Dissertation

Post-resuscitation pneumothorax – an underestimated complication?

Submitted by

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For the Academic Degree of

Doctor of Medical Science

(Dr. scient. med.)

At the

Medical University of Graz

Department of Anaesthesiology and Intensive Care Medicine

under the Supervision of

Ao.Univ.-Prof. Dr. med. univ. Gerhard Prause

2025

Statutory Declaration

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Graz, 11/07/2025
Dr. med. univ. Daniel Auinger eh

Disclosures

Part of this thesis has been published in the following two articles:

Daniel Auinger[1], David Hötzer[1], Paul Zajic[1], Simon Orlob[2], Stefan Heschl[1], Stephanie Fida[2], Philipp Zoidl[1], Gabriel Honnef[1], Herwig Friedl[3], Freyja-Maria Smolle-Jüttner[4] and Gerhard Prause[1]: *Post-resuscitation pneumothorax: retrospective analysis of incidence, risk factors and outcome-relevance. Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine volume 32, Article number: 82 (2024)*

https://sjtrem.biomedcentral.com/articles/10.1186/s13049-024-01260-8

Daniel Auinger[1], Simon Orlob[2], Johannes Wittig[1,5,6], Gabriel Honnef[1], Stefan Heschl[2], Georg Feigl[7,8], Gerhard Prause[1]: *Pneumothorax in a Thiel cadaver model of cardiopulmonary resuscitation. World Journal of Emergency Medicine 2023, Vol. 14, Issue (2): 143-147.*

http://wjem.com.cn/EN/10.5847/wjem.j.1920-8642.2023.029

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Both articles are published as open-access and are available for download via the provided links. All co-authors have given their consent for the use of the associated data in this thesis.

Conflict of interest/Funding

"Pneumothorax in a Thiel Cadaver Model of Cardiopulmonary Resuscitation" was carried out as a co-project alongside *"Reliability of Mechanical Ventilation During Continuous Chest Compressions: A Crossover Study of Transport Ventilators in a Human Cadaver Model of CPR,"* led by Simon Orlob, who received funding to support his research. The project was financed through the Reinhard Malzer Award granted by the Austrian Association of Emergency and Disaster Medicine (ÖNK). The association had no role in the study design, data collection, analysis, or interpretation of results in either project.

The medical devices and equipment used in these studies were generously provided on loan by the following companies: CHEMOMEDICA Medizintechnik und Arzneimittel VertriebsgmbH, Löwenstein Medical Austria GmbH, Sanitas GmbH, GS Elektromedizinische Geräte G. Stemple GmbH, Dräger Austria GmbH, WEINMANN Emergency Medical Technology, and RWM Medizintechnik GmbH. None of these companies had any influence on the study design, data collection, analysis, or interpretation of results in either project.

Gerhard Prause has given a talk at a national symposium upon invitation by RWM Medizintechnik GmbH. All other authors declare no personal conflict of interest.

Acknowledgements

I would like to take this opportunity to express my gratitude to all those who, in various ways, contributed their time and expertise in support of this dissertation, whether directly or indirectly.

First and foremost, I wish to express my profound gratitude to my primary supervisor, Professor Gerhard Prause, for his unwavering support throughout my journey. From my earliest steps in Anaesthesiology, Intensive Care, and Emergency Medicine to my first scientific presentations and publications, his guidance and encouragement have been invaluable. He has been not only a role model and a pioneer in the field of emergency medical care but also someone who has always remained grounded and approachable.

Furthermore, I sincerely thank Professor Freyja-Maria Smolle-Jüttner for supporting my first steps in scientific research as my diploma thesis supervisor and for her continued guidance, expertise, and pragmatism throughout my scientific journey. I am also deeply grateful to Professor Herwig Friedl for his exceptional statistical expertise and meticulous analyses, as well as for his kindness and patience in guiding me through numerous scientific projects.

I would also like to thank Priv.-Doz. Stefan Heschl for his guidance and support throughout this study and the preparation of this dissertation. I deeply appreciate his clinical and scientific expertise, his collegiality, and his pragmatic approach.

Finally, and most importantly, I wish to express my heartfelt gratitude to my partner, family, and friends for their unwavering love, support, and the countless treasured memories, laughter, and experiences we have shared together. Words cannot fully express how much you mean to me.

The author received support and funding from the Medical University of Graz through the Doctoral School Sustainable Health Research. I sincerely thank the body donors whose generous contributions make anatomical research possible.

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Abbreviations and Definitions

ABC – Airway, Breathing, Circulation

ACLS – Advanced Cardiac Life Support

AED – Automated External Defibrillator

AHA – American Heart Association

ALS – Advanced Life Support

ASA – American Society of Anaesthesiologists

AUC – Area Under the Curve

BLS – Basic Life Support

BVM – Bag-Valve-Mask

CAHP – Cardiac Arrest Hospital Prognosis

cm – Centimetre

cm H_2O – Centimetres of Water

CPC – Cerebral Performance Category

CPR – Cardiopulmonary Resuscitation

CT – Computed Tomography

CVC – Central Venous Catheter

CXR – Chest X-Ray

ECG – Electrocardiogram

eCPR – Extracorporeal Cardiopulmonary Resuscitation

eFAST – Extended Focused Assessment with Sonography for Trauma

EMS – Emergency Medical Services

EMT – Emergency Medical Technician

ERC – European Resuscitation Council

$EtCO_2$ – End-Tidal Carbon Dioxide

f – Frequency

GO-FAR – Good Outcome Following Attempted Resuscitation

HEMS – Helicopter Emergency Medical Service

HIV – Human Immunodeficiency Virus

I:E – Inspiration-to-Expiration Ratio

ICU – Intensive Care Unit

IHCA – In-Hospital Cardiac Arrest

ILCOR – International Liaison Committee on Resuscitation

IV - Intravenous

IO – Intraosseous

IQR – Interquartile Range

IRB – Institutional Review Board

kg – Kilogram

M-mode – Motion Mode

MAP – Mean Arterial Pressure

min – Minutes

MIND3 – Minimal Dataset in German Emergency Medicine

mmHg – Millimetres of Mercury

OHCA – Out-of-Hospital Cardiac Arrest

OR – Odds Ratio

PAROS – Pan-Asian Resuscitation Outcomes Study

PBW – Predicted Body Weight

PCI – Percutaneous Coronary Intervention

PEA – Pulseless Electrical Activity

PEEP – Positive End-Expiratory Pressure

PESA – Pre-Emergency Status Assessment

PMAX – Maximum Pressure

POCUS – Point-of-Care Ultrasound

PSP – Primary Spontaneous Pneumothorax

PTOP – Top Pressure

Ptx – Pneumothorax

ROC – Receiver Operating Characteristic

ROSC – Return of Spontaneous Circulation

SD – Standard Deviation

SGA – Supraglottic Airway

SSP – Secondary Spontaneous Pneumothorax

STROBE – Strengthening the Reporting of Observational Studies in Epidemiology

TOR – Termination of Resuscitation

TTM – Target Temperature Management

VA-ECMO – Veno-Arterial Extracorporeal Membrane Oxygenation

VATS – Video-Assisted Thoracic Surgery

VF – Ventricular Fibrillation

V_T – Tidal Volume

VT – Ventricular Tachycardia

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Zusammenfassung

Einleitung

Pneumothorax kann bei der kardiopulmonalen Wiederbelebung (CPR) als unerwünschte Komplikation auftreten, welche fallweise sogar potentiell lebensbedrohlich sein kann. Ziel war es, in zwei Studienprojekten die Inzidenz des Pneumothorax sowohl in Patient*innen nach außerklinischem Herz-Kreislaufstillstand, als auch im Thiel-konservierten Leichenmodell unter simulierter CPR zu untersuchen. Darüber hinaus war in der klinischen Studie die Identifikation von möglichen Risikofaktoren für die Entstehung des Pneumothorax nach CPR sowie dessen Assoziation mit Outcomes von besonderem Interesse.

Methoden

Die klinische Studie wurde durchgeführt als retrospektive Datenanalyse von Patient*innen im Zeitraum von 03/2014 bis 12/2021, die nach außerklinischem Herz-Kreislaufstillstand vom Notarzteinsatzfahrzeug des Universitätsklinikum Graz in Österreich versorgt und anschließend hospitalisiert wurden. Es wurde ein Datensatz entsprechend der Utstein-Style-Empfehlungen erstellt und zur Beurteilung des Vorliegens eines Pneumothorax die erste bildgebende Untersuchung des Thorax nach Krankenhausaufnahme ausgewertet.

Im Rahmen der experimentellen Studie wurden 11 Leichen, die mit der Thiel'schen Methode konserviert wurden, einer simulierten kardiopulmonalen Reanimation mittels mechanischer Kompressionshilfe und mechanischer Beatmung unterzogen. Nach der initialen Rekrutierung der Lunge sowie nach jedem zweiminütigen CPR-Zyklus wurde bilateral eine Lungensonografie zur Pneumothorax-Detektion durchgeführt. Am Ende des Protokolls erfolgte eine bilaterale Finger-Thoracostomie zur Identifikation eines Spannungspneumothorax (erkennbar durch Entweichen von Luft aus dem Pleuraspalt).

Ergebnisse

Wir konnten 237 Patient*innen nach außerklinischem Herz-Kreislaufstillstand in unsere klinische Studie einschließen. Bei 26 Patient*innen (11,0%) war nach Aufnahme im Krankenhaus ein Pneumothorax nachweisbar. Vorbestehende obstruktive Lungenerkrankungen waren signifikant mit dem Auftreten eines Pneumothorax nach CPR assoziiert, diese Subgruppe zeigte eine Inzidenz von 23,0%. Eine signifikante Assoziation des Pneumothorax mit Outcome-Parametern konnte nicht festgestellt werden.

In der experimentellen Studie war bei 8 von 11 (72.7%) Thiel-konservierten Leichen im Verlauf des Studienprotokolls ein Pneumothorax nachweisbar. Dieser zeigte sich in 4 Fällen unilateral, während in den übrigen 4 Fällen ein bilateraler Spannungspneumothorax vorlag.

Die Wahl eines höheren Beatmungsdrucks bei der Rekrutierung der Lunge (35cm H_2O statt 30 cm H_2O) war signifikant (p=0.0024) mit dem Auftreten eines Spannungspneumothorax assoziiert.

Schlussfolgerung

Das Auftreten eines Pneumothorax nach kardiopulmonaler Reanimation ist keine seltene Komplikation und tritt bei mehr als einem von zehn Patient*innen nach außerklinischem Herz-Kreislaufstillstand auf. Vorbestehende obstruktive Lungenerkrankungen scheinen ein relevanter Risikofaktor in der Entstehung zu sein.

Im Rahmen von simulierter CPR an Thiel-konservierten Leichen konnte ein Pneumothorax deutlich häufiger beobachtet werden als in klinischen Kohorten. Der Beatmungsdruck bei der Rekrutierung der Lunge scheint maßgeblich zur Entstehung beizutragen. Diese Erkenntnis sollte bei der Konzeption zukünftiger CPR-Studien mit Thiel-konservierten Leichen berücksichtigt werden.

Abstract

Background

Pneumothorax can arise as an adverse effect of cardiopulmonary resuscitation (CPR) and could pose a potentially life-threatening complication. In two separate study projects we sought to investigate the incidence of pneumothorax both in clinical patients experiencing out-of-hospital cardiac arrest (OHCA) and cadavers embalmed by the Thiel method undergoing simulated cardiopulmonary resuscitation. Moreover, in the clinical study the identification of possible risk factors for development of pneumothorax following CPR and its association with outcomes were of particular interest.

Methods

The clinical trial was conducted as a retrospective analysis of hospitalized OHCA cases from 03/2014 until 12/2021 to which teams of the physician-staffed ambulance based at the University Medical centre of Graz, Austria responded. The dataset was compiled in accordance with the latest Utstein style recommendations. Chest imaging after hospital admission was reviewed to evaluate whether pneumothorax was present or not. Logistic regression analysis was then performed to identify risk factors for development of pneumothorax and assess its relationship with survival to hospital discharge and neurological outcome.

In an experimental study design, eleven Thiel-embalmed cadavers underwent simulated cardiopulmonary resuscitation using a mechanical chest compression device and mechanical ventilators. After initial lung recruitment and following every two-minute cycle of chest compressions bilateral lung ultrasound was performed to test for pneumothorax. At the conclusion of the protocol, bilateral finger thoracostomy was conducted to assess for tension pneumothorax, indicated by a noticeable escape of air.

Results

In the clinical trial we were able to include 237 patients hospitalized after OHCA. In 26 patients (11.0%) pneumothorax was present after admission. History of obstructive pulmonary was significantly associated with post-CPR pneumothorax, with an incidence of 23.0% in this subgroup. Pneumothorax was not identified as a relevant factor to predict outcome.

We detected pneumothorax in 8 out 11 (72.7%) Thiel cadavers at various stages of the study protocol. Pneumothorax was present unilaterally in 4 cases, while the remaining 4 cases showed bilateral tension pneumothorax. Higher recruitment pressure (35cmH2O instead of

30cmH2O) was found to be significantly (p=0.024) associated with the development of tension pneumothorax.

Conclusion

Pneumothorax after cardiopulmonary resuscitation is not an uncommon finding, occurring in more than one out of ten patients after out-of-hospital cardiac arrest. History of obstructive pulmonary disease seems to be a relevant risk factor for development of post-CPR pneumothorax.

In the Thiel cadaver model of simulated CPR, pneumothorax was observed with notably greater frequency than in clinical cases. Recruitment pressure emerged as a key factor influencing its development and should be carefully considered in the design of future CPR studies utilizing Thiel-embalmed cadavers.

Introduction

Summary of the recent state of knowledge

Epidemiology of Out-of-Hospital Cardiac Arrest

Sudden cardiac arrest poses a major health burden and is among the leading causes of death in Europe and worldwide. In a summary including data from the year 2017 from registries in North America, Oceania, Asia and Europe the International Liaison Committee on Resuscitation (ILCOR) estimated an annual incidence of out-of-hospital cardiac arrest (OHCA) treated by emergency medical services (EMS) of 40.8-100.2 individuals per 100,000 population (2). Overall number of OHCA patients in the United States of America and Europe combined has been estimated to be around 700.000 (3). The prospective Europe-wide EuReCa (European Registry of Cardiac Arrest) TWO study found an overall incidence of 56 (range 21-91) per 100.000 population per year (4). Survival to hospital discharge or 30-day survival following EMS-treated OHCA was reported to range from 4.6%-16.4% in 2017 in the above-mentioned ILCOR summary (2). EuReCa TWO found an overall survival rate of 8.0% after OHCA in cases where cardiopulmonary resuscitation (CPR) was initiated.

Variation may arise from many different factors including structures (e.g. EMS systems, first responder utilization, health care system, geographical differences), process and quality of care provided in the individual case (e.g. response times, intra- and post resuscitation treatment), differences in data collection (e.g. use of different definitions, search and verification methods) and the mix of cardiac arrests cases in the particular resuscitation registry (e.g. age structure, socio-economic status, lifestyle, co-morbidities) (5).

In an approach to address these issues in the context of research, the so-called “Utstein style” has been established, a standardised template for reporting data from out-of-hospital cardiac arrest. It was initially developed at a conference at the Utstein abbey in Norway which was attended by representatives from the European Resuscitation Council (ERC), the American Heart Association (AHA), the Heart and Stroke Foundation of Canada and Australian Resuscitation Council (6). It was first published in 1991 and has been repeatedly updated, complemented (e.g. for in-hospital cardiac arrest or special circumstances like drowning) and revised since then (7-10).

Aetiology and Pathophysiology of Cardiac Arrest

In the literature aetiology of cardiac arrest is typically dichotomised as presumed cardiac or non-cardiac, sometimes also as presumed medical or non-medical, based on the initial assessment. On-site assessment, particularly in the out-of-hospital setting and in absence of

obvious causes like trauma only allows for a preliminary diagnosis which sometimes does not reflect the true aetiology. A trial from Melbourne, Australia found 38.6% coroner confirmed non-cardiac causes among 841 young adult OHCA patients with presumed cardiac cause (11). A study analysing patient data from an OHCA registry followed up with hospital data found the majority of non-traumatic OHCA arrest being of cardiac origin (53% - including myocardial infarction, primary arrhythmia, structural heart disease, chronic/prior ischaemia) followed by respiratory (18% - including respiratory failure, hanging and other asphyxia), toxicological (6%), neurological (3%), other (9%) and unknown aetiology (12). Gässler et al. performed a retrospective data analysis of cases from the German Resuscitation Registry including more than 33.000 prehospital cardiac arrest patients. 62.2% cardiac arrests were of cardiac origin, 11.1% due to hypoxia, 3.2% were traumatic cardiac arrests, 1.7% due to exsanguination, 1.4% caused by intoxication and another 1.0% due to metabolic causes. The remaining cases had an aetiology less frequent than 1.0% (including drowning, intracranial bleeding, sudden infant death syndrome, stroke and sepsis) or were of unknown/other aetiology. Significant differences in outcomes (ROSC, survival to hospital discharge, neurological outcome) could be observed in regards of cardiac arrest cause (13). Utstein style classified the following causes of cardiac arrest: Medical (including cases in which there is no obvious cause of cardiac arrest), Traumatic, Drug overdose, Drowning, Electrocution, Asphyxial (10).

History and Development of Cardiopulmonary Resuscitation

First guidelines for cardiopulmonary resuscitation were published in 1966, however the very first attempts to revive apparently dead human beings and animals date back to ancient Rome, Greece and Egypt. There are some reports from 2000 BC of providing breathing support by obtaining direct access to the trachea. The first report of mouth-to-mouth artificial ventilation dates back to 1743 where the British surgeon William Tossach successfully resuscitated a suffocated coal miner. Heartbeat and pulses have been described for more than 3000 years. Friedrich Mass is credited with being the first person to deliver successful closed-chest cardiac massage in 1892 after inhalation of chloroform. This technique was forgotten for nearly 70 years and was re-discovered in 1958 by William Kouwenhoven. Before that, in 1933, he demonstrated circulation to the brain due to external cardiac massage in a canine model. The ability to cause muscle contractions by electricity was described by Galvani. In 1775, the Danish Abildgaard found that chicken could be stunned and revived by electrical shocks. The first successful human defibrillation was performed by Beck in 1947 during open surgery for sternal deformity repair and intraoperative ventricular fibrillation. Zoll recorded the first successful closed-chest defibrillation in a human in 1955.

Elam proved in 1954 that expired air can provide adequate oxygenation during resuscitation and two years later together with Peter Safar he introduced mouth-to-mouth breathing as a life-saving technique. Cardiopulmonary resuscitation as a bundle of circulatory and respiratory support, consisting of external cardiac massage and artificial rescue breathing was then established and advocated in the early 1960's (14-16).

Prehospital emergency medicine, Rescue systems

Prehospital emergency care and emergency medical systems (EMS) may vary greatly between different countries and regions. Historically, two different approaches in prehospital emergency medicine have been distinguished: In the "Anglo-American" model, prehospital emergency care is provided by non-physician emergency medicine personnel (often called "paramedics or emergency medical technicians (EMT)"). This EMS structure is mainly found in the English-speaking countries of the world and is often characterized by the principle of "bringing the patient to the doctor". In contrast, the "Franco-German" system strongly relies on emergency physicians who provide prehospital emergency care in conjunction with paramedics. This type of EMS system is commonly attributed to central European countries and is often recognized by the principle of "bringing the doctor to the patient". However, clear-cut distinctions have become inadequate as EMS systems today combine elements from both archetypical models to unique systems to address specific needs of populations worldwide (17-20). EMS systems also show significant differences in terms of level of training of ambulance staff and whether they are allowed to perform medical procedures in absence of a physician, availability of helicopter emergency medical service (HEMS), dispatch characteristics and involvement of first-responders (21).

Basic Life Support

Basic Life Support (BLS) guidelines are designed to enable any person, irrespective if layperson or health care professional, to start life-saving measures in individuals who become suddenly unresponsive. These measures are organized into a straightforward algorithm (see Figure 1) that consists of:

- Recognition of cardiac Arrest
- Alert of Emergency Medical Services (EMS)
- Chest compressions
- Rescue breaths
- Use of an Automated External Defibrillator (AED)

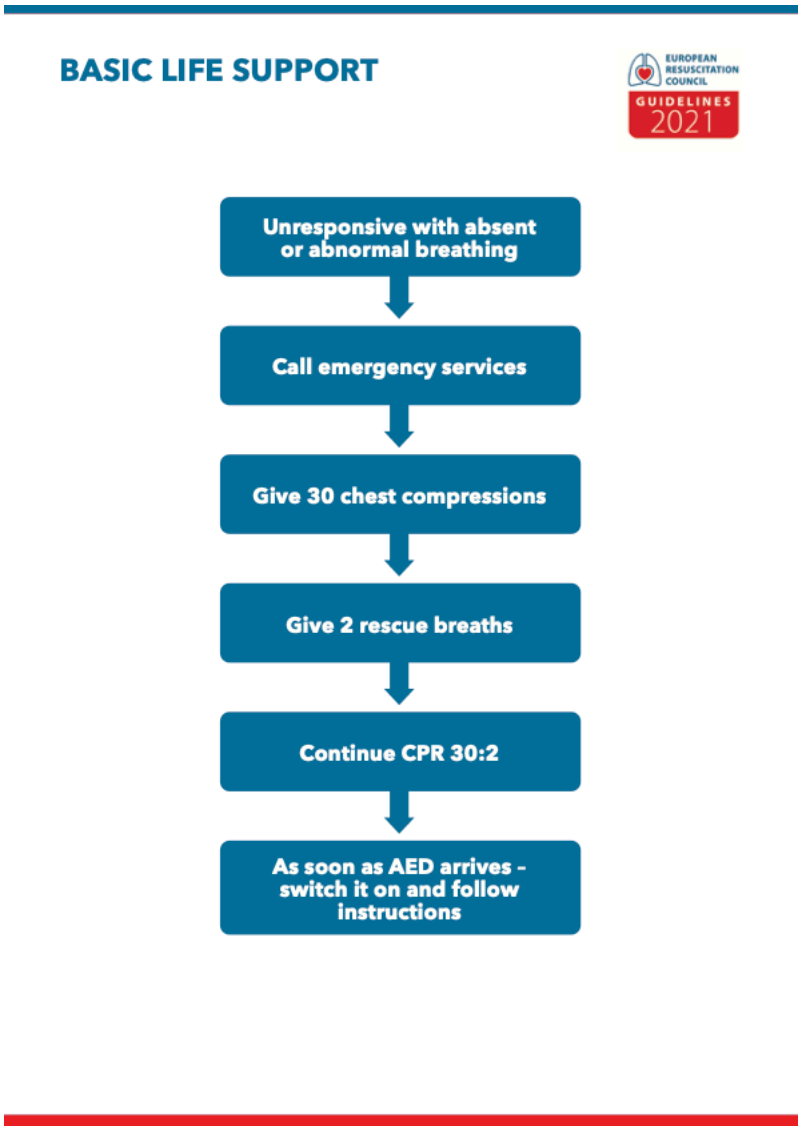

Figure 1: Basic life support algorithm, from (1)

For the initial assessment of an unresponsive patient, he or she should be rolled into supine position. The airway should be opened and breathing assessed for no longer than 10 seconds (look, listen, feel). If normal breathing is present, the person should be placed in the so-called “recovery position” and monitored closely. If there is no normal breathing (which includes “agonal breathing” characterized by slow and noisy gasps occurring in up to 50% of cardiac arrest patients), initiation of cardiopulmonary resuscitation is indicated.

High-quality chest compressions should be started as soon as possible. Compressions are 5-6cm in depth, delivered at a rate of 100-120/minute, and applied in the centre of the chest, represented by the lower half of the sternum. Full recoil of the chest is important to allow the heart to refill, and interruptions should be minimized.

2 rescue breaths attempts should be performed after every 30 chest compressions using the mouth-to-mouth technique. If this is not safe or possible, “compressions-only-CPR” is also feasible. As soon as possible, an AED should be brought to the patient, switched on, and its instructions followed. The electrodes should be attached to the bare chest to allow the device to assess the heart rhythm. If a shockable electrocardiogram (ECG) rhythm is detected, a shock can be delivered by the CPR provider (1, 22).

The core elements of basic life support have largely remained unchanged since the ILCOR recommendation for a “30 chest compressions to 2 rescue breaths”-ratio and a single shock strategy in patients with a shockable ECG rhythm (23).

For cardiac arrest in infants and children, specific guidelines exist, however CPR providers only trained in adult BLS should follow the recommendations of the adult BLS algorithm in such cases (24).

Advanced Life Support

Interventions of Advanced Life Support (ALS) are added to the measures of Basic Life Support. They include:

- Manual defibrillation
- Advanced airway management and ventilation
- Vascular access, drugs, fluids
- Point-of-care ultrasound (POCUS)
- Mechanical chest compression devices
- Extracorporeal CPR (eCPR)
- Peri-arrest arrhythmias

This is incorporated into the ALS algorithm, as illustrated in Figure 2:

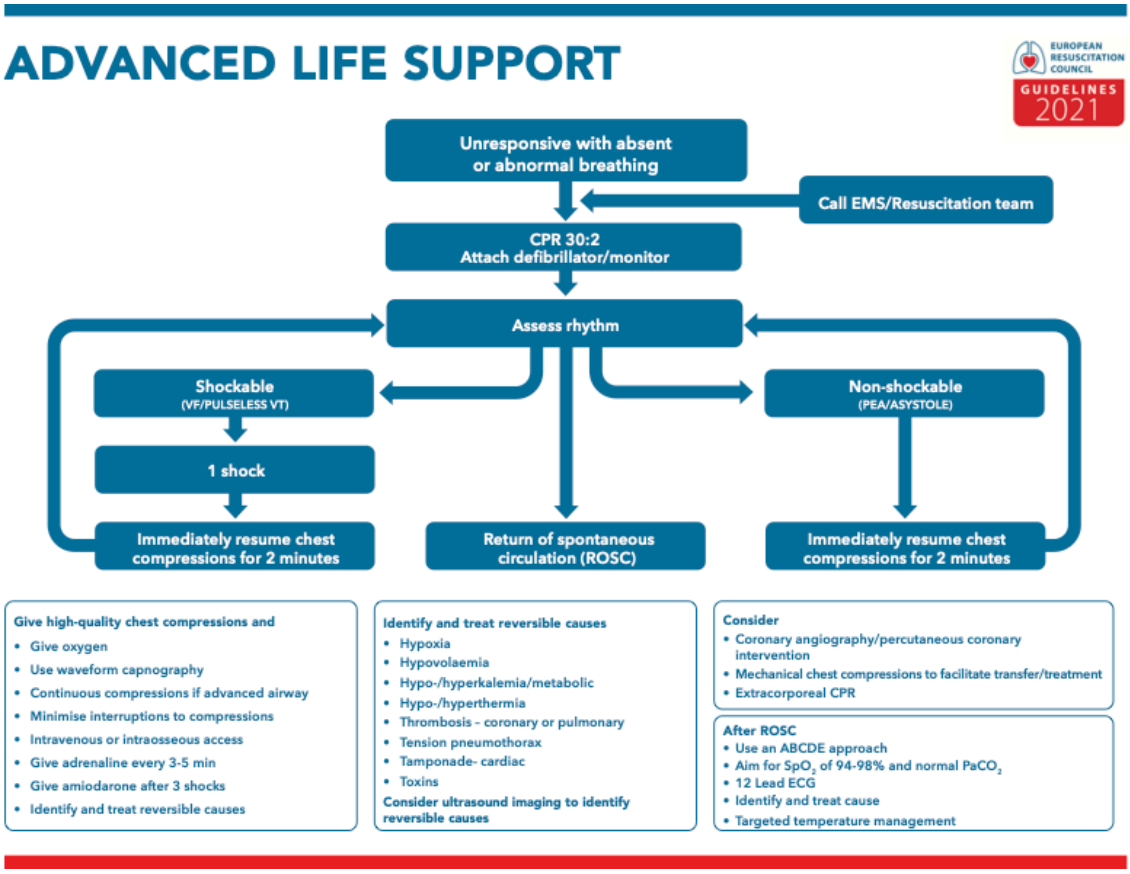

Figure 2: Advanced life support algorithm, from (25)

Similar to AED use in basic life support, as soon as possible defibrillator pads should be attached to the patient and the ECG rhythm assessed. Depending on the skills and training of the ALS provider in ECG recognition, semi-automatic or manual mode may be feasible. Ventricular fibrillation (VF) and pulseless ventricular tachycardia (pulseless VT) are considered as shockable ECG rhythms that should be immediately treated with a shock. Interruptions of chest compressions, commonly referred to as “hands-off time”, should be minimized, therefore, cardiac massage is only paused for the actual shock delivery and resumed immediately afterwards. Pulseless electrical activity (PEA) and asystole, on the other hand, are non-shockable ECG rhythms. ECG rhythm assessment is conducted every 2 minutes (1, 22, 25-27).

For ALS providers, bag-mask ventilation or advanced airway management is recommended. The latter includes the use of supraglottic airway devices (SGA) and tracheal intubation via direct or video laryngoscopy. Tracheal intubation, however, should only be attempted by experienced users with a high success rate as the potentially harmful effect of prolonged interruptions in chest compressions may outweigh the benefit of the airway intervention. The highest possible inspiratory oxygen concentration during CPR should be used. With an

advanced airway in place (and for SGAs when there is no significant air leakage), continuous chest compressions can be delivered instead of the 30:2 ratio for chest compressions and ventilations. Correct tracheal tube placement confirmation and ventilation monitoring should be performed with waveform capnography showing the end-tidal expiratory carbon dioxide (etCO2), which can monitor CPR quality and - in case of a sharp rise - indicate a possible return of spontaneous circulation (ROSC). Moreover, etCO2 monitoring may aid in decision-making regarding the termination of CPR, as low values - though not used in isolation, but as part of the overall assessment - may be predictive of poor outcome (25-28).

Venous access should be the first-line strategy for vascular access. If this is not feasible or possible, intraosseous access is recommended as the second-line strategy. Adrenaline (1mg intravenous (IV) or intraosseous (IO)) should be administered as soon as possible in patients with PEA or asystole. Amiodarone (300mg IV or IO) and adrenaline (1mg IV or IO) are indicated in cardiac arrest patients with shockable ECG rhythm after the 3rd shock. Adrenaline is then repeated every 3-5 minutes during advanced life support. Another dose of amiodarone (150mg IV or IO) is recommended after fifth shock in patients with shockable ECG rhythm. Lidocaine can be used as an alternative for amiodarone. Thrombolytic drugs may be considered when an embolic event is the suspected or confirmed cause of cardiac arrest. Fluids are only recommended when hypovolaemia is a confirmed or suspected cause of cardiac arrest (25-27).

The use of point-of-care ultrasound (POCUS) may be useful to examine the patient for potentially reversible causes of cardiac arrest such as pneumothorax or cardiac tamponade. As with tracheal intubation, POCUS should be performed only by experienced operators, as additional or prolonged interruptions in chest compressions may contribute to poor outcomes (29). Mechanical chest compression devices are not recommended for routine use. There is no strong evidence for superior outcomes and some studies found a higher rate of CPR-related injuries when using a mechanical chest compression device (30, 31). Their use is only recommended under circumstances where safe, high-quality manual chest compressions cannot be provided, and solely in skilled teams. Examples include helicopter or ambulance transport under CPR, during percutaneous coronary intervention (PCI) or during diagnostic imaging. Extracorporeal cardiopulmonary resuscitation (eCPR) is the rapid deployment of a veno-arterial extracorporeal membrane oxygenation (VA-ECMO) as a rescue therapy in selected patients (32). The guideline section on peri-arrest arrhythmias includes the assessment and management of both tachycardia and bradycardia. Synchronized electrical cardioversion for tachycardia and transcutaneous pacing for

bradycardia are indicated in the presence of life-threatening features such as shock, syncope, severe heart failure, or myocardial ischemia (25, 27).

As with basic life support, specific guideline recommendations also exist for advanced life support in infants, children, and neonates (24, 33). The guideline section titled 'Cardiac Arrest in Special Circumstances' provides recommendations for diagnosing and treating potentially reversible causes of cardiac arrest, along with adaptations for special situations (e.g., traumatic cardiac arrest, hypothermia), specific locations (e.g., cardiac catheterization laboratory), and particular patient conditions (e.g., pregnancy). For easier recall of potentially reversible causes of cardiac arrest ALS providers commonly use the acronyms “4 H’s and 4 T’s”, which represent:

- Hypoxia
- Hypovolaemia
- Hypo-/hyperkalaemia and other electrolyte disorders
- Hypo-/hyperthermia
- Thrombosis (coronary and pulmonary)
- Tamponade (cardiac)
- Tension pneumothorax
- Toxic agents (34)

Post-resuscitation Care

This bundle of care starts immediately after a sustained return of spontaneous circulation (ROSC) is achieved. First, the patient should be assessed using a structured ABC approach (Airway, Breathing, Circulation). If not already in place, an advanced airway (preferably tracheal intubation if skilled personnel are available) should be inserted unless the cardiac arrest episode has been very brief and the patient immediately returns to normal respiratory and neurological function. Again, waveform capnography should be used for confirmation of tube placement and ventilation monitoring. The goals for breathing are to maintain normoxaemia (PaO_2 75–100 mmHg) and normocapnia ($PaCO_2$ 35–45 mmHg), as deviations such as hypoxaemia, hyperoxaemia, hypocapnia, and hypercapnia may have harmful effects. If not obtained during CPR, safe intravenous access should be obtained. Crystalloids should be given to correct hypovolaemia. Invasive blood pressure monitoring using an arterial line is recommended, and in cases of haemodynamic instability cardiac output monitoring should also be considered. A 12-lead ECG and echocardiography should be performed as soon as possible to detect cardiac pathologies and assess cardiac function. There is limited evidence regarding specific goals for optimal blood pressure management.

Guidelines recommend avoiding hypotension which is interpreted as the maintenance of a mean arterial pressure (MAP) of at least 65mmHg, adequate urine output and clearance of lactate. To achieve haemodynamic goals, fluids, vasopressors, inotropes and/or mechanical circulatory support may be used. Whenever a cardiac origin is the suspected cause of cardiac arrest - particularly with ST-elevation in 12-lead ECG after ROSC - immediate transfer to the cardiac catheterization laboratory is recommended. In other patients, and if coronary angiography does not reveal a causative lesion, a brain and chest CT - including angiography of pulmonary arteries - should be performed to identify a possible neurological or pulmonary aetiology of cardiac arrest. Target temperature management (TTM) is recommended for 24 hours in patients who remain unresponsive after ROSC with a temperature goal of 32-36°C. Fever (body temperature >37.7°C) should be avoided for at least 72 hours in patients who remain comatose after ROSC. Other intensive care principles for patients after cardiac arrest include the treatment of seizures, the maintenance of normal blood glucose levels, thrombosis prophylaxis, stress ulcer prophylaxis and the use of short-acting drugs for sedation and analgesia. Multimodal prognostication for neurological outcome should begin 72 hours after cardiac arrest and involves clinical examination, imaging, electrophysiological examinations and biomarkers (35, 36).

CPR Injuries in general

Traumatic injuries may occur as a negative side effect of cardiopulmonary resuscitation. A variety of pathologies attributable to cardiopulmonary resuscitation have been described in several studies (37-47), including:

Cardiac injuries

- Atrial/ventricular lacerations
- Atrial/ventricular ruptures
- Contusion of the heart wall (endo-, myo-, epi- and/or pericardium)
- Papillary muscle tear
- Hemopericardium, cardiac tamponade
- Subendocardial/intramural/subepicardial/intracavitary haemorrhage
- Prosthetic valve dehiscence
- Conduction system injuries

Chest wall injuries

- Rib fracture, multiple rib fractures, flail chest
- Sternal fracture
- Separation of the costochondral junction

- Clavicle fracture
- Mediastinal/subcostal/retrosternal haemorrhage
- Vertebral fracture
- Scapula fracture

Pulmonary and airway injuries

- Pneumothorax, tension pneumothorax
- Haemothorax
- Pneumomediastinum
- Lung contusion/haemorrhage/herniation/laceration
- Pulmonary fat/bone marrow embolism
- Trachea injury
- Upper airway injuries

Vascular injuries

Aneurysm, pseudoaneurysm, rupture, laceration, dissection of

- Coronary arteries and coronary artery bypass grafts
- Aorta
- Subclavian artery and vein
- Vena cava superior and inferior

Abdominal injuries

- Liver laceration/rupture
- Gastric perforation
- Bowel rupture
- Splenic laceration/rupture
- Haemo/Pneumoperitoneum
- Retroperitoneal haemorrhage
- Omentum haemorrhage
- Mesenterial injury
- Pancreas injury
- Kidney injury
- Diaphragm injury

Prevalence rates of the injuries reported vary considerably across the literature and are strongly dependent on the diagnostic method used - such as chest X-ray, computed tomography, lung ultrasound, or autopsy. However, CPR-related injuries are a very common

occurrence. In a systematic review and pooled meta-analysis, van Wijck et al. reported that the overall prevalence of any injury associated with cardiopulmonary resuscitation was approximately 60%. The most frequently observed injury were rib fractures, with a pooled prevalence of 55% in the same study (46). Even higher rates of rib fractures - up to 97% - have been reported in studies using computed tomography for diagnosis (39-42). Sternal fractures is also a relatively common post-CPR finding, with van Wijck et al. reporting a pooled prevalence of 24% (46).

Along with skin lesions and minor burns, both sternal and rib fractures are often considered in the literature as “non time-critical”, “minor trauma”, “inconsequential” or “insignificant” (38, 40, 41, 43). Champigneulle et al. reported a 6.9% incidence of major traumatic injuries following cardiopulmonary resuscitation (CPR) for out-of-hospital cardiac arrest (OHCA). Major injuries were defined by the author team as those that were either life-threatening - causing cardiovascular and/or respiratory compromise - or consequential, requiring medical intervention such as surgical repair, pain relief, or resulting in prolonged hospitalization. Only 5.0% were attributed to CPR measures with the remaining findings being considered as collapse-related injuries (38). Karatasakis et al. reported a 14% rate of time-critical findings in their study (40).

Pneumothorax

Definitions

Pneumothorax is defined as a collection of air in the pleural space, the area between the inside of the chest wall (parietal pleura) and the lung surface (visceral pleura). Usually, under spontaneous breathing, there is a negative pressure in the pleural space keeping the lungs expanded and therefore inflated. Pneumothorax is a condition where this pressure balance is disrupted, either due to damage of the chest wall or the lung itself, which can lead to partial or complete lung collapse (48-50).

Any pneumothorax can potentially develop into tension pneumothorax. This is a life-threatening condition where pleural pressure exceeds atmospheric pressure due to a one-way-valve mechanism that allows air to enter the pleural space with every breath but does not allow it to escape during expiration. The accumulation of air leads to increased pressure within the affected pleural space. Besides respiratory impairment, there is also haemodynamic instability due to a mediastinal shift leading to the collapse of major blood vessels, impaired venous return to the heart and consequently low cardiac output. Positive-pressure ventilation increases the risk of conversion from pneumothorax into a tension pneumothorax (49, 51, 52).

Aetiology and types

Origin of pneumothorax is usually classified as spontaneous and non-spontaneous. Spontaneous pneumothorax occurs without a history of trauma and can be further subclassified as primary and secondary. Non-spontaneous pneumothorax may result from trauma (traumatic pneumothorax) or a medical procedure (iatrogenic pneumothorax) (48, 49, 51).

Primary spontaneous pneumothorax (PSP) occurs in healthy individuals with no history of lung disease. Male gender, age between 20 and 40 years, smoking, family history of pneumothorax and asthenic physiognomy are known risk factors for the development of PSP, however the exact cause remains unknown. Annual incidence in males is reported as 7.4-18 cases per 100.000 population, while in females it is significantly lower, at 1.2–6 cases per 100,000 population (48, 53).

Secondary spontaneous pneumothorax (SSP) occurs in patients with pre-existing lung disease with chronic obstructive pulmonary disease (COPD) being the most common. Several pulmonary conditions have been described in the context of SSP, including:

- Airways diseases (asthma, cystic fibrosis, emphysema)
- Infectious diseases (HIV-associated pneumocystis carinii pneumonia, tuberculosis, necrotising pneumonia)
- Interstitial disease (pulmonary fibrosis, sarcoidosis, histiocytosis X, lymphangioleiomyomatosis)
- Connective tissue disease (rheumatoid arthritis, scleroderma, ankylosing spondylitis, Marfan’s syndrome, Ehlers Danlos syndrome)
- Endometriosis
- Malignancies (lung carcinoma, sarcoma)

In the literature, general incidence of secondary spontaneous pneumothorax is stated to be quite similar to that of PSP. Unlike primary spontaneous pneumothorax (PSP), which is generally regarded as a relatively benign disorder, secondary spontaneous pneumothorax (SSP) tends to be a more serious event due to impaired pulmonary function resulting from underlying lung pathology. Additionally, recurrence of SSP is more frequent than that of PSP (48-51, 53).

Traumatic pneumothorax results from direct or indirect chest injury. The underlying trauma mechanism can be blunt (e.g. fall, transport accident) or penetrating (e.g. stab wound, gunshot wound). Traumatic pneumothorax may also be accompanied by haemothorax, a

collection of blood in the pleural space (48, 49, 51). Pneumothorax is a relatively frequent finding in patients with severe trauma. Lundin et al. reported a 35% incidence of pneumothorax among trauma patients referred to a tertiary trauma care unit, however, prevalence varies widely depending on the underlying trauma mechanism (54, 55). In general, thoracic trauma ranks as the third leading cause of death in polytraumatized patients, following head injuries and abdominal trauma (56).

Iatrogenic pneumothorax results from pleural injury incurred during a medical procedure. This can be deliberately, for instance in video-assisted thoracic surgery (VATS) to facilitate inspection of the pleural cavity. After finishing the procedure, a chest tube is inserted to re-expand the lung (48). A variety of medical interventions have the potential to inadvertently introduce air into the pleural space. Most commonly described in literature are transthoracic needle biopsy, subclavian vein catheterization, thoracentesis, transbronchial biopsy, pleural biopsy and positive pressure ventilation (57). Less common aetiologies include pacemaker manipulation, hypoglossal nerve stimulation, tracheostomy, breast surgery, chest acupuncture, gastroscopy, colonoscopy, bronchoscopy and shoulder surgery. In addition to the type of procedure performed, factors such as pre-existing pulmonary conditions, patient age, corticosteroid use, and the operator's level of experience may influence the risk of developing a procedure-related pneumothorax (51, 57).

Diagnosis

Diagnosis of pneumothorax usually involves history-taking, physical examination and diagnostic imaging.

Patients with pneumothorax typically present with a sudden onset of shortness of breath and ipsilateral pleuritic chest pain, however in some cases pneumothorax can be entirely asymptomatic and discovered incidentally. Symptoms tend to be more severe in cases with large volume of air in the pleural space (large size of pneumothorax) and in patients with limited pulmonary reserve due to an underlying pulmonary condition (48, 57).

Physical examination may reveal diminished or absent breath sounds on the affected side, decreased unilateral chest excursion, hyper-resonant percussion, absent tactile or vocal fremitus as well as subcutaneous emphysema. Respiratory distress (laboured breathing, use of accessory breathing muscles) may suggest a significant pneumothorax. Tracheal deviation away from the affected side is a late sign of tension pneumothorax, often accompanied by haemodynamic instability such as tachycardia and hypotension, which can

progress to cardiac arrest. Patients on mechanical ventilation with pneumothorax may show elevated pressures and signs of respiratory insufficiency (48, 52).

Chest radiography (chest X-ray) has traditionally been the most commonly used imaging modality for diagnosing pneumothorax. Presence of pneumothorax is indicated by a visible sharp, thin white line representing the visceral pleura, with no lung marking peripheral to this line. Signs of tension pneumothorax such as tracheal deviation and mediastinal shift may also be present as well as subcutaneous emphysema and pneumomediastinum (58).

Chest computed tomography (chest CT) is considered the gold standard for detecting pneumothorax and thoracic injuries in general. However, CT has some limitations, as it requires the patient to be stable enough for a transport to the CT scanner and involves significant exposure of ionizing radiation. Chest ultrasound is increasingly utilized in the emergency setting. It is rapid, safe and can be used bedside or in the field. Chest ultrasound has shown superior sensitivity compared to chest radiography in the supine position, which is often required when assessing and treating critically ill or trauma patients. Characteristic ultrasound findings of pneumothorax include absence of lung sliding, absence of B-lines, presence of a lung point, and absence of lung pulse. On M-mode, the presence of the characteristic “barcode sign” (also known as the “stratosphere sign”) further supports the diagnosis of pneumothorax (59-62).

Treatment

Pneumothorax treatment depends on several factors, including the clinical presentation, size of the pneumothorax, and underlying aetiology. Small asymptomatic pneumothoraces may be managed conservatively with careful follow-up. Tension pneumothorax requires immediate decompression either by needle or by open thoracostomy and chest tube insertion. Needle decompression can by an initial treatment option, usually performed in the 2nd intercostal space at the mid-clavicular line. This technique is quicker and technically easier to perform than chest tube placement, however high failure rates have been reported (49, 63, 64).

Chest tubes are the most definitive initial treatment option as they evacuate air and re-establish the negative pressure in the pleural space, allowing the lung to re-expand. The optimal insertion site is the anatomical landmark region known as the “triangle of safety”, which is bordered by the anterior margin of the latissimus dorsi muscle and the lateral edge of the pectoralis major muscle together with the transverse to the nipple line or the inframammary fold (usually representing the fifth intercostal space or higher), and an apex

below the axilla. Insertion can be performed dissective, with Seldinger-technique or trocar technique, with the latter two often under ultrasound guidance. Regardless of the chosen technique, the operator must always target the superior edge of the lower rib within the intercostal space to avoid injuries to the intercostal neurovascular bundle located in the costal groove of the rib above. The dissective technique starts with a small (1-2cm) skin incision, followed by careful blunt dissection through subcutaneous tissue and the three intercostal muscle layers - external intercostal muscle, internal intercostal muscle and innermost intercostal muscle - as well as the parietal pleura. Digital exploration confirms the entry into the pleural space as well as the presence of lung adhesions. This step is important for minimizing complications and may contribute to the lower rate of intrathoracic injuries observed with this technique compared to the trocar method (57, 65, 66).

Finger thoracostomy represents an alternative approach in which the pleural space is decompressed, as previously described, without the insertion of a chest drain. Alongside needle decompression, it is regarded as a rapid initial management option; however, it carries a risk of recurrent tension pneumothorax. As an alternative to purpose-designed chest tubes, a sterile endotracheal tube may also be utilized (thoracostomy tube). Inflation of the cuff within the pleural cavity secures the tube in place and minimizes the risk of dislocation, rendering this technique both efficient and reliable (1, 2).

CPR-associated pneumothorax

The reported incidence of pneumothorax following cardiopulmonary resuscitation varies widely in the literature. In a systematic review and meta-analysis published in 2024 Van Wijck et al. found a pooled prevalence of CPR-related pneumothorax of 7.03% (545 out of 8038 cases) compromising 43 studies (46). An earlier review of Miller et al. from 2014, reported a pneumothorax rate of 2.5% (29 out of 1167 cases) (37).

Karatasakis et al. and Branch et al. prospectively studied the same set of patients who were examined with computed tomography after survived OHCA and found a pneumothorax rate of 4.8% (n=104) (40, 45). Kim et al. conducted a prospective study including both in-hospital and out-of-hospital cardiac arrest patients undergoing a CT scan after ROSC. They reported of a pneumothorax rate of 8.5% (n=71) (44).

Champigneulle et al. found a rate of 2.3% in their observational study (n=1310) (38). Kashigawi et al., Katasako et al. and Viniol et al. retrospectively studied CT scans of cardiac arrest patients and found pneumothorax rates of 7.62% (n=223), 10.5% (n=306) and 26.0%

(n=100), respectively (39, 42, 67). Importantly, all studies mentioned in this section exclusively studied patients after non-traumatic cardiac arrest.

Kleber et al. analysed clinical and autopsy data of fatal major trauma patients and found tension pneumothorax as cause of traumatic cardiac arrest in 13.5% of cases (n=52) (68).

As previously noted, tension pneumothorax is among the potentially reversible causes of cardiac arrest. This condition compromises both respiratory and circulatory function and requires quick diagnosis and treatment. During cardiac arrest, pneumothorax can be diagnosed clinically and by sonography. Treatment should be performed by open thoracostomy and/or insertion of a chest tube. Decompression of a tension pneumothorax is given the highest priority in this certain situation (34).

To the best of our knowledge, no published literature has particularly focused on aetiology, pathophysiology and implications for outcome of CPR-associated pneumothorax.

Cadaver models in CPR research

There has been some previous research in the field of cardiac arrest and cardiopulmonary resuscitation utilizing different cadaver models. This research field, in general, is subject to numerous limitations. Heterogeneity among health care providers, patients and their underlying pathologies are complicating factors in design and execution of clinical trials. Additionally, ethical concerns may arise, as patients experiencing cardiac arrest require urgent medical care in situations where resources - both personnel and time - are often limited. Moreover, these patients are not able to provide informed consent to any study intervention. Animal models, especially the swine model, play a significant role in this field, however there are several limitations in terms of methodology, reporting and transferability (69-71).

Compared to clinical research and animal models, human cadaver models have some strengths and potentials. They provide a more anatomically and mechanically realistic lung-thorax-model and enable sophisticated data recordings. In their systematic review, Duhem et al. described following human cadaver models: fresh cadavers, fresh-frozen cadavers, Thiel-embalmed cadavers and newly deceased cadavers. Each of these models presents unique advantages and disadvantages (69, 72).

Thiel cadaver model

The “Thiel method” is a technique developed by the anatomist Walter Thiel (Graz, Austria) and was described in 1992 and 2002 (73, 74). The embalmment is a complex process carried out with the “Thiel solution”, a mixture of chemical agents, which includes ammonium

nitrate, boric acid and ethylene glycol. The solution is applied through intravascular and visceral injection, as full-submersion fluid in a container and as moistening solution. Thiel cadavers are known for close to in-vivo tissue properties and lifelike anatomical aspect and therefore not only used in anatomical research but also in undergraduate and postgraduate medical training (75).

Charbonney et al. extensively studied the Thiel-embalmed cadaver model in the setting of simulated cardiopulmonary resuscitation, with particular focus on thoracic and pulmonary behaviour. They found that the respiratory characteristics of Thiel-embalmed cadavers closely resembled those of OHCA patients, however, the model appeared to be susceptible to lung derecruitment. (72)

To the best of our knowledge, there is currently no published literature reporting on the occurrence of injuries - or their potential implications - arising from simulated cardiopulmonary resuscitation performed on Thiel-embalmed cadaver models.

Aims and scope

The aim of this doctoral thesis was to study pneumothorax in the context of cardiopulmonary resuscitation, carried out in two different settings and addressed through two separate research projects.

In Project 1, the occurrence of pneumothorax following cardiopulmonary resuscitation in out-of-hospital cardiac arrest patients was investigated. The study was conducted in the prehospital emergency medical service (EMS) setting of Graz, a midsize European city in Austria, along with its surrounding suburban areas. The primary objectives were to determine the incidence of post-CPR pneumothorax in this particular environment and EMS setting, identify possible risk factors for its development and elucidate its potential impact on outcome. We hypothesized that pre-existing pulmonary conditions, advanced age and prolonged duration of CPR would be associated with a higher incidence of pneumothorax. Furthermore, a key focus of the study was to evaluate whether the development of pneumothorax influenced survival to hospital discharge and the likelihood of a favourable neurological outcome. A major limitation of this study project is its retrospective design, however the data reflects real-life emergency medicine situations, decisions and procedures. To the best of our knowledge, no clinical trial has yet been specifically designed to study the phenomenon of post-CPR pneumothorax. Additionally, we are not aware of any prior systematic analysis examining possible aetiological factors contributing to the development of pneumothorax following CPR or its potential relevance to patient outcomes. To ensure

comparability with other rescue systems and to incorporate a reasonable set of potential confounding factors, we created a dataset based on the Utstein style standardized reporting template for out-of-hospital cardiac arrest (10).

In Project 2, we investigated the occurrence of pneumothorax and tension pneumothorax in simulated cardiopulmonary resuscitation using Thiel-embalmed cadavers. This experimental study was conducted in the course of a project led by Orlob et al., which focused on ventilatory and mechanical properties in the Thiel cadaver model (76). In their 2019 systematic review Duhem et al. identified four studies involving CPR research with Thiel-embalmed human cadavers (69). Our subsequent literature search yielded three more papers published in the more recent years (77-79). To the best of our knowledge, there are no reports of pneumothorax in the available scientific literature dealing with cardiopulmonary resuscitation in the Thiel-embalmed human cadaver model. One major limitation of this project arises from the fact that the study protocol was originally designed for a different study with distinct goals and research questions. Transferability to the clinical setting is limited, as tissue properties may be altered by to the embalming process. However, future CPR research using the Thiel cadaver model could benefit from the knowledge gained in this experimental study.

Materials and Methods

Parts of this section have been published in a similar fashion in journal articles by Auinger et al. (80, 81).

Project 1: Post-resuscitation pneumothorax: retrospective analysis of incidence, risk factors and outcome-relevance

Study design and setting

This was a retrospective analysis of out-of-hospital cardiac arrest cases attended by the physician-staffed ambulance based at the University Hospital of Graz, Austria. In Austria, the emergency medical services operate predominantly within a tiered response system. For emergencies perceived as non-life-threatening an ambulance staffed by two paramedics with a minimum of 260 hours of training ("Rettungssanitäter") is typically dispatched. In cases involving potentially life-threatening conditions, an additional response unit – either a ground-based vehicle or a rescue helicopter – is deployed. This unit is staffed by an emergency physician and a paramedic with higher-level training ("Notfallsanitäter").

The city of Graz – unlike the rest of the Austria - is serviced by a three-level system of emergency care. In addition to standard EMS personnel, Graz employs an intermediate level of EMS staff – known as "Rettungsmediziner". These are advanced medical students who have completed extended emergency medicine training of more than 3.000 hours. They form a suborganization within the Graz branch of the Red cross with a long-standing history, the "Medizinercorps". Two truck-based ambulances – referred to as "Notfallwagen" or more commonly as "Jumbo" - are each staffed with at least one Rettungsmediziner and minimum crew of four personnel. To emergencies with unclear or intermediate urgency the Jumbo responds solely, in critical cases the Jumbo team assists the emergency physician. Two Jumbo units provide emergency medical coverage within the city of Graz. In addition, the two physician-staffed ambulances ("Notarzteinsatzfahrzeuge") based at the University hospital of Graz and the State hospital Graz II serve both Graz and its suburban area (districts "Graz" and "Graz-Umgebung") which have a combined population of approximately 466.000 (82). During daytime hours, the physician-staffed rescue helicopter "Christophorus 12" based at Graz Thalerhof airport also responds to primary and secondary missions in the greater Graz area and the eastern part of the province of Styria (83, 84).

Advanced life support (ALS) was provided in accordance with the most recent guidelines issued by the European Resuscitation council (25, 85, 86). Patients were transported to one of the two designated cardiac arrest centres in Graz: the University hospital of Graz and the

State hospital Graz II. Post-resuscitation care was provided in line with the latest applicable clinical guidelines (35, 87, 88). In cases where pneumothorax was diagnosed, the on-call surgeon was consulted for further management.

Selection of patients

Adult patients (≥18 years) hospitalised after out-of-hospital cardiac arrest (OHCA) who received chest compressions and underwent imaging of the chest region (chest X-ray, chest computed tomography or lung ultrasound) within the first 12 hours after hospital admission were eligible for inclusion. Exclusion criteria included traumatic cardiac arrest, pneumothorax, thoracic surgery or chest trauma occurring within one month prior to cardiac arrest, as well as cases with insufficient data quality.

Ethics approval and trial registration

Approval for the study was obtained from the Ethics Committee of the Medical University of Graz (IRB00002556, decision number 28-168 ex 15/16) prior to commencement. The requirement for informed consent was waived, as data were collected retrospectively in a pseudonymized manner. All methods and analyses adhered to the applicable STROBE guidelines (89). The study was retrospectively registered at ClinicalTrials.gov and can be found under the identifier NCT06182007.

Data collection, variables and outcomes

Clinical data from missions of the physician-staffed ambulance based at the University Hospital of Graz are routinely collected using the electronic documentation system and database MEDEA (ilogs healthcare GmbH, Klagenfurt, Austria). The dataset utilizes the Minimal Dataset in German Emergency Medicine (MIND3), which is a documentation standard for prehospital physician-staffed emergency systems (90). Eligible cases from 1st March 2014 until 31st December 2021 were identified within the database and subsequently followed up in the hospital information system “openMEDOCS”.

The dataset of this study is composed of the core elements from the 2015 updated version of the Utstein Resuscitation Registry Template for out-of-hospital cardiac arrest (10). Additional variables ascertained were Pre-emergency status assessment (PESA), history of pre-existing lung disease, no-flow time, use of a mechanical chest compression device, duration of prehospital CPR, chest imaging modality, occurrence of pneumothorax, and chest tube placement.

The medical condition prior to the emergency was assessed using the Pre-Emergency Status Assessment (PESA), a five-level scale closely aligned with the ASA-classification

(American Society of Anaesthesiologists risk classification) commonly used in perioperative medicine (91).

- Unknown
- PESA 1 – normal healthy person
- PESA 2 – mild systemic disease, no functional limitations, well controlled disease
- PESA 3 – severe systemic disease that is not life threatening, some functional limitation due to disease
- PESA 4 – severe systemic disease that is a constant threat to life, severe functional limitation due to disease
- PESA 5 – moribund patient who is not expected to survive the next 24 hours with and without medical help

The radiology report from the first chest imaging procedure performed after hospital admission was reviewed to determine whether pneumothorax was present or not. In cases where a prehospital lung ultrasound had been performed, relevant information was obtained from the emergency physician's protocol. If a pneumothorax was identified, it was further evaluated whether a chest tube had been inserted.

An overview of all variables of our dataset is provided in Table 1.

Table 1: Variables ascertained for Project 1 ***"Post-resuscitation pneumothorax: retrospective analysis of incidence, risk factors and outcome-relevance" (80)****, categorized according to the Utstein style (10)*

Category	Variable	Options / Units
Patient	Sex	Female, Male
	Age	Years
	Etiology of arrest	Not recorded Medical Traumatic Drug overdose Drowning Electrocution Asphyxia
	Witnessed cardiac arrest	Bystander Emergency Medical Service Unwitnessed Not recorded
	Bystander CPR	Yes No
	Bystander AED	Yes, shock delivered Yes, no shock delivered No
	Arrest location	Home Work Recreation/Sports Public Education Nursing Other Not recorded

	First monitored ECG rhythm	Ventricular fibrillation (VF) Pulseless ventricular tachycardia (pulseless VT) Pulseless electrical activity (PEA) Asystole Not recorded
Process	Response time of first EMS team	Minutes
	Response time of emergency physician	Minutes
	Defibrillation time	Minutes
	Drugs administered	Adrenaline (yes/no) Amiodarone (yes/no)
	Reperfusion attempted	Yes No
	Target temperature management (TTM)	Yes No
Outcome	Survived Event (Sustained ROSC at admission)	Yes No
	Any ROSC	Yes No
	Survival to hospital discharge	Yes No
	CPC at discharge	CPC 1-5
Additional variables	PESA (Pre-Emergency Status Assessment)	Unknown, PESA 1–5
	Pre-existing lung disease	None Obstructive Infectious/inflammatory Interstitial Neoplasm

No-flow time	Minutes Unknown
Mechanical chest compression use	Yes No
Duration of prehospital CPR	Minutes
Chest imaging method	Chest X-ray CT Lung ultrasound
Pneumothorax	Yes No
Chest tube	Yes (out/in hospital) No

Abbreviations: CPR: cardiopulmonary resuscitation, VF: ventricular fibrillation, VT: ventricular tachycardia, PEA: pulseless electrical activity, EMS: emergency medical service, AED: automated external defibrillator, ECG: electrocardiogram, TTM: target temperature management, ROSC: return of spontaneous circulation, CPC: cerebral performance category, PESA: Pre Emergency Status Assessment, CT: computed tomography

Primary outcome was incidence of pneumothorax, secondary outcomes were survival to hospital discharge and favourable neurological outcome at hospital discharge defined by a Cerebral Performance Category (CPC) of 1 or 2.

Statistical analysis

For statistical analysis, we used R version 4.2.2, a free software environment for statistical computing and graphics (92). The set of predictors for the logistic regression models was chosen based on a preliminary exploratory analysis and recommendations from the literature (93). This approach ensured that, on one hand, bias due to the omission of relevant predictors was minimized, and on the other hand, the variance of the estimates did not increase due to the inclusion of many irrelevant terms in the model. Changes in the respective adjusted odds ratios caused either by increasing the size of a predictor by one unit or by changing its category were also examined. An effect was considered statistically significant if the two-sided 95% confidence interval of the odds ratio did not include the value of one.

The area under the receiver operating characteristic (ROC) curve was estimated to evaluate the classification accuracy of the logistic regression model. For this purpose, the available data were randomly divided into a training set (70%) and a test set (30%). The model was estimated using only the training part and this estimate was then applied to the test part. Since this classification result depends strongly on the split between training and test sample, this random partitioning was repeated 1,000 times and the median of all Monte Carlo replicates of the area under the curve (AUC) was calculated and reported.

Project 2: Pneumothorax in a Thiel cadaver model of cardiopulmonary resuscitation

This investigation was carried out during the development and execution phases of the study titled “Reliability of mechanical ventilation during continuous chest compression: a crossover study of transport ventilators in a human cadaver model of CPR” by Orlob et al. The primary objective of this study was to systematically assess and compare the performance of three different common transport ventilators under simulated CPR conditions. The three devices tested were “MEDUMAT Standard^{2}“ (WEINMANN Emergency Medical Technology GmbH + Co. KG, Hamburg, Germany), “Oxylog 3000 plus” (Drägerwerk AG & Co. KGaA, Lübeck, Germany) and “Monnal T60“ (Air Liquide Medical Systems, Antony Cedex, France). Their ability to provide sufficient alveolar ventilation during continuous mechanical chest compressions was evaluated using a human cadaver model designed to closely replicate the conditions of cardiopulmonary resuscitation (76).

Cadavers, Ethics approval

Eleven cadavers were randomly selected for the study. None showed visible signs of pre-existing injuries to the thoracic region. All bodies had been embalmed using the “Thiel method”. The embalmment process is described earlier in the introduction section (73, 74).

All bodies donated to science were investigated under the strict regulations of the body donation program of the Gottfried Schatz Research Centre, Division of Macroscopic and Clinical Anatomy at the Medical University of Graz as well as the burial law of the province of Styria, Austria. Written informed consent was obtained from all donors to donate their bodies for scientific and educational purposes. Hence, no additional approval of the local ethics committee was required.

Study procedure

The experiment was conducted according to a standardised study protocol (see Figure 3). First of all, oral endotracheal intubation was performed using direct laryngoscopy.

Subsequently, bronchoscopy (aScope™ 4 Broncho Large, Ambu™, Ballerup, Denmark) was carried out to confirm correct tracheal tube placement. Intrapulmonary fluid collections and residual substances from the embalming process were removed via suctioning, and, when necessary, by lavage through the working channel of the bronchoscope.

Initial ventilation was carried out using an intensive care respirator (Hamilton-C6, Hamilton Medical AG, Bonaduz, Switzerland). Height of each body donor was measured, and the predicted body weight (PBW) was calculated with the use of an adjusted Broca's formula (94). This calculation was essential for determining the target tidal volumes (VT), which were then set to the closest possible value supported by each respective ventilator. Lung recruitment was performed by two quasi-static inflation manoeuvres with peak inspiratory pressures of 25 and 35 cmH_2O, respectively. After tension pneumothorax developed in the first three cadavers, the peak pressure of the second inflation manoeuvre was subsequently reduced to 30 cmH_2O for all remaining cases. This was followed by a 15-minute period of volume-controlled ventilation with the following settings: V_T 6ml/kg of predicted body weight (PBW); respiratory rate (f) 12/min; positive end-expiratory pressure (PEEP) 5 cmH_2O; inspiratory-to-expiratory ratio (I:E) 1:2; maximum pressure (P_{MAX}) 40 cmH_2O).

During the ventilator trial, we assessed mechanical properties of each cadaver in three separate sequences - ventilation only, chest compressions only, ventilation and chest compressions combined - lasting two minutes each. Chest compressions were administered in a standardised manner using an automated chest compression piston device ("Corpuls CPR", GS Elektromedizinische Geräte G. Stemple GmbH, Germany). Compressions were set to a depth of 5cm and frequency of 103 compressions per minute. Ventilation throughout this study period was provided by the previously mentioned intensive care respirator with the following settings: V_T 6ml/kg PBW; f 12/min; PEEP 5 cmH_2O in the ventilation only sequence, PEEP 0 cmH_2O in the combined sequence; I:E 1:5; P_{MAX} 60 cmH_2O.

During the intervention phase, the three transport ventilators "MEDUMAT Standard^2", "Oxylog 3000 plus" and „Monnal T60" were tested in a three-period crossover design. Each period comprised two sequences of simulated cardiopulmonary resuscitation, each lasting two minutes. The order of ventilator application was randomly assigned using sealed envelopes. Ventilation settings were as follows: V_T 6ml/kg PBW; f 10/min; PEEP 0 cmH_2O; I:E 1:5 (I:E 1:4 for MEDUMAT Standard^2); P_{MAX} 60 cmH_2O. Chest compressions were delivered at a depth of 5 cm and a frequency of 103 compressions per minute. The entire experiment consisted of 17 minutes of ventilation only, two minutes of chest compressions only, and 14 minutes of combined ventilation and chest compressions.

Testing for pneumothorax was performed using bilateral lung ultrasound with a portable sonography device (“Sonosite M-Turbo”, FUJIFILM Sonosite GmbH, Frankfurt, Germany) by two clinicians trained and experienced in eFAST (extend focused assessment with sonography for trauma). Pneumothorax assessment was carried out after the initial recruitment phase and following every two-minute cycle of chest compressions. A phased array ultrasound probe was positioned at the highest point of the anterior chest wall - typically represented by the third or fourth intercostal space along the mid-clavicular line - in a sagittal orientation (60). Presence of pneumothorax was defined by absence of lung sliding. At the conclusion of the experiment, bilateral finger thoracostomy was performed. Particular attention was given to the occurrence of escaping air, indicative of tension pneumothorax.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics version 27. Continuous variables were tested for normality using the Kolmogorov-Smirnov test. Variables demonstrating a normal distribution were compared between groups using an independent samples t-test. Categorical variables were analysed using Fisher’s exact test. A two-sided p-value of ≤ 0.05 was considered statistically significant.

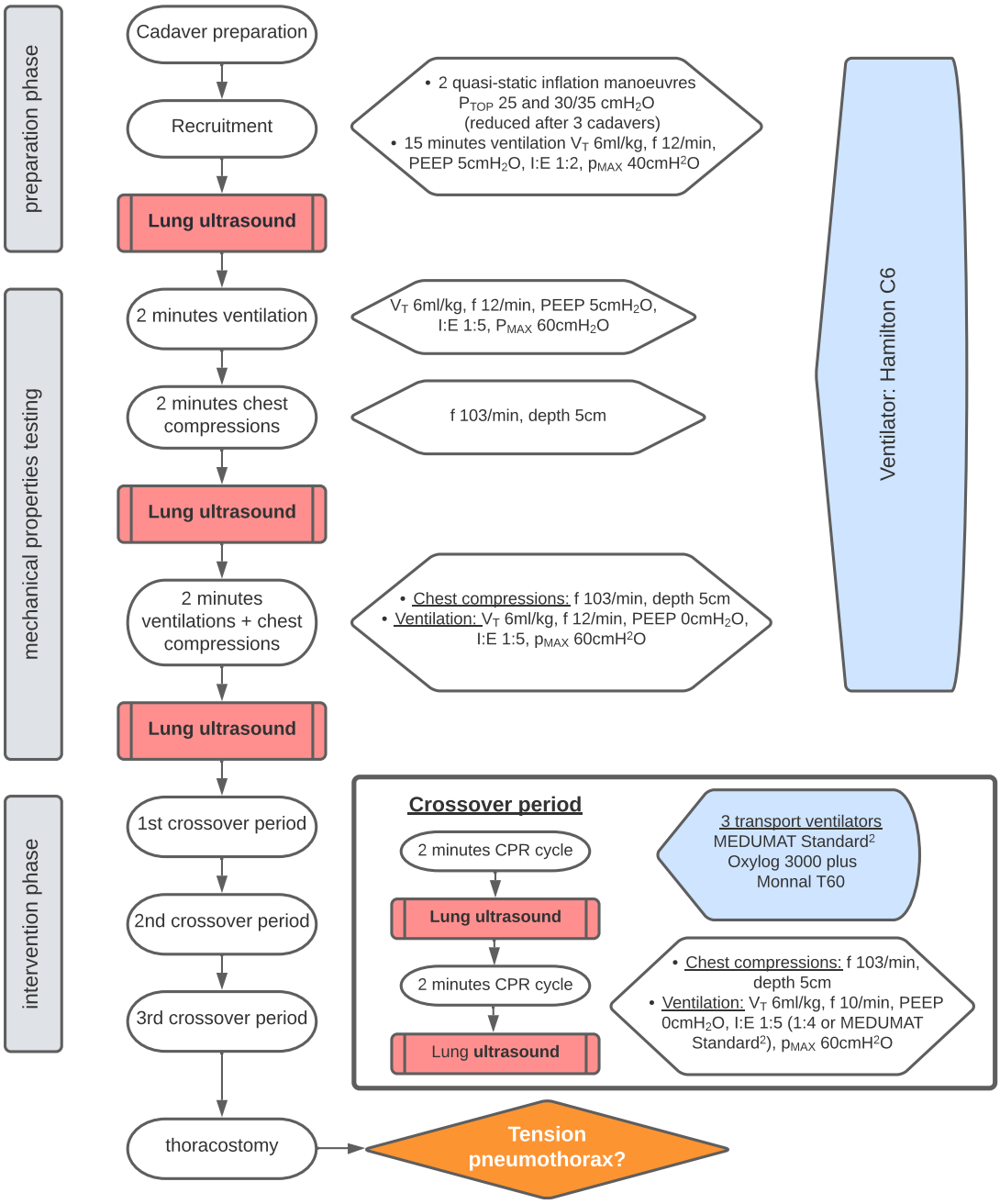

Figure 3: Experiment flow chart from Project 2 ***"Pneumothorax in a Thiel cadaver model of cardiopulmonary resuscitation" (81)***
Abbreviations: P_{TOP}: top pressure; V_T: tidal volume; f: frequency; PEEP: positive end-expiratory pressure;
I:E: inspiration/expiration ratio; P_{MAX}: upper pressure limit; CPR: cardiopulmonary resuscitation

Results

Project 1: Post-resuscitation pneumothorax: retrospective analysis of incidence, risk factors and outcome-relevance

Selection process

We identified 1,557 out-of-hospital cardiac arrest cases in the MEDEA database to which the physician staffed ambulance based at the University hospital of Graz was dispatched in the period between 1st March 2014 and 31st December 2021. Resuscitation was not attempted in 454 cases. Among the 1,103 cases where resuscitation measures was initiated, 339 patients aged over 18 years were eventually hospitalised. 102 patients were excluded for the following reasons: 11 patients had traumatic cardiac arrest, 7 patients did not receive chest compressions, chest imaging was unavailable in 51 cases, and 33 were excluded due to insufficient data quality preventing ascertainment of variables and outcomes. Ultimately, 237 patients were included into our analysis. The selection process is also illustrated in Figure 4.

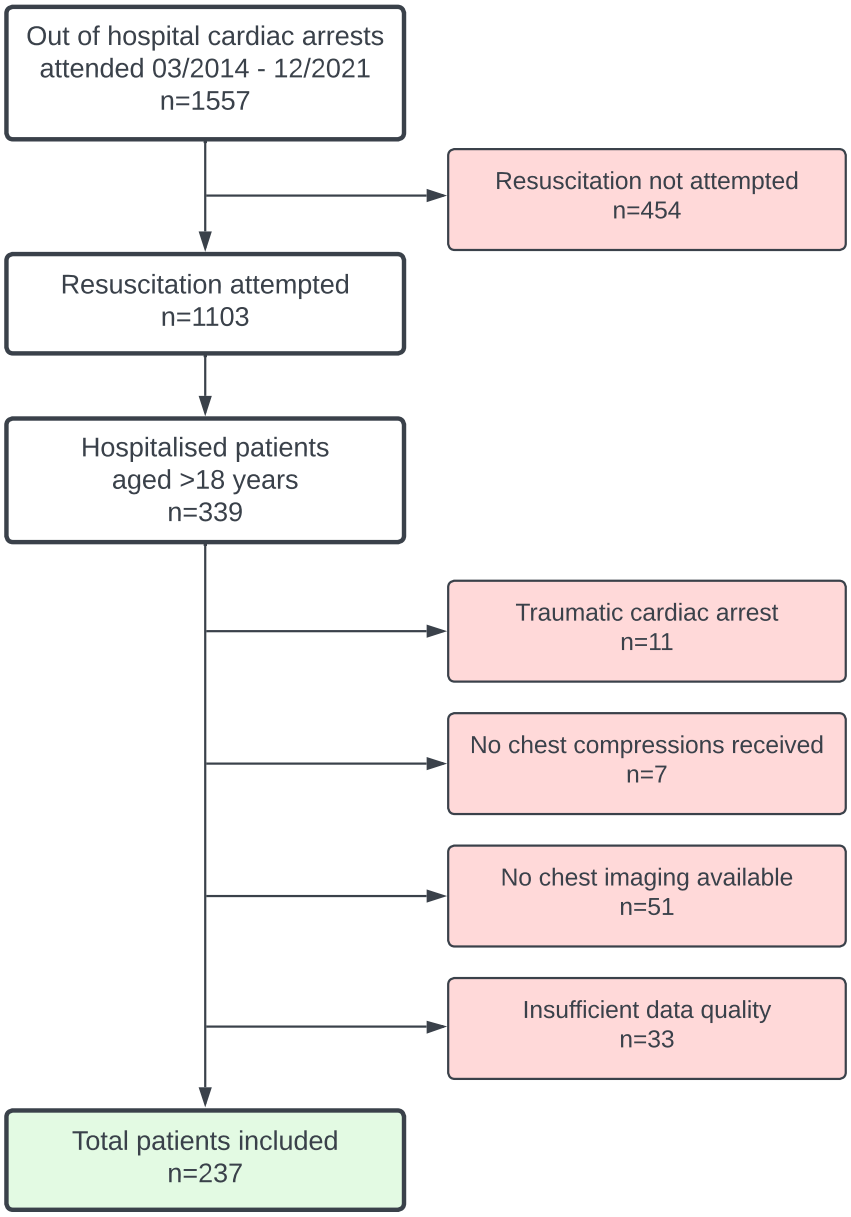

*Figure 4: Patient selection flow chart from Project 1: "**Post-resuscitation pneumothorax: retrospective analysis of incidence, risk factors and outcome-relevance"** (80)*

Patient characteristics

Of the 237 patients included in the analysis, 172 were male (72.6 %) and 65 were female (27.4%). The mean age 65.3 years with a standard deviation (SD) of ± 15.3, with an age range of 18 to 95 years. Cardiac arrest was witnessed by bystanders in 140 cases (59.1%) and by emergency medical services (EMS) personnel in 42 cases (17.7 Bystander CPR was performed in 127 patients (53.6%), and an automated external defibrillator (AED) was used by bystanders in 27 cases (11.4%), with shock delivery occurring in 21 of these (8.9%). A shockable initial ECG rhythm - ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT) - was documented in 93 cases (39.2%). A comprehensive overview of patient characteristics is provided in Table 2.

Table 2: Patient characteristics of Project 1 ***"Post-resuscitation pneumothorax: retrospective analysis of incidence, risk factors and outcome-relevance"*** *adapted from* ***(80)***

	n=237	
Sex		
Female	65	27.4%
Male	172	72.6%
Age (mean ± SD [years])	65.3	15.6
PESA		
1	25	10.5%
2	80	33.8%
3	111	46.8%
4	21	8.9%
5	0	0
Etiology		
Medical	172	72.6%
Traumatic	0	0%
Drug Overdose	4	1.7%
Drowning	1	0.4%
Electrocution	0	0%
Asphyxia	35	14.8%
Not recorded	25	10.5%
History of lung disease		
None	162	68.4%
Obstructive	61	25.7%
Inflammatory/Infectious	9	3.8%
Interstitial	1	0.4%
Neoplasm	4	1.7%

Witnessed cardiac arrest		
Bystander witnessed	140	59.1%
EMS witnessed	42	17.7%
Unwitnessed	49	20.7%
Not recorded	6	2.5%
Bystander CPR	127	53.6%
Bystander AED		
Used, shock delivered	21	8.9%
Used, no shock delivered	6	2.5%
Not used	210	88.6%
Location		
Home	139	58.6%
Work	6	2.5%
Recreation/Sports	5	2.1%
Public	53	22.4%
Nursing	17	7.2%
Other	16	6.8%
Not recorded	1	0.4%
Initial ECG rhythm		
Shockable	93	39.2%
VF	88	37.1%
Pulseless VT	5	2.1%
Non-shockable	127	53.5%
PEA	66	27.8%
Asystole	61	25.7%
Not recorded	17	7.2%

Abbreviations: SD: standard deviation, PESA: Pre Emergency Status Assessment, EMS: emergency medical service, CPR: cardiopulmonary resuscitation, AED: automated external defibrillator, ECG: electrocardiogram, VF: ventricular fibrillation, VT: ventricular tachycardia, PEA: pulseless electrical activity

Process data

The mean no-flow time, defined as the interval between collapse and the initiation of cardiopulmonary resuscitation (CPR), was 2.8 minutes (standard deviation ± 4.9), where available. In 30 cases (12.7%), the no-flow time could not be determined. The mean duration of prehospital CPR was 21.8 minutes (standard deviation ± 18.2). A mechanical chest compression device was utilised in four cases. Chest X-ray was the most frequently employed imaging modality (n = 125, 52.7%), followed by lung ultrasound (n = 62, 26.2%)

and computed tomography (n = 50, 21.1%). A detailed overview of process-related data is presented in Table 3.

*Table 3: Process data of Project 1 ""**Post-resuscitation pneumothorax: retrospective analysis of incidence, risk factors and outcome-relevance"** adapted from **(80)***

	n=237	
Response times (mean ± SD [mins])		
EMS	8.8	4.2
Emergency physician	11.3	5.1
Defibrillation time (if applicable; mean ± SD [mins])	8.8	7.1
No-flow-time (mean ± SD [min])	2.8	4.9
Unknown no-flow-time	30	12.7%
Prehospital CPR duration (mean ± SD [mins])	21.8	18.2
Mechanical CPR use	4	1.7%
Drugs given		
Adrenaline	180	75.9%
Amiodarone	56	23.6%
Reperfusion attempted	132	55.7%
TTM	113	47.7%
Chest imaging		
X-Ray	125	52.7%
CT	50	21.1%
Lung ultrasound	62	26.2%

Abbreviations: EMS: Emergency Medical Service, SD: standard deviation, mins: minutes, CPR: cardiopulmonary resuscitation, TTM: target temperature management, CT: computed tomography

Outcomes

Of the 237 patients hospitalised, 201 (84.8%) achieved sustained return of spontaneous circulation (ROSC) upon hospital admission – classified as "survived event" according to the Utstein style. A total of 230 patients (97.0%) exhibited any ROSC during the peri-resuscitation period. 90 patients (38.0%) survived to hospital discharge, and 75 (31.6%) had a favourable neurological outcome, defined as a Cerebral Performance Category (CPC)

score of 1 or 2 at discharge. When considering all 1,103 patients in whom cardiopulmonary resuscitation was initiated, the overall survival to hospital discharge was 8.2%, and the rate of favourable neurological outcome was 6.8%. A detailed summary of outcomes is presented in Table 4.

*Table 4: Outcome data of Project 1 ""**Post-resuscitation pneumothorax: retrospective analysis of incidence, risk factors and outcome-relevance"** adapted from **(80)***

	n=237	
Survived Event	201	84.8%
Any ROSC	230	97.0%
Survival to hospital discharge	90	38.0%
CPC at hospital discharge		
Favourable	75	31.6%
1	60	25.3%
2	15	6.3%
Non-favourable	162	68.4%
3	9	3.8%
4	6	2.5%
5	147	62.0%

Abbreviations: ROSC: Return of Spontaneous Circulation; CPC: Cerebral Performance Category

Statistical model "Survival to hospital discharge"

Our statistical model identified several factors significantly associated with decreased probability of survival to hospital discharge. These included higher age (Odds Ratio [OR] 0.968; 95% Confidence Interval [CI] 0.942–0.996), a higher Pre-Emergency Status Assessment (PESA) category (PESA 3 vs. PESA 1: OR 0.218, 95% CI 0.052–0.909; PESA 4 vs. PESA 1: OR 0.065, 95% CI 0.008–0.551), longer duration of prehospital cardiopulmonary resuscitation (OR 0.921; 95% CI 0.891–0.952), and increased no-flow time (OR 0.784; 95% CI 0.689–0.891). Additionally, a non-shockable initial ECG rhythm was significantly associated with lower odds of survival compared to a shockable rhythm (OR 4.796; 95% CI 2.098–10.961).

Model estimates indicated that each additional minute of prehospital CPR reduced the predicted odds of survival by 7.9%, while a 5-minute increase corresponded to a 33.7% reduction. Similarly, each minute of additional no-flow time was associated with a 21.6% decrease in survival probability; a 2-minute increase led to a 38.6% reduction. Regarding

age, each additional year was linked to a 3.2% lower chance of survival, and a 10-year increase was associated with an estimated 33.7% decline in survival probability.

The occurrence of pneumothorax was not identified as a significant predictor of survival (OR 0.579; 95% CI 0.188–1.781). The predictive performance of the model, as measured by the area under the receiver operating characteristic curve, was 0.849 (95% CI 0.755–0.923).

Key results of this statistical model are illustrated in Figures 5-8.

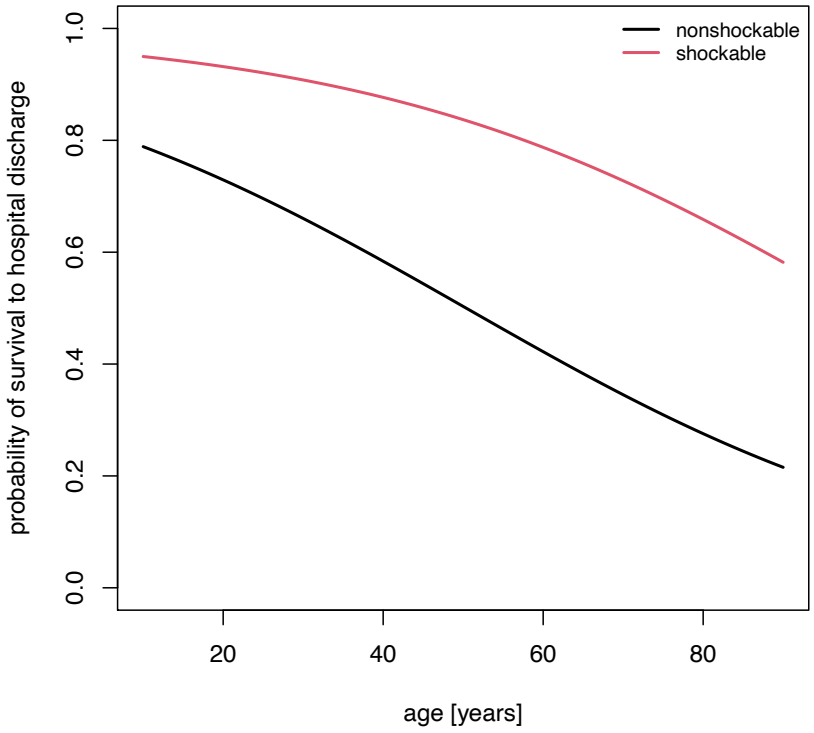

Figure 5: Survival probability of patients hospitalised after out-of-hospital cardiac arrest in the context of initial ECG rhythm (shockable = red, non-shockable = black) and age
Patients variables in the model were set as follows: PESA1, prehospital CPR duration 20 minutes, no-flow-time 3 minutes

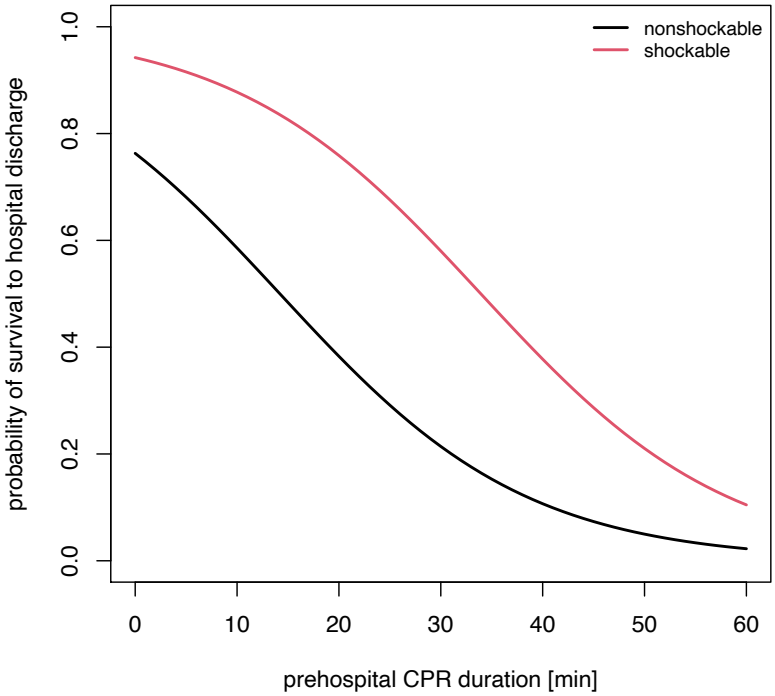

Figure 6: Survival probability of patients hospitalised after out-of-hospital cardiac arrest in the context of initial ECG rhythm (shockable = red, non-shockable = black) and prehospital CPR duration
Patients variables in the model were set as follows: age 65 years, PESA1, no-flow-time 3 minutes

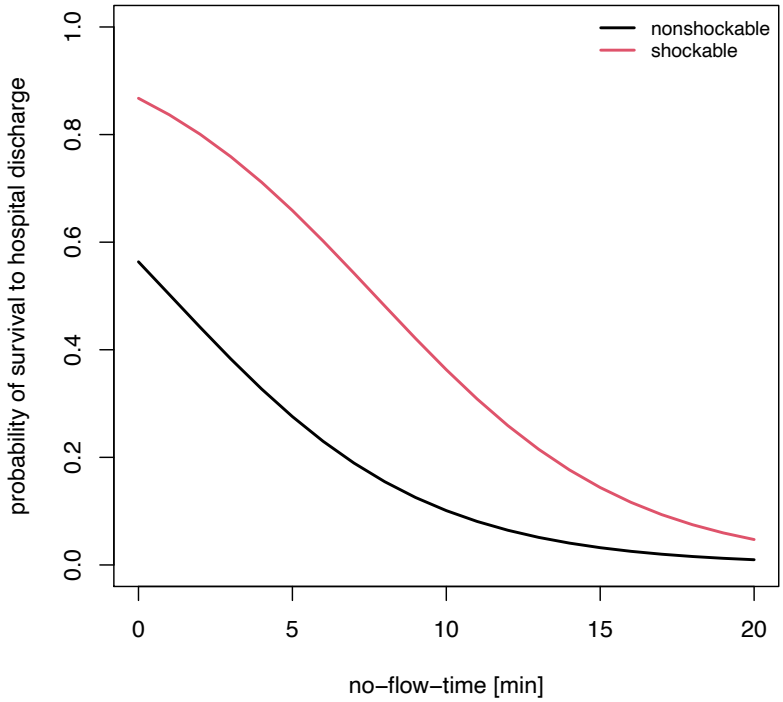

Figure 7: Survival probability of patients hospitalised after out-of-hospital cardiac arrest in the context of initial ECG rhythm (shockable = red, non-shockable = black) and no-flow-time
Patients variables in the model were set as follows: age 65 years, PESA1, prehospital CPR duration 20 minutes

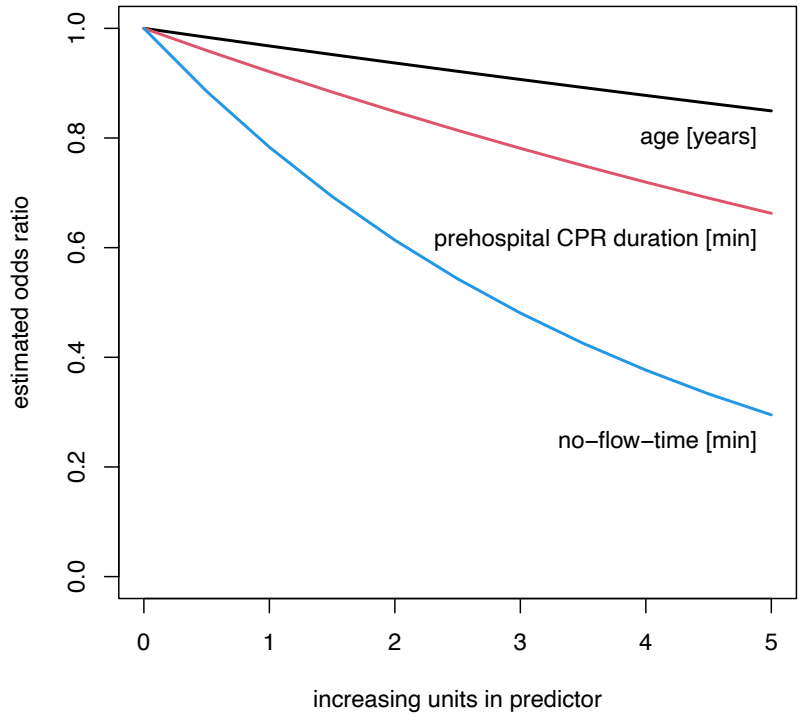

Figure 8: Estimated odds ratios for survival to hospital discharge of patients hospitalised after out-of-hospital cardiac arrest and the estimated effects of increase of age (black), prehospital duration of cardiopulmonary resuscitation (red) and no-flow-time (blue)

Statistical model "Neurological outcome at hospital discharge"

The statistical model revealed multiple statistically significant predictors of decreased probability for achieving a favourable neurological outcome (CPC 1–2) upon hospital discharge. These included higher age (Odds Ratio [OR] 0.955; 95% Confidence Interval [CI] 0.923–0.988), higher PESA category (PESA 3 vs. PESA 1: OR 0.058; 95% CI 0.010–0.344; PESA 4 vs. PESA 1: OR 0.039; 95% CI 0.003–0.434), non-shockable initial ECG rhythm (OR 12.75; 95% CI 4.211–38.62), longer duration of prehospital CPR (OR 0.863; 95% CI 0.813–0.916), and increased no-flow time (OR 0.629; 95% CI 0.499–0.792). This same set of predictors was also found to be relevant in the "survival to hospital discharge" model.

Specifically, the probability of achieving a neurologically favourable outcome declined by 13.7% with each additional minute of prehospital CPR and by 52.0% with a 5-minute increase. Likewise, increases in no-flow time were strongly associated with reduced odds of CPC 1–2: a 1-minute increase resulted in a 37.0% decrease, and a 2-minute increase was

associated with a 60.3% reduction. Age also emerged as a significant predictor, with each additional year reducing the odds of neurologically intact survival by 4.5%, and a 10-year increase associated with a 36.9% decrease.

Pneumothorax was again not identified as a significant predictor in this model (OR 1.183; 95% CI 0.325–4.303). The model demonstrated excellent discriminatory ability, with an area under the receiver operating characteristic curve (AUC) of 0.893 (95% CI 0.801–0.954). Key results are illustrated in Figures 9 and 10.

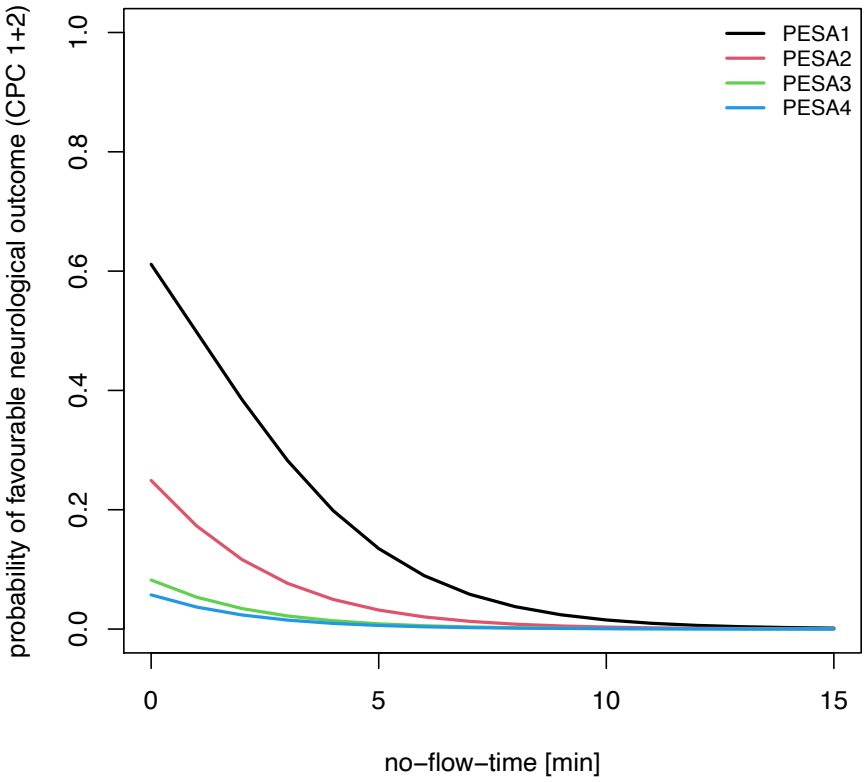

Figure 9: Probability of survival with favourable neurological outcome (cerebral performance category (CPC) 1+2) after out-of-hospital cardiac arrest in the context of PESA-Score (Prehospital Emergency Status Assessment) and no-flow-time, estimated for an age of 65 years and non-shockable ECG rhythm

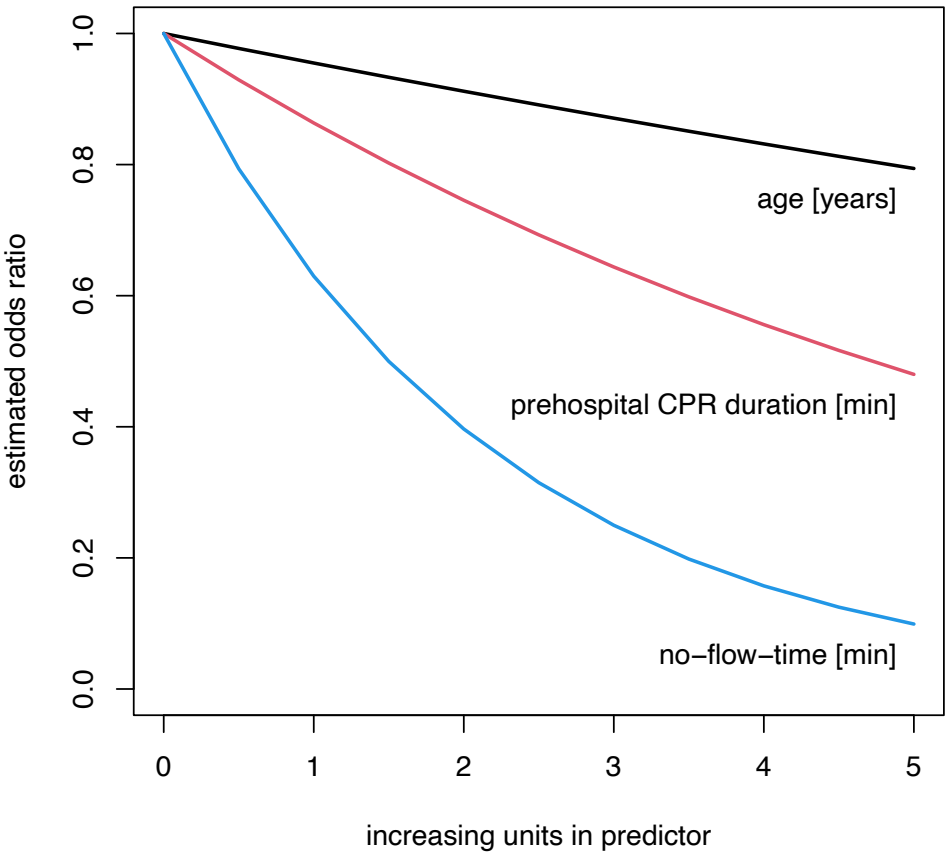

Figure 10: Estimated odds ratios for survival with favourable neurological outcome (CPC1+2) of patients hospitalised after out-of-hospital cardiac arrest and the estimated effects of increase of age (black), prehospital duration of cardiopulmonary resuscitation (red) and no-flow-time (blue)

Pneumothorax

Pneumothorax was identified upon hospital admission in 26 out of 237 out-of-hospital cardiac arrest cases (11.0%). Chest tube insertion was performed in 17 of these patients (65.4%), with 8 thoracostomies carried out prehospitally. The incidence of pneumothorax varied by imaging modality: 7.2% in chest X-ray, 8.1% in lung ultrasound, and 24.0% in computed tomography.

Table 5 provides an overview of the 26 patients diagnosed with pneumothorax on hospital admission, including patient characteristics, imaging modality used, radiological findings, clinical course, and outcomes. Table 6 presents a comparison of patient characteristics, process variables, and outcomes between the 'no pneumothorax' and 'pneumothorax' subgroups.

*Table 5: Characteristics, chest imaging method, radiology report, clinical course and outcomes of patients diagnosed with pneumothorax upon hospital admission following CPR for out-of-hospital cardiac arrest from Project 1 ""**Post-resuscitation pneumothorax: retrospective analysis of incidence, risk factors and outcome-relevance**"*

Sex	Age	History of lung disease	CPR duration	Chest imaging	Radiology report	Clinical course	Survival to hospital discharge	CPC
Female	33	Obstructive	11	Sonography (pre-hospital), CT (in-hospital)	Chest tube left, suspected minor Ptx right	Absent lung sliding on both sides in lung ultrasound, chest tube insertion left, needle decompression right by emergency physician	No	5
Male	71	None	28	Sonography (pre-hospital), CT (in-hospital)	Chest tube left, soft tissue emphysema left	Absent lung sliding left in lung ultrasound, chest tube insertion left by emergency physician	No	5
Female	51	None	10	CT	Ptx bilateral (3mm)	Conservative treatment	No	5
Male	60	None	5	CT	Ptx right (7mm)	Chest tube right by surgeon	Yes	1

Female	74	Obstructive	23	Sonography (pre-hospital), CT (in-hospital)	Thoracostomy tubes bilateral, soft tissue emphysema bilateral	Absent lung sliding left in lung ultrasound, thoracostomy tube left by emergency physician, Re-Arrest during PCI due to tension pneumothorax right, chest tube right by cardiologist	No	5
Male	48	None	34	CT	Ventral minor Ptx bilateral	Conservative treatment	Yes	1
Male	75	Obstructive	16	Sonography (pre-hospital), CT (in-hospital)	Thoracostomy tubes bilateral	Absent lung sliding bilateral in lung ultrasound, thoracostomy tubes both sides by emergency physician	No	5
Female	93	Obstructive	20	Sonography (pre-hospital), CT (in-hospital)	Haemopneumothorax bilateral, Soft tissue emphysema, Chest tubes bilateral	Absent lung sliding bilateral in lung ultrasound, Chest tubes both sides by emergency physician; Emergency surgery for haemothorax	No	5
Female	79	None	10	CT	Ventro-basal Ptx left (5mm)	Conservative treatment	Yes	1

Female	40	Obstructive	23	Sonography (pre-hospital), CXR (in-hospital)	Thoracostomy tube left	Absent lung sliding left in lung ultrasound, thoracostomy tube left by emergency physician	Yes	1
Male	72	Obstructive	14	CXR	Ptx left (8mm)	Conservative treatment	No	5
Male	84	None	32	CXR	Ptx bilateral (right 1,4cm, left 7mm)	Chest tube right by surgeon	No	5
Male	76	Obstructive	12	CXR	Ptx and soft tissue emphysema left, deep sulcus sign left	Conservative treatment	Yes	1
Female	80	Obstructive	26	CT	Ptx right (4.3cm)	Chest tube right by surgeon	No	5
Female	73	Obstructive	25	CT	Chest tubes bilateral, generalised soft tissue emphysema	Re-Arrest during PCI, tension pneumothorax, chest tubes both sides by surgeon	No	5
Male	73	Obstructive	5	CXR	Generalised soft tissue emphysema, suspected minor Ptx bilateral	Chest tubes both sides by surgeon	No	5

Female	82	None	1	CT	Bilateral Ptx (ventral right 6mm, left 1.2cm)	Conservative treatment	No	5
Male	71	Obstructive	4	CXR	Thoracostomy tube left, soft tissue emphysema left	Absent breath sounds left, haemodynamic instability, thoracostomy tube by emergency physician	Yes	2
Male	83	None	6	CXR	Haemopneumothorax right, soft tissue emphysema	Chest tube right by surgeon	No	5
Female	50	None	42	CXR	Tension Ptx right (7.5cm)	Chest tube right by surgeon	No	5
Female	70	Obstructive	17	Sonography (pre-hospital), CXR (in-hospital)	Thoracostomy tubes bilateral, generalised soft tissue emphysema	Absent lung sliding bilateral in lung ultrasound, thoracostomy tubes both sides by emergency physician	No	5
Male	74	Obstructive	11	CXR	Bilateral Ptx (left 1.5cm, right 3cm)	Conservative treatment	Yes	1
Male	71	None	23	CT	Tension Ptx left	Chest tube by surgeon	No	5

Male	88	None	19	CT	Minor ventral Ptx left	Conservative treatment	No	5
Female	65	Obstructive	6	CT	Bilateral Ptx (left 7mm, right minor)	Conservative treatment	No	5
Male	47	None	26	CT	Ventral Ptx right (1.8cm)	Chest tube by surgeon	No	5

Abbreviations: CPR: cardiopulmonary resuscitation, CPC: Cerebral Performance Category, CT: computed tomography, Ptx: Pneumothorax, CXR: Chest X-Ray

Our logistic regression analysis identified a history of pre-existing obstructive pulmonary disease as a statistically significant factor associated with the occurrence of pneumothorax following cardiopulmonary resuscitation. Specifically, patients with obstructive lung disease had significantly higher odds of developing pneumothorax following CPR, with an odds ratio (OR) of 3.723 and a 95% confidence interval (CI) of 1.611–8.606.

The incidence of pneumothorax in the overall study cohort was 11.0% (26 out of 237 patients). Stratified by lung disease status, the pneumothorax rate was 7.4% among patients without any documented history of lung disease, while patients with pre-existing obstructive pulmonary disease exhibited a rate of 23.0%. This association is illustrated in Figure 11.

The discriminatory ability of the logistic regression model was evaluated using the area under the receiver operating characteristic curve (AUC), yielding a value of 0.671 (95% CI 0.508–0.809).

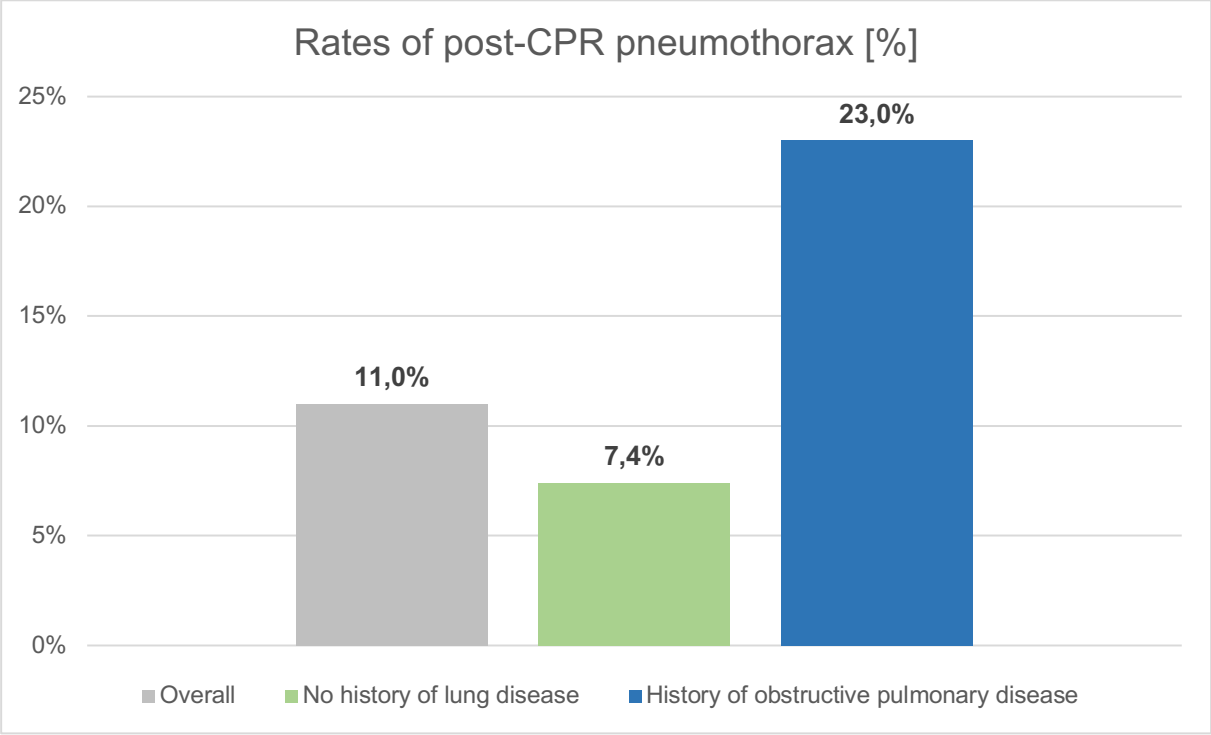

*Figure 11: Pneumothorax rates of the overall study population and the subgroups "no history of lung disease" and "history of obstructive pulmonary lung disease" from Project 1: **"Post-resuscitation pneumothorax: retrospective analysis of incidence, risk factors and outcome-relevance"(80)***

*Table 6: Patient characteristics, process and outcome data of the subgroups "no pneumothorax" and "pneumothorax" of Project 1 **""Post-resuscitation pneumothorax: retrospective analysis of incidence, risk factors and outcome-relevance"** adapted from **(80)***

	No pneumothorax n=211		Pneumothorax n=26	
Patient characteristics				
Sex				
Female	53	25.1%	12	46.2%
Male	158	74.9%	14	53.8%
Age (mean ± SD [years])	64.6	15.6	68.6	15.2
PESA				
1	22	10.4%	3	11.5%
2	73	34.6%	7	26.9%
3	98	46.4%	13	50.0%
4	18	8.5%	3	11.5%
5	64.6	15.6	68.6	15.2
Etiology				
Medical	154	73.0%	18	69.2%
Traumatic	0	0..0%	0	0.0%
Drug Overdose	4	1.9%	0	0.0%
Drowning	0	0.0%	1	3.8%
Electrocution	0	0.0%	0	0.0%
Asphyxia	30	14.2%	5	19.2%
Not recorded	23	10.9%	2	7.7%
History of lung disease				
None	150	71.1%	12	46.2%
Obstructive	47	22.3%	14	53.8%
Inflammatory/Infectious	9	4.3%	0	0.0%
Interstitial	1	0.5%	0	0.0%
Neoplasm	4	1.9%	0	0.0%
Witnessed cardiac arrest				
Bystander witnessed	121	57.3%	19	73.1%
EMS witnessed	38	18.0%	4	15.4%
Unwitnessed	47	22.3%	2	7.7%
Not recorded	5	2.4%	1	3.8%
Bystander CPR	113	53.6%	14	53.8%
Bystander AED				
Used	26	12.3%	1	3.8%
Shock delivered	20	9.5%	1	3.8%
No shock	6	2.8%	0	0.0%

delivered				
Not used	185	87.7%	25	96.2%
Location				
Home	127	60.2%	12	46.2%
Work	6	2.8%	0	0.0%
Recreation/Sports	5	2.4%	0	0.0%
Public	44	20.9%	9	34.6%
Nursing	15	7.1%	2	7.7%
Other	13	6.2%	3	11.5%
Not recorded	1	0.4%	0	0.0%
Initial ECG rhythm				
Shockable	87	41.2%	6	23.1%
VF	82	38.9%	6	23.1%
Pulseless VT	5	2.4%	0	0.0%
Non-shockable	124	58.8%	20	76.9%
PEA	55	26.1%	11	42.3%
Asystole	55	26.1%	6	23.1%
Not recorded	14	6.6%	3	11.5%
Process				
Response times (mean ± SD [mins])				
EMS	8.9	4.3	8.3	3.1
Emergency physician	11.4	5.3	10.2	3.5
Defibrillation time (if applicable; mean ± SD [mins])	8.9	7.3	8.4	3.2
No-flow-time (mean ± SD [min])	2.8	5.12	1.9	3.7
Unknown no-flow-time	28	13.3%	2	7.7%
Prehospital CPR duration (mean ± SD [mins])	22.3	18.8	17.3	10.5
Mechanical CPR use	4	1.9%	0	0.0%
Drugs given				
Adrenaline	157	74.4%	23	88.5%
Amiodarone	53	25.1%	3	11.5%
Reperfusion attempted	120	56.9%	12	46.2%
TTM	96	45.5%	17	65.4%

Chest imaging				
X-Ray	116	55.0%	9	34.6%
CT	38	18.0%	12	46.2%
Lung ultrasound	57	27.0%	5	19.2%
Outcomes				
Survived Event	176	83.4%	25	96.2%
Any ROSC	204	96.7%	26	100.0%
Survival to hospital discharge	83	39.3%	7	26.9%
CPC at hospital discharge				
Favourable	68	32.2%	7	26.9%
1	54	25.6%	6	23.1%
2	14	6.6%	1	3.8%
Non-favourable	143	67.8%	19	73.1%
3	9	4.2%	0	0.0%
4	6	2.8%	0	0.0%
5	128	60.7%	19	73.1%

Abbreviations: SD: standard deviation, PESA: Pre Emergency Status Assessment, EMS: emergency medical service, CPR: cardiopulmonary resuscitation, AED: automated external defibrillator, ECG: electrocardiogram, VF: ventricular fibrillation, VT: ventricular tachycardia, PEA: pulseless electrical activity, mins: minutes, TTM: target temperature management, CT: computed tomography, ROSC: Return of Spontaneous Circulation, CPC: Cerebral Performance Category

Project 2: Pneumothorax in a Thiel cadaver model of cardiopulmonary resuscitation

Pneumothorax was detected by lung ultrasound in 8 out of the 11 cadavers examined, corresponding to a detection rate of 72.7%. Of these, four cadavers (36.4%) had bilateral pneumothoraces, while two cases (18.2%) had left-sided and two (18.2%) right-sided pneumothorax. All cadavers with bilateral pneumothorax also exhibited tension pneumothorax. Detailed characteristics and outcomes for each cadaver are presented in Table 7 and illustrated in Figure 12.

The timing of pneumothorax detection varied throughout the experiment. The median cumulative chest compression time at which the first pneumothorax was identified was 12 minutes (interquartile range: 9.5 minutes; range: 0–16 minutes). An analysis of cadaver-specific variables - height, sex, and recruitment pressure - revealed one statistically

significant association: tension pneumothorax was observed in all three cadavers that underwent recruitment at a pressure of 35 cm H_2O. In comparison, only one of the eight cadavers subjected to a recruitment pressure of 30 cm H_2O developed tension pneumothorax. This difference was statistically significant (p = 0.024).

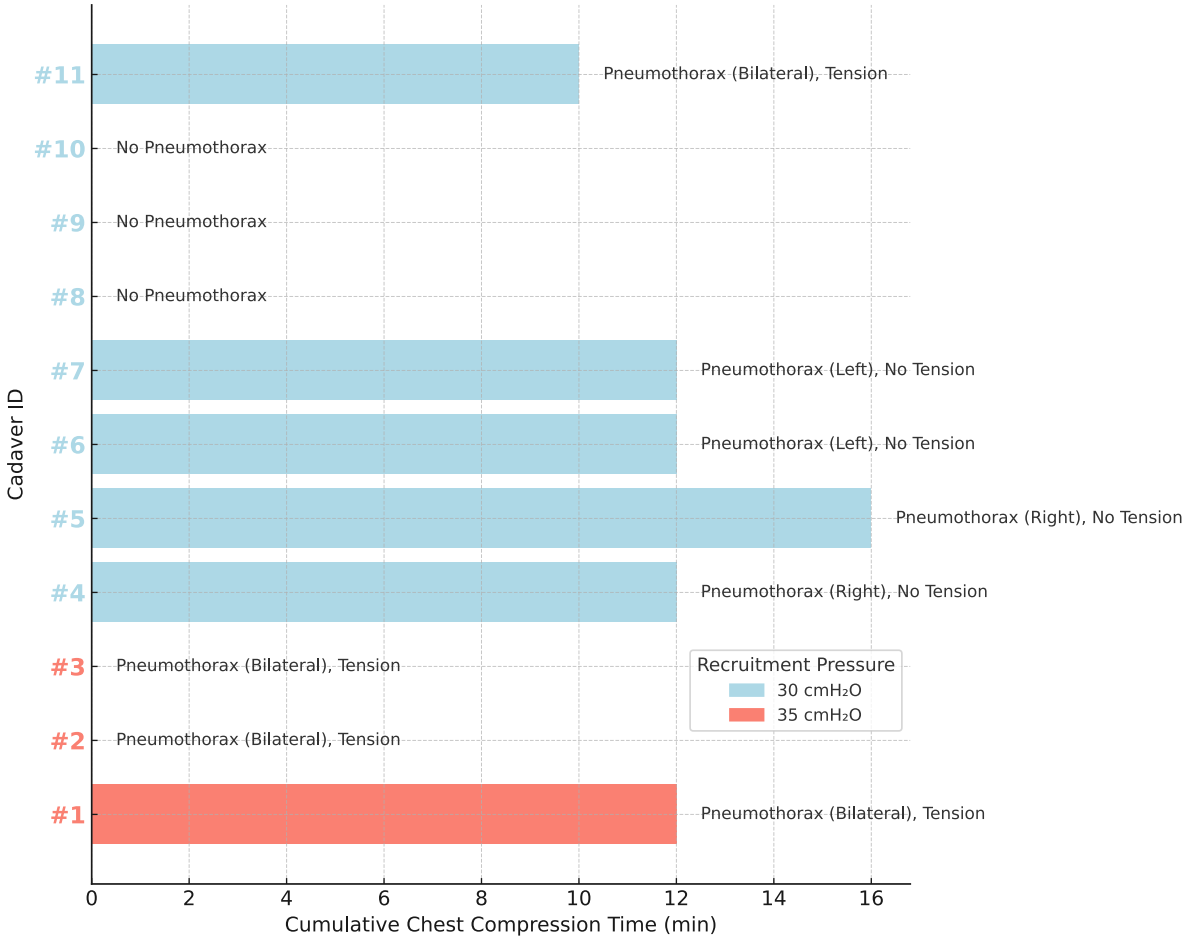

Figure 12: Cumulative chest compressions times until detection of pneumothorax for the individual cadavers with corresponding recruitment pressure and tension pneumothorax occurrence
(Prompt: bar chart with cadaver ID and cumulative chest compression time until pneumothorax detection, ChatGPT (June 2025 Version), OpenAI, 09.05.2025, https://chatgpt.com)

Table 7: Characteristics and results of the individual cadavers from Project 2: ***"Pneumothorax in a Thiel cadaver model of cardiopulmonary resuscitation"*** *adapted from* ***(81)***

Cadaver ID	Sex	Height [cm]	Occurrence/ Site of Pneumothorax	Maximum applied recruitment pressure [cmH_2O]	Study period when pneumothorax was detected	Cumulative chest compression time until first pneumothorax detection [min]	Escape of air when performing thoracostomy
#1	Male	175	Bilateral	35	2nd crossover period	12	Yes, bilateral
#2	Male	161	Bilateral	35	Recruitment phase	0	Yes, bilateral
#3	Female	163	Bilateral	35	Recruitment phase	0	Yes, bilateral
#4	Male	171	Right	30	2nd crossover period	12	No
#5	Male	167	Right	30	3rd crossover period	16	No
#6	Female	166	Left	30	2nd crossover period	12	No
#7	Female	172	Left	30	2nd crossover period	12	No
#8	Male	168	None	30	-	-	-
#9	Male	166	None	30	-	-	-
#10	Female	154	None	30	-	-	-
#11	Female	155	Bilateral	30	2nd crossover period	10	Yes, bilateral

Discussion

Project 1: Post-resuscitation pneumothorax: retrospective analysis of incidence, risk factors and outcome-relevance

In this retrospective study of patients hospitalized after non-traumatic out-of-hospital cardiac arrest we found pneumothorax to be present in more than one out of ten cases. The 11.0% pneumothorax rate in our cohort falls within the midrange of the widely varying rates (2.5%-26.4%) reported in literature (37-42, 44-47, 67, 95). This variation can be attributed to differences in study designs, patient population and diagnostic methods.

Study collectives, in which computed tomography was used as the sole imaging modality demonstrated higher rates of pneumothorax compared to study cohorts with other (chest X-ray, sonography, autopsy) or mixed diagnostic methods (37-42, 44-47, 67, 95). Similarly, in our study, the subpopulation examined with computed tomography showed a higher pneumothorax rate compared to the overall study collective (24.0% versus 11.0%). Computed tomography is widely considered as being the gold standard for pneumothorax detection, which likely accounts for some of the detected differences (96). This may suggest that chest X-ray and lung ultrasound fail to detect a considerable number of pneumothoraces. However, it remains unclear whether a pneumothorax missed by chest X-ray or sonography is of clinical significance. Additionally, pre-test probability appears to be an important contributing factor. Patients with higher clinical suspicion for a non-cardiac cause of OHCA (such as pneumothorax) or those after exclusion of a cardiac cause are more likely to be selected for computed tomography. This approach is also consistent with guideline recommendations for post-resuscitation care (35). Therefore, the CT-subpopulation may be more likely to yield positive findings indicating that variations in the baseline risks, rather than the diagnostic method alone, could also account for the differences in pneumothorax rates. Kim et al. prospectively enrolled out-of-hospital and in-hospital cardiac patients over a 6-month period. Chest computed tomography was performed in those, who achieved sustained ROSC, revealing a pneumothorax rate of 8.5%. Similarly, Branch et al. prospectively included patients that survived an OHCA and observed a pneumothorax rate of 4.8%, however patients with urgent need for coronary catheterization were excluded from their analysis. To the best of our knowledge, no other studies have prospectively enrolled OHCA patients and utilized CT as diagnostic modality.

History of pre-existing obstructive pulmonary disease was found to be associated with the occurrence of pneumothorax after cardiopulmonary resuscitation. This subgroup showed a

pneumothorax rate of 23.0% (14 out of 61 cases) which is more than three times higher compared to the “no lung disease” subgroup (7.4%). Several chronic pulmonary conditions are known risk factors for development of spontaneous pneumothorax (secondary spontaneous pneumothorax) with chronic obstructive pulmonary disease (COPD) being the most common (48-51, 53). It is likely that underlying lung diseases make the lung tissue less resilient and therefore more susceptible to the mechanical stress during cardiopulmonary resuscitation. Structural and functional pulmonary changes including emphysema, reduced compliance, decreased elasticity and air trapping may lead to elevated ventilation pressures further increasing the risk of lung injury and subsequent pneumothorax. Secondary spontaneous pneumothorax due to underlying pulmonary conditions may also progress to tension pneumothorax leading to haemodynamic and respiratory compromise, eventually resulting in cardiac arrest.

To date and to the best of our knowledge, only a limited number of case reports and a single conference abstract have addressed pneumothorax following CPR in the context of pre-existent pulmonary conditions that may predispose to this complication (95, 97-101). Notably, some of the cases involved the use of mechanical chest compression devices and some patients had underlying chest trauma. This further highlights the novelty and clinical relevance of this particular finding of our study. Based on this, we strongly recommend the use of lung ultrasound for pneumothorax detection during and after cardiopulmonary resuscitation, especially in the high-risk subpopulation of patient with pre-existent obstructive lung disease. Pleural sonography is quick and relatively easy to perform. It is of non-invasive nature, can be done repeatedly and on scene without exposing health care providers and patients to radiation. Diagnostic accuracy has been reported to be superior over supine chest X-ray (59-62).

The literature presents conflicting evidence regarding the relationship between CPR-related injuries and the duration of cardiopulmonary resuscitation. While some studies report that longer resuscitation efforts are associated with higher rates of rib fractures (39, 43, 102) and CPR-related injures generally (103), others were not able to show a clear link (38, 40, 44). To the best of our knowledge, the impact of CPR duration on the occurrence of pneumothorax following CPR has not been discussed in the available literature. In our study cohort, we were not able to observe a significant association.

Mixed results in literature can be found regarding the association of age and the occurrence of CPR-related injuries. Several authors report of higher rates of rib fractures (39, 43, 102, 104) or CPR-related injuries in general (40) with increasing age while others could not

identify any association (44). Some studies showed an association of female gender with occurrence of rib fractures (44, 104) or any injury (38) following cardiopulmonary resuscitation whereas others did not find any gender-related differences (39, 40, 43, 102). Possible explanations for the higher incidence of rib fractures in females discussed in literature include the greater prevalence of osteoporosis and higher age at the time of cardiopulmonary resuscitation (41, 44, 104). In our study collective no significant difference in age between males and females was observed. To date, we were not able to find any literature that examined the occurrence of pneumothorax after CPR in the context of patient age or gender. Although the subgroup “pneumothorax” was slightly higher in age (68.6 years versus 64.6 years) and had a greater proportion of female patients compared to the subgroup “no pneumothorax” (46.2% versus 25.1%), our logistic regression analysis did not reveal any association between age or gender with development of post-CPR pneumothorax.

In our study population the observed rate of survival to hospital discharge was 38.0%, corresponding to 90 out of 237 patients admitted to hospital after OHCA. The prospective, European-wide multicentre EURECA TWO trial (105), published in 2020, reported of a hospital survival rate of 26.4% among more than 37.000 patients with out-of-hospital cardiac arrest. In the Austria subset of the study collective, a hospital survival rate of 26.0% was reported by the authors. The observed difference is likely caused by some degree of positive-selection of patients due to our study design, which will be discussed extensively in the limitations section. However, among patients where resuscitation was attempted survival to hospital discharge in our study population (before applying exclusion criteria) was 8.2% (90 out of 1103 patients), closely aligning with the 8.0% reported in the EURECA TWO trial. The 2025 Heart Disease and Stroke Statistics published by the AHA (American Heart Association) reports of a hospital survival rate of 10.2% among patients with non-traumatic OHCA in the United States in the year 2023 (106).

Factors associated with a higher likelihood of survival to hospital discharge were younger age, lower PESA (Pre Emergency Status Assessment) category, shockable initial ECG rhythm, shorter CPR duration and shorter no-flow-time (time from collapse until initiation of cardiopulmonary resuscitation). This set of variables corresponds well with known predictors for survival following cardiopulmonary resuscitation from current literature (107, 108).

In our study collective of 237 hospitalized out-of-hospital cardiac arrest patients, 75 (31.6%) survived with favourable neurological outcome. Out of all 1103 patients in our dataset, in whom CPR measures were initiated, 6.8% had survival in favourable neurological condition. The 2025 Heart Disease and Stroke Statistics reported that, in 2023, 8.1% of out-of-hospital

cardiac arrest patients in the United States survived with a CPC of 1 or 2 (106). An analysis of the Pan-Asian Resuscitation Outcomes Study (PAROS) dataset found rates of favourable neurological outcome in patients living in high-income countries and middle-income countries of 3.65% and 0.75%, respectively (109).

The set of predictors for survival with favourable neurological outcome at hospital discharge identified in our study included younger age, lower PESA category, shockable initial ECG rhythm, shorter CPR duration and shorter no-flow-time – mirroring the set of variables identified by the statistical model for survival to hospital discharge. The prediction of neurological outcome following cardiopulmonary resuscitation has been extensively studied, driven by the need for early and accurate prognostication in cardiac arrest survivors. Several scoring systems (e.g. OHCA score – out of hospital cardiac arrest score; CAHP score– cardiac arrest hospital prognosis score, GO-FAR – good outcome following attempted resuscitation score) have been developed to assess the likelihood of survival in good neurological condition in order to guide physicians in their clinical decision-making (110-113). The variables identified in our analysis are largely reflected, either directly or indirectly, in the previously mentioned scoring systems. This alignment of predictive variables identified by our statistical models – for both survival to hospital discharge and favourable neurological outcome at hospital discharge – with reported CPR outcome predictors in the existing literature strongly supports the validity and representativeness of our dataset.

We would like to highlight the dramatic impact of longer no-flow-time, defined as the period from collapse until initiation of resuscitation efforts, on outcome after cardiopulmonary resuscitation. One additional minute of no-flow-time was estimated to lower the chances for hospital survival and favourable neurological outcome by 21.7% and 37.0%, respectively. An increase in no-flow-time by two minutes was predicted to reduce the probability to survive to hospital discharge by 52.0%, and the probability to survive with favourable neurological outcome by 60.3%. This dose-response relationship has already been demonstrated in previous studies (114, 115). Interestingly, similar findings were observed in an experimental animal model utilizing rats, where low quality immediate CPR had superior results over high quality delayed CPR (116). Among the set of predictors identified for both outcome measures, no-flow-time is the only one that is potentially modifiable. This underscores the importance of the bundle of measures encompassed by the concept of “systems saving lives” (117). Several public health campaigns aim to raise cardiac arrest awareness and promote intervention by laypersons including the start of CPR and the use of an automated external defibrillator (AED). Notably, several initiatives are actively working to enhance

cardiac arrest awareness and improve CPR knowledge and skills among laypersons in Austria (118-120). Emergency dispatchers also play a crucial role in this process as they should be able to quickly recognize cardiac arrest and – if appropriate – instruct bystanders to initiate CPR until emergency medical service arrives on scene. Across all levels of education CPR training should be integrated to ensure widespread knowledge and skills about cardiac arrest and life saving measures. Technologies that facilitate the rapid alerting of first responders and help to locate public access defibrillators play another important part further strengthen the early links of the so-called chain of survival (121).

Both survival to hospital discharge and favourable neurological outcome were less frequent among patients presenting with pneumothorax at hospital admission following CPR compared to those without pneumothorax (25.9% versus 39.5% and 25.9% versus 32.1%, respectively). These findings suggest a tendency towards worsened outcome the pneumothorax subgroup, however, this numeric trend failed to reach statistical significance in our logistic regression analysis. Nevertheless, it is thinkable pneumothorax contributes to increased morbidity and mortality among cardiac arrest survivors. The presence of pneumothorax may necessitate additional medical procedures such as chest tube placement or – in some cases - even more extensive thoracic surgery. Additionally, it may cause prolonged mechanical ventilation due to difficult weaning and haemodynamic and/or respiratory impairment, particularly if untreated tension pneumothorax is present. Notably, tension pneumothorax may not only complicate post-resuscitation care but also carries the potential to cause cardiac arrest.

At this stage, we would like to acknowledge what may be considered a “the chicken or the egg” dilemma: Pneumothorax may represent either the underlying cause leading to cardiac arrest – such as in the case of tension pneumothorax causing severe haemodynamic and respiratory compromise. Conversely, pneumothorax may also develop as an iatrogenic complication due to the mechanical stress of chest compressions and positive-pressure ventilation. Distinguishing whether pneumothorax preceded cardiac arrest or resulted as an adverse effect from resuscitation efforts is, in most cases, virtually impossible for health care providers at the time of resuscitation., However, it may be questionable, if this distinction holds any immediate clinical relevance in the acute peri-CPR setting, where the primary focus is on rapid identification and treatment of life-threatening conditions, irrespective of their exact origin.

Limitations

First and foremost, it is important to acknowledge that this study is subject to limitations inherent to retrospective analysis of clinical data. Retrospective studies, obviously, rely on previously collected data, that were originally gathered rather for clinical, rather than research, purposes. As a result, the dataset may be incomplete or contain missing values, and there may be variability in the accuracy and consistency of the recorded information. Furthermore, the retrospective design limits the ability to control for all potential confounding factors. (122) We sought to address this issue by utilizing a dataset structured in accordance with the Utstein-style reporting guidelines (10). Overall, missing data were not a significant issue in our dataset. The only exception involved 30 cases in which the no-flow time—the interval between cardiac arrest and the initiation of CPR measures—was not documented. This type of missing information is frequently encountered in real-world resuscitation scenarios.

Research in the field of cardiopulmonary resuscitation, generally, faces numerous challenges. Conducting high-quality research is complicated by ethical and practical constraints as well as the time-critical nature of cardiac arrest, heterogeneity among health care providers and institutions, patients and underlying pathologies, high mortality rates and the inability to obtain patient consent for study participation. (123)

Furthermore, our study population does not reflect the entire population of cardiac arrest victims as we only included adult, non-traumatic, hospitalized, out-of-hospital cardiac arrest patients who underwent chest imaging. Therefore, certainly some degree of selection bias may have arisen due to several reasons.

Paediatric and newborn life support algorithms differ from that used in adults for several reasons (24, 33). In terms of CPR-related injuries, the injury patterns observed in children and infants differ from those seen in adults due to distinct biomechanical properties, most notably the greater elasticity of the thoracic skeleton. In literature, significant injuries (such as pneumothorax) due to resuscitation efforts in paediatric populations are described as being extremely rare. Among 351 deceased children younger than 12 years who received CPR Bush et al. conducted a review of clinical and autopsy records. They identified rib fractures in approximately 3% of cases – significantly lower than in adult CPR populations, where rib fractures are the most frequently observed CPR-related injury, with a reported prevalence ranging approximately from 50% to as high as 97% (39-41, 46, 124). If significant traumatic injuries are present after CPR the possibility of child abuse should be taken into consideration. (41, 125, 126) Given the low incidence of paediatric cardiac arrest, the

extremely rare occurrence of CPR-related injuries in this population, the different treatment algorithm for paediatric cardiac arrest, and distinct biomechanics and pathophysiology of infants and children, we decided to exclude patients younger than 18 years from our study cohort.

In traumatic arrest, the treatment strategy is modified from the universal advanced life support algorithm. Immediate treatment of reversible causes such as catastrophic haemorrhage or tension pneumothorax is given highest priority - even over chest compressions (34). In our study, traumatic cardiac arrest cases were excluded as we considered “post-CPR pneumothorax” in our methodology rather as a negative side-effect of cardiopulmonary resuscitation than a cause of cardiac arrest. As noted earlier, perfect discrimination is impossible as pneumothorax can occur both as a cause and as a complication from CPR measures, even in non-traumatic cases.

We included only hospitalized patients in our study, as our inclusion criteria required thoracic imaging for detection of pneumothorax. Obviously, this inherently introduced a considerable positive selection bias. On one hand, patients declared dead on scene were excluded, a population likely to differ significantly from the hospitalized cohort. On the other hand, hospitalized patients had to be sufficiently stable to undergo chest imaging. A considerable number of patients died immediately after hospital admission before any diagnostic imaging was performed, adding another layer of positive selection.

Transport under ongoing CPR is rather unusual, especially in cases without prior return of spontaneous circulation (ROSC) and no apparent reversible cause. This applies particularly to rescue systems where physicians and/or paramedics are authorized to apply termination of resuscitation (TOR) rules on-scene. Furthermore, transport under ongoing cardiopulmonary resuscitation poses practical challenges and may not be feasible under certain circumstances (25, 127, 128). This practice was also evident in our study collective, where 97,0% of patients had achieved any ROSC before hospital admission. Prehospital imaging could also include cardiac arrest victims pronounced dead on scene, thereby helping to reveal the true incidence of pneumothorax in out-of-hospital cardiac arrest patients. Lung ultrasound is a feasible diagnostic tool for pneumothorax detection on-scene that is becoming increasingly available in emergency medical systems (29, 60, 129). In our opinion, prehospital lung ultrasound for pneumothorax detection in OHCA patients could provide valuable insights and represents a promising future research direction.

In-hospital cardiac arrest (IHCA) patients were also not covered by our study. Seung et al. compared CPR-related complications in OHCA and IHCA cohorts and found a higher

incidence of rib fractures in the out-of-hospital group. Pneumothorax occurred more frequently in OHCA patients (21.4% versus 10.2%), however this trend did not reach statistical significance (102). Aetiology of cardiac arrest may also differ between the OHCA and IHCA populations. In-hospital cardiac arrest is often characterized by preceding physiological deterioration in patients already hospitalized for acute medical illness. In their systematic review and meta-analysis, Allencherill et al. identified hypoxia, acute coronary syndrome, arrhythmias, hypovolemia, infection, and heart failure as the most common aetiologies for IHCA. Interestingly, three of the most common underlying causes reported in their study were not represented by the “4H’s and 4T’s” mnemonic, while some of the conditions listed in the mnemonic were found to be very uncommon, including pneumothorax (0.1%). (25, 130, 131)

Pneumothorax is also a recognized complication of central venous catheter (CVC) placement, a procedure frequently performed in critically ill patients. Indications for CVC insertion include the administration of particular medications or fluids (e.g., catecholamines, parenteral nutrition), the measurement of central venous pressure, the establishment of long-term venous access or to facilitate haemodialysis. Common sites for central venous catheter insertion include the internal jugular, subclavian, and femoral veins. Among these, catheterization of the subclavian vein carries the highest risk of pneumothorax (132). A systematic review and meta-analysis by Smit et al. reported the incidence of pneumothorax following CVC placement to range from 0.1% to 3.3% (133). In our study cohort we screened for cases, where insertion of a central venous line was performed prior to chest imaging and pneumothorax was subsequently detected. This scenario was observed in three patients, however, all of them showed bilateral pneumothoraces while attempts for CVC placement were made unilaterally.

Due to the study design centred on a single, physician-staffed ambulance system, there is limited generalizability to other EMS settings and environments. This also resulted in a relatively small study cohort, which may negatively the robustness and wider applicability of our findings.

As previously noted, the imaging method used can affect pneumothorax detection rates. Our study collective was heterogeneous in this regard, with chest X-ray, computed tomography (CT), and lung ultrasound all employed. Therefore, we were unable to assess for additional CPR-related injuries. Rib or sternal fractures, for example, can be easily diagnosed by computed tomography but not by sonography. Investigating whether such fractures

contribute to the development of pneumothorax following CPR would be a valuable focus for future research.

Several studies have suggested that the use of a mechanical chest compression device, compared to manual chest compressions, may be associated with a higher risk of CPR-related injuries, including pneumothorax. (30, 31, 134). In our study cohort, none of the four patients who received mechanical compressions presented with pneumothorax upon hospital admission. However, the small sample size precluded any meaningful analysis.

Project 2: Pneumothorax in a Thiel cadaver model of cardiopulmonary resuscitation

Pneumothorax was observed in eight out of eleven (72.7%) Thiel-embalmed cadavers used in simulated cardiopulmonary resuscitation utilizing a mechanical chest compression device and mechanical ventilation, appearing at various stages throughout the experiment. This incidence is notably higher compared to pneumothorax rates reported in clinical studies, which range from 2.5% to 26.4% (37-42, 44-47, 67, 95).

Previous studies found Thiel-embalmed cadavers to be suitable for simulated cardiopulmonary resuscitation and the study of mechanical and respiratory characteristics (69, 72). Similarly, our experimental study confirmed the suitability of this cadaver model for such applications. We found lung ultrasound to be a feasible diagnostic method for detecting pneumothorax in the Thiel cadaver model. To the best of our knowledge, there are no prior reports in the literature describing the use of pleural sonography for pneumothorax detection in cadavers embalmed by the Thiel-solution.

Thiel cadavers are valued for their lifelike anatomical appearance and mechanical properties, particularly the preserved tissue flexibility and elasticity. Charbonney et al. reported a high degree of consistency between Thiel-embalmed cadavers, patients with out-of-hospital cardiac arrest or critically illness in terms of mechanical properties of the respiratory system, including parameters such as compliance, resistance and airway closure (72). However, the high incidence of pneumothorax in our experimental setting raises the possibility that the embalming process may compromise the pulmonary resilience to the mechanical stress imposed by cardiopulmonary resuscitation. Thus, we conclude that transferability of our experimental findings to the clinical setting is very limited.

Recruitment pressure also appears to play a significant role in the development of pneumothorax. All three cadavers which were subject to a recruitment pressure of 35cm H_2O, developed bilateral tension pneumothorax. Notably, in two of the cadavers, this

condition was already present after the 15-minute recruitment phase with no chest compressions having been performed. As a result, we revised the study protocol and reduced the maximum recruitment pressure to 30cm H2O. Subsequently, only one out of eight cadavers exposed to the lower recruitment pressure developed tension pneumothorax. We are aware that this adjustment introduces an inconsistency in the study protocol - presenting a major limitation; however, we also acknowledge this as one of the key learning points that can be derived from our experimental results.

Limitations

Firstly, the study protocol was primarily designed for the project by Orlob et al. which investigated whether three different transport ventilators could achieve sufficient ventilation under ongoing chest compressions (76). This background explains some of the limitations of the current study, such as the use of different ventilators, the cross-over design and the sample size.

As previously noted, several limitations are inherent to the use of a cadaver model, mainly restricting transferability of the findings to clinical patients. Moreover, we were not able to assess the medical history of the body donors which may have included relevant pre-existing conditions, in particular pulmonary diseases.

Additionally, current evidence remains insufficient to clearly support or refute the use of automated mechanical ventilation instead of manual bag-valve ventilation during cardiopulmonary resuscitation (135). However, the use of mechanical ventilation and standardized ventilatory settings were integral parts of the study design. Settings were selected in accordance with applicable guidelines and experts' recommendations (25, 136).

Mechanical chest compressions were delivered using an automated chest compression piston device ("Corpuls CPR", GS Elektromedizinische Geräte G. Stemple GmbH, Germany). The use of such a mechanical chest compression device may be associated with an increased risk of CPR-related injuries, including pneumothorax, which could have contributed to the high incidence of pneumothorax observed in our experiment (30, 31, 134).

We are aware that computed tomography is considered the gold-standard imaging method for detecting pneumothorax. In our experimental study, we employed lung ultrasound, a diagnostic method also recognized for its suitability in pneumothorax detection, though with lower sensitivity compared to CT (62, 96). However, computed tomography was not deemed feasible within the facilities of the anatomy institute for the purposes of our study.

Conclusions

Pneumothorax after cardiopulmonary resuscitation should not be considered an uncommon phenomenon, particularly in certain high-risk populations. Among out-of-hospital cardiac arrest patients, those with pre-existing obstructive lung diseases appear to be at elevated risk for development of pneumothorax.

In simulated cardiopulmonary resuscitation using cadavers embalmed by the Thiel method pneumothorax incidence was notably high. Airway pressure during the recruitment process seems to play a crucial role. Future research involving Thiel cadavers should account for these findings in the design of their study protocols.

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Appendix

AI Tools

Use of AI Language Support

To enhance the quality of written communication in this thesis, ChatGPT (developed by OpenAI) was used for grammar and spelling checks, as well as to improve clarity, readability, and overall comprehension of the text. All content was authored and critically reviewed by the thesis author, with AI assistance serving solely as a language and editorial support tool.