ischaemia and Q-T syndrome.7

Myocardial stunning/myocardial ischemia

Extended periods of myocardial dysfunction following an episode of myocardial ischemia can occur. Following this, functional recovery of the myocardium can take several hours.

An acute cardiac event was the most frequently identifiable cause of Lazarus phenomenon in a comprehensive review.1,5

Transient asystole

Asystole or pulseless electrical activity following countershock or ventricular fibrillation (prolonged) occurs in around 60% of patients. There has been a reported case in which an asystole which primarily appeared refractory could be transformed into a sinus rhythm after an approximate resuscitation time of 45 min without leaving a severe neurological deficit.1,4–6

Cardiomyopathy

There has been a reported case of the Lazarus phenomenon occurring in a patient with underlying cardiomyopathy. Patients with underlying cardiac conditions have a poorer response to CPR as compared to those with an absence of a cardiac condition. However, in a reported case, the patient demonstrated a delayed response to CPR and additionally even underwent a complete recovery of higher cortical functions after 10 min of cardiac arrest.1

Unobserved minimal vital signs

The so-called revival of the patient can also be attributed to an inadequacy on the part of the physician as well where he/she is unable to monitor minimal vital signs,2 such as the carotid pulse and the spontaneous breathing of the patient before pronouncing him as dead.7 It must be clarified that unobserved minimal vital signs do not obviously lead to a resurrection. It is merely to underscore the importance of the fact that a physician may be led to believe that a resurrection occurred, while it was an oversight on his/her part to have overlooked the presence of vital signs in the first place.

In one relatively unconventional study involving traditional Chinese medicine, the stimulation of the Yongquan K1 point was described. This involves stimulation of the said point located one-third the antero-posterior distance of the plantar surface of the foot.

Thirty in-hospital patients with life-threatening conditions were treated using this technique and the results reported by the author, in general, pointed towards the conclusion that this is a viable method to induce spontaneous return of circulation in patients with life-threatening pathologies such as: severe arterial hypertension, ischaemia, crushed chest, skull trauma, post-surgical shock, gas embolism, sepsis-induced renal failure and ventricular fibrillation. The author reported that one such patient reporting with an incident of electrocution could not be revived by this method.12

Diagnoses at the time of death

Patients reported with the occurrence of the Lazarus phenomenon have been noted to have a cardiac accident2,4 namely arrhythmia, ischaemic stroke, haemorrhage, brainstem death as the diagnoses at the time
of death. Incidentally, the heart attack survival rate of patients has been noted to be 35–40% for out hospital and 10–12% for patients on discharge.\textsuperscript{6}

Electromechanical dissociation has also been noted to be an associated pathology at the time of death in patients exhibiting autoresuscitation.\textsuperscript{6} Additionally, a case has been reported in which a patient reporting with autoresuscitation was suffering from Duchenne’s muscular dystrophy accompanied by dilated cardiomyopathy. This particular case was reported to have had a complete recovery of higher cortical functions 10 min subsequent to cardiac arrest.\textsuperscript{1}

Recreational drug\textsuperscript{1,5} use, asystole, multiple trauma, intoxication and drowning have also been reported to be diagnoses at the time of death in patients exhibiting autoresuscitation.\textsuperscript{2} Autopsy findings in a case exhibiting autoresuscitation revealed early inferior wall myocardial infarction and hypoxic brain damage.\textsuperscript{4}

Time that has been spent on resuscitative efforts has not been correlated with the phenomenon of autoresuscitation. Cases in which CPR efforts lasted 30 min,\textsuperscript{1} 45 min,\textsuperscript{3} 75 min,\textsuperscript{1} 15 min, 26 min and 40 min have been reported to have subsequently gone on to produce autoresuscitation.

Pulseless electrical activity (PEA) has been touted as the usual reason due to which CPR efforts were ceased for a patient.\textsuperscript{1}

Recovery

Neurological recovery

The neurological recovery in patients can range from partial to complete, i.e. 100%. Such recovery has been reported in 45% of cases.\textsuperscript{1,4,5} There has been a reported case of Lazarus phenomenon who went on to achieve a neurological recovery of 100%.\textsuperscript{1}

Krarup et al.\textsuperscript{10} reported on one of the few cases of autoresuscitation with good neurological outcome.\textsuperscript{2} It has been reported that survival with minimal neurological disability is possible after extracorporeal membrane oxygenation (ECMO). This has been noted in cases with refractory cardiac arrest in which CPR efforts were instituted.\textsuperscript{3}

After autoresuscitation, patients have made neurological recovery to place them in the cerebral performance category of 1–2.\textsuperscript{12} Another case was reported to have been placed in a CPC of 3.\textsuperscript{7}

The concept of neurological recovery has been compared to hibernation, where certain mammals survive in conditions mimicking those of cardiac arrest without neurological damage. This is however speculative.\textsuperscript{1}

Functional recovery

Maleck et al. reported that out of a total of 25 patients examined, only one survived for a period greater than 180 days subsequent to functional recovery.

This case was that of a 36-year-old woman with a cardiac arrest secondary to a serious asthma attack. Spontaneous recovery of cardiovascular and respiratory functions occurred a mere 3 min after 25 min of resuscitative efforts were discontinued.\textsuperscript{6}

Three other patients survived for a period greater than 90 days, two of which had a myocardial infarction, while only one of these suffered from asystolia having an apparent death interval of 20 min, while the other recovered in a few seconds after receiving 50 min of CPR during which electromechanical dissociation was demonstrated. A number of patients failed to survive beyond 24 h or did not show a functional recovery.\textsuperscript{6}

Reasons for underreporting

The Lazarus phenomenon is a grossly underreported event. The reason for these can be attributed to the fact that medicolegal\textsuperscript{1,5,7} issues are brought to light in cases which are pronounced dead which later turn out to have been alive. The professional expertise of the resuscitating doctor can be brought into question, not to mention the fact that such an event can lead to disrepute among colleagues.\textsuperscript{13} Another pertinent question that arises is whether the death of a particular patient occurred as a result of premature cessation of resuscitative efforts or the omission of continued resuscitation.\textsuperscript{5}

Recommendations

A watchful waiting period of 10–15 min after cessation of CPR is advisable.\textsuperscript{1,2,7,11,14}

Five minutes of absent arterial pulse when determining circulatory death after 30 min of unsuccessful CPR before proceeding with organ donation in uncontrolled non-heart beating.

A period of careful observation to confirm death subsequent to discontinuation of resuscitation to provide appropriate medical care, regardless of the duration or quality of the advanced life-supporting efforts instituted.

The absence of return of spontaneous circulation anytime during 30 min of cumulative advanced cardiac life support is a criterion for termination of resuscitative efforts.\textsuperscript{4}

Careful bed-side observation for 10 min to confirm death after discontinuation of CPR assisted by multiple lead electrocardiogram monitoring (since, such a
spontaneous recovery has been observed within a period of 10 min after cessation of CPR efforts in most cases.\textsuperscript{4}

Rules of termination of resuscitation – (1) event not witnessed by EMS personnel (2) no automated external defibrillator used or manual shock applied in out-of-hospital setting (3) no Return of Spontaneous Circulation in hospital setting (4) arrest not witnessed by by-stander. (5) No by-stander administered CPR.\textsuperscript{14}

The European Resuscitation Council recommends upholding treatment during an ongoing ventricular fibrillation.\textsuperscript{14} Spontaneous termination of ventricular fibrillation is an uncommon event with only a few reported cases.\textsuperscript{7} According to the European Resuscitation Council guidelines for Resuscitation, resuscitation is generally recommended to be continued as long as ventricular fibrillation persists.\textsuperscript{7}

Awareness

A national survey based on a randomized sample of French pre-hospital emergency physicians was performed in March 2013.\textsuperscript{13} None of the assessed physicians were aware of the term ‘Lazarus phenomenon’; however, the majority of them knew that autoresuscitation exists.

Physicians reported that they knew of the existence of autoresuscitation by:

Facing it – 54%, Sharing a colleague’s experience – 31% and through post-graduate and continuing medical education events – 4%.\textsuperscript{13}

Conclusion

Despite numerous cases of spontaneous restoration of circulation being reported, the Lazarus phenomenon remains an underreported entity. Trauma surgeons and physicians, who are constantly dealing with emergency situations, should be aware of such an occurrence, the pathophysiology surrounding it and the medico-legal implications that it entails. Recognition of this phenomenon and addressing medical negligence issues surrounding it are warranted in order to promote further reporting of this little known entity.

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