Tampere University

PIRITTA SETÄLÄ

Out-of-Hospital Cardiac Arrest and the Critically Ill Pre-Hospital Patient

Factors Affecting Cardiopulmonary Resuscitation and Patient Outcomes

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ACADEMIC DISSERTATION
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”Do not go gentle into that good night.
Rage, rage against the dying of the light.”

Dylan Thomas

To those who resuscitate

ABSTRACT

Background: The outcome of out-of-hospital cardiac arrest (OHCA) varies between countries, and the prognosis remains modest despite improvements in quality of care. International OHCA registries and Utstein guidelines aim to gather comprehensive epidemiological data that could be better compared between communities.

Cardiopulmonary resuscitation (CPR) may cause injuries. Although a majority of CPR-related injuries are considered to be non-life-threatening, their predictors are poorly known.

End-tidal carbon dioxide ($ETCO_2$) is a marker for CPR quality and CPR effectiveness during the resuscitation attempt. The role of active compression-decompression (ACD) devices in improving resuscitation quality by enhancing the $ETCO_2$ output has had controversial results, while previous studies lack quality measurements of CPR attempts.

Emergency medical service (EMS) staff meet their patients in situations where the underlying severity of the patient's condition may not be easily resolved. Therefore, a reliable assessment tool for early recognition of a deteriorating patient would be valuable in the pre-hospital setting.

The aims of this study were to 1) describe the epidemiology of OHCA in the Pirkanmaa area of Finland, 2) evaluate the impact of futile resuscitation attempts on the outcomes in OHCA according to the Utstein reporting template, 3) determine the incidence of and predictors for CPR-related injuries in non-survivors of OHCA, 4) assess whether ACD-CPR provides better overall resuscitation quality than manual CPR in terms of $ETCO_2$ output when both methods are used under the guidance of an audio-visual feedback system defibrillator in the pre-hospital setting, and 5) determine whether a simplified pre-hospital medical emergency team (MET) score could provide a risk assessment tool in the pre-hospital setting and predict in-hospital outcomes.

Materials and methods: Study data were collected prospectively from 314 OHCA cases, including forensic autopsy records, during a 12-month study period and retrospectively from 610 adult patients' pre-hospital MET scores during a 6-month study period. The emergency medical service (EMS) adhered to the European Resuscitation Council Resuscitation Guidelines (2010) during the study. CPR-quality data from ten witnessed OHCAs resuscitated with alternating two CPR methods, ACD-CPR and manual CPR, were collected together with continuous $ETCO_2$ measurements. Differences between the CPR methods were analysed within each OHCA case to minimise the confounding factors between the cases. Pre-hospital vital signs were scored to receive a simplified pre-hospital MET score.

Results: In the prospective study, the incidence of EMS-treated OHCA was 52 per 100,000 population per year. EMS attended a total of 314 OHCA cases in which resuscitation was not attempted due to futility in 34 (11%) cases, and efforts were soon discontinued due to dismal prognostic factors in 74 (24%) cases. The discontinued cases were classified as partial resuscitations. Removing these partial resuscitation attempts from the outcome calculations increased the percentage of survival to hospital discharge from 14% to 19%. The overall survival from EMS-witnessed CA was low (16%) but resulted in good neurological recovery (cerebral performance category 1-2) at hospital discharge among all survivors. In this study, the shockable initial rhythm (OR 3.91, 95% CI 1.61-9.51, P = 0.003) and bystander CPR (OR 3.48, 95% CI 1.29-9.39, P = 0.014) were strong independent predictors of survival after OHCA. A total of 149 cases underwent a forensic autopsy after OHCA. The incidence of CPR-related injuries was 47%, and the most common injuries were multiple rib fractures (43%) and sternum fracture (15%). The independent predictors for CPR-related injuries were OHCA in a public location (OR 4.98, 95% CI 2.02–12.31, P < 0.001), male gender (OR 4.11, 95% CI 1.79–9.43, P = 0.001), and older age (OR 1.04, 95% CI 1.01–1.07, P = 0.013). The duration of CPR attempts did not affect the incidence of injuries.

In the study comparing the two CPR methods, the interaction between the method and the patient was significant ($P < 0.001$) for $ETCO_2$ output. The mean length of the CPR episodes was 37(±8) minutes, and in six out of ten cases, the $ETCO_2$ output was higher with manual CPR, indicating similar effectiveness of CPR-methods.

Higher simplified pre-hospital MET scores were associated with hospital morbidity and mortality. A simplified pre-hospital MET score was an independent predictor for hospital mortality (OR 2.42, 95% CI 1.84-3.18, $P < 0.001$), regardless of the patient's age or previous physical health.

Conclusions: The incidence and survival rates of EMS-treated OHCA in the Pirkanmaa area of Finland are similar when compared to the European registries. However, partial resuscitations formed a considerable amount of OHCA cases, and this interfered with the outcome calculations. The incidence of CPR-related injuries was lower compared to previous studies, and this study presents a novel finding that OHCA in public locations is an independent risk factor for these injuries. A novel method of comparing the effectiveness of two CPR methods on their $ETCO_2$ output by monitoring the quality of CPR during the resuscitation attempt found that quality-controlled ACD-CPR was not superior to quality-controlled manual CPR. A simplified pre-hospital MET score predicts patient outcome regardless of age or physical health and could serve as a pre-hospital risk assessment tool.

TIIVISTELMÄ

Äkillinen sydänpysähdys on maailmanlaajuisesti yksi suurimmista kansanterveydellisistä ongelmista. Sairaalan ulkopuolella tapahtuvan sydänpysähdyksen ennuste on vaatimaton, sillä Euroopassa vain 9-11% kaikista sydänpysähdyspotilaista kotiutuu sairaalahoidosta. Viime vuosikymmenten aikana ennustetta on pyritty parantamaan kehittämällä monia menetelmiä ja uusia hoitomuotoja, kuten elvytyksen jälkeinen välitön sydämen sepelvaltimoiden angiografia ja pallolaajennus sekä teho-osastolla toteutettava potilaan elimistön ydinlämpötilan hallinta. Pyrkimyksistä huolimatta sairaalan ulkopuolisen sydänpysähdyksen ennuste ei ole viime vuoksikymmenten aikana muuttunut paremmaksi.

Kansainväliset elvytysohjeistot pyrkivät parantamaan potilaan koko hoitoketjun laatua ja siten potilaan selviytymistä äkillisestä sydänpysähdyksestä. Lisäksi monet kansalliset ja kansainväliset elvytysrekisterit keräävät tietoa sydänpysähdystapahtumista Utsteinin mallin mukaisesti. Tämä Utstein-ohjeistus pyrkii yhdenmukaistamaan elvytystapahtumien raportointimallia, jotta lukuisiin elvytysrekistereihin kerättyä tietoa voitaisiin verrata keskenään.

Elvytyksen laatu ja siten potilaan ennuste ovat riippuvaisia mahdollisimman varhain aloitetusta elvytyksestä, oikeasta rintakehän painelutekniikasta, mahdollisimman varhaisesta sydäniskurin käytöstä silloin kun kyseessä on defibrilloitava rytmi, sekä painelutaukojen minimoinnista. Elvytyksen aikana voidaan käyttää painelulaatua mittaavaa anturia, joka neuvoo elvyttäjää suorittamaan laadukasta paineluelvytystä. Lisäksi elvytyksen aikaisella potilaan uloshengitysilman hiilidioksidin mittauksella voidaan arvioida elvytyksen laadukkuutta. Elvytyksen aikainen potilaan rintakehän painelu voi aiheuttaa potilaalle vammoja. Tyypillisimmät vammat esiintyvät luisen rintakehän alueella, mutta elvytys voi aiheuttaa vammoja myös sisäelinten alueelle. Suurin osa elvytykseen liittyvistä vammoista on lieviä eivätkä ne ole vältettävissä laadukkaankaan paineluelvytyksen aikana.

Ensihoidon kohtaamien potilaiden kokonaisvaltainen tilanarviointi ja hoidon tarpeen kiireellisyyden arviointi on haastavaa, sillä potilaan äkillisen sairastumisen yhteydessä voi olla vaikea saada tietoja potilaan aiemmista sairauksista sekä nykytilan kehittymisestä. Sairaaloissa on käytössä potilaan elintoimintojen mittauksiin perustuvia arviointityökaluja, joilla voidaan ennustaa potilaan tilan kehittymistä ja hoitaa nopeasti uhkaava elintoimintojen romahtaminen. Vastaavanlainen arviointityökalu olisi hyödyllinen myös ensihoidossa, mutta toistaiseksi käytössä olevien menetelmien herkkyys ja tarkkuus eivät ole kovin korkeita ensihoidon valikoitumattomassa potilasmateriaalissa.

Tämän väitöskirjatyön tarkoituksena oli tutkia sairaalan ulkopuolisten sydänpysähdysten epidemiologiaa Pirkanmaan alueella ja määrittää elvytyksen tehokkuuteen tai

tuloksettomuuteen liittyviä tekijöitä selvittämällä osittaisten elvytysyritysten luonnetta sekä vertaamalla kahden elvytysmenetelmän laatua toisiinsa. Lisäksi väitöskirjatyössä tutkittiin sairaalan ulkopuolella elvytettyjen oikeuslääketieteellisessä ruumiinavauksessa todettuja elvytysvammoja ja ensihoidon aikana laskettavan yksinkertaisen riskipisteytyksen hyötyä kriittisesti sairaan potilaan sairaalahoitojakson ennusteen arvioinnissa.

Epidemiologisessa työssä todettiin sairaalan ulkopuolisten ensihoidon hoitamien sydänpysähdysten ilmaantuvuudeksi 52 tapausta 100 000 henkeä kohden vuodessa, joka on vastaavaa tasoa eurooppalaisiin tutkimuksiin verrattuna. Pirkanmaan ensihoito osallistui vuodessa 314 sairaalan ulkopuoliseen elvytykseen. Näistä tapauksista 34 potilaan (11%) kohdalla elvytysyrityksen todettiin olevan hyödytön eikä elvytystä aloitettu, 280 potilaan kohdalla elvytys aloitettiin. Näiden elvytysyritysten joukosta 24% oli osittaisia elvytysyrityksiä, joissa aloitetusta elvytyksestä luovuttiin lyhyen elvytysyrityksen jälkeen huonon kokonaisennusteen vuoksi. Kokonaisselviytyminen oli aineistossa 14%, mutta osuus nousi 19%:iin, kun aineistosta vähennettiin osittaisten elvytysyritysten osuus. Maallikkoelvytys (OR 3.48, 95% CI 1.29-9.39, P = 0.014) sekä defibrilloitava alkurytmi (OR 3.91, 95% CI 1.61-9.51, P = 0.003) olivat itsenäisiä ennustekijöitä sairaalan ulkopuolisesta sydänpysähdyksestä selviytymiseen. Niistä potilaista, jotka menivät elottomaksi ensihoidon ollessa paikalla, 16% selvisi sairaalasta kotiin.

Sairaalan ulkopuolisen elvytyksen jälkeen 149 vainajalle suoritettiin oikeuslääketieteellinen ruumiinavaus. Elvytyksestä aiheutuvia vammoja oli aineistossa 47%:lla vainajista, mikä on vähemmän verrattuna viimeisimpiin tutkimuksiin Euroopassa. Tyypillisimmät elvytyksestä aiheutuneet vammat olivat kylkiluunmurtuma (43%) sekä rintalastan murtuma (15%). Lisäksi todettiin, että elvytys julkisella paikalla (OR 4.98, 95% CI 2.02–12.31, $P < 0.001$), miessukupuoli (OR 4.11, 95% CI 1.79–9.43, $P = 0.001$) sekä ikä (OR 1.04, 95% CI 1.01–1.07, $P = 0.013$) lisäävät elvytysvammojen riskiä.

Kahden elvytysmenetelmän vertailu ei tuottanut eroa menetelmien välillä tutkittaessa elvytyksen aikaisen potilaan uloshengitysilman hiilidioksidipitoisuutta sekä laadukkaan painantaelvytyksen mitattavia muuttujia. Elvytystapahtuman keston keskiarvo oli 37 (±8) minuuttia, ja kuudessa tapauksessa kymmenestä uloshengitysilman hiilidioksidipitoisuus oli korkeampi käsin suoritetulla elvytystekniikalla kuin elvytyslaitteella mikä kertoo menetelmien yhdenvertaisuudesta. Ensihoidon aikana laskettava yksinkertainen riskipisteytys ennusti potilaan kuolleisuutta sairaalahoitojakson aikana (OR 2.42, 95% CI 1.84-3.18, P < 0.001) riippumatta potilaan iästä tai sairauksista.

Väitöskirjatyön päätelminä voidaan todeta että osittaisten elvytysyritysten huomioiminen raportoitaessa potilaiden selviytymislukuja parantaisi tulosten yhdenmukaisuutta ja vertailtavuutta. Painantaelvytyksen laatudata tulisi liittää elvytyksen aikaisten menetelmien vertailuun. Potilaan elvytysvammat ovat yleisiä ja vammoihin liittyvät riskitekijät tulisi huomioida potilaan hoitoketjussa. Yksinkertainen ensihoidon riskipisteytys voi soveltua riskinarvioinnin työkaluksi kenttäolosuhteissa kriittisesti sairaan potilaan jatkoennusteen arviointiin.

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ABBREVIATIONS

ACD	Active compression-decompression
AED	Automated external defibrillator
ALS	Advanced life support
ASA	American Society of Anesthesiologists classification
bCPR	Bystander CPR
BLS	Basic life support
CA	Cardiac arrest
CPC	Cerebral performance category
CPR	Cardiopulmonary resuscitation
DNAR	Do not attempt resuscitation
ECPR	Extracorporeal cardiopulmonary resuscitation
ED	Emergency department
EMS	Emergency medical service
ERC	European Resuscitation Council
ESI	Emergency severity index
$ETCO_2$	End-tidal carbon dioxide
EWS	Early warning score
FRU	First responding unit
GCS	Glasgow coma scale
HEMS	Helicopter emergency medical service
HR	Heart rate
ICU	Intensive care unit
IHCA	In-hospital cardiac arrest
MET	Medical emergency team
OHCA	Out-of-hospital cardiac arrest
PAD	Public access defibrillator
PEA	Pulseless electrical activity
pPCI	Primary percutaneous coronary intervention
ROSC	Return of spontaneous circulation
RR	Respiratory rate
RRT	Rapid response team
SBP	Systolic blood pressure
SpO_2	Peripheral capillary oxygen saturation
STEMI	ST-elevation myocardial infarct
Tays	Tampere University Hospital
TOR	Termination of resuscitation
VF	Ventricular fibrillation
VT	Ventricular tachycardia

LIST OF ORIGINAL PUBLICATIONS

This thesis is based on four original publications, which are referred to in the text by the Roman numerals I to IV. The publications are reprinted with the kind permission of the publishers Wiley-Blackwell (I, II, IV) and BMJ Publishing Group (III).

I Setälä P, Hoppu S, Virkkunen I, Yli-Hankala A, Kämäräinen A. Assessment of futility in out-of-hospital cardiac arrest. *Acta Anaesthesiologica Scandinavica*, 2017;61:1334-1344.

II Setälä P, Hellevuo H, Huhtala H, Kämäräinen A, Tirkkonen J, Hoppu S. Risk factors for cardiopulmonary resuscitation-related injuries sustained during out-of-hospital cardiac arrests. *Acta Anaesthesiologica Scandinavica*, 2018;62:1290-1296.

III Setälä P, Virkkunen I, Kämäräinen A, Huhtala H, Virta J, Yli-Hankala A, Hoppu S. End-tidal carbon dioxide output in manual cardiopulmonary resuscitation versus active compression-decompression device during prehospital quality controlled resuscitation: a case-series study. *Emergency Medicine Journal*, 2018;35:428-433.

IV Jokela K, Setälä P, Virta J, Huhtala H, Yli-Hankala A, Hoppu S. Using a simplified pre-hospital 'MET' score to predict in-hospital care and outcomes. *Acta Anaesthesiologica Scandinavica*, 2015;59:505-513.

1. INTRODUCTION

Sudden cardiac arrest (CA) outside the hospital is a major public health problem globally, and its incidence and outcomes vary greatly between continents (Berdowski et al. 2010). The burden of out-of-hospital cardiac arrest (OHCA) results from its overall dismal prognosis despite manifold methods that try to improve survival by enhancing the quality of treatment with updated clinical practice guidelines, such as the European Resuscitation Council (ERC) resuscitation guidelines, and novel treatments, such as immediate primary percutaneous coronary intervention (pPCI) and targeted temperature control in the post-resuscitation phase (ERC 2015). Still, the overall survival rate to hospital discharge remains 6% to 11% globally (Berdowski et al. 2010; Gräsner et al. 2016). To better describe the epidemiology of OHCA, many national and international communities have created joint registries for reporting OHCA (Gräsner et al. 2016; Hasegawa et al. 2013; McNally et al. 2009; Morrison et al. 2008a; Ong et al. 2015). Moreover, the Utstein-style guidelines recommend direct reporting of OHCA data in a uniform manner (Perkins et al. 2015b).

In CA, blood flow ceases when the mechanical function of the heart muscle stops. This cessation of circulation can be due to either cardiac disease or a non-cardiac disorder, and it leads to critical failure in organs dependent on continuous oxygen flow, such as the brain and heart muscle (Pell et al. 2003). Cardiopulmonary resuscitation (CPR) attempts to reverse the deathly situation and restore the circulation by restarting heart muscle function (Perkins et al. 2015a). The quality of CPR is composed of proper technique in providing chest compressions, minimal delay in defibrillation, and minimal interruptions of chest compressions. End-tidal carbon dioxide ($ETCO_2$) serves as a measurable marker for CPR effectiveness during the resuscitation attempt (Paiva et al. 2018) because this value reflects the low-flow state cardiac output and predicts the return of spontaneous circulation (ROSC) but also reacts to alterations in chest compression quality (Sheak et al. 2015).

Although chest compressions are necessary to manage CPR treatment, they may induce resuscitation-related injuries to the OHCA victim. The most typical injury areas include the thorax and rib cage, while severe injuries in thoracic and abdominal viscera seem to be rare (Miller et al. 2014). When compared to in-hospital resuscitation, these injuries are more common among OHCA patients (Hellevuo et al. 2013; Seung et al. 2016). Although the majority of CPR-related injuries are considered to be non-life-threatening and somewhat unavoidable, serious injuries that contribute to death do occur (Beom et al. 2017).

In pre-hospital care, emergency medical service (EMS) staff are the first healthcare professionals meeting the patient in a resource- and time-limited situation, where the underlying severity of the patient's condition may not be easily resolved. Therefore, a reliable assessment tool for the early recognition of a deteriorating pre-hospital patient could benefit the patient's outcome and the quality of care. Several track and trigger systems based on monitoring alterations in a patient's vital signs and caregiver's concern predict subsequent adverse effects, and they are used daily in hospitals and emergency departments (ED) (Harrison et al. 2006; Herod et al. 2014). However, a validated assessment tool for an unselected patient population with high sensitivity and specificity is still missing from the pre-hospital setting (Hoikka et al. 2018; Williams et al. 2016).

The purpose of this study was to describe the epidemiology of OHCA in the Pirkanmaa area of Finland and evaluate the impact of different factors associated with OHCA resuscitation futility and effectiveness by characterising partial resuscitation attempts and comparing two CPR methods on their CPR quality. The study also determined the incidence and predictors of CPR-related injuries sustained during OHCA and the usefulness of simplified pre-hospital medical emergency team (MET) score on prediction of critically ill pre-hospital patients' in-hospital outcomes.

2. REVIEW OF THE LITERATURE

2.1 Out-of-Hospital Cardiac Arrest: Epidemiology and Reporting Systems

Unexpected CA in coronary artery disease is the most frequent cause of sudden death, and two-thirds of these deaths occur outside hospitals (Nikolaou et al. 2015; Safar 1981). Past studies have reported various incidences and a vast range of survival rates for OHCAs, as the challenge has been the marked variations in the reported populations, methodological and terminological differences, and heterogeneous reporting data (Atwood et al. 2005; Becker et al. 1993; Berdowski et al. 2010; Nichol et al. 2008). There is a tenfold global variation in reported OHCA incidences (Berdowski et al. 2010). The estimated overall incidence of EMS-treated cardiac arrests is 38 per 100,000 population per year in Europe (Atwood et al. 2005; Gräsner et al. 2016) and 55 per 100,000 population per year in the United States (Rea et al. 2004). The survival to hospital discharge rates for all initial rhythms is 9-11% in Europe (Gräsner et al. 2016), 6-8% in North America and 11% in Australia (Berdowski et al. 2010).

The previous Finnish epidemiological studies of OCHA (Hiltunen et al. 2012; Kuisma et Määttä 1996; Kämäräinen et al. 2007; Silfvast 1990) in Table 1 show that the regional incidences of EMS-treated OCHA in Finland seem to be in the middle of European ranks (19 to 104 per 100,000 population per year). The survival rates for all initial rhythms in Finland exceed the average estimates of Europe (Gräsner et al. 2016). To date, Finland lacks a national registry for reporting OHCA, and none of the previous studies have evaluated the overall national incidence of OHCA with a total population of 5,521,000 inhabitants (January 2019) in Finland.

Table 1. Epidemiological studies of out-of-hospital cardiac arrests in Finland.

Community and study year	Study data collection period	Population	EMS-treated CAs/ 100,000 inhabitants/ year	Survival to hospital discharge in EMS-treated CAs (%)
1987 city of Helsinki	12 months	500,000	53	14.7
1994 city of Helsinki	12 months	516,000	67	16.6
2004-2005 city of Tampere	12 months	203,000	46	12.9
2010 southern, central, and eastern Finland	6 months	2,644,200	51	19.9

CA indicates cardiac arrest; EMS, emergency medical service.

The International Liaison Committee on Resuscitation (ILCOR) reviews and identifies relevant scientific information on CPR and emergency cardiovascular care, and also provides consensus on treatment recommendations (Nolan et al. 2015). These evidence-based CPR guidelines aim to improve survival after sudden CA (American Heart Association 2015; ERC 2015). The concept of "chain of survival" describes the sequence of events that are linked together to improve the quality of care in sudden CA (Cummings et al. 1991; Nolan et al. 2006). These events are early recognition and call for help, early CPR, early defibrillation and standardised post-resuscitation care. Some studies have reported improvements in outcome by strengthening the links in their local chains such as focusing on good-quality CPR (Lindner et al. 2011; Lund-Kordahl et al. 2010) and goal-directed post-resuscitation care, such as immediate pPCI (Dumas et al. 2010) and targeted temperature management (Sunde 2013), but despite these encouraging reports, the overall survival in OHCA has remained low over the last decade (Berdowski et al. 2010; Gräsner et al. 2016).

2.1.1 Factors Associated with Out-of-Hospital Cardiac Arrest Outcomes

The most important factors associated with improved outcomes are witnessed CA (Sasson et al. 2010), bystander-initiated CPR before EMS arrival (Adielsson et al.

2011; Stiell et al. 2004), shockable initial rhythm and early defibrillation (Adielsson et al. 2011; Becker et al. 2008), good-quality chest compressions (Christenson et al. 2009; Stiell et al. 2012), and the availability of public access defibrillators (PADs) (Ringh et al. 2015). These factors indicate that well-informed communities and educated EMS systems are needed to save a sudden CA victim. Dispatch centres have an important role in recognising a sudden CA by asking a standard series of questions and subsequently assisting callers in starting CPR (Vaillancourt et al. 2007). Recognition of OHCA during the emergency call varies substantially, the sensitivity ranging from 14% to 97% (Viereck et al. 2017). Abnormal breathing during OHCA is the most significant barrier in recognising sudden CA (Vaillancourt et al. 2007). Interventions such as improving medical dispatcher competence and relevant tools for support enhance the timely recognition of OHCA (Bobrow et al. 2016; Bohm et al. 2009). Dispatcher CPR provides effective guidance to bystanders without prior CPR training to commence resuscitation, although their initiation of CPR after a collapse takes longer compared to previously trained persons (Nebsbjerg et al. 2018). The OHCA victim is almost four times more likely to survive the event when receiving bystander-CPR (bCPR) (Stiell et al. 2004). Dispatcher CPR has resulted in a marked increase in the incidence of community bCPR rates and improved outcomes after OHCA (Rea et al. 2001).

Early defibrillation in shockable monitored rhythm is crucial for patient outcomes, as delays decrease the effectiveness of the defibrillation attempt and diminish the incidence of ventricular fibrillation (VF) (Sasson et al. 2010). PADs that are easily available to lay responders diminish the delay to the first delivered shock and impact survival (Bækgaard et al. 2017; Kitamura et al. 2016). VF as the initial rhythm is associated with better survival in OHCAs (Keller and Halperin 2015), but its frequency has decreased over the last 20 years (Cobb et al. 2002; Lund-Kordahl et al. 2010) to 35% in Europe, 28% in North America, and 40% in Australia (Berdowski et al. 2010). At the same time, the frequency of pulseless electrical activity (PEA) as the initial rhythm has increased (Cobb et al. 2002). PEA is associated with a non-cardiac aetiology, including traumatic CA, overdose, drowning, electrocution, and asphyxia. Although PEA has an overall poor outcome, the rapid recognition of a possible reversible cause for sudden CA plays an important role in the outcome (Wolbinski et al. 2016).

Traumatic CAs are small but an important CA subgroup whose survival rates (4-8%) are comparable to other non-cardiac aetiologies and are dependent on the sustained injuries and rapid treatment on scene (Lockey et al. 2006; Stockinger and McSwain 2004). They often present potential reversible causes, such as hypovolaemia, hypoxemia, tension pneumothorax, or cardiac tamponade leading to traumatic CA that requires rapid and effective intervention. Therefore, the management of traumatic CA is best dealt with a specific algorithm that differs from the conventional advanced cardiac support (ALS) guidelines (Lockey et al. 2013).

EMS-witnessed OHCA with presumed cardiac origin is associated with better survival when compared to bystander-witnessed or unwitnessed sudden CAs (Gold and Eisenberg 2010; Nehme et al. 2015). In these cases, trained healthcare professionals are able to start CPR without delay. Today, the rate of EMS-witnessed CAs is 8-11% of all resuscitation attempts (Sasson et al. 2010). The variation indicates regional differences in EMS response times but also the severity of illness of the pre-arrest patient encountered by EMS (Skrifvars et al. 2009) and the public awareness of a patient's critical condition and an urgent need for medical help (Nehme et al. 2018). Earlier contact with EMS results in better survival and neurological outcomes (Nishiyama et al. 2013; Takei et al. 2015).

The neurological outcome of the CA patient is described with Cerebral Performance Category (CPC), a scale that combines functional and cognitive areas to assess brain recovery after sudden CA and subsequent post-arrest care. The scale is divided in five points (CPC 1: good cerebral performance; CPC 2: moderate cerebral disability, sufficient function for independent activities of daily life; CPC 3: severe cerebral disability, conscious but dependent on others for daily support due to impaired brain function and limited cognition; CPC 4: coma / vegetative state; CPC 5: brain death). Each CPC score presents several domains of function, for example impairment, level of activities performed and level of participation, but it has not been established that CPC has sufficient sensitivity to assess all these domains and other metrics may possess greater predictive characteristics (Becker et al. 2011). Still, CPC is a useful surrogate measure of long-term survival as more favourable CPC at the time of hospital discharge independently predicts better long-term prognosis (Phelps et al. 2013).

2.1.2. Out-of-Hospital Cardiac Arrest Registries and the Utstein Template

Epidemiological data are time-sensitive, meaning that the available interventions, life expectancy, the age pyramid of the studied population, and prevention methods change over time (Gräsner and Bossaert 2013). Therefore, OHCA registries continuously collect data on sudden CAs and provide up-to-date and uniform information on the subject and describe changes over time in incidence, survival, and the methods of treatment. A number of registries, both regional and national, have been built across the world, the largest ones being the Cardiac Arrest Registry to Enhance Survival (CARES) in the United States (McNally et al. 2009) and the Resuscitation Outcomes Consortium (ROC) Epistry in North America (Morrison et al. 2008a), the Pan-Asian Resuscitation Outcomes Registry (PAROS) (Ong et al. 2015), and the All-Japan Utstein Registry (Hasegawa et al. 2013). European countries are building a pan-European registry, EuReCa, to provide a high-quality European overview and monitoring of the outcomes of CA and resuscitation (Gräsner et al. 2011; Gräsner et al. 2016).

To ensure uniform reporting across registries, the Utstein template was created in 1990. It describes uniform terms and definitions for reporting OHCA. The original

Utstein definitions were revised in 2004 to update data elements, reduce complexity, and provide a template that would serve research, evaluation of the systems, and continuous quality improvement (Jacobs et al. 2004). The data elements include the description of the population, the EMS and the EMS dispatch systems studied, the incidence and aetiology of OHCA, the critical time points of the events, the patient and event characteristics of the resuscitation attempt, the description of the goal-directed post-resuscitation care, and the neurological outcomes of OHCA patients. The template was further updated in 2015, and the decision was made to report OHCA and in-hospital cardiac arrest (IHCA) as separate reporting templates (Perkins et al. 2015b). The refined template includes several new or modified elements that help to distinguish the impact of the availability of PADs, the use of dispatcher CPR, prognostication tools, and emerging field treatments on outcome (Table 2). Despite these advances, the Utstein template has not been able to fully explain the variability in OHCA survival across populations (Fredriksson et al. 2005; Rea et al. 2010), and there has been increased recognition of the importance to further investigate the additional factors associated with survival after OHCA.

Table 2. Elements of the Utstein template for reporting outcomes from out-of-hospital cardiac arrest.

EMS description: *total population served by EMS, total number of CA cases, response times*
Dispatcher: *identification of CA, dispatcher-CPR, response times*
Resuscitation not attempted: *DNAR, obviously dead, signs of life*
Patient and event characteristics: *Age, gender, the initial rhythm, location, aetiology, bystander-witnessed, EMS-witnessed, unwitnessed, bystander response (bCPR, use of PAD)*
EMS process: *Defibrillation time, drugs given, targeted temperature control*
Hospital process: *Reperfusion, targeted temperature control, organ donor*

bCPR indicates bystander CPR; CA, cardiac arrest; CPR, cardiopulmonary resuscitation; DNAR, do not attempt resuscitation; EMS, emergency medical service; PAD, public access defibrillator.

2.2 The Presumed Futility and Decision-Making in Out-of-Hospital Cardiac Arrest

2.2.1 Ethical Considerations

Futile medical treatment is defined by the World Medical Association as a treatment that "offers no reasonable hope of recovery or improvement" or from which "the patient is permanently unable to experience any benefit" (World Medical Association 2015). Futile treatment may offer false hope to the patient and patient's family, causing unrealistic expectations about the success of a treatment (Waisel and Truog 1995). Determination of the futility of the resuscitation attempt has an important role among factors associated with OHCA survival, as the "do not attempt resuscitation" (DNAR) order policies and procedures differ from country to country and thus may affect the variability in survival rates. In recent years, decisions regarding a patient's treatment have shifted from the doctor-centred approach emphasising beneficence to a more patient-centred approach underlining patient autonomy (Bossaert et al. 2015). The common principles in ethical considerations and decision-making strive to optimise the resuscitative results for the individual patient and societies by appropriately allocating resources with justice and equality (Committee on Bioethics of the Council of Europe 2014). There are various ethical principles that need to be considered during decision-making in OHCA. Patient autonomy and personal preferences have to be respected and expressed in advance directives. However, if the wishes of the individual patient are not readily available in a sudden CA situation, they may remain unknown (Field et al. 2014). Attending staff are responsible for the decisions on starting CPR, continuing the effort beyond the normal practices in special circumstances, and proper prognostication. They should make a clear distinction between a sudden CA and the expected cessation of cardiac function in terminal situations and practice non-maleficence, including DNAR orders, withholding or terminating the resuscitation attempt according to futility, and allowing a natural death (Committee on Bioethics of the Council of Europe 2014; Field et al. 2014).

2.2.2 Decision-Making in the Pre-Hospital Setting

Pre-hospital emergency medical practitioners use life-sustaining treatments and frequently participate in tending to dying patients (Ferrand and Marty 2006). Current resuscitation guidelines acknowledge the challenges regarding the decision to start or discontinue CPR in the pre-hospital setting due to a lack of sufficient information of a patient's comorbidities and the patient's wishes (Bossaert et al. 2015). Therefore, prognostic assessments in the pre-hospital setting are often insufficient to reliably predict survival and subsequent quality of life (Ranola et al. 2015). However, some well-established factors associated with increased or decreased chance of survival become apparent during the resuscitation attempt and dictate the subsequent course of the event (Herlitz et al. 2005). Dismal prognostic factors, such as prolonged interval between collapse and the start of CPR (Vukmir et al. 2006), previous general condition and the underlying disease, and a highly advanced age, diminish the probability of obtaining a good future quality of life (Bunch et al. 2004; Herlitz et al. 2005). For this reason, resuscitative efforts in OHCA are usually promptly started, and the assessment of futility is made during the resuscitation attempt when more information becomes available. In situations where conditions are incompatible with life, the resuscitation guidelines recommend that a non-physician in the field is entitled to withhold a resuscitation attempt. These conditions are as follows: dependent lividity with rigor mortis, decomposition or putrefaction, incineration, massive cranial and cerebral destruction, decapitation, and foetal maceration (Bossaert et al. 2015). Other futile situations where resuscitation should be withheld arise when asystole persists for more than 20 minutes despite the ongoing resuscitation attempt when there is no treatable, reversible cause of sudden CA (Nehme et al. 2016), or when valid patient values and preferences or advance directives become available (Bossaert et al. 2015).

In order to diminish the variability in pre-hospital decision-making in determining the futility in OHCA, the Termination of Resuscitation (TOR) rule was established in Canada in 2002 (Verbeek et al. 2002) and further validated in 2006 (Morrison et al. 2006). The most important function for this rule is to determine the futility of a resuscitation attempt: The rule recommends termination of basic life support (BLS) resuscitation when the CA is not witnessed by EMS personnel, no defibrillation is delivered, and there is no ROSC. Implementing the TOR rule has significantly diminished the transportation of futile OHCA victims to hospital and improved the comfort of paramedics and physicians with decision-making in EMS systems where all OHCAs have previously been transported to hospital with ongoing resuscitation (Morrison et al. 2014). The rule is validated to have 100% specificity; that is, the rule will reliably recognise all patients who might have a chance for survival (Morrison et al. 2006; Morrison et al. 2008b). However, the comparisons of the TOR rule's effectiveness between regions and countries are difficult due to variability in regional EMS systems where paramedics have previously been allowed to terminate or withhold resuscitation according to local protocols (Kämäräinen et al. 2007; Verhaert et al. 2016).

Pre-hospital physicians make decisions to withhold or terminate resuscitation attempts by assessing the probability of fatal outcome expected in the short term (Ferrand and Marty 2006). In the majority of cases, the decision is based on presumed prolonged anoxia (Horsted et al. 2004). Decisions regarding futility in OHCA are either needed in the acute onset of critical illness or trauma, or when a serious illness has slowly advanced into a terminal state. OHCA patients suffering from multiple trauma or prolonged asphyxia have a dismal prognosis that could lead to not starting CPR (Duchateau et al. 2008; Ferrand and Marty 2006). In the case of terminal illness, such as advanced cancer with metastasis or poor overall previous health status with a deterioration of functional independence, the condition will prevent the opportunity from resuscitating the patient to a good quality of life (Horsted et al. 2004). Advanced age is an ambiguous predictive factor, as its significance in determining resuscitation futility has varied among studies (Søholm et al. 2014). The aforementioned factors of futility result in a higher rate of withholding and terminating resuscitation due to ethical considerations by pre-hospital physicians (Duchateau et al. 2008; Ferrand and Marty 2006; Horsted et al. 2004).

Two previous Finnish OHCA studies have investigated the proportion of CAs considered for resuscitation where resuscitation was not attempted due to futility. In the city of Tampere, resuscitation was not initiated by EMS in 51% of cases due to secondary signs of death, over 15 min delay in starting CPR when the initial rhythm was asystole or PEA, massive trauma, end-stage malignant disease, or DNAR order (Kämäräinen et al. 2007). A study from southern, central, and eastern Finland reported that, in 36% of cases, EMS crews rapidly discontinued CPR after initial assessment due to the considered futility of the situation (Hiltunen et al. 2010). To date, the termination of resuscitation attempts due to presumed futility of the attempt is not included in the reporting templates describing OHCA epidemiology.

2.3 Approaches to Improving Cardiopulmonary Resuscitation Quality

2.3.1 Chest Compressions

The resuscitation guidelines emphasise the importance of providing high-quality chest compression components during the resuscitation attempt, including the optimal position of the rescuer and the victim, the right hand position on the lower half of the sternum (Baubin et al. 1997), the rate and depth of the compressions (100 to 120 compressions/min, depth more than 50 mm but not over 70 mm), duty cycle of 50:50, and allowing chest decompression to fully recoil (Perkins et al. 2015a). The ventilation rate should be held constant at ten breaths per minute (Soar et al. 2015). High-quality CPR also denotes following the protocol of minimal interruptions of chest compressions when assessing the underlying rhythm (Christenson et al. 2009; Wik et al. 2003) and during defibrillation (Cobb et al. 1999; Steen et al. 2003; Yu et al. 2002). Suboptimal chest compressions are insufficient to maintain perfusion pressure to the vital organs (Ristagno et al. 2007) and have adverse effect on patient outcomes (Stiell et al. 2012). Also, when the chest compression rate exceeds 120 compressions/min, the compressions might become shallow and thus ineffective (Idris et al. 2015). The coronary arteries are perfused during the diastole in the decompression phase; thus, leaning on the chest during that phase reduces venous return and decreases the coronary and cerebral perfusion pressures (Yannopoulos et al. 2005). Additionally, excessive ventilation during CPR results in increased intrathoracic pressure and decreased coronary perfusion pressure (Aufderheide et al. 2004). Maintaining consistent compressions during prolonged periods of time is a difficult task due to rescuer fatigue (Hightower et al. 1995; Ochoa et al. 1998), which can lead to suboptimal chest compressions and incomplete chest wall decompression (Yannopoulos et al. 2005). High-quality CPR also requires teamwork, advance planning, and orderly performed tasks during the resuscitation attempt to avoid unnecessary hands-off time. These elements are often not optimal, and as a result, chest compressions often do not achieve guideline recommendations regarding the rate, depth, hands-on time, and ventilation rates in the clinical context (Abella et al. 2005; Wik et al. 2005). In a clinical setting, conducting a team performing CPR is a high-stress situation where the team leader needs good communication skills and reliable situational awareness to ensure high-quality resuscitation performance. Today, the application of these non-technical skills, together with team-building skills, is an integral part in rapid response team (RRT) and MET performance, as well as CPR education to improve clinical performance and ensure positive effects on the chain of survival (Chalwin and Flabouris 2013; Greif et al. 2015).

2.3.2 Ancillary Cardiopulmonary Resuscitation Devices

In an aim to improve the outcome after sudden CA, several devices have been developed to improve the consistency and quality of compressions during the resuscitation attempt. Due to insufficient data, these devices are not currently recommended for routine use, but they serve as alternative circulatory adjuncts to the standard manual chest compressions (Brooks et al. 2015). The devices for augmenting chest compression efficiency include a manual active compression-decompression (ACD) device based on suction cup technology with a force gauge and a metronome, and automated devices that perform chest compressions at specific rates and depths and use either a load-distributing band or piston technology (Brooks et al. 2015). Manual ACD-CPR device has shown to enhance both myocardial perfusion and aortic systolic pressure and increase the myocardial and cerebral blood flow compared to manual CPR in experimental animal and human studies (Chang et al. 1994; Shultz et al. 1994), but clinical studies have not consistently shown improved results in survival rates when compared to manual CPR (Wang et al. 2015). Automated mechanical devices have demonstrated improved organ blood flow and higher $ETCO_2$ output during CPR (Axelsson et al. 2009; Timerman et al. 2004). However, their contribution to improved patient outcomes in large trials has remained controversial (Axelsson et al. 2009; Ong et al. 2006). The ASPIRE (Hallstrom et al. 2006) and CIRC (Wik et al. 2014) trials studying mechanical CPR with a load-distributing band did not show a survival benefit over manual CPR, and the LINC (Rubertsson et al. 2014) and PARA-

MEDIC (Perkins et al. 2015c) trials studying mechanical CPR with piston technology did not show a survival benefit to hospital discharge. While the studies lacked a survival benefit, they also reported high quality of manual CPR performance during the resuscitation attempts, and this may impact the generalisability of their results. On the other hand, mechanical CPR devices may introduce injuries to patients (Koster et al. 2017). However, these devices offer the rescuer the possibility to start and continue high-quality CPR in a pre-hospital setting in circumstances that either prevent or risk providing high-quality manual standard CPR, such as in confined spaces or when the situation demands patient transfer and specific treatment during resuscitation attempts, such as performing a pPCI on a patient with recurring VF (Nikolaou and Christou 2013; Wagner et al. 2010). Therefore, these aforementioned studies have established a platform for the clinicians to decide about the possible harm or benefit of using a mechanical CPR device in their clinical practice.

A novel approach to enhance survival from OHCA is the implementation of extracorporeal cardiopulmonary resuscitation (ECPR) in the pre-hospital setting by starting veno-arterial extracorporeal membrane oxygenation during ongoing CPR on scene. ECPR improves blood flow and oxygen delivery when compared to manual CPR (Ahn et al. 2016; Wang et al. 2017) and has the potential for substantial improvement in OHCA outcomes, the overall survival rate in previous studies being 15% (Singer 2018). Longer low-flow times in manual CPR prior to commencement of ECPR result in poor outcomes (Debaty et al. 2017). Therefore, the desirable therapeutic window for ECPR is under 60 minutes from CA (Fagnoul et al. 2014). Although evidence supports its use, pre-hospital ECPR requires careful consideration for patient selection, timing for treatment initiation, required personnel, and logistical achievements (Singer et al. 2018). In a sparsely inhabited country like Finland, with long distances to hospital and anaesthesiology-staffed helicopter emergency medical service (HEMS) units, implementation of this novel method might improve patient outcomes in specifically defined patient subgroups.

Another recent approach to improve resuscitation quality is the use of real-time audio-visual feedback system monitor defibrillators (Yeung et al. 2009). Studies have shown that the retention of CPR-performing skills starts to deteriorate within months after training (Kaye and Mancini 1986) despite of well-established programs of resuscitation training (Wik et al. 2002). Rescuers are unable to recognise the quality changes of the provided CPR during the resuscitation attempt (Hightower et al. 1995; Ochoa et al. 1998). The real-time audio-visual feedback system defibrillator gathers CPR quality information through measuring chest compression rates, depths, duty cycles, and no-flow times during the resuscitation attempt via an accelerometer and impedance changes across the defibrillation electrodes. Real-time audio-visual guidance prompts the CPR provider directly for performing CPR according to resuscitation guideline specifications (Hostler et al. 2011). Despite its improvement in CPR performance, patient outcomes have not improved after implementation of real-time audio-visual feedback guidance during resuscitation attempts (Hostler et al. 2011; Yeung et al. 2009).

2.4 Evaluating Injuries from Out-of-Hospital Cardiac Arrest

Performing chest compressions during sudden CA is a violent manoeuvre that can lead to iatrogenic injuries during the resuscitation attempt. The most common injuries involve the thoracic wall, but more uncommon injuries are found in the thoracic and abdominal viscera and in the retroperitoneum (Buschmann and Tsokos 2009; Hashimoto et al. 2007; Olds et al. 2015). Skin lesions, subcutaneous injuries, and injuries in the head and neck may result from airway management and the insertion of intravenous lines (Olds et al. 2015; Raven et al. 1999; Stoppacher et al. 2004). The majority of these injuries are non-life-threatening and considered unavoidable, but also serious injuries contributing to patients' deaths are reported (Beom et al. 2017). In addition to thoracic wall injuries, such as rib fractures and sternum fractures, major cardiac and large vessel injuries such as cardiac contusions, cardiac haematomas, haemopericardium, myocardial rupture or laceration, coronary artery rupture or laceration, aortic rupture or laceration, aortic dissection or vena cava injury may occur during CPR (Miller et al. 2014). The majority of rib fractures are situated in the thoracic wall anteriorly, and sternal fractures are typically seen in the middle third of the torso (Kashiwagi et al. 2015).

The incidence of CPR-related injuries varies widely. A meta-analysis including 15 studies of adult populations (n ranging from 20 to 705 cases) in 2004 reported an incidence of rib fractures ranging from 13% to 97% and an incidence of sternum fractures from 1% to 43% after standard manual CPR (Hoke and Chamberlain 2004). The more recent OHCA studies have reported the incidence of rib fractures as high as 85% and sternal fractures as high as 79% (Kralj et al. 2015; Rudinská et al. 2016). The incidence of thoracic wall injuries after manual ACD-CPR ranges from 4% to 87% for rib fractures and from 0% to 93% for sternal fractures (Hoke and Chamberlain 2004). The injury patterns are different when mechanical CPR devices are used during the resuscitation attempt. The injuries sustained during mechanical CPR with distributing-load band are posterior rib fractures, abrasions located along the chest, and even vertebral fractures and liver lacerations, splenic lacerations, haemoperitoneum, and retroperitoneal haemorrhage (Koga et al. 2015; Pinto et al. 2013). Mechanical CPR with piston technology causes more frequently rib fractures than manual CPR, but otherwise these two methods do not differ in their iatrogenic injury patterns (Lardi et al. 2015; Smekal et al. 2014). Mechanical CPR with load-distributing bands seems to induce more injuries compared to manual CPR (Koga et al. 2015; Koster et al. 2017 Pinto et al. 2013), whereas mechanical CPR with piston technology does not significantly increase injury frequency (Koster et al. 2017; Lardi et al. 2015; Smekal et al. 2014). Population characteristics, anatomical differences, and the feasibility of applying these devices safely during a highly stressful situation may contribute to the injury findings.

Past studies have suggested various risk factors for CPR-related injuries. Age is considered to be a strong risk factor, mostly due to the degenerative skeletal changes and a higher frequency of osteoporosis in older populations (Black et al. 2004; Kashiwagi et al. 2015; Seung et al. 2016; Smekal et al. 2014). Some studies have reported female gender as a risk factor (Black et al. 2004; Kim et al. 2013), whereas other studies have suggested male gender to be a risk factor for CPR-related injuries (Hellevuo et al. 2013) or have not found any difference between genders (Smekal et al. 2014). Other reported risk factors are the duration of the resuscitation attempt (Kashiwagi et al. 2015; Seung et al. 2016), the increased depth and rate of chest compressions (Beom et al. 2017; Hellevuo et al. 2013; Kralj et al. 2015), and the lower rate of ROSC (Kashiwagi et al. 2015). OHCA survivors sustain more injuries compared to IHCA survivors (Seung et al. 2016), and the occupational groups who participate in CPR attempts can affect the incidence of injuries (Kim et al. 2013). Common to all aforementioned studies is that their vast variability in the incidence of and risk factors for CPR-related injuries reflect the differences in their study populations, pre-hospital care, and hospital procedures, including autopsy rates.

2.4.1 The Role of Forensic Autopsies

Sudden CA may be the first symptom of underlying pathology in previously healthy patients. The accuracy of diagnosis in sudden CA can be ascertained only with proper investigations, including autopsy. In general, a clinical diagnosis may not be adequate to successfully address the cause of death (Ornelas-Aguirre et al. 2003), and when a patient deteriorates suddenly or suffers from OHCA, the clinical diagnosis is often inaccurate (Mushtaq and Ritchie 2005). Both forensic physicians and emergency physicians examining these patients are required to have updated knowledge of CPR techniques and CPR-related injuries when determining the cause of death (De Leeum and Jacobs 2010). Although novel studies have investigated injury frequencies utilising post-mortem computed tomography (Kashiwagi et al. 2015), forensic autopsy is considered to be the most reliable method to investigate CPR-related injuries for revealing the more obscure lesions that are not readily visible in the conventional imaging methods (Lederer et al. 2004; Oberladstaetter et al. 2012; Roberts et al. 2012; Schulze et al. 2013). Moreover, injury frequencies and accurate post-mortem diagnoses in forensic autopsies will help emergency physicians working in the field or ED to suspect these injuries in their OHCA patients who survive to hospital.

2.5 Prevention of Patient Morbidity and Mortality

2.5.1 Track and Trigger Systems

Prevention of CA by early recognition of the deteriorating patient and subsequent immediate treatment remain the first link in the chain of survival (Nolan et al. 2006). Only about 20% of CA patients will survive in an in-hospital setting (Nolan et al. 2014; Sandroni et al. 2007). In minimising the risk of CA, chain of prevention includes monitoring of patients, recognition of patient deterioration, and a system call for help with subsequent rapid response and staff education (Smith 2010). In wards, the deteriorating patient has often had progressive physiological deterioration during a sustained period of time that has been insufficiently managed or unnoticed by ward staff, and thereby CA is not usually an unpredictable event (Hodgetts et al. 2002; Kause et al. 2004; Taenzer et al. 2011). This phenomenon has been known over 40 years (Castagna et al. 1974) and the prognosis for these patients is poor; in the majority of cases, the initial rhythm is non-shockable, and the survival among those patients is 9% (Nolan et al. 2014; Skrifvars et al. 2006).

Alteration in patient vital signs reflects the onset of acute illness. Early warning systems have been increasingly employed in the inpatient setting throughout the world in recent years and provide a means of identification of potential deterioration (Jones et al. 2011). The alterations in physiological variables, singly or in combination, with caregiver's concern (Douw et al. 2015; Santiano et al. 2009) can be used to predict the occurrence of adverse effects such as patient morbidity and mortality (Buist et al. 2004; Harrison et al. 2006; Herod et al. 2014) with varying sensitivity and specificity (Smith et al. 2008a; Smith et al. 2008b). This has led many hospitals to use METs, RRTs or critical care outreach teams alongside physiological scores that will facilitate objective decision-making and trigger the escalation of care (Ball et al. 2003; DeVita et al. 2006; Jones et al. 2011). These "track and trigger" systems, or early warning scores (EWSs), are based on scoring systems that offer guidance to either a graded escalation of care (Smith et al. 2013; Subbe et al. 2003) or a trigger for calling expert help (Bell et al. 2006). Team interventions often involve starting basic treatment according to the ABCDE approach, such as supplemental oxygen therapy and opening an intravenous access with fluid therapy (Chan et al. 2008; Dacey et al. 2007; Kenward et al. 2004). Nevertheless, the majority of the interventions offered by these teams have included critical care type treatments (Flabouris et al. 2010). The effect of these teams on patient outcomes is difficult to measure reliably, because the hospitals have evolved during the same time period when these teams have emerged into hospital environments, contributing to various aspects with improved focus on patient safety (Jones et al. 2011).

2.5.2 Estimating Patient Urgency in the Emergency Department

Alongside the aforementioned track and trigger systems, EDs utilise triage tools that take into consideration the resources that are needed to treat deteriorating patients and identify the order in which patients should be given care according to the severity of their medical condition. These tools help staff in planning, prioritising, and preparing for arriving patients. However, the scientific evidence of the triage scales' validity and reliability to assess patient outcomes is limited (Farrohknia et al. 2011). Emergency Severity Index (ESI) classification is a validated five-level triage tool that estimates patient urgency with staff resource requirements (Wuerz et al. 2001). The classification is as follows: ESI 1: an intubated, apnoeic, pulseless *or* unresponsive patient; ESI 2: a high-risk situation *or* confused, lethargic or disoriented patient *or* severe pain/distress *or* two or more resources required and the patient's vitals are in the danger zone; ESI 3: two or more resources required but the patient's vitals are not in the danger zone; ESI 4: only one resource needed; ESI 5: no resources needed. What is unique in this tool is that a detailed triage evaluation is not required; only certain information is needed to predict the resources the patient needs, and vital signs marked in the "danger zone" only determine whether certain category 3 patients will be recategorized to category 2. This makes the ESI classification a fast and reliable tool for urgent evaluation of patients in the ED (Tanabe et al. 2004).

2.5.3 Identification of Critically Ill Patients in the Pre-Hospital Setting by Pre-Hospital Care Providers

Pre-hospital patients may suffer from various symptoms for extended amounts of time before the situation leads to the emergency call. The patient or bystander on scene may not always be aware of the critical situation. The prodromal symptoms of the pre-hospital patient with chest pain, such as vomiting, dyspnoea and abnormal systolic blood pressure, are warning symptoms preceding OHCA, and every 30-minute increase in delay to call emergency medical centre for help decreases survival to hospital discharge (Nehme et al. 2015). This means that public awareness plays a critical role in the process of identifying critically ill pre-hospital patients.

In the pre-hospital setting, identifying critically ill patients is challenging for EMS paramedics because patients often have non-specific signs and symptoms, and the availability of their clinical history may be limited. Moreover, the heterogeneous reasons for dispatching and variable utilisation of EMS, incomplete information gained on scene, and subjective assessments of a patient's status may limit accurate identification of critical illness, and many studies have raised the concern that the severity of a patient's situation might not be recognised by pre-hospital staff (Brown and Bleetman 2006; Brown et al. 2009; Brown and Warwick 2001; Challen and Goodacre 2011).

Pre-hospital pathology-specific protocols, such as stroke or ST-elevation myocardial infarction, offer disease-specific assessment tools for objective triage and risk stratification for pre-hospital patients, ensuring accurately made diagnoses and improvements in morbidity and mortality (Bray et al. 2010; Lidal et al. 2013; Ortolani et al. 2007). However, uncertainty exists whether the EWSs would be applicable to pre-hospital settings, where the scores would be obtained prior to commencing any treatment, as the scores were developed by analysing clinical observations in hospital inpatients, in whom a course of treatment had already been started (Challen and Roland 2016). In this situation, the score may be used as a triage aid contributing to a decision-making, a role that differs from the original track and trigger role for which these scores have been primarily intended.

Using pre-hospital EWS may prompt earlier recognition of deteriorating patients and facilitate early pre-alert to the receiving hospital, early involvement of senior ED staff on patient care, and appropriate transfer to critical care (Dawson et al. 2013; Leung et al. 2016; Shaw et al. 2017). Recent studies suggest that EWS is more reliable in recognising a critically ill patient compared to clinical judgement in the pre-hospital setting (Bayer et al. 2015; Booth and Bloch 2013; Guerra et al. 2013; Suffoletto et al. 2011; Wallgren et al. 2014), and it has a prognostic value on clinically important adverse outcomes, such as hospital mortality and admission to ICU (Fullerton et al. 2012; Seymour et al. 2010; Silcock et al. 2015). However, the best suitable EWS for pre-hospital settings is yet to be determined (Williams et al. 2016).

3. AIMS OF THE STUDY

The purpose of this thesis was to evaluate the overall effectiveness of CPR attempts and determine the impact of different factors associated with OHCA resuscitation attempts and the prediction of critically ill pre-hospital patients' in-hospital outcomes. The specific aims were:

1. To describe the epidemiology of OHCA according to the Utstein template and the incidence of EMS-treated OHCA in the Pirkanmaa area of Finland and evaluate the impact of futile resuscitation attempts when assessing the outcome of resuscitations (I).

2. To determine the incidence of and associated risk factors for CPR-related injuries after OHCA by analysing forensic autopsy records and assessing the patient and event characteristics according to the Utstein template during the resuscitation attempt (II).

3. To assess manual CPR and ACD-CPR for overall resuscitation quality in terms of $ETCO_2$ output by comparing the methods during the resuscitation attempt under the guidance of an audio-visual feedback system defibrillator in the pre-hospital setting (III).

4. To determine whether a simplified pre-hospital MET score would be useful in identifying patients at risk to deteriorate in pre-hospital care and subsequent hospital care by comparing pre-hospital vital signs to hospital morbidity and mortality (IV).

4. MATERIALS AND METHODS

4.1 The Emergency Medical Service System and the University Hospital in the Pirkanmaa Area

During the study period, the Pirkanmaa area had approximately 500,000 inhabitants, including the city of Tampere, with 220,500 inhabitants. The EMS in the Pirkanmaa area consists of a two-tiered system that is activated by a national emergency medical dispatching centre and serves a total catchment area of 12,600 km^2 with urban, suburban, and rural areas. During the data collection period (I, II, III, IV), the EMS comprised 45 first response units (FRUs) with lay rescuers or firefighters who are trained in first aid and provide immediate life support, including the use of automated external defibrillators (AEDs), 10 BLS units staffed by emergency medical technicians and firefighters, and 25 ALS units staffed with paramedic-nurses who have the capability of providing drug-assisted CPR. One field commander unit and one physician-staffed HEMS unit operate in the area 24 h a day. HEMS crew physicians are mainly specialists in anaesthesiology and intensive care medicine, with pre-hospital critical emergency care training. HEMS is dispatched to all high-risk medical emergencies and trauma in the Pirkanmaa area. EMS dispatch is provided by a joint emergency dispatch service that also dispatches police, fire, rescue, and social services. In the case of sudden CA, the dispatch centre provides telephone-assisted instructions for CPR and dispatches the FRU and either BLS or ALS unit alongside the field commander unit and the HEMS unit. The FRUs are permitted to refrain from CPR attempts in cases of secondary signs of death, i.e., rigor mortis, dependent lividity, or physical injuries incompatible with life. The EMS has a standing order that permits withholding CPR attempt in cases of obvious futility, i.e., unwitnessed CA with asystole as the initial rhythm or DNAR order presented at the scene. According to local protocol based on national resuscitation guidelines, EMS is allowed to withhold resuscitation if the downtime is substantially prolonged and all reversible treatable causes are excluded. In cases of ongoing CPR, the decision to terminate a full resuscitation attempt is made by a HEMS physician.

All critically ill patients are transported to Tampere University Hospital (Tays), a tertiary referral centre for 1.1 million people. Tays is one of the five university hospitals in Finland, with 1,195 beds for somatic patients, including 24 ICU beds and 8 cardiosurgical post-operative ICU beds (in 2017). Tays' multidisciplinary ED treats approximately 100,000 patients every year, and Tays provides over 33,800 surgical procedures and approximately 2,100 ICU admissions annually, with pPCI 24 h a day and goal-directed intensive care with targeted temperature management for the OHCA post-resuscitation phase.

4.2 Data Collection

A total of 924 patients were studied for this thesis. Six hundred ten patients were included in the study for simplified pre-hospital MET score (IV). Three hundred fourteen patients were studied in the evaluation of OHCAs (I); 149 of those patients were included in the autopsy study of CPR-related injuries (II), and 10 patients contributed to the ACD-CPR study (III). The summary of the studies is presented in Table 3. The data were collected retrospectively between 1 January 2012 and 30 June 2012 for study IV, prospectively between 1 June 2013 and 31 May 2014 for studies I and II, and prospectively between September 2013 and March 2014 for study III. During the study periods, all OHCAs were treated according to the ERC Guidelines 2010 (Deakin et al. 2010).

Table 3. Summary of the studies.

Study characteristics	Study I	Study II	Study III	Study IV
	314 OHCA patients	149 forensic autopsies from the 314 OHCA patients	10 ACD-CPR cases from the 314 OHCA patients	610 pre-hospital MET score patients
Study design	Prospective observational study	Prospective observational study	Prospective case series study	Retrospective cohort study
Study question	What is the impact of futile resuscitation attempts on outcome of OHCA in Pirkanmaa?	What are the incidence and associated risk factors of CPR-related injuries in non-survivors after OHCA?	Does ACD-CPR provide better overall resuscitation quality than manual CPR during quality-controlled resuscitation attempts?	Do abnormal vital signs, based on in-hospital MET activation criteria, predict patient outcomes in an unselected patient population met by HEMS?

ACD-CPR indicates active compression-decompression CPR; CPR, cardiopulmonary resuscitation; HEMS, helicopter emergency medical service; MET, medical emergency team; OHCA, out-of-hospital cardiac arrest.

4.3 Study Design and Setting

4.3.1 Assessment of Futility and Cardiopulmonary Resuscitation-Related Injuries in Out-of-Hospital Cardiac Arrest (I, II)

The prospective observational study of epidemiology and the futility of OHCAs in the Pirkanmaa area (I) was conducted during a one-year study period. The EMS filled in a standardised chart according to the Utstein OHCA template while on scene and supplementary data were obtained from defibrillator records and hospital medical records. Neurological outcome was determined according to the CPC. The event and patient characteristics were compared between full and partial resuscitation attempts, and the incidence of OHCA, survival, and neurological outcome were determined according to the Utstein reporting template.

All OHCA non-survivors who received EMS-provided CPR and underwent a forensic autopsy were examined for CPR-related injuries (II). CAs with pre-arrest trauma in the thoracic or abdominal area were excluded from the study (II). CA patients who survived the event and were admitted to hospital but died later were either examined by medical autopsy when the cause of death was uncertain or they were issued a death certificate by the attending physician. Automated mechanical CPR devices were not used during the study period.

4.3.2 Definitions and Core Data Elements (I, II)

In the assessment of futility in OHCA (I), the data variables were used according to the updated Utstein definitions (Perkins et al. 2015a) as described in Table 2. Additionally, a prolonged downtime was determined as 1) no CPR attempts for ten minutes or more after collapse when the initial monitored rhythm was asystole or 2) no CPR attempts for 15 minutes or more when the initial rhythm was PEA. The response time was defined by the time interval between the incoming call to the dispatch centre and the time the first emergency response unit stopped at a point closest to the patient's location. The defibrillation time was defined by the time interval between the incoming call to the dispatch centre and the time the first shock was delivered.

The investigated CPR-related injuries (II) included rib fracture, rib fracture-associated haematoma, sternal fracture, mediastinal haemorrhage, haemothorax, lung contusion, haematoma or rupture of the heart muscle, haematoma or injury of the great vessels, liver injury, splenic injury, gastric injury, and laryngeal haematoma. Rib fractures were examined by side (bilateral or unilateral) and the number of fractures.

4.3.3 Quality-Controlled Active Compression-Decompression Cardiopulmonary Resuscitation Versus Manual Cardiopulmonary Resuscitation on End-Tidal Carbon Dioxide Output (III)

Study III was conducted as an observational self-controlled case-series study in the physician-staffed Pirkanmaa HEMS. Adult, non-hypothermic CA patients were enrolled in the study if the HEMS crew decided to continue resuscitative efforts for at least five minutes after securing the airway with endotracheal intubation. Patients were resuscitated on a two-minute cycle with standard manual CPR followed by a two-minute cycle of ACD-CPR, and the cycles were alternated as long as the resuscitation was attempted. ACD-CPR was performed with a manual lightweight ACD-CPR device (Ambu CardioPump, Ambu International Inc., Copenhagen, Denmark). The device was placed over the defibrillator's compression quality sensor to perform the ACD-CPR cycles. Ventilation was maintained manually constant during the cycles. The CPR quality data and $ETCO_2$ values were continuously recorded with the defibrillator during the resuscitation attempt and analysed with dedicated analysis software (RescueNet Code Review™, ZOLL Medical Corporation, Chelmsford, MA, USA). The differences in $ETCO_2$ output between the two resuscitation methods were compared in each individual patient separately to minimise confounding factors between the cases.

4.3.4 The Simplified Pre-Hospital Medical Emergency Team Score and In-Hospital Patient Outcomes (IV)

This retrospective study (IV) examined adult pre-hospital patients treated by physician-staffed HEMS in Tampere and Turku University Hospital areas and subsequently transported with or without accompanying physician to a university hospital. Patients' pre-hospital vital signs were measured on-scene before the commencement of any treatment and compared with the MET activation criteria used in Tampere University Hospital and scored accordingly (Table 4).

Table 4. Tampere University Hospital medical emergency team activation criteria and the simplified pre-hospital medical emergency team score.

Tampere University Hospital MET criteria	Simplified pre-hospital MET score	
SpO_2 < 90%	Respiratory dysfunction:	SpO_2 < 90% and/or
RR < 5/min or RR >24/min		RR < 5/min or RR >24/min
SBP < 90mmHg	Circulatory dysfunction:	SBP < 90mmHg and/or
HR < 40/min or >140/min		HR < 40/min or >140/min
GCS < 14 or decrease in GCS of ≥ 2 points	GCS < 14	
Caregivers concern	Caregivers concern	

GCS indicates Glasgow coma scale; HR, heart rate; MET, medical emergency team; SpO_2, peripheral capillary oxygen saturation; RR, respiratory rate; SBP, systolic blood pressure.

The measurements included peripheral capillary oxygen saturation (SpO2), respiratory rate (RR), heart rate (HR), systolic blood pressure (SBP), Glasgow Coma Scale (GCS), and nurse-paramedics' or HEMS physicians' concerns about the patients. This concern is based on a documented worry about the patient with or without any abnormal vital signs. To minimise errors due to missing data, the measurements of the pre-hospital vital signs were combined as follows: respiratory dysfunction (abnormal SpO2 and/or abnormal RR), circulatory dysfunction (abnormal HR and/or SBP), lowered GCS (<14), and caregiver concern. All these measurements were scored as one point, giving the simplified pre-hospital MET score a maximum value of 4. Patients' health status prior to acute onset of illness was evaluated according to the American Society of Anesthesiologists (ASA) classification system.

Data were collected from the HEMS database, EMS datasheets, and hospitals medical records. The simplified pre-hospital MET score was compared with patients' ESI classification on arrival to the hospital. The primary outcome was hospital mortality, and the secondary outcomes were the need for ICU treatment and the length of the ED stay, the ICU stay, and the hospital stay.

4.4 Statistical Methods

The statistical analysis was performed using SPSS software, versions 21.0 to 24.0 (IBM SPSS statistics for Windows, IBM Corp., Armonk, NY, USA). The demographic data were presented as medians and quartiles [Q_1–Q_3] (II, IV), as means and standard deviations (±SD) (I, III), or with 95% confidence limits (CLs) (I), as appropriate. In studies I, II, and IV, the comparisons between groups were analysed with Chi-square tests (I, II, IV), Student's *t*-tests (IV), Mann-Whitney *U*-tests (I, II, IV), and Kruskall-Wallis tests (IV) as appropriate.

Binary logistic regression analysis was used for crude odds ratios (ORs) to determine the contributing factors associated with OHCA survival (I), the variables associated with CPR-related injuries (II), and the variables associated with hospital mortality and morbidity in pre-hospital critically ill patients (IV), and further analysis with forward stepwise logistic regression was applied for adjusted ORs. The goodness-of-fit was assessed by the Hosmer-Lemeshow test (II).

The design in study III was based on preliminary results of a pilot study of a continuous response variable from matched pairs of both CPR methods in four study subjects. A pair consisted of measurements on both methods within a same-subject patient. According to the pilot study data, the difference in responses of matched pairs was normally distributed, with a standard deviation of 0.35 kPa, and the true difference in the mean response of matched pairs was 0.7 kPa. At power 0.8 and the Type I error 0.05, this study needed four pairs of subjects to be able to reject the null hypothesis. Linear mixed models were used to analyse the differences in $ETCO_2$ output between manual CPR and ACD-CPR where the patient was used as the random effect and the method as the fixed effect.

In all studies, statistical significance was defined as two-tailed $P < 0.05$.

4.5 Ethical Considerations

All studies were conducted according to the principles of the Declaration of Helsinki (World Medical Association 2013). The study protocols were approved by the Institutional Review Board and the Ethics Committee of Tays (ETL:R08116). Studies I, II, and IV were observational studies that were based on routinely obtained data from medical records. Therefore, the need for patients' informed consent was waived. In study II, the forensic autopsies were not performed as a part of the study protocol, as the decision to proceed with the forensic autopsy is stipulated in national legislation. Hence, consent from relatives was not needed. In study III, both CPR methods were considered as standard treatment, and the Ethics Committee of Tays thus approved the study and waived the need for informed consent.

5. RESULTS

5.1 Patient Characteristics

During the study period, the incidence of all EMS-treated OHCA was 52 per 100,000 population per year in the Pirkanmaa area, where the EMS attended a total of 314 OHCAs. Survival from hospital discharge was 14%, and 74% of survivors had good neurological outcome (CPC 1-2). Full system descriptions, process elements, patient variables, and outcomes are presented in Tables 5a and 5b. In this OHCA population, 70 (47%) non-survivors had CPR-related injuries. The most common injuries were multiple rib fractures (43%) and sternum fracture (15%). In the critically ill patient population with pre-hospital MET scores, the hospital mortality among the 610 patients treated by HEMS physician on scene was 11%.

Table 5a. The epidemiology of out-of-hospital cardiac arrests according to the Utstein template form (Perkins et al. 2015b) in the Pirkanmaa area between 1 June 2013 and 31 May 2014.

Population Served	Cardiac Arrests Attended
Total Population Served by EMS	Total Number of Cases
n=600 000	n=314

Resuscitation Attempted			Resuscitation not attempted			
All Cases	Partial attempts	Full attempts	All cases	DNAR or end stage terminal disease	Prolonged downtime	Unseen collapse with asystole
n=280	n=74	n=206	n=34	n=11	n=13	n=10

EMS response time	Resuscitation attempted	Resuscitation not attempted
	mean (SD)	mean (SD)
	10 (4.5)	14 (5.6)

Initial rhythm (n=280)	AED shock-able	AED non-shock-able	VT	VF	PEA	Asystole	Un-known	Not recorded
	n=9 (3%)	n=10 (3%)	n=5 (2%)	n=68 (24%)	n=77 (28%)	n=107 (38%)	n=4 (1%)	n=0

Location (n=280)	Home	Work	Rec	Public	Nursing home	Other	EMS transport	Un-known
	n=162 (58%)	n=3 (1%)	n=1 (0.4%)	n=65 (23%)	n=17 (6%)	n=17 (6%)	n=15 (5%)	n=0

Patient (n=280)	Age		Gender	
	mean (SD)	Unknown	Male	Female
	70 (15)	n=0	n=187 (67%)	n=93 (33%)

Witnessed (n=280)	Bystander	EMS	Unwitnessed	Unknown
	n=156 (56%)	n=62 (22%)	n=62 (22%)	n=0

Bystander Response (n=218)	Bystander CPR			Bystander AED	
	No bCPR	bCPR	Unknown	Analyse/ shock	Unknown
	n=100 (46%)	n=118 (54%)	n=0	n=0	n=0

Aetiology (n=280)	Medical	Trauma	Overdose	Drown-ing	Electro-cution	Asphyxial	Not recorded
	n=251 (90%)	n=3 (1%)	n=4 (1%)	n=7 (3%)	n=0	n=15 (5%)	n=0

EMS process (n=280)	First Defib Time n=82	Targeted Temp Control			Drugs given
	min, mean (SD)	Indicated	Not indicated	Unknown	
	12 (4.3)	n=0	n=280	n=0	n=138 (49%)

Hospital Process (n=67)	Reperfusion	Targeted Temp Control			
	pPCI attempted	Indicated/ Done	Indicated/ Not done	Not indicated	Unknown
	n=15	n=29	n=0	n=38	n=0

Forensic autopsies (n=149)	CPR-related injuries	No CPR-related injuries
	n=70 (47%)	n=79 (53%)

Table 5b. Out-of-hospital cardiac arrest patient outcomes by Utstein subgroups.

Patient outcomes reporting population		Any ROSC		Survived event		Survival to hospital discharge		Favourable neurological outcome CPC ≤ 2	
		Yes	Un-known	Yes	Un-known	Yes	Un-known	Yes	Un-known
EMS witnessed included n=280	All EMS treated arrests	n=100 (36%)	0	n=66 (24%)	0	n=39 (14%)	0	n=29 (10%)	1 (0.4%)
EMS witnessed excluded n=218	Shockable bystander witnessed n=57	n=35 (61%)	0	n=27 (47%)	0	19 (33%)	0	n=13 (23%)	0
	Shockable bCPR n=42	n=23 (55%)	0	n=19 (45%)	0	16 (38%)	0	n=12 (29%)	0
	Non-shockable witnessed n=99	n=30 (30%)	0	n=19 (19%)	0	6 (6%)	0	n=5 (5%)	0
Partial resuscitations excluded n=206	All EMS treated arrests	n=98 (48%)	0	n=65 (33%)	0	n=39 (19%)	0	n=29 (14%)	0

AED indicates automated external defibrillator; bCPR, bystander cardiopulmonary resuscitation; CPC, cerebral performance category; CPR, cardiopulmonary resuscitation; Defib, defibrillation; DNAR, do not attempt resuscitation; EMS, emergency medical service; PEA, pulseless electrical activity; pPCI, primary percutaneous coronary intervention; Rec, sports/recreation event; ROSC, return of spontaneous circulation; SD, standard deviation; VF, ventricular fibrillation; VT, ventricular tachycardia.

Resuscitation was not attempted due to futility in 34 OHCA cases. In 74 cases, the EMS started CPR, but the resuscitation attempt was soon discontinued due to additional information that confirmed the dismal prognosis of the situation, and the patient was declared dead on scene. These attempts were considered partial resuscitation attempts, and they comprised 24% of all CPR attempts. When these partial resuscitation attempts were removed from the survival analysis, the calculated percentage of survival to hospital discharge increased from 14% to 19%.

Table 6 presents CPR-related injury findings in OHCA non-survivors, divided into all resuscitation attempts, partial resuscitation attempts, and EMS-witnessed CAs. The incidence of injuries in partial resuscitation attempts and EMS witnessed attempts were similar when compared to all resuscitation attempts despite the differences in the duration of the attempt or persons involved in the CPR attempt. In EMS-witnessed CPR attempts, bystanders did not participate in providing CPR.

Table 6. Cardiopulmonary resuscitation-related injury findings in out-of-hospital cardiac arrest non-survivors.

	All attempts n=277, forensic autopsies n=149	Partial attempts n=74, forensic autopsies n=43	EMS witnessed n=62, forensic autopsies n=29
Duration of the resuscitation attempt (min), mean (SD)	20 (13)	9.5 (6)	30 (15)
CPR-related injuries in non-survivors, n (%)	70 (47)	15 (35)	12 (41)
Rib fracture, n (%)	64 (43)	11 (26)	10 (34)
Sternum fracture, n (%)	22 (15)	4 (9)	3 (10)
Rib fractures with haematoma, n (%)	11 (7)	0	4 (14)
Haematoma in cardiac muscle, n (%)	11 (7)	3 (7)	2 (7)
Haemothorax, n (%)	4 (3)	0	0

CPR indicates cardiopulmonary resuscitation; EMS, emergency medical service; SD, standard deviation.

Sixty-two (22%) OHCA patients were witnessed by EMS. These cases are described in detail in Table 7. In nine (15%) cases, EMS started CPR but soon discontinued the effort due to revealed futility, resulting in partial resuscitation attempts. Twenty-nine of 52 (56%) EMS-witnessed OHCA non-survivors underwent forensic autopsy. Their CPR-related injury incidence was 41%. All EMS witnessed OHCA survivors had good neurological outcomes (CPC 1–2) at hospital discharge. Simplified pre-hospital MET scores were available retrospectively for calculation in 47% of all EMS-witnessed OHCA cases. In these cases, vital signs were measured before any medical treatment was commenced.

Table 7. The characteristics of emergency medical service-witnessed out-of-hospital cardiac arrest patients (n=62).

Age (years), median [Q_1–Q_3]	70 [61 – 82]
Male gender, n (%)	44 (71)
Presumed cardiac origin, n (%)	36 (58)
Initial rhythm shockable, n (%)	13 (21)
Initial rhythm PEA, n (%)	35 (57)
Partial resuscitation attempt, n (%)	9 (15)
terminal illness	8
DNAR revealed during resuscitation attempt	1
Time interval between the EMS arrival on scene and the cardiac arrest (min), median [Q_1–Q_3]	19 [6 – 31]
Cardiac arrest during EMS transport, n (%)	14 (23)
Any ROSC, n (%)	25 (40)
Survived the event, n (%)	13 (20)
Survived to hospital discharge, n (%)	10 (16)
CPC 1-2, n (%)	10 (16)
CPR-related injuries in non-survivors, n (%)	12 (41)
Total simplified pre-hospital MET score, median [Q_1 – Q_3]	3 [2 – 4]

CPC indicates cerebral performance category; CPR, cardiopulmonary resuscitation; DNAR, do not attempt resuscitation; EMS, emergency medical service; MET, emergency medical service; PEA, pulseless electrical activity; Q_1 – Q_3, quartiles; ROSC, return of spontaneous circulation; SD, standard deviation.

Ten bystander-witnessed OHCA patients were resuscitated, alternating two resuscitation methods, manual CPR and ACD-CPR, and comparing the $ETCO_2$ output during the resuscitation attempt. A prior pilot study was conducted to ensure adequate power calculations. The patients were similar to the overall OHCA patient population regarding age and initial rhythm (mean age 75 (±10) years vs. 70 (±15) years; VF as initial rhythm 20% vs. 24%), but there were more males when compared to overall OHCA population (80% vs. 67%). The quality measurements during the resuscitation attempts were as follows: mean compression rate 100 (±6.7)$^{min-1}$ vs. 105 (±4.9)$^{min-1}$, mean compression depth 76 (±1.3) mm vs. 71 (±1.0) mm, and mean ventilation rate 11 (±2.9) $^{min-1}$ vs. 11 (±2.6) $^{min-1}$ between ACD-CPR and manual CPR, respectively.

Simplified pre-hospital MET score frequencies of points from 0 to 4 were 25%, 5%, 39%, 17%, and 15%, respectively. The majority of patients with scores of 3 and

4 (44% and 61%) were admitted to the ICU, the majority of patients with scores of 1 and 2 (32% and 40%) were admitted to the internal medicine department, and the majority of patients with a score of 0 (42%) were admitted to the ED monitoring unit. Those critically ill pre-hospital patients who died later were older, their ASA classification score prior to acute onset of illness was higher, they had higher simplified pre-hospital MET scores and more urgent ESI classification on arrival to the ED, and they stayed longer in the ICU ($P < 0.001$, respectively).

5.2 Predictors of Patient Outcomes

In the OHCA population, the initial rhythm was shockable in 29% of all attempted resuscitation cases, and 54% of OHCA patients received bCPR before EMS arrival (Table 5a). The shockable initial rhythm (OR 3.91, CI 95% 1.61–9.51, $P = 0.003$) and bCPR (OR 3.48, 95% CI 1.29–9.39, $P = 0.014$) were independent predictors for survival to hospital discharge and together resulted in survival to hospital discharge in 38% of cases. Seventy-five per cent of these patients had a favourable neurological outcome. Fifteen OHCA patients (23%) presented an ST-elevation myocardial infarct (STEMI) after ROSC and were admitted for immediate pPCI. Thirteen of those patients (87%) survived to hospital discharge; 12 had a good neurological outcome (CPC 1-2).

Partial resuscitation attempts were associated with dismal prognostic factors: an unwitnessed OHCA, initial rhythm being asystole or PEA, prolonged downtime, end-stage terminal disease, multiple trauma, and FRU being the first unit on the scene ($P < 0.05$). The mean time to cease resuscitation attempts after partial resuscitation attempts was 9.5 (±6) minutes. After futility was revealed, EMS discontinued CPR in 13 (18%) cases, and a HEMS physician (either present on the scene or by telephone consultation) ordered CPR termination in all other cases of partial resuscitation.

CPR-related injuries were associated with older age, male gender, initial shockable rhythm, and OHCA in a public location, as shown in Table 8. Of these variables, older age, male gender, and a public place were independently associated with CPR-related injuries (Hosmer-Lemeshow test $P = 0.350$). Table 9 presents the durations of the bCPR, EMS-provided CPR, and the overall duration of resuscitation attempts, divided into injured and non-injured groups, and shows that the duration of the resuscitation attempt in these groups did not affect the incidence of CPR-related injuries.

Table 8. Predictors of cardiopulmonary resuscitation-related injuries in out-of-hospital cardiac arrest.

	CPR-related injuries			CPR-related injuries		
	Univariate			Multivariable		
Variables	OR	95% CI	*P*-value	OR	95% CI	*P*-value
Age	1.02	1.00 - 1.05	0.045	1.04	1.01 - 1.07	0.013
Male gender	3.02	1.45 - 6.31	0.003	4.11	1.79 - 9.43	0.001
Public location	4.60	1.97 - 10.72	<0.001	4.98	2.02 - 12.31	<0.001
Initial rhythm shockable	2.23	1.00 - 4.99	0.050	Variable not entered		

CI indicates confidence interval; CPR, cardiopulmonary resuscitation; OR, odds ratio.

Table 9. Characteristics of the duration of the resuscitation attempt divided into injured and non-injured groups.

		Forensic autopsies		
	Total cohort n=280	Injuries n=70	No injuries n=79	
	median [Q_1- Q_3]	median [Q_1- Q_3] min - max	median [Q_1- Q_3] min - max	*P*-value
Duration of bCPR attempt (min)	8 [5 - 11]	8 [7 - 11] 2 - 21	10 [6 -14] 2- 29	0.411
Duration of EMS CPR attempt (min)	17 [10 - 26]	21 [13 - 30] 0 - 83	19 [11 -25] 1 - 70	0.232
Duration of overall CPR attempt (min)	21 [13 - 30]	25 [17 - 38] 0 - 83	23 [15 - 30] 1 - 74	0.145

bCPR indicates bystander cardiopulmonary resuscitation; CPR, cardiopulmonary resuscitation; EMS, emergency medical service; Q_1–Q_3, quartiles.

Patients resuscitated with the quality-controlled manual CPR and ACD-CPR underwent a mean of 37 (±8) minutes of CPR. The HEMS crew arrived on scene in a mean of 17 (±8) minutes after the onset of CA. The interaction between the resuscitation method and the patient was significant ($P < 0.001$), but although manual CPR showed a trend for increasing $ETCO_2$ output compared to ACD-CPR in 6/10 patients, this difference was not statistically significant.

Higher scores in simplified pre-hospital MET score were associated with hospital mortality, the need for ICU treatment, and patient's more urgent ESI classification in the ED ($P < 0.001$, respectively). Also, the time intervals for stays in the ED were shorter and the time intervals for stays in the ICU and in the hospital were longer with higher MET scores ($P < 0.001$, respectively). The simplified pre-hospital MET score was an independent predictor for hospital mortality (OR 2.42, 95% CI 1.84–3.18, $P < 0.001$) regardless of patients' previous physical health or age.

6. DISCUSSION

This thesis studied the epidemiology of OHCA, with a special interest in the futility aspects and the characteristics of CPR-related injuries in OHCAs in the Pirkanmaa area of Finland (I, II). The study also determined whether there would be difference between quality-controlled ACD-CPR and quality-controlled manual CPR when $ETCO_2$ output was used as a quantitative measure of CPR effectiveness (III) and whether a simplified pre-hospital MET score of the critically ill patients would predict in-hospital outcomes (IV).

The thesis addresses the main findings as 1) the considerable amount of partial resuscitation attempts where futility was revealed only after the commencement of resuscitation attempts and the interference that the partial resuscitation attempts have on the outcome calculations in the Utstein reporting template; 2) the independent predictors of CPR-related injuries being a public location for the resuscitation attempt, male gender, and older age, while the duration of the resuscitation attempt did not affect the incidence of injuries; 3) quality-controlled manual CPR produces similar or slightly better $ETCO_2$ rates than ACD-CPR, indicating equal performance of these methods on CPR effectiveness; 4) the overall low survival of EMS-witnessed CA but resulting in good neurological recovery at hospital discharge among all survivors; and 5) the simplified pre-hospital MET score presents an independent predictor of hospital morbidity and mortality regardless of patient age or previous physical health.

6.1 Out-of-Hospital Cardiac Arrest Epidemiology in the Pirkanmaa Area

The previous epidemiological OHCA study was conducted in Tampere, the largest city in the Pirkanmaa area ten years ago (Kämäräinen et al. 2007). This thesis shows that the incidence of EMS-treated OHCA in the area has increased during this time period, from 46 to 52 per 100,000 population per year (I). The current incidence ranks in the midst of European regional incidences where CPR attempts ranged from 19 to 104 per 100,000 population per year (Gräsner et al. 2016). At the same time, the population in the Pirkanmaa area has grown 2%, and the mean age of the population has risen, explaining the increased numbers (Statistics Finland 2017). At the beginning of 1980, one in five Finns was aged under 15 years, but the population projection predicts that the share of persons under 15 years would decrease to 14% by 2060 (Statistics Finland 2017). The accelerated ageing population could decidedly increase Finland's incidence of OHCA in the future, as has happened in Japan (Hasegawa et al. 2013).

This study shows that the incidence of VF as the initial rhythm has decreased in the Pirkanmaa area from 30% to 24% even though the EMS response time has not increased when comparing the results between the Tampere city area in 2004 (Kämäräinen et al. 2007) and the Pirkanmaa area in 2013 (I). This phenomenon is recognised throughout the world (Berdowski et al. 2010), and it challenges survival rates, as the initial non-shockable rhythms are known to have a more dismal prognosis (Wolbinski et al. 2016). The incidence of bCPR seems to have improved remarkably during the last ten years in Finland when comparing the results from Tampere in 2004 (Kämäräinen et al. 2007) and the FINNRESUSCI study in 2010 (Hiltunen et al. 2012) with the results (I) of this thesis: 31%, 47%, and 54%, respectively. This favourable trend impacts patients' survival and improves patients' long-term functional outcomes by decreasing the risk of brain damage (Kragholm et al. 2017a). However, the socioeconomic status of the patient and neighbourhood characteristics influence the likelihood of OHCA victims receiving bCPR (Sasson et al. 2011; Vaillancourt et al. 2008), indicating a need for community CPR training programmes.

The study shows that, in the Pirkanmaa area, OHCA patients presenting STEMI after ROSC who were admitted to immediate pPCI had high (87%) rates of survival to hospital discharge (I). According to a recent meta-analysis, the mean survival to hospital discharge rates of OHCA patients presenting STEMI after ROSC and receiving immediate pPCI is 67%, and the overall survival rates in the early angiography group versus the conservative management group were 58% and 31%, respectively (Camuglia et al. 2014). Survival is not affected by transportation time; thus, patients with STEMI after ROSC should be taken directly to a PCI centre (Kragholm et al.2017b). The incidences of shockable initial rhythm and bCPR, and the rate of immediate pPCI are the most influential factors on the overall survival rates (I) presented in this thesis.

6.2 Factors Leading to Partial Resuscitation Attempts

As shown in study I, partial resuscitation attempts remain unavoidable and count as a significant amount (24%) of futile resuscitation attempts in OHCA. Their association with dismal prognostic factors and the reality that most of the factors were discovered only after the commencement of resuscitation attempts make this patient subgroup very different from the other OHCA patient subgroups, namely those where CPR was not attempted at all and those where CPR was fully attempted. A recent retrospective study including over 34,800 patients reported that, during a 10-year period, partial resuscitations in the studied area increased from 8.6% to 18.8% (Nehme et al. 2014). Those cases were independently associated with non-shockable rhythm, prolonged downtime, older age, and female gender. The skill level of the first unit on the scene was also a significant factor leading to partial resuscitation attempt. This may be due to resuscitation guidelines (ERC 2015) and local protocols that direct the first responders on scene to promptly start chest compressions and deliver the first defibrillation as soon as possible if secondary signs of death are not obvious. While these guidelines aim to ensure that resuscitative actions are not delayed unnecessarily, which would have dismal effects on patient survival, this will sustain the significant incidence of partial resuscitation attempts. To date, the OHCA Utstein template divides cases only based on whether resuscitation was attempted or was not (Perkins et al. 2015a). This approach fails to recognise cases where resuscitation attempts were withheld after the commencement of CPR when futility was revealed. As previously reported (Nehme et al. 2014), and also as found in this thesis, the mean duration of partial resuscitation was less than ten minutes, but during that time, these patients did receive a factual resuscitation attempt (I). This patient subgroup leads to ambiguous results when included in the survival analysis, deviating from the Utstein template purpose of describing the system effectiveness of treating OHCA patients (Perkins et al. 2015a).

6.3 Cardiopulmonary Resuscitation-Related Injuries and Cardiopulmonary Resuscitation Quality

In this thesis, the most common injury findings in OHCA non-survivors were multiple rib fractures and sternum fractures (II). The incidence of CPR-related injuries reflects the characteristics of OHCA events and also denotes the counterproductive effect on resuscitation guidelines' directions on chest compression depth and compression rate. On the contrary for IHCA patients, OHCA patients often lack any previous medical history, and their critical illness often manifested unexpectantly (Mushtaq and Ritchie 2005). The first helpers are usually bystanders that might not have any previous experience in performing CPR and receive instructions via telephone from the dispatch centre; however, this does not seem to increase the incidence of CPR-related injuries (II) as found in this thesis and in previous studies (Seung et al. 2016). There are nevertheless many distracting and hampering issues when performing CPR in OHCA. Giving quality chest compressions and performing timely procedures during the resuscitation attempt in crowded places or confined spaces, places with hostile weather or insufficient lighting, or when moving patients to a more appropriate place for full resuscitation attempts lead to higher risk for CPR-related injuries (Seung et al. 2016). In study II, the duration of the resuscitation attempt did not affect the incidence of injuries, and the incidences were similar between full resuscitation attempts, partial attempts and EMS-witnessed CAs. It is more plausible that injuries do occur at any time of resuscitation attempt when the compression force and depth are non-optimal and exceed the recommendations in the resuscitation guidelines (Hellevuo et al. 2013). When several rescuers participate in performing chest compressions (Kim et al. 2013), or when a patient is moved on scene or transported to hospital with ongoing manual CPR, the risk for injuries increases (Seung et al. 2016). In this thesis, the studied OHCA non-survivors received all resuscitative efforts on scene according to Pirkanmaa EMS protocols (I, II).

Study II showed an association between CPR-related injuries and public location of OHCA, initial shockable rhythm, male gender, and older age. While some of the findings, such as age, could be due to degenerative skeletal changes or osteoporosis, and gender could be explained by differences in tissue stiffness, the other findings are highly associated with possible improved prognosis. As in this thesis, with initial shockable rhythm and bCPR, survival to hospital discharge is high (I) and thus explains the rescuer's desire to perform chest compressions with considerable strength, which may lead to higher frequency of injuries, especially if a CPR feedback device is not available to guide performance to avoid too-deep compressions (Hellevuo et al. 2013).

One of the collective objectives for the OHCA Utstein template and autopsies performed on OHCA non-survivors is to evaluate the quality of the medical care. The CPR-related injury incidences vary greatly and reflect the composition of population pyramids and the effect of application of the resuscitation guidelines in that time span (Hoke and Chamberlain 2004, Kralj et al. 2015, Miller et al. 2014). While all these studies lack data on quality measurements of the CPR attempts, the underlying mechanics spur a need for future investigations.

6.4 End-Tidal Carbon Dioxide as the Surrogate Marker for Cardiopulmonary Resuscitation Quality

The thesis evaluated two CPR methods based on their capability to produce $ETCO_2$ during the resuscitation attempt (III). These methods provided equal performance on CPR effectiveness with $ETCO_2$ as the surrogate marker (III). $ETCO_2$ reflects cardiac output and pulmonary blood flow during low-flow states by estimating carbon dioxide production, its alveolar tension and the elimination from the lungs (Idris et al. 1994; Trillò et al. 1994). Increasing values of $ETCO_2$ predict ROSC and serve as a surrogate for the quality of CPR performance (Touma and Davies 2013). But even though $ETCO_2$ is an important tool during resuscitation, there are many confounding factors that affect $ETCO_2$, such as the cause of CA, bCPR, initial rhythm, and the time delay between CA and the time of capnography measurement commencement (Heradstveit et al. 2012). Tracheal intubation is the only reliable way to measure $ETCO_2$ and capnography; however, OHCA patients are more difficult to intubate, as a recent study showed higher first-attempt intubation failure when compared to non-CA patients (Sunde 2015). According to the studies to date, the initial $ETCO_2$ values or values at 20 min of CPR being less than 2.67 kPa (20 mmHg) serve as a better predictor for ROSC than the 1.33 kPa (10 mmHg) cut-off values (Paiva et al. 2018). It should be noted, though, that the initial value of $ETCO_2$ may not necessarily be truly the initial encounter, for CPR may be performed several minutes before the airway is secured with intubation and the measurement of $ETCO_2$ is started. Another important factor is the ventilation rate and the tidal volumes when estimating $ETCO_2$: hyperventilation or hypoventilation will introduce falsely low or high values. The overall evidence of any cut-off value for $ETCO_2$ and ROSC is low, and most importantly, the initial low $ETCO_2$ levels do not predict futility and do not justify withholding the CPR attempt (Paiva et al. 2018; Rognås et al. 2014).

In study III, the confounding factors were eliminated by analysing $ETCO_2$ values between the two CPR methods for each individual patient separately and keeping the ventilation rate constant. Therefore, when estimating CPR effectiveness and the chances of obtaining ROSC, one should include all quality parameters that estimate overall CPR quality: chest compression rate and depth, duty cycle, and ventilation rate, together with ventilation-associated $ETCO_2$ values.

6.5 The Critically Ill Pre-Hospital Patient and Emergency Medical Service-Witnessed Cardiac Arrests

EMS-witnessed CAs form a subgroup of patients where many confounding factors, such as witness status, EMS response time, and whether the patient received bCPR, are all equalised. In this thesis, survival to hospital discharge after EMS-witnessed OHCA was 16%, all patients having a good neurological recovery. Most patients (57%) presented PEA as the initial rhythm. In a vast cohort study in North America, the EMS-witnessed OHCA survival was 18%, and the most common initial rhythm in this patient subgroup was PEA (43%), similar to our result, and a factor to affect survival from OHCA (Hostler et al. 2010). Our survival rates are significantly lower than some of the previous studies that report 35% survival rates after EMS-witnessed OHCA and describe EMS-witnessed CA enhancing the likelihood of survival and favourable neurological recovery 12 months after the incident when compared to bystander-witnessed or unwitnessed OHCA (Gold and Eisenberg, 2010; Nehme et al. 2015). However, our numbers represent all EMS-witnessed OHCAs, whereas the previous studies have usually reported only OHCAs with presumed cardiac aetiology (Gold and Eisenberg, 2010; Nehme et al. 2015). When comparing the efficacy of the emergency system to save OHCA patients, these dissimilarities are needed to take into consideration when comparing data.

The rate of EMS-witnessed CA is dependent on community and the response times of the EMS, reflecting both the effectiveness of the system to reach the patient before the CA but also whether immediate care can reverse the patient's condition and prevent the CA. In this thesis, retrospectively calculated simplified pre-hospital MET score was high among EMS-witnessed CAs, but those patients who survived the event had good neurological recovery at hospital discharge. The most common symptoms preceding CA are dyspnoea, chest pain, and syncope (Nehme et al. 2018;

Nishiyama 2013; Skrifvars et al 2009). This information may not be readily apparent when seeking alterations in vital signs in the pre-hospital setting, but rather reflect the overall habitus and complaint of the patient (Douw et al. 2015). Applying healthcare professional's worry to the pre-hospital evaluation of the acute situation will also address many questions that are important when treating patients in the pre-hospital setting: limitations of resources, including staff and available treatment; distance to the appropriate hospital and transportation times; hostile environment; or difficult transfer of the patient due to confined spaces. This knowledge is difficult to apply to EWS calculations (Shaw et al. 2017). The good neurological outcome of all survivors after EMS-witnessed OHCA indicates high performance of the EMS in Pirkanmaa, Finland.

In study IV, hospital mortality of the critically ill pre-hospital patients treated by HEMS physician on scene was 11%, and the simplified pre-hospital MET score predicted patient outcomes during the hospitalization, irrespective of age and previous physical health. Older age, lower pulse oximetry measurements, abnormal respiratory rate, lower systolic blood pressure and lower GCS score have all shown an association with development of critical illness during hospitalisation (Seymour et al. 2010). The vast variation of the mortality rates in the pre-hospital studies from 35% (Seymour et al. 2010) to less than 1% (Leung et al. 2016; Shaw et al. 2017) results from heterogeneity in patient populations, in the EMSs and in the timing of mortality calculation (24 h after admission, during ED care, or during hospitalisation). In this thesis, the patient population consisted of patients treated by HEMS physician (IV), whereas other studies examined all patients treated by EMS and brought to hospital.

EWSs present only one important aspect when looking at the manifold challenges in safely treating the patient from a pre-hospital setting to the ED and transferring care from the pre-hospital team to the in-hospital team. Detecting patient deterioration is dependent on numerous factors during that phase: respectful and effective communication, identification of staff in the ED, and the application of a structured handover tool (Dawson et al. 2013). Therefore, it is also difficult to measure the effectiveness of track and trigger system scores when other patient safety-related issues may greatly vary between EMSs and hospitals, and these factors are under focus for better quality management. Early intervention improves outcomes; however, some critically ill patients in the pre-hospital setting will not improve no matter how quickly the initial treatment is administered, and only the subsequent hospitalisation and treatments during the hospital stay will determine patient outcome. In this study, the ESI classification assigned by the ED triage nurse correlated strongly with the simplified pre-hospital MET score (IV). This indicates that the pre-hospital concern for the patient was respected, and subsequent treatment and use of resources was allocated accordingly.

Ambulance services need a reliable tool for early estimation of critically ill patients' subsequent risk of deterioration and for rapid decision-making to escalate the level of care. To date, the scoring systems based on physiological measures, such as MET scores and NEWS scores, have been evaluated in the pre-hospital setting for their ability to predict adverse outcomes, but a validated assessment tool for unselected patient populations with high sensitivity and specificity on patient outcomes is yet to be discovered (Williams et al. 2016).

6.6 Strengths and Limitations

The strengths and the limitations of this thesis are described according to the studies.

In Finland, the police are primarily dispatched to the scene when the secondary signs of death are indisputable at the time of the emergency call. Therefore, these calls were not included in study I. The data for all CPR attempts according to the Utstein standardised template for OHCA were included in the study without any missing cases. During study periods I and II, the Pirkanmaa EMS was not equipped with audio-visual feedback system defibrillators, hence the data on epidemiology and CPR-related injuries did not include the quality measurements of CPR attempts. The overall frequency of autopsies in study II was high, but the patient population that comprised only OHCA non-survivors for computed tomography radiographs were not routinely obtained from patients with ROSC at the time of hospital admission; therefore, the results may have varied if the OHCA survivors were included in the study. Forensic autopsies are performed under the restrictions of Finnish law; hence, the study II protocol could not stipulate any details of the forensic autopsies.

In study III, the confounding factors of resuscitation attempts between the cases were minimised by analysing the $ETCO_2$ differences between the two CPR methods separately for every patient. All CPR quality data were continuously recorded during the CPR attempt, and the constant ventilation rate was evaluated with capnography during data analysis, but the minute ventilation could not be controlled due to manual ventilation during the CPR attempt. Prior to study III, a pilot study was conducted to ensure adequate power calculations. The patients were not randomised by the CPR method, but the $ETCO_2$ and quality measurements commenced when all parameter sensors were ready, and this could have affected the results.

In study IV, the retrospective collection of data resulted in missing data in patients' vital signs. Moreover, the cold climate restricted the possibility of obtaining SpO_2 measurements in some cases. To minimise these errors, the parameters were combined to form respiratory dysfunction (sPO2 and RR parameters) and circulatory dysfunction (HR and SBP parameters) points. The 30-day mortality was not evaluated; thus, the results may underestimate long-term mortality in the studied patient population.

Additional studies are needed to compensate for the limitations of the design of the studies in this thesis.

6.7 Future Implications

The research in resuscitation science aims to identify and prioritise gaps in knowledge and help the progress of quality improvement. Current resuscitation guidelines emphasise immediate action when encountering OHCA patients to ensure high-quality CPR attempts and positive impacts on patient survival. However, this will lead to unavoidable partial resuscitation attempts. To date, the OHCA registries and the Utstein template definitions do not recognise this subgroup of patients. Defining and separating this subgroup from the outcome calculations may help to further standardise the registry reports and may better reflect true OHCA outcomes.

Due to the great variability in CPR-related injuries after OHCA, the studies investigating injuries should include CPR quality measurement data in the analysis. This would enhance the knowledge of the impact of true high-quality CPR on CPR-related injuries and help to distinguish the thresholds that might increase injury incidence. Applying this information to the incidence and characteristics of CPR-related injuries, as well as the CPR quality data to the Utstein template, would help to compare the significance of these factors to OHCA survival. Moreover, when considering the incidence of CPR-related injuries and the predictors of positive outcome after OHCA, hospitals receiving OHCA patients should consider having a standard protocol for observing and diagnosing the sometimes obscure and underlying injuries after OHCA by radiography imaging to ensure appropriate quality of subsequent medical care.

In the future, new CPR techniques may emerge and be suggested as alternative choices to rescue OHCA patient. When these techniques are compared with existing techniques on CPR effectiveness and the chances of obtaining ROSC, the data should include all of the quality parameters that estimate the overall CPR quality, together with ventilation-associated $ETCO_2$ values.

Currently, there are no recommendations on how to manage the urgency and appropriate scale of clinical response with EWS systems in the EMS pre-hospital setting. The EMS would benefit from a validated pre-hospital assessment tool with high sensitivity and specificity for unselected patient populations to help with decision-making in the pre-hospital setting.

7. SUMMARY AND CONCLUSIONS

This thesis aimed to evaluate the overall quality in resuscitation in the field by addressing the contents of uniform reporting templates to better reflect the outcome of, incidence of, and risk factors for CPR-related injuries in OHCA, pointing to the importance of overall quality control when comparing CPR methods and the usefulness of a simplified pre-hospital MET score for predicting patient outcomes after hospital admission.

The incidence and survival rates of OHCA in the Pirkanmaa area of Finland are similar when compared to the other regional Finnish studies and European registries. However, partial resuscitations formed a considerable amount of OHCA cases where futility was revealed only after the commencement of CPR. Excluding these futile cases from the outcome calculations improved the rate of hospital survival from 14% to 19%. Terminating resuscitation is a distinctive subgroup in OHCA that interferes with the reporting outcome calculations and thus should be included in the reporting templates to better reflect the true effectiveness of CPR attempts and outcomes of OHCA. The incidence of CPR-related injuries was lower than in the recent previous studies, and this study presents a novel finding that public location is an independent risk factor for these injuries. This may be explained by the implication of more aggressive treatment during OHCA in situations where the hope for possible positive outcomes and the stress of public situations affect the rescuer on scene.

The quality of the CPR attempt plays the utmost important role when evaluating patient outcome, including injury findings or when comparing different resuscitative methods. This study presented a novel method of comparing the effectiveness of two CPR methods on their $ETCO_2$ output by monitoring the quality of CPR during the resuscitation attempt and minimising the confounding factors by alternating these methods within the same patient. The quality-controlled ACD-CPR was not superior to quality-controlled manual CPR.

EMS providers benefit from a risk assessment tool to help identify critically ill patients in unselected patient populations where patients' previous medical history may not be readily available. A simplified pre-hospital MET score predicts patient outcomes regardless of age or previous physical health. Further studies are needed to validate a suitable early warning tool in the pre-hospital setting with high sensitivity and specificity.

8. ERRATA

I. Page 1337, Figure 1, “Prolonged downtime n=23” should be “Prolonged downtime n=13”.

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APPENDIX: ORIGINAL PUBLICATIONS

PUBLICATION
I

Assessment of futility in out-of-hospital cardiac arrest

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ORIGINAL ARTICLE

Assessment of futility in out-of-hospital cardiac arrest

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Conflicts of interest
The authors confirm that there are no conflicts of interest to report.

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Background: Our aim was to evaluate the impact of futile resuscitation attempts to the outcome calculations of attempted resuscitation in out-of-hospital cardiac arrest (OHCA). Defined as partial resuscitations, we focused on a subgroup of patients in whom cardiopulmonary resuscitation (CPR) was initiated, but further efforts were soon abandoned due to evidence of futility.

Methods: We conducted this study using the Utstein template during a 12-month study period. We compared the event characteristics between full and partial resuscitation attempts and determined the incidence, survival and neurological outcome.

Results: Emergency Medical Services (EMS) attended a total of 314 OHCA cases. In 34 cases, resuscitation was not attempted due to futility. Seventy-four cases were partial resuscitation attempts where resuscitation was soon discontinued due to dismal prognostic factors. Partial attempts were associated with an unwitnessed OHCA, prolonged downtime, end-stage malignant disease, multiple trauma, asystole or pulseless electrical activity as the initial rhythm, and a first responding unit being the first unit on the scene ($P < 0.05$, respectively). The calculation of survival to hospital discharge rate was 14% and increased 5% when partial resuscitation attempts were excluded from the analysis. Seventy-four percentage had a Cerebral Performance Category 1–2 at hospital discharge. Shockable initial rhythm, public location and bystander CPR had a positive impact on survival.

Conclusions: Resuscitative efforts were considered futile in 11% of cases and resuscitation was discontinued due to evidence of futility in additional 24% cases based on additional information. Terminating resuscitation should be identified as a separate subgroup of OHCA cases to better reflect the outcome.

Editorial Comment
In a cohort of out-of-hospital cardiac arrest patients, details leading to cardiac arrest were analyzed, with focus on determinations of futility and discontinuation of treatment. The authors suggest that terminated resuscitation should be reported as a separate cardiac arrest subgroup to better reflect resuscitation outcome.

During the preceding fifteen years, several methods have been proposed to improve the survival of out-of-hospital cardiac arrest (OHCA) victims. These methods include the application of the clinical practice guidelines for cardiac arrest patient care,[1] primary percutaneous coronary intervention (pPCI) and post-resuscitation care with targeted temperature management. Some centres have reported a significant increase in survival rates from OHCA, but variability is high and overall survival remains low.[2]

The European Resuscitation Council (ERC) recommends the updated Utstein style template to report data on OHCA.[3,4] It presents important subgroups that allow the evaluation of the effect of the initial rhythm and bystander actions on outcome.[4]

The purpose of this study was to evaluate the impact of futile resuscitation attempts when assessing the outcome calculations of attempted resuscitation in OHCA. Taking into account our previous observations regarding futility in the context of pre-hospital cardiac arrest,[5] we focused on a subgroup of patients in whom resuscitation was initiated, but further efforts were abandoned due to evidence of futility.

Methods

Study design

Our study was a 1 year observational study. We collected data prospectively from all OHCAs treated by the EMS between 1 June 2013, and 31 May 2014. During the study period cardiac arrest treatment was administered according to the ERC guidelines 2010.[6] The EMS personnel filled in a standardized chart on scene and supplementary data were obtained from monitor-defibrillator record sheets and hospital records.

EMS system in Pirkanmaa area

The EMS serves approximately 600,000 inhabitants in the Pirkanmaa area including the city of Tampere with 220,500 inhabitants. The total catchment area of Pirkanmaa is 12,600 km^2 and includes urban, suburban and rural areas. All critically ill patients are transported to Tampere University Hospital, which provides pPCI 24 h a day and goal directed intensive care including targeted temperature management.

All resuscitative efforts are performed on scene and OHCA patients are transported to hospital only if return of spontaneous circulation (ROSC) is achieved with the exception of hypothermic OHCA patients, who are transported during ongoing CPR. One field commander unit of advanced ALS-level and one physician staffed HEMS unit operate in the area 24 h a day. During the data collection period the EMS consisted of 45 first responding units (FRU) staffed mostly by lay rescuers with first aid training providing immediate life support including defibrillation, ten basic life support (BLS) units staffed by emergency medical technicians and firemen and 25 paramedic-nurse staffed advanced life support (ALS) units.

In the case of a sudden cardiac arrest, the FRU and either an ALS or BLS unit are dispatched alongside the field commander and the HEMS unit. EMS dispatch is provided by a joint emergency dispatch service centre also dispatching fire, rescue, police and social services. The dispatch centre provides telephone-assisted instructions for cardiopulmonary resuscitation (CPR) in cases of a suspected cardiac arrest.

First responding units are permitted to withhold resuscitation attempts in cases of secondary signs of death (e.g. dependent lividity, rigor mortis, and physical injuries incompatible with life). As a standing order, EMS personnel are permitted to withhold resuscitative attempts in cases of obvious futility (e.g. unwitnessed arrest with asystole as the initial rhythm or when a 'do not attempt resuscitation' (DNAR)-order is presented on scene. EMS was entitled to refrain from resuscitation if downtime was prolonged according to local protocol based on national guidelines when reversible treatable causes were excluded. In the study area, all reasons to withhold the resuscitative manoeuvres are written to the patient records. In cases of ongoing resuscitation, the decision to terminate a full resuscitation attempt is taken by the HEMS physician.

Definitions and core data elements

All data variables were used according to the updated Utstein definitions.[4] Prolonged downtime was determined as no CPR attempts for over 10 min after the collapse and the initial rhythm being asystole, or no CPR attempts over 14 min and the initial rhythm being pulseless electrical activity (PEA). The response time was by definition the time interval from the incoming call to the time the first emergency response vehicle stops at a point closest to the patient's location, and the defibrillation time was the time interval from the incoming call to the time the first shock is delivered. These core time data did not include arrests witnessed by EMS personnel. Neurological outcome at hospital discharge was determined according to Cerebral Performance Category (CPC).[7]

Statistical analysis

Statistical analysis was performed using SPSS software version 23.0 (IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp). Demographic data are presented as numbers and percentages and as means, standard deviations (SD) and 95% confidence limits (CL) for proportions as appropriate. Chi-square test and Mann–Whitney *U*-test were used for comparison between groups as appropriate. The association with survival, neurological outcome and event characteristics were analysed using binary logistic regression analysis for crude odds ratios (ORs) and these results are presented as ORs and 95% confidence intervals (CI). No sample size calculation was performed but we estimated that data collection for a full year would allow a meaningful description in this observational study. Statistical significance was defined as two-tailed $P < 0.05$.

Ethical considerations

This study was conducted in accordance to the principles of the Declaration of Helsinki and the study protocol was approved by the institutional review board of Tampere University Hospital (Ethics committee date of approval 12.04.2013, ETL:R08116. The Regional Ethics Committee of Pirkanmaa Health District, Tampere University Hospital, PO Box 2000, FI-33521 Tampere, Finland). The study was a prospective observational study based on routinely obtained data from EMS and medical records. Therefore, the need for patients' informed consent was waived.

Results

The one year study period resulted in 314 OHCA cases. The study flow chart is presented in Fig. 1. OHCA incidence was 52/100,000/year. The core data of all OHCA cases where resuscitation was attempted were obtained without any missing data. In cases where resuscitation was not attempted by the EMS, gender and age data were missing in two cases and bystander CPR status in one case. Supplementary data on whether the first unit on scene was an FRU or an EMS unit, was missing in 43 (14%) cases.

Futility and partial resuscitation attempts

Based on standing order principles, resuscitative efforts were immediately considered futile on scene thus CPR was not attempted in 11% ($n = 34$), 95% CL [0.08, 0.15] of cases (Fig. 1). In 24% ($n = 74$), 95% CL [0.19, 0.29] of cases resuscitation was initiated, but further efforts were soon discontinued due to evidence of futility per additional information. Therefore, these cases were considered as partial resuscitation attempts.

Primary rhythm

The primary rhythm was shockable in 29% ($n = 82$), 95% CL [0.24, 0.35] of cases. In four cases the patient achieved ROSC before a

Fig. 1. The study flowchart according to the Utstein standardized template for reporting outcomes from out-of-hospital cardiac arrest in Pirkanmaa area. AED, automated external defibrillator; bCPR, bystander cardiopulmonary resuscitation; CPR, cardiopulmonary resuscitation; Defib, defibrillation; DNAR, do not attempt resuscitation; EMS, emergency medical service; full attempts, defined as complete adherence to resuscitation protocol and continuing efforts until return of spontaneous circulation or observed lack of response partial attempts, resuscitation was initiated, but further efforts were ceased due to evidence of futility; PEA, pulseless electrical activity; pPCI, primary percutaneous coronary intervention; Rec, sports/recreation event; SD, standard deviation; Temp, temperature; VF, ventricular fibrillation; VT, ventricular tachycardia. *Prolonged downtime indicates no CPR attempts over 10 min after the collapse and the initial rhythm being asystole, or no CPR attempts over 15 min and the initial rhythm being pulseless electrical activity.

Population Served	Cardiac Arrests Attended
Total Population Served by EMS	Total Number of Cases
n = 600 000	*n* = 314

Resuscitation Attempted			Resuscitation not attempted			
All Cases	Partial attempts	Full attempts	All cases	DNAR or end stage terminal disease	Prolonged downtime*	Unseen collapse with asystole
n = 280	*n* = 74	*n* = 206	*n* = 34	*n* = 11	*n* = 23	*n* = 10

Primary Rhythm (*n* = 280)	AED shockable	AED non-shockable	VT	VF	PEA	Asystole	Unknown	Not recorded
	n = 9 (3%)	*n* = 10 (3%)	*n* = 5 (2%)	*n* = 68 (24%)	*n* = 77 (28%)	*n* = 107 (38%)	*n* = 4 (1%)	*n* = 0

Location (*n* = 280)	Home	Work	Rec	Public	Nursing home	Other	EMS transport	Unknown
	n = 162 (58%)	*n* = 3 (1%)	*n* = 1 (0.4%)	*n* = 65 (23%)	*n* = 17 (6%)	*n* = 17 (6%)	*n* = 15 (5%)	*n* = 0

Patient (*n* = 280)	Age		Gender	
	mean (SD)	Unknown	Male	Female
	70 (15)	*n* = 0	*n* = 187 (67%)	*n* = 93 (33%)

Witnessed (*n* = 280)	Bystander	EMS	Unwitnessed	Unknown
	n = 156 (56%)	*n* = 62 (22%)	*n* = 62 (22%)	*n* = 0

Bystander Response (*n* = 218)	Bystander CPR			Bystander AED	
	No bCPR	bCPR	Unknown	Analyse/shock	Unknown
	n = 100 (46%)	*n* = 118 (54%)	*n* = 0	*n* = 0	*n* = 0

Etiology (*n* = 280)	Medical	Trauma	Overdose	Drowning	Electrocution	Asphyxial	Not recorded
	n = 251 (90%)	*n* = 3 (1%)	*n* = 4 (1%)	*n* = 7 (3%)	*n* = 0	*n* = 15 (5%)	*n* = 0

EMS process (*n* = 280)	First Defib Time *n* = 82	Targeted Temp Control			Drugs given
	min, mean (SD)	Indicated	Not indicated	Unknown	
	12 (4.3)	*n* = 0	*n* = 280	*n* = 0	*n* = 138 (49%)

Hospital Process (*n* = 67)	Reperfusion	Targeted Temp Control			
	pPCI attempted	Indicated/Done	Indicated/Not done	Not indicated	Unknown
	n = 15	*n* = 29	*n* = 0	*n* = 38	*n* = 0

defibrillator was attached: one drowning incident patient with successful bystander CPR before EMS arrival, one asphyxial patient with carbon monoxide poisoning resuscitated by fire fighters before EMS arrival, one patient with heart disease with 14 min of bystander CPR and presenting ROSC upon EMS arrival and one patient with EMS witnessed cardiac arrest presenting ROSC in 2 min before commencing rhythm monitoring. In these cases the primary rhythm remained unknown (Fig. 1).

Full and partial resuscitation attempts, baseline characteristics

The baseline characteristics of all OHCA patients stratified by resuscitation attempt are presented in Table 1. Altogether 74% (n = 206), 95% CL [0.68, 0.78] of patients underwent a full resuscitation attempt, defined as complete adherence to resuscitation protocol and continuing efforts until ROSC or observed lack of response. Two of these patients were successfully resuscitated by bystanders and presented ROSC at EMS arrival. In three cases a DNAR order was presented only after a full attempt at resuscitation was terminated due to presumed futility.

Those patients on whom resuscitation was attempted only partially presented with dismal prognostic factors such as an unwitnessed OHCA, prolonged downtime, end-stage terminal disease, multiple trauma and asystole or PEA as the initial rhythm. An FRU was the first unit on the scene in 15% (n = 31), 95% [CL 0.11, 0.21] of full resuscitation attempt cases and in 28% (n = 21), 95% CL [0.19, 0.40] of partial resuscitation attempt cases (P = 0.015). Resuscitative efforts were terminated after the decision of an HEMS physician either present on the scene or via telephone consultation in 82% (n = 61), 95% CL [0.72, 0.89] of partial resuscitation attempts (Table 2). In 18% (n = 13), 95% CL [0.11, 0.28] of cases the EMS discontinued the resuscitation attempt after receiving additional information that revealed futility.

Outcome results and contributing factors for survival

Sixty-seven patients went through the hospital process (as presented in Fig. 1), but only 66 patients survived the event as one hypothermic patient was admitted with ongoing resuscitation. Outcome results by patient subgroups are presented in Table 3. CPC at hospital discharge was 1–2 in 74% (n = 29), 95% CL [0.59, 0.85] of cases. Selectively excluding partial resuscitation attempts from outcome data calculations resulted in a higher proportion of patients getting any ROSC, event survival, survival to hospital discharge and favourable neurological outcome. Seventy-five percentage of patients achieved favourable neurological outcome at hospital discharge in the shockable bystander CPR subgroup.

Twenty-three percentage (n = 15), 95% CL [0.14, 0.34] of patients who survived the event presented with acute myocardial infarction and were admitted for immediate pPCI. Of these patients, 87% (n = 13), 95% CL [0.62, 0.96] survived to hospital discharge, 12 patients with CPC 1–2 and one patient with CPC 3–4 at the time of discharge.

The factors contributing to overall survival to hospital discharge with full resuscitation attempts not witnessed by EMS are described in Table 4. Shockable initial rhythm, public location and bystander CPR had a positive impact on survival. With full resuscitation attempts the fact whether the cardiac arrest was witnessed or not did not affect the survival.

Discussion

In this population-based cohort study we evaluated the impact of futile resuscitation attempts to the outcome calculations of OHCA in Pirkanmaa area, Finland, with a special focus on factors leading to a partial resuscitation attempt. We found a high rate of partial resuscitation attempts. In these cases the futility became obvious only after the initiation of resuscitation. Excluding these partial resuscitation attempts from our outcome analysis calculations resulted in a 5% increase in hospital survival.

Partial resuscitation attempts

Partial resuscitation attempts were made in 24% of cases during the study period. These were associated with unfavourable prognostic factors such as unwitnessed OHCA, prolonged downtime, end-stage terminal disease, multiple

Table 1 Baseline characteristics of all out-of-hospital cardiac arrests (n = 314) stratified by resuscitation attempt.

	Resuscitation not attempted	Resuscitation attempted			
	n = 34	All n = 280	Partial attempt n = 74	Full attempt n = 206	P-value
Age, mean (SD); years	73 (16)	69 (15)	68 (19)	70 (13)	0.921
Unknown	2	0	0	0	
Male gender, no. (%)	24 (71)	187 (67)	46 (62)	141 (68)	0.388
Unknown	2	0	0	0	
Witnessed, no. (%)	18 (53)	156 (56)	25 (34)	131 (64)	< 0.001
Witnessed by EMS, no. (%)	1 (3)	62 (22)	9 (12)	53 (26)	0.015
Bystander CPR, no. (%)	9 (27)	118 (54)	29 (45)	89 (58)	0.075
Unknown	1 (3)	0	0	0	
Presumed cardiac origin no. (%)	25 (74)	210 (75)	48 (65)	162 (79)	0.028
Location of arrest, no. (%)					
Home	18 (53)	162 (58)	45 (61)	117 (57)	0.585
Work	0	3 (1)	2 (3)	1 (0.5)	0.172
Recreational/sport	0	1 (0.4)	0	1 ((0.5)	0.264
Public place	1 (3)	65 (23)	9 (12)	56 (27)	0.010
Nursing home	8 (24)	18 (6)	8 (10)	10 (5)	0.095
Other	6 (18)	18 (6)	9 (12)	9 (4)	0.027
EMS transportation	1 (3)	16 (6)	3 (4)	13 (6)	0.573
EMS response time min, mean (SD)	14 (5.6)	10 (4.5)	13 (6.5)	9 (3.7)	0.226
Prolonged downtime*, no. (%)	13 (38)	12 (4)	12 (16)	0	< 0.001
Unwitnessed arrest with asystole	10 (29)	37 (13)	37 (50)	0	< 0.001
End-stage terminal disease	1 (3)	17 (6)	17 (23)	0	< 0.001
DNAR-order present	10 (29)	8 (3)	5 (7)	3 (1)	0.032
Multiple trauma	1 (3)	3 (1)	3 (4)	0	0.018
First unit on scene no. (%)					
FRU	3 (9)	52 (19)	21 (28)	31 (15)	0.015
BLS	2 (6)	16 (6)	4 (5)	12 (6)	1.000
ALS	24 (71)	174 (62)	42 (57)	132 (64)	0.268
Unknown	5 (15)	38 (14)	7 (9)	31 (15)	
Initial ECG rhythm, no. (%)					
AED shockable	0	9 (3)	0	9 (4)	0.118
AED non-shockable	0	10 (4)	5 (7)	5 (2)	0.136
VT	0	5 (2)	0	5 (2)	0.330
VF	1 (3)	68 (24)	4 (5)	64 (31)	< 0.001
PEA	3 (9)	77 (28)	11 (15)	66 (32)	0.004
Asystole	29 (85)	107 (38)	54 (73)	53 (26)	< 0.001
Unknown	1 (3)	4 (1)	0	4 (2)	0.576
Drugs given	0	138 (49)	4 (5)	134 (65)	< 0.001
ROSC at any time, no. (%)	NA	100 (36)	2 (3)	98 (48)	< 0.001
Duration of resuscitation attempt min, mean, (SD), when terminated on scene	NA	20 (13)	9.5 (6)	26 (13)	< 0.001

AED indicates automated external defibrillator; ALS, advanced life support; BLS, basic life support; CPR, cardiopulmonary resuscitation; DNAR, do not attempt resuscitation; EMS, emergency medical service; FRU, first responding unit; PEA, pulseless electrical activity; response time, the time interval from incoming call to the time the first emergency response vehicle stops at a point closest to the patient's location; ROSC, return of spontaneous circulation; SD, standard deviation; VF, ventricular fibrillation; VT, ventricular tachycardia. *Prolonged downtime indicates no CPR attempts for over 10 min after the collapse and the initial rhythm being asystole, or no CPR attempts over 15 min and the initial rhythm being pulseless electrical activity.

Table 2 Partial resuscitation attempts initiated by emergency medical service and terminated by helicopter emergency service physician or emergency medical service due to additional information.

	Partial resuscitations terminated by HEMS physician		Partial resuscitations terminated by EMS
	On scene (%) n = 48	By consultation (%) n = 13	On scene n = 13
Unwitnessed asystole	32 (66)	3 (23)	2 (15)
End-stage malignant disease	11 (23)	5 (38)	1 (8)
Prolonged downtime*	2 (4)	4 (31)	6 (46)
Multiple trauma	2 (4)	0	1 (8)
DNAR presented after commencement of CPR	1 (2)	1 (8)	3 (23)

CPR indicates cardiopulmonary resuscitation; DNAR, do not attempt resuscitation; HEMS, helicopter emergency medical service. *Prolonged downtime indicates no CPR attempts for over 10 min after the collapse and the initial rhythm being asystole, or no CPR attempts over 15 min and the initial rhythm being pulseless electrical activity.

trauma and non-shockable rhythm as the initial rhythm. These confounding factors are comparable with those in an earlier study[8] reporting 19% of OHCA patients to have received resuscitative efforts lasting < 10 min due to futility, that is, partial resuscitation. The reasons for partial resuscitations may lie within the resuscitation protocols that direct the first unit on the scene to initiate resuscitative efforts if irreversible signs of death are not obvious. The personnel will start chest compressions before connecting the patient to a defibrillator and additional information is collected concurrently during the resuscitation attempt. As a result, the evidence of futility emerges only after the immediate initiation of resuscitative efforts. While most procedures are initiated during the first minutes of the resuscitation attempt, these patients receive full attempted resuscitative efforts exactly as do non-futile patient groups, including advanced airway management and drug administration. In Finland, FRUs are not allowed to withhold resuscitation if there are no obvious signs of futility, that is, secondary signs of death.

To date, the Utstein template lacks definition of this futile patient subgroup which skews the outcome results and may thus underestimate the overall effectiveness of CPR.[4] Our outcome results improved considerably when partial resuscitations were selectively excluded from the patient outcome calculations.

OHCA incidence and outcome

The incidence of OHCA has changed from 46 to 52/100,000/year during the last 10 years in the Pirkanmaa area, and is comparable to that of other European countries.[9] The baseline characteristics of OHCA such as age, gender, location of arrest and response times have not altered in Pirkanmaa.[5]

In this study, the rate of overall hospital survival was 14% and 74% (n = 12) of patients had a favourable neurological outcome (CPC 1–2) at hospital discharge. The Utstein Guidelines recommends the use of CPC category when determining the neurological outcome. The CPC at the time of discharge has been associated with long-term outcome, more favourable CPC independently predicts better long-term prognosis.[7] Our survival rate is somewhat higher than the average survival rate of 11% in the 2005 European survey.[10] Nevertheless, we saw no vast improvement in overall survival when comparing our findings to the earlier study in Tampere.[5] Other studies have reported increasing survival rates by improving the overall quality of the local chain of survival.[2,11,12] Pirkanmaa area has evolved in recent years with its physician staffed HEMS, 24 h availability of immediate pPCI, and standardized ICU-care with targeted temperature management for OHCA patients. Interestingly, excluding the partial resuscitation attempts from our outcome analysis calculations resulted in a 5% increase in hospital survival. It has been reported earlier that the differences between survival rates can partly be explained by varying definitions of OHCA.[13] Therefore, the assessment of futility and the role of partial resuscitation attempts in OHCA outcomes needs further evaluation.

The contributing factors for survival

Survival from witnessed OHCA with a shockable primary rhythm has improved in recent decades in urban areas in Finland.[14] Immediate

Table 3 Patient outcomes by Utstein subgroups (a) in Pirkanmaa 2014 with all resuscitation attempts included, *n* = 280; (b) in Pirkanmaa 2014 with partial resuscitation attempts excluded, *n* = 206.

Patient outcomes reporting population	Any ROSC		Survived event		Survival to hospital discharge		Favourable neurological outcome CPC ≤ 2	
	Yes	Unknown	Yes	Unknown	Yes	Unknown	Yes	Unknown
(a)								
EMS witnessed included *n* = 280								
All EMS treated arrests	*n* = 100 (36%)	0	*n* = 66 (24%)	0	*n* = 39 (14%)	0	*n* = 29 (10%)	1 (0.4%)
EMS witnessed excluded *n* = 218								
Shockable bystander witnessed* *n* = 57	*n* = 35 (61%)	0	*n* = 27 (47%)	0	19 (33%)	0	*n* = 13 (23%)	0
Shockable bystander CPR *n* = 42	*n* = 23 (55%)	0	*n* = 19 (45%)	0	16 (38%)	0	*n* = 12 (29%)	0
Non-shockable witnessed *n* = 99	*n* = 30 (30%)	0	*n* = 19 (19%)	0	6 (6%)	0	*n* = 5 (5%)	0
(b)								
EMS witnessed included *n* = 206								
All EMS treated arrests	*n* = 98 (48%)	0	*n* = 65 (33%)	0	*n* = 39 (19%)	0	*n* = 29 (14%)	1 (0.5%)
EMS witnessed xcluded *n* = 153								
Shockable bystander witnessed* *n* = 53	*n* = 35 (66%)	0	*n* = 27 (51%)	0	*n* = 19 (36%)	0	*n* = 13 (25%)	0
Shockable bystander CPR *n* = 39	*n* = 23 (59%)	0	*n* = 19 (49%)	0	*n* = 16 (41%)	0	*n* = 12 (31%)	0
Non-shockable witnessed *n* = 78	*n* = 30 (39%)	0	19 (24%)	0	*n* = 6 (8%)	0	*n* = 5 (6%)	0

CPC, Cerebral Performance Category; CPR, cardiopulmonary resuscitation; EMS, emergency medical services; ROSC, return of spontaneous circulation. *Utstein comparator group (system efficacy).

pPCI is an independent predictor of survival in OHCA.[15,16] In this study, 23% of those patients who survived the event received immediate pPCI and 87% of them survived to hospital discharge. Eighty percentage of these patients had a favourable neurological outcome. In comparison, a recent review reported a mean survival to hospital discharge in 67% and a mean survival with good neurological outcome in 68% of patients receiving immediate pPCI.[17] One large cohort study reported similar survival rates with an overall survival of 79% at 5-year follow-up.[18] However, the proportion of shockable rhythm as the initial rhythm was considerably higher in that patient population compared that in our study (70% vs. 28%, respectively). Our study showed that with full resuscitation attempts survival was not affected by whether the collapse of the patient was witnessed or not. We believe that the local protocol permitting EMS to refrain from resuscitation when futility was evident explains this effect.

The decision-making in withholding or discontinuing resuscitation attempts presents ethical dilemmas that are not always immediately resolved. In cases of prolonged anoxia, end stage terminal disease or multiple trauma the decision is commonly straightforward.[19] The decision to withhold efforts among elderly patients and patients living in a nursing home is more complicated.[20,21] EMS practitioners' annual exposure to OHCA patients is reported to be four to nine cases per year - however, there is no clear evidence that career experience or exposure to OHCA patients affects practitioners' ALS procedures.[22] Continuing education for EMS practitioners and implementation of clear rules for terminating resuscitation on scene reduces futile efforts and enhances practitioner assurance.[23]

In this study HEMS physicians terminated sixty-one (22%) primarily futile, partial resuscitation attempts on the scene or by telephone consultation. Comparing these results to those in our area 10 years ago reveals that nowadays

Table 4 Univariate and multivariable logistic regression analysis for overall survival to hospital discharge in full resuscitation attempts of out-of-hospital cardiac arrests not witnessed by emergency medical service.

	Survival					
	Univariate			Multivariable		
	Odds ratio	95% CI	*P*-value	Odds ratio	95% CI	*P*-value
Age	0.97	0.94–1.00	0.084			
Hands-on-time	1.00	0.91–1.11	0.977			
Shockable vs. non-shockable rhythm	3.80	1.60–9.06	0.003	3.91	1.61–9.51	0.003
Cardiac vs. non-cardiac aetiology	1.15	0.36–3.70	0.811			
Public vs. non-public location	2.42	1.05–5.53	0.037	Variable not entered	Variable not entered	Variable not entered
Witnessed vs. non-witnessed	1.08	0.34–3.48	0.895			
Bystander CPR vs. no bystander CPR	3.36	1.28–8.84	0.014	3.48	1.29–9.39	0.014

CI, confidence interval; CPR, cardiopulmonary resuscitation; hands-on-time, from collapse to start of cardiopulmonary resuscitation by emergency medical service.

having a physician in the field, more resuscitative efforts are terminated on scene. In these cases, the HEMS physicians' decisions seemed justified and were based on both futility and ethical considerations for the patient's best interests. We emphasize that expert opinion on scene or by consultation in these cases is mandatory. Defining the futility of a resuscitation attempt is difficult, and ethical practices and legislation vary between countries. Therefore, such specific guidelines that try to harmonize the variation in practices appeared only recently in the ERC 2015 Guidelines.[24] These guidelines could contribute to the Utstein-style outcome reports in recognizing that partial resuscitation may serve as a defined patient group and that this group may affect the outcome results and should thus be taken into consideration in future outcome reports.

Limitations of the study

There are some limitations to our study. Patients in whom secondary signs of death were already present at the time of emergency call were not included in this study as these calls result in the dispatch of the police instead of the EMS. However, if the EMS on scene decided to initiate CPR on to these patients, they were included in the study. To ensure the quality of the data, the corresponding author continuously collected the data in a designated database and cross-checked data from EMS record sheets and hospital records.

Conclusion

Strict adherence to the guidelines in the EMS system resulted in partial resuscitation attempt situations and resuscitative efforts were considered futile in 11% of cases and resuscitation was discontinued due to evidence of futility in additional 24% cases based on additional information. Terminating resuscitation should be identified as a separate subgroup.

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PUBLICATION
II

Risk factors for cardiopulmonary resuscitation-related injuries sustained during out-of-hospital cardiac arrests

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ORIGINAL ARTICLE

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Risk factors for cardiopulmonary resuscitation-related injuries sustained during out-of-hospital cardiac arrests

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Background: We aimed to determine the incidence of and associated risk factors for cardiopulmonary resuscitation (CPR)-related injuries in non-survivors of out-of-hospital cardiac arrests (OHCAs) in an emergency medical service (EMS) system in which all CPR procedures are performed on scene and patients are not routinely transported to the hospital with ongoing CPR.

Material and methods: We conducted this prospective observational study between 1 June 2013, and 31 May 2014. Data were collected from EMS datasheets and forensic autopsy records. The exclusion criteria were OHCAs due to trauma in the thoracic or abdominal area. EMS adhered to the European Resuscitation Council Resuscitation Guidelines (2010) during the resuscitation attempts.

Results: Emergency medical service provided CPR in 280 attended OHCAs with 207 cases terminated on scene. A total of 149 patients underwent a forensic autopsy and 47% had a CPR-related injury. The most common injuries were multiple rib fractures (43%), with 22% of patients having more than eight fractured ribs. Abdominal visceral injuries or injuries related to airway management were rare. The injuries were associated with older age, male gender, initial shockable rhythm and public location of the cardiac arrest ($P < .05$ respectively). In the multivariable regression analysis, older age, male gender, and public location were independent predictors for injuries. There were no differences in the durations of the CPR attempt between the injured and non-injured groups.

Conclusion: Older age, male gender, and public location were independently associated with CPR-related injuries. The duration of the resuscitation attempts did not affect the incident of injuries.

KEYWORDS
autopsy study, cardiac arrest, cardiopulmonary resuscitation, complication, CPR-related injuries, out-of-hospital cardiac arrest, rib fractures, risk factors, thoracic injuries

1 | INTRODUCTION

Cardiopulmonary resuscitation (CPR) may cause iatrogenic injuries due to the force and depth of the chest compressions, rescuer's hand position and the direction of the chest compression and airway management. Injuries related to CPR attempts involve the chest, abdomen, retroperitoneum, face and neck; they also contribute to air and fat embolisms.[1-3] The most common injuries involve the thoracic cage and thoracic viscera.[4-6] The reported incidence of CPR-related injuries varies widely among studies; a recent systematic review conducted a pooled analysis of reported post-resuscitation injuries and

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found a 31% overall incidence for rib fractures and a 15% incidence for sternum fractures.[5]

The past studies have reported some risk factors for CPR-related injuries, including older age, gender, longer duration of CPR, increased compression depth and rate, lower rate of return of spontaneous circulation (ROSC) and out-of-hospital cardiac arrests (OHCAs).[4,6-10] These studies have included both in-hospital cardiac arrest (IHCA) patients and OHCA patients, with great variability regarding patient populations, EMS systems and hospital procedures.

To the best of our knowledge, no previous studies have investigated CPR-related injuries in OHCAs with a specific focus on their association with patient and event characteristics. Therefore, the purpose of this study was to determine the incidence and associated risk factors of CPR-related injuries in non-survivors after OHCA according to the Utstein Style guidelines. The information gained from this analysis would (1) help medical personnel understand the incidence and relevance of CPR-related injuries and (2) increase provider comfort with performing proper CPR without unnecessary concerns. The study was conducted using data from an emergency medical service (EMS) system in which OHCA patients are not routinely transported to the hospital with ongoing CPR; instead, all CPR efforts are performed at the scene of the event.

Editorial comment

Possible injuries caused by potentially lifesaving cardiopulmonary resuscitation to a cardiac arrest victim may create fear and reluctance to respond with the necessary determination and force. This paper reports the injuries found in victims of deceased cardiac arrest in a system with good registration and a high frequency of autopsy.

2 | METHODS

2.1 | Study design, population and setting

This observational study was a part of an Utstein Style analysis of OHCAs between 1 June 2013 and 31 May 2014 in the Pirkanmaa area, Finland. The cohort was collected prospectively and planned originally for 2 substudies conducted by the corresponding author in Tampere University Hospital. The OHCA incidence in the Pirkanmaa area during the study period was 52/100 000. All adult OHCA patients who received EMS-provided CPR did not survive the event or died on the hospital admission and subsequently underwent a forensic autopsy were included in the study (n = 149), as shown in Figure 1. Cardiac arrest patients with trauma in the thoracic or abdominal area were excluded from the study. The patients were either declared dead on scene after an unsuccessful resuscitation attempt or were transported to the hospital after successful resuscitation with ROSC. Three elderly patients with dismal prognostic factors were transported to primary care facility. During the study period, mechanical CPR devices were not used in the prehospital setting. Patients who died later after the hospital admission were either examined by medical autopsy when the cause of death was uncertain or they were issued a death certificate by the attending physician.

2.2 | EMS system in the Pirkanmaa area

Pirkanmaa is served by a 2-tiered EMS system that is activated by a national emergency medical dispatching centre. The first tier consists of first-response units (FRU) with lay rescuers or firefighters who are trained in basic life support (BLS) and the use of automated external defibrillators (AEDs) and BLS units staffed by emergency medical technicians and firefighters. The second tier consists of advanced life support (ALS) units staffed with paramedic nurses who have the capability of providing drug-assisted resuscitation. Additionally, a field commander unit of advanced ALS-level and a physician-staffed Helicopter EMS (HEMS) unit are dispatched to sudden cardiac arrests. All resuscitated patients are transported to Tampere University Hospital, which is a tertiary referral centre for a base population of 1 200 000 persons.

2.3 | Data collection

Patient's data were collected prospectively from EMS datasheets, Pirkanmaa OHCA data according to the Utstein Style guidelines[11] and forensic autopsy records. All forensic autopsies were conducted by a protocol stipulated by the Finnish legislation and the use of autopsy descriptions was in collaboration with forensic pathologists, but this study did not affect the protocol used by the forensic pathologist when performing the autopsy. The data included age, gender, body mass index (BMI), location of the arrest, duration of the resuscitation attempt, bystander CPR and initial rhythm, and whether a transient ROSC was gained during the resuscitation attempt. Analysed injuries included rib fracture, rib fracture-associated haematoma, sternal fracture, mediastinal haemorrhage, haemothorax, lung contusion, haematoma or rupture of the heart, haematoma or injury of the great vessels, liver injury, splenic injury, gastric injury and laryngeal haematoma. Rib fractures were examined by side (bilateral or unilateral) and the number of fractures.

2.4 | Statistical analysis

The statistical analysis was performed using SPSS software version 21.0 (IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp). Data are presented as numbers and percentages or with medians and interquartiles [Q_1-Q_3], as appropriate. Binominal variables were analysed with the chi-square test, and the comparisons of continuous data were analysed with Mann-Whitney *U*-test. Binary logistic regression analysis was used for crude odds ratios (ORs) to determine variables associated with CPR-related injuries, after which forward stepwise logistic regression was applied for adjusted ORs. The goodness of fit was assessed by Hosmer-Lemeshow test. Statistical significance was defined as 2-tailed $P < .05$.

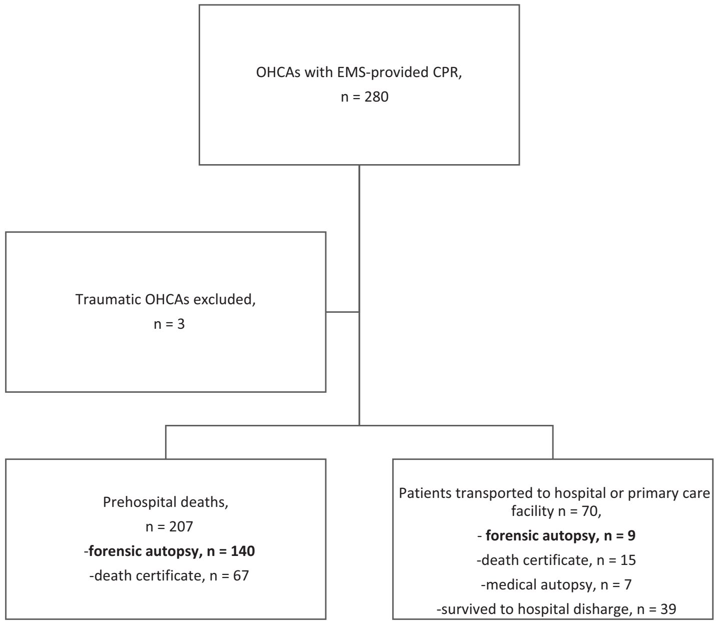

FIGURE 1 Flowchart of out-of-hospital cardiac arrest patients included in the study. CPR, cardiopulmonary resuscitation; EMS, emergency medical service; OHCA, out-of hospital cardiac arrest

2.5 | Ethical considerations

This study was approved by the Institutional Review Board and the Ethics Committee of Tampere University Hospital (ETL:R08116) and conducted in accordance to the principles of the Declaration of Helsinki. In Finland, the decision to proceed with a forensic autopsy is stipulated in national legislation; therefore, forensic autopsies were not performed as a part of the study protocol and consent from relatives was not required. The authorisation to analyse the forensic autopsy findings was issued by the National Institute for Health and Welfare. The study was an observational study based on routinely obtained data from EMS records, hospital medical records and autopsy records. Therefore, the need for informed consent was waived.

3 | RESULTS

A 1-year study period resulted in 280 attended OHCAs with EMS-provided CPR of which 207 cases were terminated on scene. The epidemiological analysis of the OHCA cases is described in our previous study.[12] A total of 149 patients had forensic autopsy records for the analysis. The event and patient characteristics are presented in Table 1. Seventy patients (47%) sustained CPR-related injuries. CPR-related injuries were associated with older age, the male gender, initial shockable rhythm and OCHA in a public location ($P < .05$, respectively), whereas a patient's BMI, bystander CPR, transient ROSC and airway management by intubation did not have an effect on injuries. The overall median duration of the resuscitation attempt in the patient population subjected to forensic autopsy was 24 [16-31] minutes. There were no differences in the durations of the EMS-provided CPR, bystander CPR or overall CPR attempt between the injured and non-injured groups.

Injuries related to CPR after OHCA are presented in Table 2. The most common injuries were multiple rib fractures: A total of 64 patients (43%) had multiple rib fractures and 51 (34%) of which had bilateral rib fractures. Every fifth patient had more than 8 fractured ribs, and 22 (15%) had a sternum fracture. Eleven patients (7%) had rib fractures with haematoma and 11 patients (7%) had haematomas in the heart or haemopericardium. Only 1 patient with haemopericardium also had a sternum fracture. Four patients had a haemothorax, with one being significant (1200 mL of blood in the right pleural space and 300 mL of blood in the left pleural space), also presenting with a rupture of the pericardium and an aortic injury (a haematoma in the wall of the thoracic aorta). One patient with multiple rib fractures also sustained a small gastric laceration, and 1 patient had liver lacerations with the aforementioned sternal fracture and haemopericardium. According to the forensic pathologist statements, the injury findings of the patient with massive haemothorax, rupture of the pericardium and an aortic injury and the injury findings of the patient with liver lacerations were potentially life-threatening. In one case, the CPR-related injuries were considered lethal: This was a patient with coronary artery disease who had a mediastinal haematoma with ruptures in the myocardium, causing a haemopericardium and cardiac tamponade.

Two patients presented with a laryngeal haematoma due to airway management; a drowned male who was intubated during the resuscitation attempt and an elderly female with severe obesity

TABLE 1 Event and patient characteristics divided into injured and non-injured groups in out-of-hospital cardiac arrest

		Forensic autopsies				
	Total cohort	Injuries		No injuries		
	n or median [Q_1-Q_3] N = 280	n or median [Q_1-Q_3] N = 70	% or min-max	n or median [Q_1-Q_3] N = 79	% or min-max	*P*-value
Age	70 [62-80]	70 [63-81]	20-91	66 [59-78]	0.1-94	.038
Male	187 (67)	56	80	45	57	.003
BMI	*NA*	27.8 [24.0-30.6]	17.6-48.3	27.1 [23.5-33.1]	18.7-66.9	.627
Bystander CPR						.127
Yes	118	39	56	31	39	
No	100	19	27	31	39	
EMS witnessed	62	12	17	17	22	
Duration of bystander CPR attempt (min)	8 [5-11]	8 [7-11]	2-21	10 [6-14]	2-29	.411
Duration of EMS CPR attempt (min)	17 [10-26]	21 [13-30]	0-83	19.0 [11-25]	1-70	.232
Duration of the overall CPR attempt (min)	21 [13-30]	25 [17-38]	0-83	23 [15-30]	1-74	.145
Initial rhythm shockable	82	20	29	12	15	.047
Location: home	162	36	51	53	67	.052
Location: public	65	26	37	9	11	<.001
Airway management intubation	108	21	30	14	18	.078
Any ROSC	100	18	26	11	14	.070

BMI, body mass index; CPR, cardiopulmonary resuscitation; EMS, emergency medical service; ROSC, return of spontaneous circulation.

whose airway was maintained with a supraglottic device during the resuscitation attempt. Neither of these patients had any other injuries.

The predictors of CPR-related injuries are presented in Table 3. In the univariate analysis age, the male gender, a public location and the initial shockable rhythm were associated with CPR-related injuries, whereas transient ROSC and the duration of the CPR attempt did not reach statistical significance. After univariate analysis, all statistically or clinically significant variables were entered into the multivariable model. Forward stepwise method was used to select the final model. The goodness of fit was assessed by Hosmer-Lemeshow test indicated a good fit of the multivariable model ($P = .350$). A multivariable logistic regression analysis showed that the independent predictors for CPR-related injuries in OHCA were older age, male gender and public location. Interactions between age and other predictors and gender and other predictors were tested. None of the interaction terms was significant.

4 | DISCUSSION

This prospective study examined CPR-related injuries and associated risk factors after OHCA. The most common injury findings were multiple bilateral rib fractures and sternum fractures. Severe injuries in the thoracic or abdominal viscera were rare. In this patient population, older age, the male gender and a public location were independent predictors for CPR-related injuries. The durations of the resuscitation attempts did not affect the incidence of injuries.

The past studies have reported variable incidences of CPR-related injuries after OHCA. The incidence of rib fractures has ranged from 13% to 97% and sternal fractures from 1% to 79%.[4-6] This wide variation is possibly due to the fact that these studies are from a 50-year time span and the methods that have been used to analyse these injuries may have varied. The most recent autopsy studies report a high frequency of thoracic injuries, rib fractures as high as 85% and sternal fractures as high as 79%.[6,13] A Japanese study examined both survivors and non-survivors of OHCA using post-mortem computed tomography and whole-body computed tomography.[8] Their reported frequency was 70% for rib fractures and 8% for sternal fractures. When comparing forensic autopsy with post-mortem computed tomography, these methods seem to be comparable in finding rib fractures.[14] Yet, forensic autopsy is considered to be the most reliable method when investigating CPR-related injuries for revealing the more obscure lesions that might not be readily visible in the conventional imaging methods.[15-17]

In the current study, we observed potentially life-threatening CPR-related injuries in 2 OHCA patients. These injuries were located in the thorax and abdominal viscera. One patient with coronary artery disease sustained a mediastinal haematoma and ruptures in the myocardium with haemopericardium and cardiac tamponade. In

TABLE 2 Injuries related to cardiopulmonary resuscitation after out-of-hospital cardiac arrest. Injuries are described by the category and some of the patients have multiple injury categories

	All patients, N = 149 n (%)
Sternum fracture	22 (15)
Rib fracture	64 (43)
Bilateral	56
Unilateral	6
Side of fractures not known	2
2-3 fractures	7 (5)
4-5 fractures	9 (6)
6-7 fractures	14 (9)
≥8 fractures	33 (22)
Number of rib fractures, median [Q_1-Q_3]	8 [5-9]
(min-max)	(0-24)
Haemothorax	4 (3)
Haematoma—rib fractures	11 (7)
Lung contusion	1 (<1)
Mediastinal haematoma	1 (<1)
Injury in great vessels	1 (<1)
Heart injury	11 (7)
Haematoma in heart	10
Haemopericardium	4
Rupture of pericardium	1
Lethal ruptures of heart	1
Other small ruptures of heart	3
Gastric injury	1 (<1)
Liver injury	1 (<1)
Spleen injury	0
Laryngeal haematoma	2 (1)

TABLE 3 Predictors of cardiopulmonary resuscitation-related injuries in out-of-hospital cardiac arrest patients

	CPR-related injuries			CPR-related injuries		
	Univariate			Multivariable		
Variables	OR	95% CI	*P*-value	OR	95% CI	*P*-value
Age	1.02	1.00-1.05	.045	1.04	1.01-1.07	.013
Male gender	3.02	1.45-6.31	.003	4.11	1.79-9.43	.001
Public location	4.60	1.97-10.72	<.001	4.98	2.02-12.31	<.001
Initial rhythm shockable	2.23	1.00-4.99	.050	Variable not entered		
Transient ROSC	2.14	0.93-4.92	.073	Variable not entered		
Duration of CPR attempt	1.02	1.00-1.05	.080	Variable not entered		

CI, confidence interval; CPR, cardiopulmonary resuscitation; OR, odds ratio; ROSC, return of spontaneous circulation; VF ventricular fibrillation.

this case, the injuries were lethal. Cardiac rupture is a known but a rare complication of CPR; it is caused by the increasing pressure from chest compressions to incompressible fluid (ie blood).[2,3,18] These ruptures are usually located in regions with a thinner wall or underneath the sternum. In patients with coronary artery disease, the coronary plaque and the weakened infarct area may result in a haemopericardium prior to CPR.[2,3,18]

Only 2% of the studied population had serious injuries. The frequency of haemopericardial injuries (7%) is comparable to other studies, in which pericardial injuries were noted in 8.9% of the study participants, haemopericardium in 7.5% and cardiac injuries in 4.4%.[5]

In this study, the incidence of injuries (ie 43% for rib fractures and 15% for sternal fractures) was lower compared to earlier studies. During the study period, the OHCA survival rate in the Pirkanmaa area was 14%. All OCHA patients received CPR at the scene of the event, and none of the patients were transported to the hospital with ongoing CPR. Chest compressions were performed by bystanders and EMS personnel. During a CPR attempt, the heel of the rescuer's hand should be placed in the centre of the patient's chest; that is, the lower half of the sternum.[19] However, the force is not equally distributed from the hands to the chest, as the hypothenar part of the hand is the dominant part of the compression force.[20] This could influence both the area and direction of the compression force, leading to a more lateral or cephalad compression point and hence causing rib and sternum fractures. Bystanders performing dispatcher-assisted CPR before the arrival of EMS differ in their knowledge and capability of providing proper CPR, which could lead to CPR-related injuries. In our study, bystander CPR and the duration of bystander CPR were not associated with CPR-related injuries. Previous studies have shown that injuries related to bystander CPR affected only 2% of patients who were not in cardiac arrest when they received the CPR[21] and that there was no difference between injuries when comparing resuscitated patients who either received bystander CPR before EMS arrival or only EMS-provided CPR.[7,22]

In our study, the median duration of prehospital resuscitation in the patient population subjected to forensic autopsy was 24 minutes. During that time period, the CPR providers shifted from bystanders to the FRU, BLS and ALS teams. While a sufficient number of rescuers performing chest compressions will prevent rescuer fatigue, too many people alternating chest compression cycles might increase the risk of CPR-related injuries. Kim et al[23] reported that the occupational groups who participated in providing CPR affected the incidence of injuries in an emergency department. In our study, we found no association between CPR-related injuries and the duration of the resuscitation attempt. Rudinská et al[13] reported a similar finding, whereas other studies have suggested that CPR duration is a risk factor for injuries.[7,8] Yet, a deeper compression depth results in an increased rate of injury.[6,9,24] These suboptimal compression forces could happen at any time during a resuscitation attempt regardless of the overall duration of the resuscitation attempt.

A recent study conducted in South Korea found that OHCA survivors had more rib fractures than IHCA survivors (83% vs 63%) and that OHCAs also presented with a higher frequency of multiple rib fractures (78% vs 58%).[7] The reported sternal fractures were 38% in OHCAs and 30% in IHCAs. When we compared our study to a previous IHCA autopsy study in our area,[24] we came to a similar conclusion that the IHCAs had less rib and sternal fractures compared to the OHCAs. However, the incidence of the injuries was much lower in our area; the rib fracture frequencies for OHCAs and IHCAs were 43% vs 27% and the sternal fractures were 15% vs 11% respectively. The differences in the EMS systems could explain this variation in injury frequency. The OHCA patients in the Korean study were transported with ongoing resuscitation to a hospital. The authors of this study suggested that these findings could have resulted from poor quality resuscitation during transport when accelerating and driving at high speeds could compromise the hand position and compression force.

In this study, we found an association between CPR-related injuries and older age, the male gender, initial shockable rhythm and a public location of the OHCA. Further analysis revealed that older age, the male gender and a public location were independent risk factors. Previous studies have suggested various risk factors for CPR-related injuries.[4,6-10,23-25] Older age is considered a strong risk factor,[7,8,10,25] and some studies have reported the female gender as a risk factor,[10,23] while others have not found any differences between gender[25] or have reported the male gender as a risk factor.[24] A higher frequency of osteoporosis in female and older populations as well as differences in increasing tissue stiffness and degenerative skeletal changes between genders could explain the variation in these findings. It is possible that the rescuer uses more force on male patient's chest compressions that might cause more injuries.

To the best of our knowledge, this is the first study to report that the initial shockable rhythm and a public location of the OHCA are associated with CPR-related injuries. Our findings can be explained by the fact that they also implicate possible positive outcomes for the resuscitation attempts. This could lead to more aggressive treatment during the resuscitation attempt including using more force on chest compressions. CPR in a public place could also be a more stressful situation because there are onlookers and that might also influence more aggressive attempt and cause rescuers on scene to "push harder." In this patient population, we did not find any association between CPR-related injuries and patient's BMI, bystander-CPR, transient ROSC during the resuscitation attempt, duration of the CPR attempt or airway management with intubation.

OHCA patients arriving in the ED are often suffering from an unexpected critical illness without any previous medical history, and the attending physician should be careful when establishing the cause of death and refrain from writing a death certificate for an OHCA patient who dies later in the ED if a radiological examination has not been performed and CPR-related injuries are not excluded.[26-28] We should bear in mind that one of the main objectives for autopsies is to evaluate the quality of medical care provided to the individual. Even though injuries related to resuscitation attempts are mostly not life-threatening in quality and are not completely avoidable, some exceptions may occur. When seeking to improve or maintain the quality of care provided to OHCA patients, verifiable diagnoses are very important.

4.1 | Limitations of the study

During the study period, we could not analyse the quality of CPR performance to ensure the right depth and rate of compressions. In addition, our patient population consisted only of OHCA non-survivors; hence, the results could have been different if the OHCA survivors were included in the study. Furthermore, computed tomography radiographs were not routinely obtained from OHCA survivors; thus, we could not compare injury findings between OHCA survivors and non-survivors using both forensic autopsy and computed tomography findings. The forensic protocol of investigating the injuries after OHCA is strictly executed according to Finnish law; hence, our study protocol could not give any guidance to the forensic pathologists during the autopsies. Radiological examination was not routinely used when performing forensic autopsy in cases without previous trauma; hence, we could not determine the presence of any pneumothorax. Finally, our sample size may have been insufficient to detect all possible predictors for CPR-related injuries.

5 | CONCLUSION

The independent risk factors for CPR-related injuries after OHCA were a public location, the male gender and older age. Durations of the resuscitation attempts had no effect on the incidence of injuries. The most common injury findings were multiple bilateral rib fractures and sternum fractures. Severe injuries in the thoracic or abdominal viscera were rare.

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CONFLICTS OF INTEREST

There are no conflicts of interests disclosed by the authors.

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PUBLICATION
III

End-tidal carbon dioxide output in manual cardiopulmonary resuscitation versus active compression-decompression device during prehospital quality controlled resuscitation: a case-series study

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End-tidal carbon dioxide output in manual cardiopulmonary resuscitation versus active compression-decompression device during prehospital quality controlled resuscitation: a case series study

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ABSTRACT

Background Active compression–decompression (ACD) devices have enhanced end-tidal carbon dioxide ($ETCO_2$) output in experimental cardiopulmonary resuscitation (CPR) studies. However, the results in out-of-hospital cardiac arrest (OHCA) patients have shown inconsistent outcomes, and earlier studies lacked quality control of CPR attempts. We compared manual CPR with ACD-CPR by measuring $ETCO_2$ output using an audiovisual feedback defibrillator to ensure continuous high quality resuscitation attempts.

Methods 10 witnessed OHCAs were resuscitated, rotating a 2 min cycle with manual CPR and a 2 min cycle of ACD-CPR. Patients were intubated and the ventilation rate was held constant during CPR. CPR quality parameters and $ETCO_2$ values were collected continuously with the defibrillator. Differences in $ETCO_2$ output between manual CPR and ACD-CPR were analysed using a linear mixed model where $ETCO_2$ output produced by a summary of the 2 min cycles was included as the dependent variable, the patient as a random factor and method as a fixed effect. These comparisons were made within each OHCA case to minimise confounding factors between the cases.

Results Mean length of the CPR episodes was 37 (SD 8) min. Mean compression depth was 76 (SD 1.3) mm versus 71 (SD1.0) mm, and mean compression rate was 100 per min (SD 6.7) versus 105 per min (SD 4.9) between ACD-CPR and manual CPR, respectively. For $ETCO_2$ output, the interaction between the method and the patient was significant (P<0.001). $ETCO_2$ output was higher with manual CPR in 6 of the 10 cases.

Conclusions This study suggests that quality controlled ACD-CPR is not superior to quality controlled manual CPR when $ETCO_2$ is used as a quantitative measure of CPR effectiveness.

Trial registration number NCT00951704; Results.

Key messages

What is already known on this subject

- Active compression–decompression (ACD) devices have improved venous return and cardiac output during cardiopulmonary resuscitation (CPR) in experimental studies.
- Earlier clinical reports comparing ACD-CPR and manual CPR have been controversial and lacked quality control measurements of CPR attempts.

What this study adds

- Our experimental study presents a novel approach to the evaluation of an ACD device versus manual CPR by applying continuous quality measurement of both CPR methods in the prehospital setting.
- This study suggests that when using end-tidal carbon dioxide ($ETCO_2$) as an indicator of CPR performance, quality controlled ACD-CPR is not superior to quality controlled manual CPR under the guidance of real time audiovisual feedback system defibrillators in the prehospital setting.

INTRODUCTION

Novel resuscitation guidelines emphasise high quality cardiopulmonary resuscitation (CPR): chest compression rate should be at least 100 per min, chest compression depth should be at least 5 cm and external defibrillation should be delivered as early as possible.[1] End-tidal carbon dioxide ($ETCO_2$) reflects cardiac output during low flow states.[2 3] Thus $ETCO_2$ is a surrogate for CPR performance and has been shown to predict return of spontaneous circulation (ROSC) and survival.[4]

Active compression–decompression (ACD) devices have enhanced negative intrathoracic pressure and improved venous return and myocardial perfusion during CPR, and thus one would expect improved resuscitation outcomes.[5] However, reported clinical results have been controversial and they lacked quality control of the resuscitation attempts; the current conclusion is that there is neither harm nor benefit from using an ACD device.[6]

A more recent approach to improve resuscitation quality is the use of real time audiovisual feedback system defibrillators that provide continuous guidance for correct performance of CPR by measuring

Figure 1 Resuscitation with the active compression–decompression device and the audiovisual feedback defibrillator.

chest compression rate, depth, duty-cycle and no-flow time during the resuscitation attempt.[7,8] The quality of chest compressions is measured with a sensor attached to the patient's chest, and automatic guidance prompts the CPR provider directly for optimal performance to match goals that are set in the resuscitation guidelines.

There is a constant need for independent quality analysis of the equipment produced by the healthcare industry, such as the ACD device, in the clinical setting. Using $ETCO_2$ as an indicator, the aim of this study was to evaluate whether ACD-CPR provides better overall resuscitation quality than manual CPR when both methods are used, alternating in 2 min cycles during the ongoing resuscitation attempt under the guidance of audiovisual feedback system defibrillator in the prehospital setting.

METHODS

Study objective

The purpose of the study was to assess whether quality controlled ACD-CPR provides better overall resuscitation quality compared with quality controlled manual CPR, using $ETCO_2$ as a surrogate marker. This observational self-controlled case series study was carried out in the anaesthetist staffed Pirkanmaa Helicopter Emergency Medical Service (HEMS) unit, Tampere University Hospital, Finland.

Organisation

The anaesthetist staffed HEMS serves approximately 6 00 000 inhabitants in the Pirkanmaa and surrounding area in Finland. In addition to the HEMS, the Emergency Medical Service (EMS) system includes first responding units (FRU) and basic life support (BLS) units, staffed with firemen–emergency medical technicians (EMT), and paramedic staffed advanced life support (ALS) units. An FRU and the nearest BLS or ALS unit with the HEMS unit are always dispatched to high-risk medical emergencies, such as sudden cardiac arrest.

Study design

The study core data comprised continuous $ETCO_2$ measurements from 10 adult out- of-hospital cardiac arrest (OHCA) patients during CPR attempts. Data were collected over 7 months, from September 2013 to March 2014. Adult patients not suffering from trauma or hypothermia were enrolled in the study if the HEMS crew decided to continue resuscitative efforts on scene for at least 5 min after securing the airway by endotracheal tube to ensure adequate collection of all ventilation associated $ETCO_2$ data. All patients were treated according to the resuscitation guidelines of the European Resuscitation Council.[9] On arrival at the scene, the HEMS crew attached a real-time audiovisual feedback defibrillator (Zoll X Series, Real CPR Help, ZOLL Medical Corporation, USA) to the patient's chest during ongoing resuscitation and the defibrillator's compression quality sensor was placed in the midsternal position on the patient's chest. The HEMS physician performed endotracheal intubation and the defibrillator's continuous sidestream CO_2 recording connector was attached to the endotracheal tube. The first ACD-CPR cycle started as soon as the previous 2 min cycle of CPR was finished, and the measurements started as soon as all parameter sensors were ready. Thereafter, patients were resuscitated using a 2 min cycle with standard manual CPR followed by a 2 min cycle of ACD-CPR with continuous guidance from the audiovisual feedback defibrillator.

These cycles were rotated as long as resuscitation was attempted. The person delivering chest compressions was changed every 2 min cycle during rhythm analysis, in accordance with the resuscitation guidelines. A manual lightweight ACD-CPR device (Ambu CardioPump, Ambu International Inc, Copenhagen, Denmark) consisting of a silicone rubber suction cup and a plastic handle containing a force gauge and a metronome, was placed over the defibrillator's compression quality sensor to perform ACD-CPR cycles (figure 1).

To ensure an adequate seal of the ACD device, the outer insulator layer of the wires from the compression quality sensor crossing under the suction cup was removed prior to the resuscitation attempt and the thin wires were under adhesive tape when crossing the suction cup. The sensor itself fitted inside the rubber suction cup without touching the cup. Compressions and decompressions were performed with a 50% duty cycle at the rate of 100 per min in accordance with the European Resuscitation Council guidelines. HEMS paramedics were responsible for delivering the ACD-CPR cycles during the resuscitation attempts. The feedback device remained attached to the patient's chest during all cycles. Ventilation rate was maintained constant manually during the cycles. The beat-by-beat CPR quality data with measurement of all values for chest compression depth, rate and duty cycle, and all ventilation associated $ETCO_2$ values were recorded continuously by the defibrillator during the resuscitation attempts.

Data were analysed using dedicated quality analysis software (RescueNet Code Review, ZOLL Medical Corporation, USA). One of the authors (PAS) compared the $ETCO_2$ values with the capnography curve data to ensure correct analysis of all associated $ETCO_2$ values during the entire resuscitation attempt. Differences in $ETCO_2$ output produced by a summary of the 2 min manual CPR cycles and by the 2 min ACD-CPR cycles were compared for each individual patient separately to minimise confounding factors between the cases.

Statistical analysis

The study was designed based on the preliminary results of a pilot study of a continuous response variable from matched pairs of both CPR methods in four study subjects. A pair consisted of measurements with both methods within the same patient. Pilot study data indicated that the difference in the response of matched pairs was normally distributed with an SD of 0.35, and the true difference in the mean response of matched pairs was 0.7 kPa. This led to the conclusion that we needed to study four pairs of subjects to be able to reject the null hypothesis, at a power of 0.8 and a type I error of 0.05.

Table 1 Patient characteristics and differences in end-tidal carbon dioxide values between manual cardiopulmonary resuscitation and active compression–decompression cardiopulmonary resuscitation with data point measurements

Patient No	Age (years)	Sex	First rhythm	$ETCO_2$ (kPa) ACD-CPR			$ETCO_2$ (kPa) Manual CPR		
				Data points (n)	Mean†	SD	Data points (n)	Mean†	SD
1	85	Female	VF	32	2.30	0.4	40	3.45	0.2
2	68	Male	ASY	50	3.47	0.6	41	3.07	0.1
3	83	Male	PEA	56	4.61	0.7	64	4.63	0.5
4	92	Male	ASY	44	4.37	0.5	53	4.76	1.0
5	59	Male	VF	54	4.76	1.1	50	4.39	0.7
6	68	Male	PEA	31	4.02	0.5	43	3.78	0.5
7*	68	Male	PEA	65	3.77	0.2	70	4.08	0.4
8	75	Male	PEA	35	4.92	0.6	31	5.05	0.5
9	76	Female	PEA	65	2.21	0.3	74	1.88	0.4
10	71	Male	PEA	66	4.30	0.7	62	4.44	0.9

*Return of spontaneous circulation achieved.
†The mean value of single ventilation associated $ETCO_2$
ACD-CPR, active compression–decompression cardiopulmonary resuscitation; ASY, asystole; CPR, cardiopulmonary resuscitation; $ETCO_2$, in end-tidal carbon dioxide; PEA, pulseless electrical activity; VF, ventricular fibrillation.

The statistical analysis was performed using SPSS software (IBM SPSS Statistics for Windows, V.21.0. Armonk, NY, IBM Corp). Data are presented as number or mean (SD), as indicated. In a linear mixed model, the $ETCO_2$ output produced by a summary of the 2 min cycles was included as the dependent variable. The model included the patient as the random factor, method as the fixed effect and the patient×method interaction effect. All comparisons were two-tailed, and a P value <0.05 was considered statistically significant.

Ethics approval

This study was carried out in the physician staffed Pirkanmaa HEMS unit, Tampere University Hospital, Finland (ClinTrials: NCT 00951704). The regional ethics committee of Pirkanmaa Health District approved the study and waived the need for informed consent as both CPR methods were considered standard of care (R08116).

RESULTS

The EMS attempted CPR in 194 OHCA cases during the study period. The HEMS unit was on scene in 108 cases and terminated the resuscitative efforts by consultation before reaching the scene in 86 cases. Twelve adult OHCA patients met the inclusion criteria during the study period. One patient suffering from submersion was excluded from the study because of inadequate attachment of the ACD-CPR device on the patient's chest and one patient was excluded from the study due to data loss.

Patient characteristics and differences in $ETCO_2$ output between manual CPR and ACD-CPR are presented in table 1. All cardiac arrests were witnessed. Mean age was 75 (SD 10) years. Mean length of the CPR episode was 37 (SD 8) min and the mean delay to arrival of the HEMS crew from the onset of cardiac arrest was 17 (SD 8) minutes. One patient achieved ROSC. In the linear mixed model analysis, the interaction between the method (fixed effect) and the patient (random factor) was significant ($P<0.001$), resulting in a significant difference in $ETCO_2$ output between manual CPR and ACD-CPR for every patient. In 6 out of 10 cases, $ETCO_2$ output was higher with manual CPR and in 4 cases ACD-CPR showed higher $ETCO_2$ values, as shown in figure 2. The quality measurements of resuscitation attempts with manual CPR versus ACD-CPR are presented in table 2. All parameters showed rescuers performing good quality CPR during both ACD-CPR and manual CPR. Ventilation rate was maintained constant during individual resuscitation attempts for both resuscitation methods.

DISCUSSION

In this observational self-controlled case series, we compared manual CPR with ACD-CPR to evaluate differences in $ETCO_2$ production during quality controlled resuscitation using a defibrillator with audiovisual feedback and continuous ventilation associated sidestream CO_2 recording with capnography. In our study, a novel approach in the evaluation of the ACD device versus manual CPR was application of continuous measurement of quality parameters for both CPR methods. Typical confounding factors that affect the interpretation of CPR attempts such as age, gender, previous medical history, cause of the cardiac arrest, primary rhythm, location of the arrest and time delay of beginning the CPR attempt were minimised by comparing both methods in each individual patient, and by controlling the quality of chest compressions and ventilation rate to ensure they would not have an impact on $ETCO_2$ production.

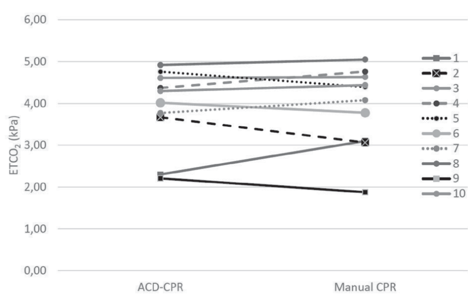

Figure 2 Mean values for end-tidal carbon dioxide ($ETCO_2$) between active compression–decompression and manual cardiopulmonary resuscitation. ACD-CPR, active compression–decompression cardiopulmonary resuscitation; CPR, cardiopulmonary resuscitation.

Table 2 Resuscitation quality measurements during cardiopulmonary resuscitation attempts

	Depth (mm)	Rate (cpm)	No-flow time (%)	Ventilations (vpm)
ACD-CPR	76 (1.3)	100 (6.7)	8 (10.4)	11 (2.9)
Manual CPR	71 (1.0)	105 (4.9)	1 (4.6)	11 (2.6)

Values are mean (SD).
ACD-CPR, active compression–decompression cardiopulmonary resuscitation; cpm, compressions per minute; CPR, cardiopulmonary resuscitation; No-flow time, ratio between all pauses between the compressions; vpm, ventilations per minute.

According to our results, quality controlled ACD-CPR is not superior to quality controlled manual CPR.

Previously, ACD-CPR has been shown to enhance aortic systolic pressure and myocardial perfusion pressure and increase myocardial and cerebral blood flow compared with manual CPR in experimental animal and human studies.[5 10] Thus one might expect ACD-CPR to create higher $ETCO_2$ output compared with manual CPR. Despite its promising effects in these studies, ACD-CPR failed to demonstrate any superiority in prehospital patient care.[6] Regarding the use of $ETCO_2$ values as a surrogate for CPR produced cardiac output, an earlier study by Mauer *et al* found no difference in $ETCO_2$ values between the ACD patient group and the manual CPR patient group in OHCA.[11] However, these $ETCO_2$ readings were recorded only every 2 min. Plaisance *et al* reported an improvement in the ACD group versus the manual CPR group in terms of hospital discharge,[12] whereas other studies did not show statistically significant differences in ROSC, hospital admission, survival or neurological prognosis.[13–15] The importance of evaluating $ETCO_2$ values by analysing capnography curves was described recently.[16] Chest compressions generate minimal tidal volumes during the resuscitation attempt and plain capnometry will monitor these numerical values as part of the $ETCO_2$. In our study, we analysed all ventilation associated $ETCO_2$ data and beat-by-beat chest compressions with associated capnography curves to exclude values that were not associated with ventilation assisted $ETCO_2$. Variations in chest compression depth and ventilation rate also affect $ETCO_2$ values during the resuscitation attempt,[17] and therefore quality parameters are essential when comparing two CPR methods. In our study, the ventilation rate was maintained constant during the resuscitation attempt as $ETCO_2$ values were compared between the two CPR methods in every patient separately.

It is currently acknowledged that delay in the commencement of CPR and insufficient chest compressions have detrimental effects on the patient's arterial and perfusion pressures.[18] A multicentre case series study in 2005 reported that prehospital personnel with advanced cardiac life support training and regular retraining failed to deliver CPR according to guidelines during OHCA by not delivering chest compressions half of the time and delivering compressions that were too shallow most of the time.[19] Regarding the earlier studies in which manual CPR without quality feedback was compared with ACD-CPR, it should be taken into consideration that the ACD device itself is a feedback device as it has a gauge in the handle for the measurement of both sufficient compression depth and upward force, and now also has a metronome to ensure an appropriate compression rate. More encouraging results with earlier ACD-CPR studies might have resulted from the active chest lift stopping the rescuer from leaning on the chest during the recoil phase that would have an undesirable effect on coronary and cerebral perfusion pressures by impeding venous return and decreasing mean arterial pressure.[18] However, performing ACD-CPR requires 25% more effort than manual CPR and thus may be more difficult to perform over sustained periods of time.[20] Multicentre studies have reported that the ACD device demanded a longer period of training and rescuer fatigue was a common problem.[12 13] These studies demonstrate the utmost importance of regularly changing the person providing CPR to avoid fatigue during the resuscitation attempt and to provide continuous high quality CPR. Parameters for high quality CPR, such as chest compression depth, compression rate, duty cycle of 50%, minimal no-flow time and full recoil of the chest during the decompression phase are easily monitored with the real time audiovisual feedback defibrillators during resuscitation.

Study strengths and limitations

The strength of this study is that we handled the confounding factors between the cases by analysing differences in $ETCO_2$ between manual CPR and ACD-CPR separately for every patient and measuring the quality parameters of chest compressions when comparing these two resuscitation methods. The data were recorded from compression to compression and from every ventilation during the entire resuscitation attempt to ensure the quality of the measurements. The ventilation rate was maintained constant during the resuscitation attempt and every ventilation associated $ETCO_2$ value was recorded continuously and data were evaluated with capnography during the analysis of the data. Changing the CPR method during the resuscitation attempt did not affect the quality, as indicated by the CPR quality parameter recordings.

There are some limitations in this study. First, the total number of patients was small. However, the study was conducted after a pilot study that provided the power calculations described in the methods section. Second, the minute ventilation of the patient was not controlled due to manual ventilation during the resuscitation attempt as mechanical ventilation during CPR is regarded as contraindicated. Third, all but one patient died on the scene which may have had an impact on the $ETCO_2$ values recorded. Fourth, in the study design, patients were not randomised by the first attempted CPR method, but the measurements started with either ACD-CPR or manual CPR depending on when all the parameter sensors were ready. This could have affected the results and caution should be exercised in the interpretation and extrapolation of the data.

CONCLUSIONS

According to our results, quality controlled ACD-CPR does not provide better overall resuscitation quality compared with quality controlled manual CPR when using $ETCO_2$ as a surrogate for CPR performance.

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Contributors All authors certify that they have participated sufficiently in the work, including participation in the concept, design, analysis, writing or revision of the manuscript. ITV, AJK and SEH planned the study design. All authors collected the patient data. PAS analysed and interpreted the patient data. PAS and HSAH performed the statistical tests. PAS was a major contributor towards writing the manuscript. AMY-H made revisions to the manuscript. All authors read and approved the final manuscript. Each author certifies that this material has not been submitted to or published in any other publication.

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Competing interests None declared.

Patient consent Not required.

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PUBLICATION IV

Using a simplified pre-hospital 'MET' score to predict in-hospital care and outcomes

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Using a simplified pre-hospital 'MET' score to predict in-hospital care and outcomes

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*These authors contributed equally to this work.

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Background: Medical emergency team (MET) activation criteria serve as a predictor of serious adverse events on hospital wards and in the emergency department (ED). We aimed to determine whether in-hospital MET activation criteria would be useful in identifying patients at risk in pre-hospital care.
Methods: The data were collected retrospectively from 610 adult patients treated by physician-staffed helicopter emergency medical services. Pre-hospital vital signs were compared with MET activation criteria and scored accordingly to receive a simplified pre-hospital 'MET' score. The primary outcome measure was hospital mortality. The secondary outcome measures were admission to intensive care unit and the length of ED stay, intensive care unit (ICU) stay and hospital stay. The simplified pre-hospital 'MET' score was also compared with Emergency Severity Index (ESI) used as a triage tool in ED.
Results: Higher simplified pre-hospital 'MET' scores were associated with hospital mortality ($P < 0.001$), the need for ICU treatment ($P < 0.001$) and a more urgent ESI class in the ED ($P < 0.001$). Higher simplified pre-hospital 'MET' scores were associated with shorter stay in the ED ($P < 0.001$), longer stay in the ICU ($P < 0.001$) and longer hospital stay ($P < 0.001$). A simplified pre-hospital 'MET' score was an independent predictor for hospital mortality (odds ratio 2.42, confidence interval 1.84 3.18, $P < 0.001$), regardless of age or patient's previous overall physical health classified by American Society of Anesthesiologists physical status classification system.
Conclusion: A simplified pre-hospital 'MET' score is a predictor for patient outcome and could serve as a risk assessment tool for the health care provider on-scene.

Editorial comment: what this article tells us
Patients with severe deterioration in vital organ functions should be identified early and a simple severity score has been used to activate a medical emergency team (MET) in hospitals. This study confirms that a simple MET score applied in the pre-hospital setting could be of similar value with regard to estimating resource use and hospital mortality.

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In the pre-hospital setting, decisions are often made without detailed information on the patient's condition and comorbidities. Therefore, vital signs play an essential role in patient evaluation, and have been used successfully as triage tools in trauma patients and in recognising septic shock.[1–4] However, at present, the pre-hospital care lacks validated tools for identifying patient deterioration in unselected patient population.[4]

Abnormal vital sign values measured in the inpatient setting are associated with greater risk for mortality.[5–10] Several response systems have been developed for recognising patient deterioration on hospital wards to allow early intervention and to prevent adverse events.[11] Additionally, several triage scales have been developed for emergency department (ED) to ascertain patient urgency.[12–14] These scales are based on systematic measurement and documentation of physiological variables and reaction when certain trigger levels are reached. There is some evidence that trigger systems in the ED can improve patient care by reducing time to therapy and predicting clinical outcomes.[15–17] One of these trigger systems, medical emergency team (MET) activation criteria, have been validated as a predictor of serious adverse events on hospital wards and in the ED.[18,19]

In this study, we aimed to determine whether abnormal vital signs, based on an in-hospital MET activation criteria, in unselected patient population met by pre-hospital helicopter emergency medical services (HEMS) team could predict patient outcome. Further we hypothesised that this simplified pre-hospital 'MET' score could serve as a risk assessment tool for emergency medical services (EMS) to recognise those patients requiring the most urgent attention and facilitate the continuing triage from the scene to the appropriate level of ED care.

Methods

Study design

This retrospective cohort study was conducted and carried out in the pre-hospital area of two Finnish university hospitals, Tampere University Hospital (TAUH) and Turku University Hospital (TUH) from 1 January 2012 to 30 June 2012. The data were collected from all patients aged over 18 years who were encountered by a physician-staffed HEMS on-scene and transported subsequently with or without accompanying physician to a university hospital. Because this was an observational study based on medical records, the statement from the Ethics Committee was waived. The study was approved by the TAUH and TUH Medical Directors.

EMS in TAUH and TUH areas

Details of the physician-staffed HEMS and the hospitals in Turku area have been described elsewhere.[20] HEMS serves approximately 800,000 inhabitants in the Turku area and 1,200,000 inhabitants in the Tampere area. The majority of HEMS physicians are specialists in anaesthesiology and intensive care medicine. In addition to the HEMS units, the EMS system in Finland includes first responding units (FRU) and basic life support (BLS) units staffed with firemen–emergency medical technicians and paramedic-staffed advanced life support (ALS) units. Alongside an FRU and the nearest BLS or ALS unit, the HEMS is always dispatched to high-risk trauma and medical emergencies. Stabilised patients are mainly transported to the university hospitals in the Finnish cities of Turku and Tampere, which are tertiary referral centres providing highest possible medical care in Finland.

Data

Patients with do-not-attempt-resuscitation (DNAR) orders or on labour, those transported to primary care, as well as patients under the age of 18 were all excluded. Data on age, sex, patient's overall physical health at that time excluding the emergency situation [classified by American Society of Anesthesiologists (ASA) physical status classification system], pre-hospital vital signs on-scene, the length of stay in ED, admission and the length of stay in intensive care unit (ICU), duration of hospitalisation and mortality were collected from the HEMS database, EMS datasheets and hospitals medical records. The primary outcome measure was hospital mortality. The secondary outcome measures were need for ICU treatment (either immediately or later during hospital stay), and the length of ED stay, ICU stay and hospital stay. A simplified pre-hospital 'MET' score was also compared with data on Emergency

Severity Index (ESI) classification. This classification is a five-level triage tool for ED that estimates both patient urgency and staff resources requirements. The ED triage nurse uses ESI to rate patient urgency from level 1 (most urgent) to level 5 (least resource intensive). This classification is routinely used in ED at TAUH.

In-hospital MET activation criteria and a simplified pre-hospital 'MET' score

TAUH utilises MET activation criteria in wards to allow rapid recognition of patient deterioration due to critical illness. These activation criteria are presented in Table 1. In this study, we collected the first vital signs measured on-scene before the commencement of any treatment and then compared these vital signs with MET activation criteria used in TAUH to calculate a simplified pre-hospital 'MET' score. The measurements included respiratory rate (RR), peripheral capillary oxygen saturation (SpO_2), blood pressure, heart rate (HR), Glasgow Coma Scale (GCS) and caregivers concern about the patient. The caregivers' concern describes a documented concern about the patient with or without any abnormal vital signs. A caregiver in this study is either a paramedic or a HEMS physician treating the patient on-scene. To minimise the error due to lack of data, the pre-hospital vital signs measurements were combined as respiratory dysfunction (abnormal SpO_2 and/or abnormal RR) and circulatory dysfunction [abnormal HR and/or abnormal systolic blood pressure (SBP)] points, the remaining two being lowered GCS (< 14) and caregivers' concern, giving the maximum simplified pre-hospital 'MET' score of 4.

Table 1 TAUH's MET activation criteria and a simplified pre-hospital 'MET' score measured during the pre-hospital care. Pre-hospital vital signs were compared with TAUH MET activation criteria and scored accordingly to receive a simplified pre-hospital 'MET' score.

TAUH MET criteria	
$SpO_2 < 90\%$	
RR < 5/min or > 24/min	
SBP < 90 mmHg	
HR < 40/min or > 140/min	
GCS < 14 or decrease in GCS of ≥ 2 points	
Caregivers concern	
A simplified pre-hospital 'MET' score	
Respiratory failure: SpO2 < 90% and/or RR < 5/min or > 24/min	1 point
Circulatory failure: SBP < 90 mmHg and/or HR < 40/min or > 140/min	1 point
GCS < 14	1 point
Caregivers concern	1 point
	4 points max

TAUH, Tampere University Hospital; SpO_2, peripheral capillary oxygen saturation; RR, respiratory rate; SBP, systolic blood pressure; HR, heart rate; GCS, Glasgow Coma Scale; MET, medical emergency team.

Statistical analysis

Demographic data are presented as numbers and percentages or as medians and quartiles (Q_1–Q_3) as indicated. Chi-square test, Student's *t*-test, Mann–Whitney *U*-test and Kruskal–Wallis test were used for the comparisons between groups, as appropriate. Binary logistic regression analysis was used for crude odds ratios (ORs) to determine variables associated with hospital mortality, after which forward stepwise logistic regression was applied for adjusted ORs. Results are shown as ORs and 95% confidence intervals (CI). Outcome groups were defined on the basis of hospital survival.

Results

Patient characteristics

A total 670 patients were treated by an HEMS physician and conveyed to a university hospital during the study period. Sixty patients were excluded due to an DNAR order made either beforehand or immediately on arrival in the ED leaving a total of 610 patient records for analysis. Patient characteristics stratified by hospital outcome are presented in Table 2. Hospital mortality was 11.0%. Non-survivors were older and had higher simplified pre-hospital 'MET' scores ($P < 0.001$), higher ASA classification ($P < 0.001$) and were triaged more urgent by the ESI classification ($P < 0.001$). They also had a longer ICU stay ($P < 0.001$). There was no significant correlation between the length of hospital stay and hospital outcome ($P = 0.53$).

A simplified pre-hospital 'MET' score and patient outcome

Hospital mortality and admissions to the ICU according to simplified pre-hospital 'MET' score

Table 2 Patient characteristics in groups stratified by hospital outcome.

	Hospital survivors		Hospital non-survivors		Hospital mortality	
	n	%	*n*	%	%	*P*-value
No. of patients	543		67		11	
Age, years, median, (min–max)	57.7	(18–95)	65.3	(22–88)		< 0.001
Male	361	66	41	61		0.23
ASA						< 0.001
I	197	36	10	15		
II	154	28	16	24		
III	133	25	26	39		
IV	59	11	15	22		
Emergency Severity Index						< 0.001
1	146	30	34	60		
2	257	52	21	37		
3	82	16	2	4		
4	14	3	0	0		
NA	44	8	10	15		
Pre-hospital 'MET' score						< 0.001
0	149	27	2	3		
1	27	5	1	2		
2	217	40	19	28		
3	88	16	13	19		
4	62	11	32	48		
Total 'MET' score, median, (Q_1–Q_3)	2	(0–3)	3	(2–4)		
Respiratory failure	207		46		18	
Circulatory failure	127		40		24	
GCS < 14	263		56		18	
Paramedics concern	376		64		15	
ICU stay, days, median, (Q_1–Q_3)	0	(0–2)	2	(1–5)		< 0.001
Hospital admission, days, median, (Q_1–Q_3)	4	(2–8)	3	(2–7)		0.53

ASA, American Society of Anesthesiologists Classification; ED, emergency department, ICU, intensive care unit; Q1–Q3, quartiles; NA, ESI classification not available, patient transferred straight to operation room; GCS, Glasgow Coma Scale; MET, medical emergency team.

are presented in Fig. 1. Higher simplified pre-hospital 'MET' scores were associated with hospital mortality ($P < 0.001$) and the need for ICU treatment ($P < 0.001$). Higher simplified pre-hospital 'MET' scores were also associated with a more urgent ESI class in the ED ($P < 0.001$).

A simplified pre-hospital 'MET' score and the duration of stay in the ED and ICU as well as the total duration of hospitalisation are presented in Table 3. There was a significant association between higher simplified pre-hospital 'MET' score and shorter stay in the ED ($P < 0.001$), longer stay in the ICU ($P < 0.001$) and longer hospital stay ($P < 0.001$).

Patient's subsequent transfer from the ED to a ward according to the simplified pre-hospital 'MET' score is presented in Fig. 2. The majority of patients with simplified pre-hospital 'MET' scores 3 and 4 (44% and 61%) were admitted to the ICU. The majority of patients with simplified pre-hospital 'MET' scores 1 and 2 (32% and 40%) were admitted to the internal medicine department. The majority of patients with simplified pre-hospital 'MET' score 0 (42%) were admitted to the ED monitoring unit facilitating patient care for a maximum of 24 h before discharging the patient.

Predictors of hospital mortality

Predictors of hospital mortality are presented in Table 4. Total simplified pre-hospital 'MET' score and all individual parameters (respiratory dysfunction, circulatory dysfunction, lowered GCS and caregivers concern), age and ASA classification were associated with hospital mortality in

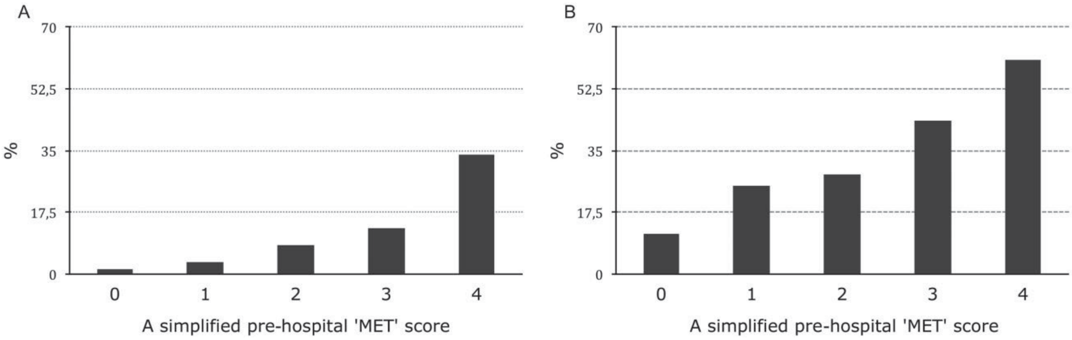

Fig. 1. Percentage distributions of a simplified pre-hospital medical emergency team (MET) score according to patient outcome. (A) Hospital mortality according to a simplified pre-hospital 'MET' score. (B) Admissions to the ICU according to a simplified pre-hospital 'MET' score.

Table 3 A simplified pre-hospital 'MET' score and the duration of stay in the ED, in the ICU and in the length of hospital stay.

	ED stay, min		ICU stay, days		Hospital stay, days	
	Median	(Q_1–Q_3)	Median	(Q_1–Q_3)	Median	(Q_1–Q_3)
MET Score						
0	177	114–233	0	0–0	2	1–5
1	134	53–171	0	0–0.75	3.5	2–7.75
2	132	68–197	0	0–2	5	2–9.75
3	117	70–191	1	0–3	5	2–10.5
4	73	44–123	3	0–4	6	3–13
P-value	< 0.001		< 0.001		< 0.001	

MET, medical emergency team.

the univariate analysis. A simplified pre-hospital 'MET' score was an independent predictor for hospital mortality in the multivariable analysis (OR 2.42, 95% CI 1.84–3.18, $P < 0.001$), regardless of age and patient's previous physical health. As expected, a high ASA class was also an independent predictor of mortality: ASA class 4 (OR 3.49, 95% CI 1.43–8.51, $P = 0.01$) and ASA class 3 (OR 2.67, 95% CI 1.20–5.94, $P = 0.02$). Age and the individual vital parameters did not reach statistical significance in the multivariable analysis.

Discussion

In this study, a higher simplified pre-hospital 'MET' score was associated with hospital mortality, the need for ICU treatment and a more urgent ESI class in the ED. A higher simplified pre-hospital 'MET' score was also associated with shorter stay in the ED, and longer ICU and hospital stay. In a multivariable analysis, both the simplified pre-hospital 'MET' score and ASA class 3 or 4 were predictors for hospital mortality, while age alone was not a predictor for hospital mortality.

In the pre-hospital setting, decisions are often made without detailed information on the patient's condition and comorbidities. In addition, the severity of the patient's acute illness may easily be overlooked by pre-hospital staff.[21] Risk scores may be used to guide patient management on-scene, but most pre-hospital triage scores are based on trauma patient evaluation or serve as a detailed evaluation and protocol tool for pathology-specific conditions such as acute stroke or acute ischaemic heart disease.[22–25] Currently, there are no available triage tools for EMS to recognise a patient in risk of deterioration in an unselected patient population.

Early identification of those patients who may need critical care is of the utmost importance for patient outcome in a country like Finland, where the distances to the nearest tertiary referral hos-

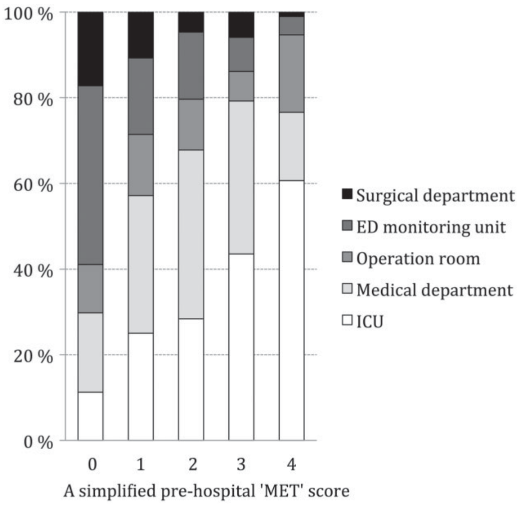

Fig. 2. Patient's admission from the emergency department (ED) to a subsequent ward according to a simplified pre-hospital medical emergency team (MET) score.

pital may be long. Fullerton et al. concluded that the addition of modified early warning scores (MEWS) to clinical judgement improved the detection of patient illness during pre-hospital care.[26] Burch et al. reported that the abbreviated MEWS was a useful tool in predicting which of the medical patients brought to the ED needed hospital admission and who had an increased risk of in-hospital death prior to admission.[27] The advantage of MET scores as well as MEWS is that the physiological parameters needed for calculating the score are routinely obtained and evaluated in a resource-limited and time critical environment like pre-hospital patient care.

The outcome of the patient is affected by both the severity of the emergency situation and previous medical history. In our analysis, in addition to a simplified pre-hospital 'MET' score, patient's overall physical health at the time of the emergency situation (ASA classification) were significantly associated with outcome. Interestingly, age was not an independent predictor of hospital mortality; thus, we should consider that a young patient with a high simplified pre-hospital 'MET' score is at equally high risk of hospital mortality as an older patient without comorbidities. This observation might encourage pre-hospital paramedics and physicians to pay more attention to elderly people and give more intense treatments if needed for correction of the vital organ dysfunction, since that might improve the outcome of patients regardless of their age. As far as we know, this is the first report to show that a scoring based on in-hospital MET activation criteria could be used to evaluate risk also in the pre-hospital setting and in an unselected patient population.

Interventions performed by the HEMS physician during pre-hospital care could present a bias when a patient is admitted to the ED as corrected vital signs may lead the ED triage nurse to assign the patient to a less severe ESI class. Delay in recognising a critically ill patient in the ED leads to delayed ICU admission and increased mortality as the underlying pathology may have advanced to an irreversible state at the time of admission.[28] In our study, a simplified pre-hospital 'MET' score correlated strongly with the ESI classification in the ED and the duration of stay in the ED, indicating that the pre-hospital information was respected and patient care was not delayed despite a possible improvement in the patient's status at the time of admission. In addition, more than 40% of patients with pre-hospital MET scores 3 and 4 were admitted from the ED to the ICU compared with patients with MET scores 1–2, who were mainly admitted to the internal medicine department or to the ED monitoring unit. Most patient's with a simplified pre-hospital 'MET' score 0 were discharged home after evaluation in ED. This information can be useful when triaging patients to different levels of hospitals.

The purpose of this study was not to validate in-hospital MET criteria for recognising a critical patient in pre-hospital care, rather it was carried out to pilot the idea whether some of the already existing tools, here the simplified pre-hospital 'MET' score, could be useful in evaluating patient deterioration on-scene, and whether this information could be used to triage patients to different levels of EDs and to allow faster and more appropriate response at the receiving hospital. Future research of both reliable documentation and recognition of deteriorating patients is needed.

Strengths and limitations of the study

This is a study from a Nordic country including all adult pre-hospital patients met by HEMS physi-

Table 4 Univariate and multivariable analysis of age, ASA, a simplified pre-hospital 'MET' score and individual vital parameters predicting hospital mortality.

	Univariate			Multivariable		
	OR	95% CI	*P*-value	OR	95% CI	*P*-value
Age	1.03	1.01–1.04	0.001			Variable not entered
ASA						
I	1	ref				
II	2.05	0.91–4.64	0.09	1.33	0.56–3.13	0.52
III	3.85	1.80–8.25	0.001	2.67	1.20–5.94	0.02
IV	5.01	2.14–11.73	< 0.001	3.49	1.43–8.51	0.01
'MET' score	2.44	1.88–3.15	< 0.001	2.42	1.84–3.18	< 0.001
Respiratory failure						
No	1	Ref				
Yes	3.56	2.06–6.13	< 0.001			Variable not entered
Circulatory failure						
No	1	Ref				
Yes	4.85	2.87–8.22	< 0.001			Variable not entered
GCS						
14–15	1	Ref				
< 14	5.42	2.78–10.57	< 0.001			Variable not entered
Caregivers concern						
No	1	Ref				
Yes	9.48	2.94–30.59	< 0.001			Variable not entered

ASA, American Society of Anesthesiologists Classification; ; GCS, Glasgow Coma Scale; MET, medical emergency team.

cians in two university-level tertiary referral hospital areas. All pre-hospital data were retrieved from the FinnHEMS database and EMS datasheets. We therefore believe that our results are generalizable to similar institutions with a comparable level of health care. The most important limitation to be considered is that our data collection was retrospective; thus, a lack of data was unavoidable. In addition, due to a cold climate and transportation, measuring SpO_2 or non-invasive blood pressure was in some circumstances impossible. To minimise the error from missing data, we combined parameters concerning respiratory (SpO_2+ RR) and circulatory (HR + systolic blood pressure) dysfunction. Caregivers concern was not handled as an independent factor, but describes a documented concern about the patient in addition to, or despite, measured vital abnormalities.

Other than that, there are few other limitations in the study. First, the data do not include paediatric or obstetric patients. Secondly, we did not evaluate 30-day mortality, which may have caused us to underestimate the long-term mortality in this patient population.

Conclusions

In a pre-hospital setting, validated tools should be offered to healthcare providers for patient evaluation. A simplified pre-hospital 'MET' score is a predictor for patient outcome regardless of patient age and overall physical health and could serve as a risk assessment tool for EMS on the scene. Further studies are required to validate the use of a simplified 'MET' score in the pre-hospital setting.

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