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Safety with Mechanical Chest Compressions in CPR

Clinical studies with the LUCAS™ device

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Abstract
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Chest compressions in cardiopulmonary resuscitation are of utmost importance although not without a risk. Many injuries are described but the incidence of these is hard to define due to methodological differences. It is strenuous to perform chest compressions and therefore mechanical chest compressions have been looked upon with interest. This thesis presents new insights on the panorama and incidence of injuries in modern CPR and a comparison of safety and efficacy between manual chest compressions and mechanical chest compressions with the LUCAS™ device.

We also evaluated if computed tomography could be an aid in the detection of these injuries.

Two pilot trials were conducted and one presented no difference in early survival with 26% and 31% having return of spontaneous circulation when comparing manual chest compressions with the LUCAS device in out-of-hospital cardiac arrest. The other revealed no difference in autopsy-detected injuries. A third multicentre autopsy trial revealed that in patients treated with manual chest compressions 78.3% had at least one injury and 63.9% had at least one rib fracture. The corresponding numbers for patients treated with the LUCAS device was 92.8% ($p = 0.002$) and 77.7% ($p=0.022$). Sternal fractures occurred in 54.2% and in 58.3% of the cases treated with manual chest compressions and the LUCAS device respectively ($p = 0.556$). The median number of rib fractures was 7 in the group receiving manual chest compressions and 6 in the group receiving chest compressions with the LUCAS device. In 31 cases a computed tomography was conducted prior to autopsy and we found a very strong correlation in the discrimination of patients with or without rib fractures (kappa=0.83). Mean difference between the two methods in detecting rib fractures was 0.16. The detection of other injuries did not have a strong correlation. In conclusion there is no difference in early survival between the two methods and mechanical chest compressions adds 14-15% more patients with rib fractures but the amount of rib fractures, sternal fractures and other injuries is equal. CT can aid but not replace autopsies in the detection of these injuries.

Keywords: Cardiac arrest, Cardiopulmonary resuscitation, Mechanical chest compressions, Active compression-decompression, Injury, Autopsy, LUCAS

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“Life is short, and Art long; the crisis fleeting; experience perilous, and decision difficult. The physician must not only be prepared to do what is right himself, but also to make the patient, the attendants, and externals cooperate.”

Hippocrates 400 BC

To those I care about

List of Papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals.

I Smekal, D., Johansson, J., Huzevka, T., Rubertsson, S. (2009) **No difference in autopsy detected injuries in cardiac arrest patients treated with manual chest compressions compared with mechanical compressions with the LUCAS™ device-a pilot study.** *Resuscitation*, 80:1104–7

II Smekal, D., Johansson, J., Huzevka, T., Rubertsson, S. (2011) **A pilot study of mechanical chest compressions with the LUCAS™ device in cardiopulmonary resuscitation.** *Resuscitation*. 82(6):702-706

III Smekal, D., Hansen, T., Sandler, H., Rubertsson, S. (2012) **Comparison of computed tomography and autopsy in detection of injuries after unsuccessful cardiopulmonary resuscitation.** *Resuscitation.* 84:357– 360

IV Smekal, D., Lindgren, E., Sandler, H., Johansson, J., Rubertsson, S. (2013) **CPR related injuries after manual or mechanical chest compressions with the LUCAS™ device. A multicentre study in victims after unsuccessful resuscitation.** *Manuscript*

Contents

Abbreviations

ACD-CPR	Active compression-decompression-CPR
AHA	American Heart Association
ALS	Advanced life support
BLS	Basic life support
BP	Blood pressure
CPR	Cardiopulmonary resuscitation
CT	Computed tomography
ECG	Electrocardiography
ECMO	Extracorporeal membrane oxygenation
EMS	Emergency medical system
ERC	European Resuscitation Council
ICU	Intensive care unit
L-CPR	LUCAS CPR
MCC	Miniaturized mechanical chest compressor
M-CPR	Manual CPR
OHCA	Out-of-hospital cardiac arrest
PACS	Picture archiving and communication system
PCI	Percutaneous coronary intervention
$P_{ET}CO_2$	Partial pressure of end-tidal carbon dioxide
ROSC	Return of spontaneous circulation

Introduction

> "For extreme diseases, extreme methods of cure, as to restriction, are most suitable."
>
> Hippocrates 400 BC

A sudden cardiac arrest is often an extremely stressful event for bystanders and ambulance personnel. Overall mortality in out-of-hospital cardiac arrests is very high and in this dreadful situation desperate measures are needed. In this situation, adherence to guidelines can be difficult and hence automated mechanical devices to aid personnel in cardiopulmonary resuscitation (CPR) have been viewed with great interest. External chest compressions involve a risk of injury but also offer a chance to save the patient's life and so the risk of harm has been accepted: the alternative would be no chest compressions and the patient's certain death.

When investigating the occurrence of injuries due to CPR it is important to remember this and also to bear in mind that some of the injuries can actually be seen as an acknowledgement of proper CPR. If we focus only on the complications of CPR, it could create a situation where rescuers might perform CPR too gingerly for fear of injuring the patient, thereby producing suboptimal chest compressions and furthermore seriously reducing the patient's chances of survival. It would therefore be inappropriate to look only at the injuries without also addressing the efficacy of the CPR performed. This thesis presents new insights on the range and incidence of injuries in modern CPR and a comparison of safety and efficacy between manual chest compressions and mechanical chest compressions with the LUCAS™ device.

Background

Modern history of CPR

There are ancient descriptions of resuscitation from Egypt and in the bible but the development of modern CPR started in the early 19th century. In 1827, Leroy d`Etiolles proposed a method of artificial respiration using manual chest compressions with or without movement of the arms. Later the idea that the compressions could be used to create blood flow was born and in 1878 Boehm described external chest compressions in animal experiments [1]. Four years later the first description of chest compressions in humans was published but it was not adopted by many [2]. The birth of general anaesthesia with the use of ether and chloroform and the subsequent complications of these drugs led to some sudden cardiac arrests in the operating theatre. A method for treating these cardiac arrests was soon developed and from the beginning of the 20th century open chest cardiac massage was the standard in CPR [3]. Obviously this method was for patients who had their cardiac arrest in the operating theatre and surgeons were needed.

In 1960, the ground breaking paper by Kouwenhoven, Jude and Knickerbocker described a resuscitation technique that required little technical expertise [4]. It was not necessary to open the chest and compress the heart directly. Instead, compressions were performed by hand compressing the thoracic wall. This was somewhat revolutionary and closed-chest cardiac massage was promptly adopted.

The first report of injuries due to the new CPR method was published only a year after the original paper by Kouwenhoven et al., but the report did not influence the worldwide adoption of the technique [5]. In 1965, an editorial was published in the journal Circulation stating that both the benefits and hazards of CPR had become apparent. A previous statement from 1962 that defined CPR as a medical procedure was revised and it was now called an emergency procedure that could be initiated by several different work groups [6]. In this editorial several *types of* injuries were listed and they stated that these injuries were more likely to occur if untrained personnel performed the resuscitation and that training programs would keep these injuries to an acceptable minimum. During the following years more reports of injuries were published and in 1974 a review by Patterson et al. was published [7]. This

review presented several different injuries but as before, this paper also had no effect on the way CPR was performed at that time.

Other subsequent studies confirmed the fact that injuries from CPR were common and that the most frequently reported complications were skeletal injuries, especially to ribs and sternum. Furthermore, complications from the upper airway, lungs, heart, great vessels and injuries to the gastrointestinal system, including lacerations of the liver and spleen and retroperitoneal haemorrhage, were reported to occur with varying frequencies [8-17].

From the 1980s to the beginning of the 21st century, new insights indicated three phases during the cardiac arrest. First, there was an electric phase where defibrillation was the top priority [18]. Second came a haemodynamic phase where adequate cerebral and coronary perfusion should be the priority with efficient chest compressions to optimize neurological survival [19]. There was also a third metabolic phase and hypothermia was thought to affect this third phase. The understanding of these different phases in CPR and the combination of studies describing inefficient CPR resulted in an increased focus on the chest compressions during CPR [20-23]. A new algorithm was constructed and in 2005, the European Resuscitation Council (ERC) and American Heart Association (AHA) revised the guidelines for resuscitation [24, 25]. Five years later the new, revised guidelines were published and the recommendations now were that all rescuers, trained or not, should provide chest compressions to victims of cardiac arrest and it was emphasised to “push hard and fast”. An increase of depth of the chest compressions by approximately one centimetre was also recommended [26]. Have the advances in the field of CPR yielded additional lives saved?

Efficacy of CPR in out-of-hospital cardiac arrest in Sweden

Out-of-hospital cardiac arrest (OHCA) is a common cause of death. In spite of recurring updates to CPR guidelines, the survival of OHCA patients was essentially unchanged from the early 1970s to the early 2000s, averaging 5% for all OHCAs. From the early 2000s onwards, survival has been increasing and in 2011, survival after one month was 10.4% [27].
The initial rhythm detected in OHCA has changed over the years. Between 1992 and 2011, the number of patients with ventricular fibrillation has declined from 34% to 25% [27]. The mean age of the patients has been constant over these years (67 years) [27].

The overall outcome of CPR is also influenced by the possible performance of CPR by bystanders. The rate of bystander CPR has increased from 33% in 1992 to 68% in 2011. Early defibrillation is also important and alarmingly, the median time from dispatch call to defibrillation has increased from 8 minutes 1992 to 11 minutes 2011 [27].
Furthermore, it has been postulated that after a long period of CPR the elastic recoil of the thoracic wall might diminish and this could impair the success of the resuscitation [28, 29].

Survival after cardiac arrest depends on prompt and effective CPR. Several factors influence the outcome: naturally, the most important factor is whether CPR is performed or not, but the quality of the CPR is also important. It has long been recognised that chest compressions are strenuous to perform and therefore mechanical chest compressions have been a field of interest for some time.

History of mechanical devices

In 1908, a device to give external chest compressions was constructed and tested in canine experiments but it was not considered noteworthy at that time [30]. Only one year after the world-wide shift from internal to external cardiac massage, a device was designed to overcome the disadvantages of performing manual chest compressions [31] (Figure 1). In 1962, several different devices were tested. Among them was the device shown in Figure 2 [32, 33]. It was claimed that this device was simple to use, cheap to produce and could also be made available to medical teams. Designed to fit over a bed or couch, it required an individual to pull a lever, which operated a plunger, placed on the patient's chest. It was stated that 17 out of 18 patients had an adequate femoral pulse when it was used. From the mid nineteen sixties to the eighties many mechanical devices were developed and tested for CPR but they were mostly considered too complicated, heavy or ineffective, or a combination of all three [34, 35].

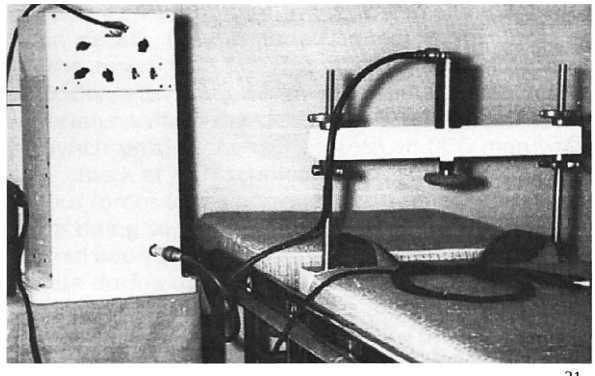

Figure 1. The Cardiac Massage Unit Source: Harkins and Bramson[31].

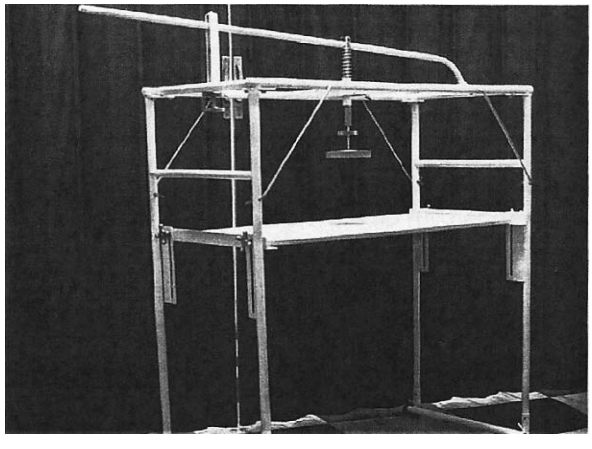

Figure 2. Source: Warltier[33].

The best known device from this period was the Thumper, which was used in clinical settings and in many laboratory investigations of CPR [36].

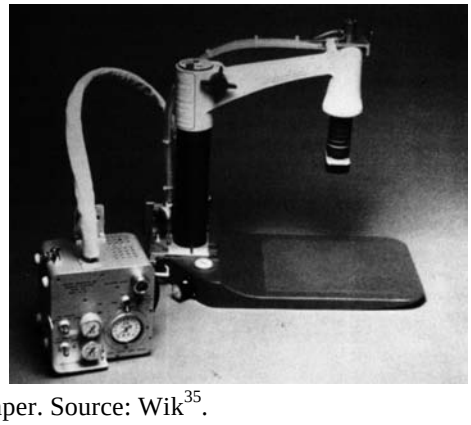

Figure 3. The Thumper. Source: Wik[35].

It consisted of a vertical column attached to a baseplate and a cantilevered arm with a cylinder and piston. Compressed gas was used to drive the device. It had a built-in ventilator that was time-cycled and pressure limited. The thought was that it would be useful in the hospital and in ambulances. It has remained in use and has been updated several times throughout the years. (Apparently the last model was actually tested in a clinical trial in China in 2010 but no abstract seems to be available [37].)

At the beginning of the 1990s, an anecdotal report of successful CPR where chest compressions had been performed with a household plunger was published [38]. This spurred Cohen et al. to test the hypothesis that a suction device could assist chest wall expansion and thereby improve haemodynamics during CPR. Active compression-decompression resuscitation (ACD-CPR) was compared with standard CPR. This device was marketed under the name of Ambu Cardiopump™ and results from early studies were promising. However, subsequent studies had varying results and from 1996 to 1999, Rabl et al. and Baubin et al. presented results showing an increase in chest wall injuries [39-46]. This doubtless affected the use of this device and it has since been used sparsely. A review investigating fractures due to CPR was published in 2004 and the occurrence of injuries due to ACD-CPR was reviewed for the first time [15].

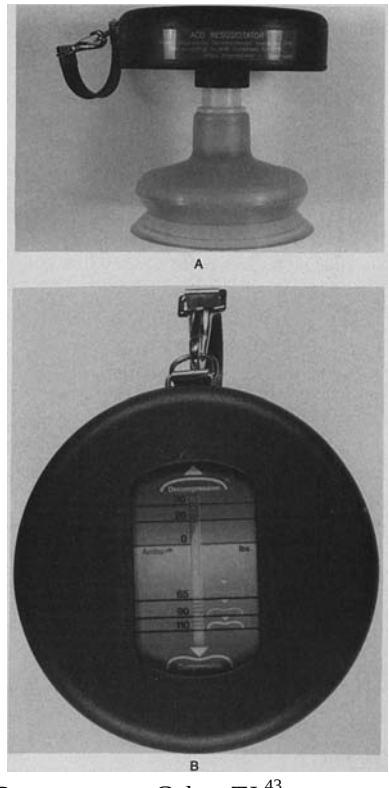

Figure 4. Ambu CardioPump, source: Cohen TJ [43].

The LUCAS device was introduced in 2002 and experimental studies were promising but there were concerns about the safety of the device [47-50]. A thorough description of the LUCAS™ device follows on Page 19.

The AutoPulse™ was introduced in 2004 [51]. It is designed as a pneumatic vest and it has a load-distributing band attached to a short backboard. The band is connected to a mechanism that can shorten the band under force in a rhythmic fashion such that the band squeezes the entire chest with each cycle. An experimental study has shown an improvement in haemodynamics compared to mechanical chest compressions with a piston but later clinical studies have had conflicting results [51-55]. Studies have shown injuries due to CPR with the Autopulse™ although the incidence of injuries is not evidently clear [56, 57]. It seems that dorsal rib fractures are more common after the use of this device than after manual and mechanical chest compressions with the LUCAS™ device.

Figure 5. Autopulse™, © ZOLL Medical Corporation.

A new miniaturized mechanical chest compressor (MCC) was tested in experimental studies in 2008 and again in 2012 [58, 59]. There are no studies looking into the safety of this device.

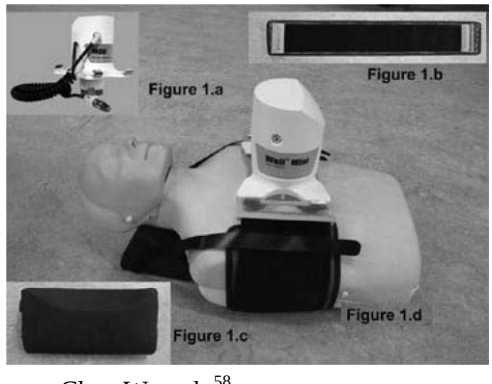

Figure 6. MCC, Source: Chen W et al. [58].

The LUCAS™ device

Two models of LUCAS™ have been developed. The first model was the LUCAS™ 1 Chest Compression System which was a pneumatic gas-driven device. As of early 2010, this was replaced by the LUCAS™ 2 Chest Compression System which is powered electrically. Both devices achieve mechanical chest compressions at a constant rate of 100 per minute and to a fixed depth of 4– 5 cm by means of a piston that has a 50% duty cycle, with the added feature of a suction cup that may assist the chest back to neutral position.

Figure 7. The LUCAS™ device, © Physio-control, Inc.

Experimental studies have shown that the device produces superior pressure and flow in a thoracic model, significantly higher cardiac output, carotid artery blood flow, end-tidal CO2, intrathoracic decompression phase, aortic and coronary perfusion pressures and a higher rate of return of spontaneous circulation (ROSC) [47]. An experimental study has shown that chest compressions with the LUCAS™ device during experimental CPR result in

higher cerebral blood flow and cardiac output than with standard manual CPR [48].

Clinical studies has shown a higher mean of $P_{ET}CO_2$ with the use of the LUCAS™ device compared to manual chest compressions in out-of-hospital cardiac arrest but still no proof of any benefit in terms of increased survival [60, 61]. The LUCAS™ device has proven to be functional in "rescue PCI" during on-going CPR [62, 63]. It has also been used in other settings such as emergency aortic valve repair, in other percutaneous non-coronary interventions during on-going CPR and during prolonged CPR due to transport or hypothermia [64-66]. In some countries where the law allows organ transplants from donors who have no heart beat after sudden cardiac arrest, the LUCAS™ device has been used as a bridge from the decision to transplant organs until the start of extracorporeal oxygenation (ECMO) [67, 68].

As stated before, there were concerns about the safety of the device. Before questions concerning the risk of harm from the device can be answered, we have to understand the range and incidence of injuries in standard CPR.

Injuries due to CPR

Although there are reports of injuries to almost every part of the trunk and head, the incidence of these injuries varies greatly in the literature. The most common injuries are rib and sternal fractures. From 1961 to date, many articles have been published and in 1974, 2004 and 2008 reviews were published [7-15, 69-93]. The first review listed many different injuries and focused on several life threatening ones. The second review concentrated on skeletal injuries and the third added a few injuries not listed by the other two reviews. When combining the three reviews we see incidences of rib fractures ranging from 8.1% to 96.6% and sternal fractures ranging from 1% to 80%. A recent trial with a multicentre design looking at patients surviving after CPR presented results where the range of rib fractures varied from 0 to 83.3% in the different centres participating [94]. Injuries due to CPR with mechanical devices were also explored in the second review and the incidence of skeletal injuries due to ACD-CPR ranged from 3.8% to 86.6% for rib fractures, 0 to 93.3% for sternal fractures and from 3.8% to 93.3% for rib and/or sternal fractures. These numbers were based on studies with the CardioPump™ presented on Page 14. No studies with the LUCAS™ device were included in any of the reviews. Table 1 presents a list of other injuries found in patients after CPR.

Table 1. *Injuries due to CPR.*

Type of injury	Patterson et al.	Hoke et al.	Buschmann et al.
Fracture of collar bone	X		
Bone marrow embolism	X	X	
Epicardial bleeding/bruising	X		X
Mediastinal bleeding/bruising	X		
Pericardial bleeding	X	X	X
Thoracic aortic laceration/rupture	X	X	X
Pneumothorax	X	X	X
Haemothorax		X	X
Subcutaneous emphysema	X		
Liver laceration/rupture	X	X	X
Splenic laceration/rupture	X	X	X
Hemiperitoneum	X		X
Retroperitoneal haematoma	X		
Left ventricular haemorrhage		X	X
Perforation of right accessory renal vein	X		
Injury to gastric muchosa			X
Gastric rupture			X

Most of the injuries shown above are infrequent and many of them do not have a known incidence. Aortic ruptures due to CPR might occur in up to 1% of patients [95]. Gastric ruptures and injuries to the spleen have an incidence lower than 1% [13, 96].

There have also been reports of injuries from other regions such as the head and eyes. There has also been a case report of Brown's syndrome (an ocular motility disorder) as a complication of cardiopulmonary resuscitation although it is likely that this injury is attributable to mouth-to-mouth ventilation and not to chest compressions [97]. Preliminary data from two as yet unpublished studies compare injuries from manual chest compressions and mechanical chest compressions with the LUCAS™ device in patients with unsuccessful CPR. Englund et al. found 93% and 65% rib and sternal fractures respectively in patients treated with LUCAS-CPR (L-CPR) and 52% and 28% rib and sternal fractures respectively in patients treated with manual CPR (M-CPR) [98]. Menzies et al. found 32.5% and 22.5% rib and sternal fractures respectively in patients treated with L-CPR and 48.7% and 41.0% rib and sternal fractures respectively in patients treated with M-CPR [99]. One experimental study in a porcine model comparing manual chest compressions with mechanical chest compressions with the LUCAS device revealed 30.2% and 33.7% rib and sternal fractures respectively after manual chest compressions and 7.5% and 3.8% rib and sternal fractures respectively after chest compressions with the LUCAS device. The mean number of rib fractures was also higher after manual chest compressions (6.0 versus 1.8). There was also a larger proportion of haematomas to the liver and spleen after manual chest compressions (17% and 15.1% versus 3.8% 0%) [100].

In conclusion CPR is an emergency measure with a high complication rate. There are several factors influencing not only the rate of complications but also the efficacy.

Factors influencing the quality and risk for injuries in CPR

Extrinsic factors

The resuscitator

Level of training has been proposed as influencing the rate of complications but there are conflicting results [12, 101]. Other studies show no difference in performance on manikins with different levels of experience or employment [102, 103].

Placement of hands/piston

Chest compressions produce an intrathoracic pressure gradient and a direct compression of the heart, which leads to cardiac output and coronary blood flow. If the hand or the piston of the LUCAS™ device were placed too high or too low, the quality of CPR would be affected. Positioning the hand/piston too high is likely to increase the risk of high rib fractures or fractures to collar bones and this could in turn lead to injuries to large vessels near the heart. Positioning the hand/piston too low increases the risk of intra-abdominal injuries. A placement that is lateral in any direction could produce rib fractures and direct injuries to the lungs. Some authors have used the term “avoidable rib fractures” and these would be a product of the hand positions presented above. It has been shown that these types of fractures could constitute up to 20% of the rib fractures due to CPR [13]. There have been experiments with alternative positions for the hands [104] and for the resuscitator [105, 106]. It has actually been postulated that a position where a right-handed rescuer kneels on the right side of the patient and uses the right hand to establish contact with the patient would be beneficial both in terms of efficacy and risk for sternal fractures. This is because the hypothenar part of the hand exerts force more effectively than the thenar part and this position would put the hypothenar part of the hand in a more caudal position on the sternum [107].

Figure 8. Placement of hands in CPR

Depth of compressions

There is a correlation between increasing blood flow and increasing compression force and/or depth although within certain limits. As manual chest compressions produce, at best, a cardiac output of approximately 20–30% of normal output, sufficient depth of the compressions is fundamental [28, 108-113]. Despite this, we know that the majority of compressions are too shallow and that they are affected by the rescuers' endurance [20, 114-117]. Not only the force of the compressions, but also back support stiffness, is important for effective chest compressions [118].

As early as 1965 Ruben and Johansen presented results from eight corpses showing that sternal displacement was proportional to the pressure exerted on the sternum until the displacement caused costochondral separation or rib and/or sternal fractures. Fractures often occurred at a compression depth of 35-45 mm [119]. Almost 50 years later, Hellevuo et al. presented results showing a correlation between increasing depth and number of CPR-related injuries [120].

The LUCAS™ device is designed to produce the same depth of the compressions and decompressions the whole time. Two manikin studies have cast some doubt on this fact although there are some limitations when using manikins in these types of studies [121-123].

In conclusion, shallow compressions are negative in terms of efficacy but would probably lead to a decreased incidence of injuries [124]. An increased depth would probably lead to the opposite situation with increased efficacy and an increase in injuries. We still do not know the perfect compromise between efficacy and injuries.

Leaning

Leaning onto the patient during CPR affects the quality of CPR [125]. If the rescuer would produce the intended depth from the leaning position it might lead to a depth beyond recommendations.

It is possible to press down the piston too hard during the mounting of the LUCAS™ device, thereby creating a situation resembling leaning.

Both of these situations could lead to more injuries.

Interruptions of CPR

When ventricular fibrillation occurs blood is pooled in the venous circulation, which results in distension of the right heart and a subsequent emptying of the left heart. When the blood pressures on the arterial and venous sides are equal, the coronary perfusion pressure and the carotid flow fall to zero. Chest compressions lead to carotid artery blood flow within 10 seconds but it takes one and a half minutes to get an adequate coronary perfusion pressure. This difference is due to the different effects of chest compressions. The brain receives perfusion pressure and flow during both the compression and decompression phases. But the heart is only perfused during the decompression phase, since the pressure in the ascending aorta is less or equal to the pressure in the right atrium during the compression. Furthermore, as the right heart becomes more and more distended, the coronary pressure needed to provide adequate perfusion increases correspondingly.

There is evidence that during up to 50% of the CPR time, no chest compressions are performed and of course the pauses will lead to a decline in pressures and flow and pooling of the blood on the right side.

This is suboptimal as it has also been shown that interruptions negatively affect the chance for return of ROSC after defibrillation [21-23, 124, 126]. One theoretical advantage with the LUCAS™ device is that it is possible to give defibrillatory shocks during mechanical chest compressions.

CPR duration

During the first few minutes the strength of the chest compressions diminishes without being noticed by the rescuer and needless to say, this affects the quality of the chest compressions [117]. It is recommended that personnel take turns and shift positions after 2 minutes to compensate for this loss in power. It is difficult to predict how this affects the risk for injuries as there could be several possible scenarios: a lower amount of injuries due to a lower percentage of compressions with sufficient depth over time, or conversely, a higher amount of injuries due to movement of the hand because of

fatigue, as seen in a study by Krischer et al. [13]. Furthermore, it has been postulated that after a long period of CPR the elastic recoil of the thoracic wall might diminish and this could impair the success of the resuscitation [28, 29].

Frequency of CPR

CPR performed with too slow a frequency has been shown to be suboptimal in terms of efficacy but whether this might affect the risk of injuries remains unknown [127].

Transport

It has been shown that it is very hard to maintain efficient, on-going CPR during transport [128, 129]. It is difficult to predict how this affects the risk for injuries as there could be several possible scenarios: a lower amount of injuries due to a lower percentage of compressions with sufficient depth over time, or conversely, a higher amount of injuries due to movement of the hand because of the difficulties of keeping the hand in the right position due to the movement of the ambulance. There is also a risk for injury to the personnel performing CPR during transport. The use of mechanical devices during transport is theoretically advantageous but only one study compares the LUCAS™ device with manual chest compressions during transport with on-going CPR [123]. In this manikin study, manual chest compressions were performed with a higher frequency and deeper than compressions with the LUCAS™ device but there were periods with no compressions in the manual group due to the change in rescuers every two minutes. There was also a higher percentage of incorrect pressure points and the speed of the ambulance had to be reduced for safety reasons in cases where manual CPR was being performed.

Intrinsic factors

Age of the patient

High age is believed to result in a lower chance of survival although conflicting results exist [130, 131]. It is also believed that advanced age could lead to a higher injury risk. Whether this increase is correlated to age or whether it is a confounder, and whether osteoporosis is the nominator, remains unknown although in living patients it seems that increasing age is the strongest risk factor for fractures [13, 132].

Gender

When a cardiac arrest occurs, females are generally older and have a higher incidence of osteoporosis [133]. There are indications that, in some settings,

female patients are less likely to receive CPR and resuscitative measures and this could explain why females could be linked to a lower chance of survival [134]. Some studies, however, show an increased survival in women [135] when trying to match age and optimal treatment. Studies looking at injuries from CPR have varying results when it comes to the correlation between gender and fractures from CPR [13, 41, 71, 94, 136].

Concomitant diseases

Several diseases obviously affect the opportunity for successful CPR and some diseases are themselves the reason for cardiac arrest (as, for example, a ruptured aortic aneurysm). There are also several diseases that could affect the possibility of complications from CPR such as, for example, osteoporosis, renal failure leading to renal osteodystrophy and myeloma, all leading to an increased risk for fractures. Diseases leading to enlarged liver and/or spleen probably increase the risk for haematomas and bleedings, and coagulopathies will of course increase the risk for bleedings.

Aims

The general aim of this thesis was to provide a new map that shows the range and incidence of injuries in modern cardiopulmonary resuscitation with the focus on injuries due to chest compressions. We also intended to compare the LUCAS™ device with manual chest compressions in cardio-pulmonary resuscitation with the focus on safety.

The specific aims of the projects were to:

- Evaluate the efficacy of the LUCAS™ device and the study design prior to a larger clinical trial.
- Evaluate the safety of the LUCAS™ device and the study design prior to a larger clinical trial.
- Compare the range and incidence of internal injuries, as assessed by autopsy, after unsuccessful CPR with the LUCAS™ device (L-CPR) or manual chest compressions (M-CPR) in out-of-hospital cardiac arrests.
- Compare autopsy and computed tomography in their ability to detect injuries in unsuccessful CPR.

Materials and methods

All studies were reviewed and approved by the regional human ethics committee in Uppsala, Sweden. The committee waived the need for informed consent.

The LUCAS pilot studies (Papers I and II)

At the time of the studies, the counties of Uppsala and Gävle had a total population of approximately 180,000 inhabitants and about 150 out-of-hospital cardiac arrests per year.

The emergency medical systems (EMS) and hospitals in these two counties participated in the studies. The Departments of Pathology in both counties and the Centre for Forensic Medicine in Uppsala County were also involved in Paper I.

The EMS systems had a first-tier design with ambulance crews consisting of at least one registered nurse. All first-tier ambulances were equipped with the LUCAS™ device. The dispatching centres simultaneously alerted two emergency ambulances. Prior to the studies and on repeated occasions, all personnel involved were informed about the design of the studies and all ambulance personnel received one day of manikin hands-on training and theoretical education. Just before the beginning of the studies there was a new training session with a repetition of the theoretical and practical items. During the studies there was an on-going process of repetition and evaluation of the use of the LUCAS™ device, the two algorithms used and standard CPR.

The LUCAS™ device and a randomization letter were brought to all patients with suspected cardiac arrest, chest pain and breathing problems. When cardiac arrest was identified, patients were eligible for inclusion and were checked for exclusion criteria (known pregnancy, age under 18 or trauma). If there were no exclusion criteria, CPR was started with manual chest compressions by one of the ambulance personnel and the other crew member opened the sealed envelope where a letter gave the randomized treatment. If the patient was randomized to manual chest compressions, CPR was contin-

ued according to the European Resuscitation Guidelines of 2000 [124]. If the patient was randomized to receive cardiopulmonary resuscitation with the LUCAS™ device, manual chest compressions were continued during the process of mounting the LUCAS™ device and until the start of its use. In this treatment arm, CPR was conducted according to a specific algorithm (Fig. 9).

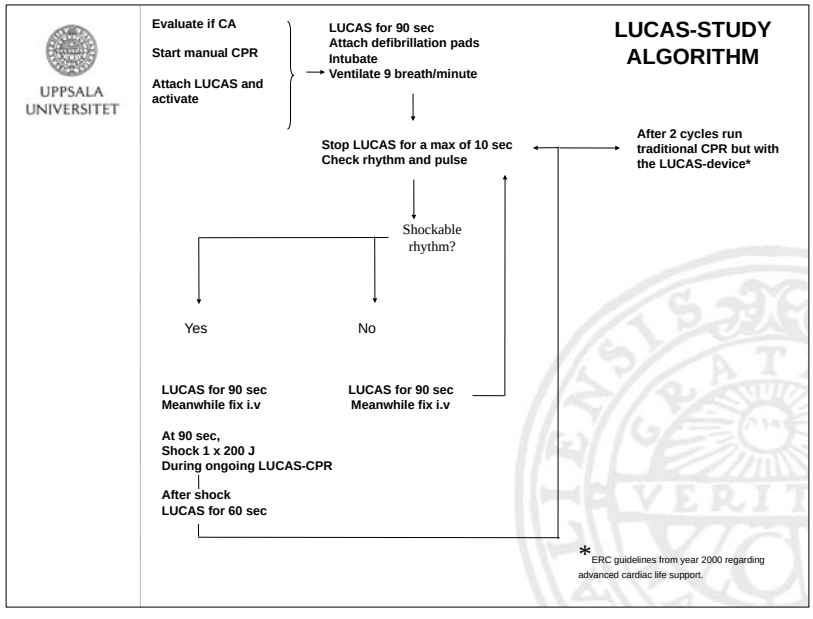

Figure 9. The LUCAS pilot study algorithm.

The main purpose of this algorithm was to enable defibrillatory shocks during the chest compression process. The European guidelines for advanced CPR suggested three defibrillations without chest compressions in between (Fig. 10) and due to the risk of too few defibrillations over time in the LUCAS group, traditional CPR was conducted but with the LUCAS™ device after two cycles with defibrillations during on-going CPR .

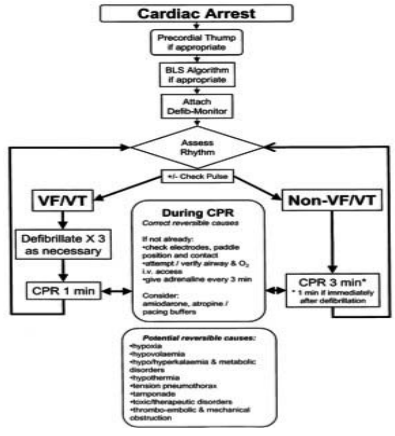

Figure 10. ERC guidelines from 2000 regarding advanced cardiac life support.

Demographic data, location of cardiac arrest, specific times to events, whether cardiac arrest was witnessed, first electrocardiography (ECG) rhythm and numbers of defibrillatory shocks were recorded.

Safety (Paper I)

Patients with unsuccessful CPR were eligible for inclusion in the autopsy study. Patients who did not survive underwent an autopsy based upon the decision of the admitting physician. Swedish law regulates the possibility of autopsy and the admitting physician must determine whether the patient's view in this matter was known. Often the relatives' views determine whether there will be an autopsy or not, unless a forensic autopsy is required. In this pilot study, 71 patients who did not survive an out-of-hospital cardiac arrest were included. The remaining 14 patients had an in-hospital cardiac arrest and could not be resuscitated by outreach intensive care teams. There was no difference in demographic data between the groups (Table 2).

Table 2. *Demographic and baseline data of patients included.*

	L-CPR **38**	**M-CPR** **47**	**p value**
Age (years)	72±12	66±17	0.38
Sex (male)	27	31	0.65
CPR duration	42±19	36±13	0.11

Mean ± SD or number of patients.

Pathologists recorded data from the autopsy through a standardised study protocol for external and internal injuries, which included recording sternal fractures, rib fractures, bleeding in the mediastinum, injuries to the heart, injuries to the thoracic aorta, haemothorax, pneumothorax and injuries to the liver and/or spleen.

Efficacy (Paper II)

In the efficacy study containing only out-of-hospital cardiac arrest patients, the LUCAS and the manual groups contained 75 and 73 patients respectively and there was no difference concerning demographic data, first recorded ECG rhythm, witnessing of cardiac arrest, or bystander CPR (Table 3).

The primary endpoint was ROSC, with blood pressure (BP) above 80/50 mmHg for at least 5 minutes. Secondary endpoints were ROSC with a palpable pulse, and whether the patient was hospitalised alive or discharged from hospital alive.

Table 3. *Demographic and baseline data of patients included.*

	L-CPR, n (%) 75	**M-CPR, n (%) 73**	**p value**
Age (years)[a]	69±16	71±16	0.52
Sex (male)	50 (68)	50 (68)	1.00
Witnessed CA (0/1)[b]	50 (68)	53 (74)	0.47
Bystander CPR (1/1)[b]	25 (34)	22 (31)	0.72
VF/VT as initial rhythm	20 (27)	20 (27)	1.00

[a] Mean ± SD.
[b] Number of patients with missing information

The LINC autopsy studies (Papers III and IV)

Three Emergency Medical Services participated in this autopsy trial. Patients were included in Gävle, Västerås and Uppsala in Sweden.

These centres fulfilled specific requirements including experience of pre-hospital studies and/or the use of the LUCAS™ device. During the study period, an efficacy study was being carried out to compare the LUCAS™ device with manual chest compressions in out-of-hospital cardiac arrests, and all of the autopsy study population was also included in the efficacy study [138]. Before the study started, all paramedics and other ambulance personnel at each site were trained in conventional manual CPR according to the 2005 guidelines [24], in the use of the LUCAS™ device, and in the algorithms of the two different treatments (Figs. 4 and 5). Retraining continued at least every 6 months during the study period and it involved training in both techniques. In addition, once every year, 20-30% randomly selected ambulance personnel were monitored using a modified CPR manikin (Laerdal, Stavanger, Norway).

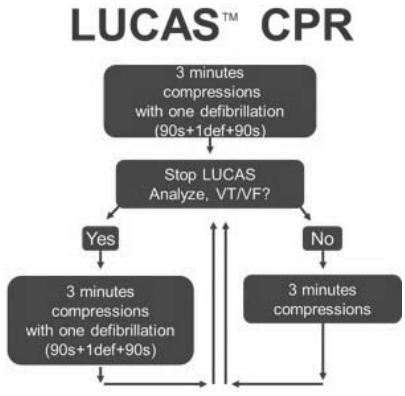

Figure 11. LUCAS™ algorithm

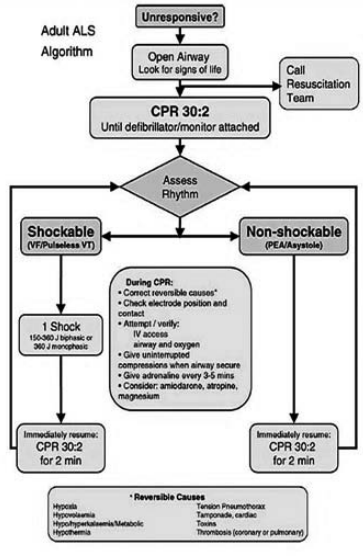

Figure 12. Standard CPR algorithm

The LUCAS™ device was brought to all patients with suspected cardiac arrests, breathing problems and chest pain. Patients with unexpected out-of-hospital cardiac arrests were eligible for inclusion. Exclusion criteria were traumatic cardiac arrest including hanging, age believed to be less than 18 years (no upper limit), known pregnancy, defibrillated before LUCAS™ was brought to the scene or patient's body size not fitting the LUCAS™ System. For obvious reasons, patients who survived were excluded from the autopsy study. Ambulance personnel performed closed letter randomization during on-going manual CPR.

If the patient did not survive, the admitting physician sought the relatives' opinion and this determined whether there would be an autopsy or not (unless a forensic autopsy was required). Demographic and baseline data of the patients included are presented in Table 4 (Paper IV).

Table 4. *Demographic and baseline data of patients included.*

	L-CPR 139	**M-CPR 83**	**p value**
Age (years)a	65.7±16 (24-100)	68.1±18 (21-92)	0.310
Sex (female)[b]	42 (30)	28 (34)	0.655
CPR duration[c]	35.0±17.3	34.7±16.0	0.904
Osteoporosis[b] (10/37)[d]	28 (27.5)	18 (24.7)	0.729
Bystander CPR[b]	77 (55.4)	51 (61.4)	0.402

[a] mean ± SD (range).
[b] number of patients (%).
[c] mean ± SD.

Three pathology departments and one centre for forensic medicine were responsible for the autopsies. All but one department had prior experience of the study type from the previous pilot study.

Pathologists in each of the four centres recorded autopsy data through a standardised study protocol for external and internal injuries. The protocol consisted of questions about different injuries and the eventual relationship of the injury to CPR (Yes/no/not possible to answer). In total, there were 40 different pathologists/forensic experts involved in the autopsies in this study.

Computed tomography (CT) was conducted prior to autopsy in 31 of the 222 patients included (Paper III). The bodies were scanned with a 64 slice CT scanner and the CT examinations were analysed on a picture archiving and communication system (PACS) station by a radiologist with 10 years' experience including 7 years of reading post mortem examinations. The autopsy procedure followed. The radiologist and the pathologists used the same standardised protocol for external and internal injuries. The pathologists and radiologist were blinded from each other's results. The demographic data from this study population is presented in Table 5.

Table 5. *Demographic and baseline data of patients included.*

	N=31
Age (years)[a]	62.3±20.3
Sex (male)[b]	19 (61.3)
Number of days from death to CT[a]	3.9±2.6
Number of days from CT to autopsy[a]	3.9±2.6
CPR duration[a] (1)[c]	33.3±16.6

[a] Mean±SD.
[b] Number of patients (%)
[c] Patients with missing data.

Statistical analyses

The statistical analyses were performed in collaboration with statisticians at the Uppsala Clinical Research Centre, Uppsala, Sweden. Data were analysed with SAS version 9.1-9.3 (SAS Institute, Cary, NC, USA) and IBM SPSS version 21 for Mac. The groups were tested for the dichotomous variables with Fisher's exact test or Chi square-test. The Wilcoxon rank sum test was used for continuous variables. The Hodges-Lehmann approach was used to estimate the median shift parameter between groups for continuous variables. Values are reported as mean ± standard deviation or median with interquartile range. A two sided p value <0.05 was considered significant.

In Paper III the incidence of injuries based on CT and autopsy was compared using Cohen's kappa coefficient. The incidence of rib fractures was also compared, using Pearson’s correlation coefficient and Spearman’s correlation coefficient. The mean difference between the two methods in detecting rib fractures was calculated with standard deviation and limits of agreement.

Results

The LUCAS pilot studies (Papers I and II)

Safety (Paper I)

In the group receiving chest compressions with the LUCAS™ device, 42% had no injuries found by autopsy. In the group receiving manual chest compressions this figure was 55% (p = 0.28). The most common injuries were rib fractures. There were 44.7% in the LUCAS group and 27.7% in the manual group, which had multiple rib fractures (p= 0.12). Sternal fractures were the second most common injury with 29% and 21% in the LUCAS and manual group respectively (p= 0.46). There were only a few patients with single rib fractures (<3). We also found occasional bleeding in different locations, from the inside of the sternum to the heart and lungs. Occasionally there were also patients with pneumothorax. None of these injuries was considered to have affected the patients' outcomes. The number of patients and type of injuries are outlined in Table 6.

Table 6. *Number of injuries detected by autopsy.*

Injury	**L-CPR, n (%) 38**	**M-CPR, n (%) 47**	**p value**
Single rib fracture (<3 fractures)	1 (2.6)	2 (4.3)	1.00
Multiple rib fracture (≥3 fractures)	17(44.7)	13(27.7)	0.12
Sternal fracture	11(29.0)	10(21.3)	0.46
Mediastinal bleeding	3 (7.9)	2 (4.3)	0.65
Retrosternal bleeding	3 (7.9)	1 (2.1)	0.32
Epicardial bleeding	4 (10.5)	1 (2.1)	0.17
Pericardial bleeding	3 (7.9)	4 (8.5)	1.00
Ruptured abdominal aortic aneurysm	1 (2.6)	0 (0.0)	0.45
Thoracic aortic dissection	1 (2.6)	0 (0.0)	0.45
Ruptured thoracic aorta	0 (0.0)	1 (2.1)	1.00
Lung parenchymal bleeding	1 (2.6)	0 (0.0)	0.45
Pneumothorax	1 (2.6)	1 (2.1)	1.00
Injury to the liver	1 (2.6)	0 (0.0)	0.45
Injury to the spleen	0 (0.0)	1 (2.1)	1.00

n = number of patients

In the original article we did not analyse the median number of rib fractures but a later analysis revealed that the median number of rib fractures was 6 (4.5 -10) in patients with L-CPR and 9 (5.25-12) in patients with M-CPR. Presented in Figure 13.

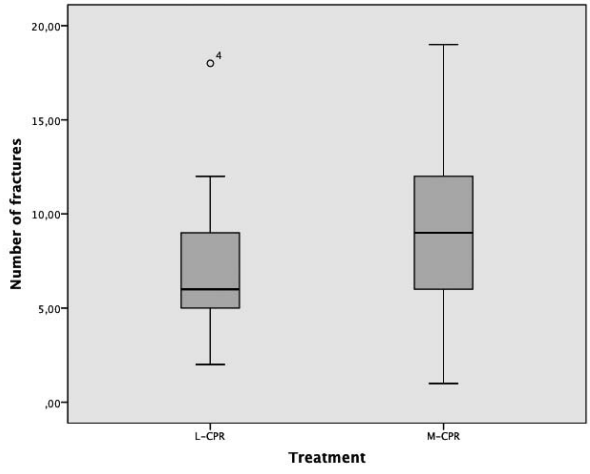

Figure 13. Median number of rib fractures among patients with rib fractures

Efficacy (Paper I)

In the efficacy pilot there was no difference in the primary and secondary outcome measures between the groups that received CPR with the LUCAS™ device compared with manual chest compressions (Table 7).

Table 7. *Study objectives.*

	L-CPR, n (%) 75	**M-CPR, n (%) 73**	**p value**
ROSC (1/1)[a]	30 (41)	23 (32)	0.30
ROSC with BP >80/50 mmHg > 5 min(0/1)[a]	23 (31)	19 (26)	0.59
Hospitalised alive (0/1)[a]	18 (24)	15 (21)	0.69
Discharged alive (0/1)[a]	6 (8)	7 (10)	0.78

n = number of patients.
[a] number of patients with missing information.

The mean time from dispatch call to start of CPR was 8.3 min in the LUCAS group and 7.5 min in the manual group (p = 0.38). The mean time taken to apply the device in the LUCAS group was 2.7 min from the start of CPR (Table 8).

Table 8. *Time variables (minutes).*

	L-CPR 75	M-CPR 73	p value
CA to start of CPR (24/21)[a]	10.4±6.6	10.2±5.9	0.87
CA to start of L-CPR (28)[a]	13.1±7.2		
Call from dispatch centre to CPR (1/4)[a]	8.3±5.8	7.5±3.6	0.38
Team arrival to CPR (8/8)[a]	1.0±1.1	1.1±1.1	0.63
CA to ROSC with BP >80/50 mmHg > 5 min (6/23)(6/19)[b]	35.1±20.7	31.1±19.5	0.59

Mean ± SD.
[a] number of patients with missing information
[b] number of patients with missing information/total number of patients, L-CPR and M-CPR respectively.

When looking at the whole population, about 37% of the patients had ROSC with a palpable pulse. ROSC with blood pressure above 80/50 mmHg for at least 5 minutes was achieved in 29% of the patients and the number of patients hospitalised alive >4 hours was 23%. At hospital discharge 9% were alive.

The LINC autopsy studies (Papers III and IV)

CT and autopsy correlation study (Paper III)

A CT scan was conducted prior to autopsy in 31 patients and the correlation between the two methods was investigated. This study was designed to give an indication of whether CT could be an aid or could even replace autopsy as the gold standard in examining post mortem injuries after unsuccessful CPR. The CT and the subsequent autopsy revealed rib fractures in 22 and 24 patients respectively (kappa=0.83, Table 9, Fig 14).

Table 9. *Correlation of rib fractures between CT and autopsy.*

Rib fractures	Type of Coefficient	Value
All fractures	Pearson	0.79 (95% C.I. 0.61 – 0.90)
	Spearmen	0.76 (95% C.I. 0.55 – 0.88)
	Kappa	0.83 (95% C.I. 0.61 – 1.00)
	Weighted kappa	0.65 (95% C.I. 0.50 – 0.81)

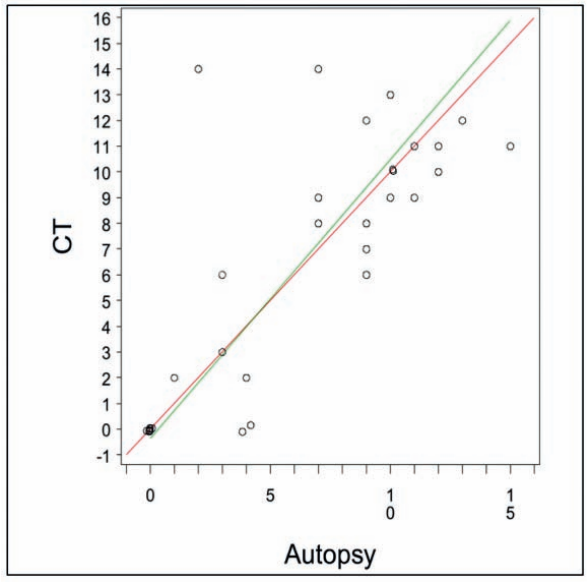

Figure 14. Number of rib fractures detected by CT and autopsy. A random jitter has been added to points lying on the same spot as others to make them visible.

In 12 cases, the autopsy revealed more rib fractures than CT whereas in eight cases, CT revealed more rib fractures than the autopsy. In seven patients, neither method showed any rib fractures. The mean difference between the two methods in detecting rib fractures was 0.16 (SD: ± 3.174, limits of agreement: -6.19–6.51). CT detected a total of 197 fractures and autopsy 192 fractures. The average patient had a median of eight rib fractures detected by CT and seven fractures detected at autopsy respectively. Other injuries are outlined in Table 13.

Table 13. *Correlation of other injuries.*

Injury	**CT**	**Autopsy**		**Kappa**
		No	**Yes**	
Retrosternal bleeding	No	21	4	0.32 (-0.08 – 0.71)
	Yes	3	3	
Mediastinal bleeding	No	27	3	-0.05 (-0.13 – 0.03)
	Yes	1	0	
Epicardial bleeding	No	25	5	-0.06 (-0.15 – 0.04)
	Yes	1	0	
Pericardial bleeding	No	21	1	0.34 (-0.01 – 0.70)
	Yes	6	3	
Pneumothorax right	No	30	0	-0.00 (-0.00 – -0.00)
	Yes	1	0	
Pneumothorax left	No	30	0	-0.00 (-0.00 – -0.00)
	Yes	1	0	
Haemothorax right	No	15	1	0.00 (-0.17 – 0.18)
	Yes	14	1	
Haemothorax left	No	19	0	0.20 (-0.05 – 0.44)
	Yes	10	2	
Injury to liver capsule	No	27	4	-0.00 (-0.00 – -0.00)
	Yes	0	0	
Injury to liver parenchyme	No	28	1	0.00 (0.00 – 0.00)
	Yes	0	0	
Ruptured thoracic aorta	No	29	1	0.65 (0.02 – 1.00)
	Yes	0	1	
Sternal fracture	No	11	6	0.49 (0.20 – 0.79)
	Yes	2	12	
Osteoporosis	No	15	7	-0.00 (-0.00 – -0.00)
	Yes	1	2	
Dissected thoracic aorta	No	29	1	0.19 (-0.15 – 0.53)
	Yes	0	0	
Dissected abdominal aorta	No	30	1	-0.00 (-0.00 – -0.00)
	Yes	0	0	

Safety (Paper IV)

Of the 222 patients included in the study, 83 patients (37.4%) had been treated with M-CPR only and 139 patients (62.6%) with L-CPR. There was no difference in age, gender or duration of CPR by EMS personnel between the two groups and there was no strong correlation between these parameters and the incidence of rib and sternal fractures.

In the patients receiving L-CPR, the average duration of initial manual chest compressions by EMS personnel was 3.4 minutes (SD 3.2 min) with a range from 0 to 16 minutes before mechanical chest compression was started. Bystander CPR was performed on 61.4% of the patients receiving M-CPR and on 55.4% of the patients receiving L-CPR.

At least one injury was found in 78.3% of the patients receiving M-CPR and in 92.8% of the patients receiving L-CPR (p=0.03).

The population with at least one injury was significantly older than the uninjured population (mean age 69.0, SD 15.4, vs. 54.9, SD 21.0, (p=0.002)). The numbers of injuries are summarised in Tables 14 and 15. When analysing the population with rib fractures the median number was 6 (IQR 3-10) in the L-CPR group and 7 (IQR 4-10) in the M-CPR group (Hodge-Lehmann location shift 1.00, CI 0.00 – 2.00, p=0.197) (Figure 15).

When looking at injuries by gender across the whole study population there were 77.1% female and 70.4% male patients with rib fractures (p=0.325). When analysing the female and male population with rib fractures, the median number was 8 (IQR 3-10) in the female population and 6 (IQR 3-9) in the male population. There were 60.0% and 55.3% sternal fractures in female and male patients respectively. In the patients with osteoporosis, 100% had at least one rib fracture and 82.6% had sternal fractures. In the group without osteoporosis the numbers were 63.8% and 47.3% respectively (p<0.001).

The numbers of injuries are summarised in Tables 14 and 15.

Table 14. *Number of rib and sternal fractures detected by a utopsy.*

Injury	**L-CPR n (%) 139**	**M-CPR n (%) 83**	**P value**	**Treatment difference, percentage points (95% C.I.)**
Sternal fracture	81 (58.3)	45 (54.2)	0.578	4.1 (-9.5 – 17.7)
Any rib fracture	108 (78.8)	53 (64.6)	0.027	14.2 (2.15 – 26.3)
≥ 3 rib fractures	89 (65.0)	47 (57.3)	0.314	7.6 (-5.7 – 21.0)
< 3 rib fractures	19 (13.9)	6 (7.3)	0.188	6.6 (-2.2 – 15.3)

Table 15. *Number of other injuries detected by autopsy.*

Injury	**L-CPR n/n* 139**	**M-CPR n/n* 83**
Mediastinal bleeding	14/0 (10.1)	8/1 (9.6)
Retrosternal bleeding	45/4 (32.4)	19/0 (22.9)
Epicardial bleeding	13/4 (9.4)	7/1 (8.4)
Pericardial bleeding	5/2 (3.6)	2/1 (2.4)
Haemothorax	6/0 (4.3)	2/1 (2.4)
Pneumothorax	4/1 (2.9)	2/0 (2.4)
Injury to liver capsule	6/0 (4.3)	2/1 (2.4)
Injury to liver parenchyme	5/1 (3.6)	1/0 (1.2)
Fracture to vertebral body	2/0 (1.4)	0/0 (0.0)
Fracture to collar bone	0/0 (0.0)	1/0 (1.2)
Rupture to thoracic aorta	2/2 (1.4)	0/0 (0.0)
Lung bleeding	1/0 (0.7)	1/0 (1.2)
Bleeding in the pectoral muscle	1/0 (0.7)	0/0 (0.0)
Rupture of the abdominal aorta	1/1 (0.7)	0/0 (0.0)
Rupture to the adventitia in pulmonary artery	1/ 0 (0.7)	0/0 (0.0)
Other injuries to the heart	3/1 (2.2)	2/0 (2.4)

* n/n The first number is the total number of certain and uncertain CPR-related injuries and the second number is the number where the pathologists stated that it was impossible to say whether the injury was related to CPR or not (uncertain).

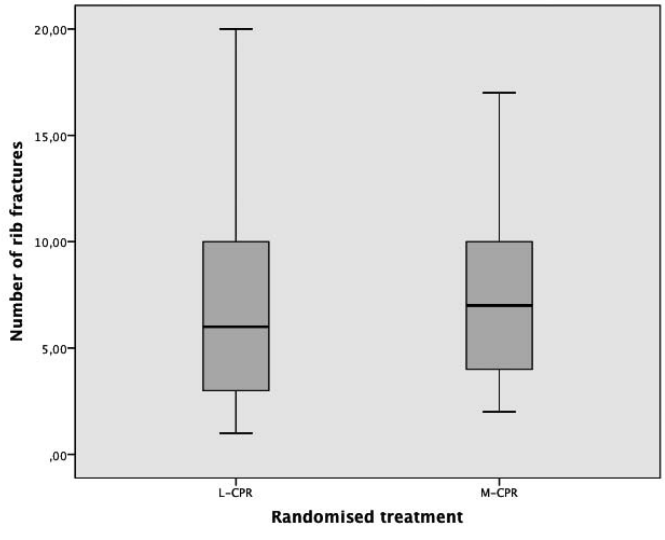

Figure 15. Median number of rib fractures among patients with rib fractures

Discussion

We have studied the LUCAS™ device, focussing on the device's safety and efficacy in a clinical setting. To be able to define the safety of a mechanical device we must know how and with whom to compare our results, and herein lies the first challenge. The most common injuries due to chest compressions are fractures to the ribs and sternum but in the literature the reported incidence of these injuries varies greatly. We will examine the reasons for this variance in previous studies before we look at the most important results of this thesis.

Is comparison with previous studies possible?
Can we compare our results with those of previous studies? Although there are a large number of articles on the subject, methodological differences have made comparisons almost impossible. The most obvious differences in previous studies are the possible inclusion of children, which of course decreases the incidence of fractures due to their more elastic rib cage, and also the inclusion of traumatic cardiac arrests, which would probably increase the incidence of injuries.

There has also been a difference in the detection of injuries and we know that this will affect the incidence rates presented here. We know that chest x-rays will underestimate the number of fractures, as will external examinations of the patients [126]. CT has been proposed as an aid to or even as a replacement for autopsy and there are somewhat conflicting results about the reliability of this method for detecting post-CPR injuries. In Paper III we looked at the correlation between CT and autopsy in their ability to detect post-CPR injuries and we could see a strong correlation in the ability to discriminate between the patients with rib fractures from those without. The ability to detect the same amount of fractures in the same patient was not as good: it could vary substantially in some of the cases and it missed all the intra-abdominal injuries found later at autopsy. We therefore cannot recommend this method as a replacement for autopsy, which has always been considered the gold standard.

In studies that have used an autopsy as a method for finding injuries it is important to verify whether the analysis has been of a retrospective or prospective type, as there appears to be a tendency for lower numbers in retro-

spective analyses. It is also important to see if the autopsies were performed routinely or with a focus on suspected injuries post-CPR. In many studies the design is not clearly described.

Case mix is also important, as age and gender are believed to be risk factors for fractures in CPR.

We were able to confirm a correlation between age and risk for injuries. We could also see a trend towards a greater number of fractures in the female population but we could not see any correlation between the duration of CPR and injuries.

Thus, when analysing results from studies dealing with injuries from CPR, it is important to remember all these different factors, any of which could affect outcomes.

There are no randomised controlled trials and there probably never will be due to the nature of the subject. As Swedish law regulates the options for an autopsy, the randomisation of such a decision would be difficult.

Safety of the LUCAS™ device

Safety is of paramount importance when introducing new medical devices. We therefore undertook a pilot study first and a subsequent prospective multicentre trial to explore the comprehensive range and incidence of injuries due to chest compressions in out-of-hospital cardiac arrests.

The first study did not present any difference in injury incidence between the CPR methods but the low number of patients included made the conclusion somewhat uncertain. The latter trial has shown that in patients with unsuccessful CPR after out-of-hospital cardiac arrests, more chest compression related injuries were found at autopsy in patients after L-CPR. Rib fractures were found more often after L-CPR although no differences in the median number of rib fractures, number of sternal fractures or other less frequently observed injuries were found compared to the group treated with M-CPR. As stated above it is difficult to compare these results with most of the studies performed earlier and there is actually only one study with a comparable design.

In 1999, Baubin et al. presented the results of a study that compared the efficacy and safety of ACD-CPR with standard CPR in a clinical setting. Autopsies focussing on injuries due to CPR were conducted and alarmingly high numbers of fractures due to ACD-CPR led to an early termination of the study by the ethics committee. At the time of termination, the incidence of rib fractures was 87% and 93% had sternal fractures. The corresponding

numbers in M-CPR were 55% rib fractures and 30% sternal fractures. A comparison with our pilot study seems adequate due to the similar (but still smaller) study size and the time when the study was conducted, although the study by Baubin had a somewhat younger population with shorter CPR duration. The numbers of M-CPR are a bit higher compared to our pilot study but the numbers of injuries due to ACD-CPR are much higher than from LUCAS-CPR. One possible explanation for the large difference between the two mechanical devices is that the Ambu CardioPump™ could produce an active decompression above the neutral position of the chest. One other possible explanation is that the CardioPump™ is manually driven and thereby it is possible to exert too much force when using it.

If there is only one well-conducted study comparing the safety of a mechanical device with standard CPR in out-of-hospital cardiac arrests, and that study was terminated prematurely, it leaves us no other alternative than to compare our own two studies.

It is important to remember that we could not present any differences in injury incidence in the pilot study. However, when looking at the percentage differences in both of the studies, we can see that the differences for any injuries and any rib fractures are similar in both studies while in multiple rib fractures and sternal fractures the difference has decreased.

Table 16. *Comparison of incidence of injuries between manual chest compressions and compressions with the LUCAS*™ device in Paper I and IV.

	Difference between the methods in the pilot study (Paper I)	**Difference between the methods in the LINC autopsy study (Paper IV)**
Any injuries	13.2%	14.5%
Any rib fractures	15.5%	14.2%
Multiple rib fractures	17.0%	7.7%
Sternal fractures	7.7%	4.1%

In the original Paper I, the median number of rib fractures was not analysed but a post hoc analysis reveals that the median number of rib fractures was 6 (4.5-10) in patients with L-CPR and 9 (5.25-12) in patients with M-CPR. The numbers in the LINC autopsy trial was 6 (IQR 3-10) in the L-CPR group and 7 (IQR 4-10) in the M-CPR group.

A conclusion that L-CPR adds about 14-15% more patients with any rib fracture does not seem far-fetched. But it would also appear that if one has rib fractures due to CPR, the number of rib or sternal fractures will not be increased if the LUCAS™ device is used.

How does this conclusion fit into the theories of how and when the fractures occur?

One existing theory is that fractures occur during the first minute of CPR but if this is true, should there be any difference in the incidence of rib fractures between the two groups in our studies, as all patients randomized to L-CPR had an initial period of M-CPR? Or does the theory hold good and is the extra 14-15% due to the active decompression of the mechanical device?

In 1965, Ruben and Johansen showed a linear relationship between force and sternal dislocation until there were fractures to the rib cage or costochondral displacement. Fractures occurred at a depth of 35-46 mm. Is it simply that the difference presented in our studies is due to the fact that 15% more of the patients reached this threshold? If this is so, it is probably not important when the rescuer is reaching the threshold during CPR. Ruben and Johansen also showed that applying force over a larger surface would not lead to a decreased risk of fractures. Could the difference between the methods be due to the fact that some of the rescuers had larger hands than the compression pad in the LUCAS™ device? The compression pad of the LUCAS™ device has a diameter of 59 mm and the suction cup adds another 7 mm. Baubin et al. presented results where the mean size of the most ulnar part to the most radial part of the hand exerting low pressure was 92 mm. When applying more pressure the area exerting pressure decreases to about 65 mm [107].

Do we have any possible confounding factors? Age, gender and CPR duration seem to be evenly matched between the groups. One factor that seems to have a large effect on fractures is osteoporosis. In our multicentre trial (Paper IV) all patients with osteoporosis had rib fractures. There was no difference between the groups in incidence of osteoporosis but in 12% of patients with M-CPR we had missing data concerning osteoporosis and the corresponding number in the L-CPR group was 27%.

As there is no difference in median numbers of rib fractures between the groups and as we did not find any correlation between rib fractures and numbers of injuries, this type of injury might not be the most important factor to examine when analysing complications of CPR.

Sternal fractures have been considered to be more hazardous than rib fractures due to sharper edges in the fractures. There is also a tendency to an inward tilting of eventual fragments, which in turn could lead to lacerations to the heart or great vessels in the vicinity of the heart [39]. As these types of internal injuries are rare, it is not likely that there is a strong correlation between them and sternal fractures. Although there was an increase in incidence of sternal fractures between the two studies, we could actually see a

decrease in numbers of pericardial bleedings when comparing the two studies. There is no difference in incidence of sternal fractures between the two methods of CPR chest compressions.

Rib and sternal fractures were the most common injuries but there were also minor bleedings and bruises to different parts of the trunk. Liver injuries are uncommon with an incidence ranging from 0-11%, mostly in case reports presenting this injury after CPR with manual or mechanical chest compressions and we present figures in the mid-range of these numbers [5, 74, 149-151]. All of the patients with injuries to the liver parenchyma had right-sided rib fractures but unfortunately, based on our protocol, we cannot determine whether these fractures were high or low. Risk factors could include improper hand positioning during CPR and anticoagulation therapies but due to the size and location of the liver, even correct hand positioning can potentially produce injuries to the liver. Heart and liver failure could possibly be other predisposing factors. In addition, prolonged time from cardiac arrest to start of CPR could lead to filling of blood to the liver but as we did not look at liver weight in this study, this is merely speculation. Injuries to the spleen are considered even more uncommon. In our pilot study we had one patient with an injury to the spleen after M-CPR and in the latter study there were no patients with spleen injuries. None of these patients had life threatening bleedings from these injuries and in fact, some had no bleeding at all. In Paper III we compared the CT with autopsy in their ability to detect post mortem injuries and CT missed the intra-abdominal injuries. However, injuries missed by computed tomography could be so minor (e.g. small bruises to the liver or spleen) that they have little or no impact on morbidity, mortality or patient comfort and thus are insignificant.

Three patients had fractured vertebral bodies and two of them had received L-CPR. This complication was described after multiple defibrillations without chest compression as well as after CPR without defibrillation [84]. Therefore the report states that it is difficult to know whether these fractures should be accounted for as complications of chest compressions or not [15]. The theory described is that muscle contractions in sedated patients during defibrillation could lead to the fractures and as cardiac arrest patients have lower muscle tone than sedated patients, we are unsure whether this theory fits into the CPR setting.

In point of fact, we do not know whether these injuries played any role in the resuscitation but none of the CPR related injuries in the pilot study was considered by the pathologist to be the cause of death. Haemodynamic consequences due to some of the injuries in the later multicentre trial study is of course possible as the amount of bleeding from liver injuries varied from 0 to 500ml, tamponades with blood ranging from 50ml to 800ml and patients

with haemothorax had bleedings from 25 to 700ml. A thorough analysis of these injuries by a forensic expert, blinded to treatment given, gave that all large tamponades must be considered as part of the primary cause of death and not caused by CPR and none of the CPR-related injuries was considered life threatening. There were two patients with severe but not life-threatening injuries. Both of them treated with the LUCAS™ device. Ruptures of the heart have been reported to occur due to CPR but this has been questioned by several studies stating that the ruptures probably are occurring prior to CPR [9, 161-163]. In this study we did not have any cardiac ruptures due to CPR. The tamponades in this study were either from cardiac ruptures due to myocardial infarcts or aortic dissections with pericardial tamponades.

Do changes in guidelines affect the incidence of injuries?
One observation is the difference in the incidence of injuries between the first and second study as presented in Table 13.

Table 17. *Comparison of differences in incidence of injuries between Paper I and Paper IV.*

CPR	**L-CPR**			**M-CPR**		
	Pilot study	LINC autopsy	Difference between the studies, %	Pilot study	LINC autopsy	Difference between the studies, %
Any injuries	57.9%	92.8%	34.9%	44.7%	78.3%	33.6%
Any rib fractures	47.4%	78.8%	31.4%	31.9%	64.6%	32.7%
Multiple rib fractures	44.7%	65.0%	20.3%	27.7%	57.3%	29.6%
Sternal fractures	29.0%	58.3%	29.3%	21.3%	54.2%	32.9%

There is a general increase in injuries from the first to the second safety study. Why?

There are several possible explanations for this increase. One could be that the changes in the European guidelines during these years have changed the way CPR has been conducted. In the first study, manual CPR was conducted according to the guidelines from 2000 and in the latter study the guidelines from 2005 were used [24, 137]. The changes made to the guidelines in 2005 have been shown to shorten the time without active chest compressions in CPR [152]. This could in turn mean that the total number of compressions has increased and that numbers of compressions have an impact on rib and sternal fractures. There is no evidence that the subsequent increase in fractures due to the changes in the guidelines have affected CPR outcomes in any negative way because most of the studies looking at survival have pre-

sented higher survival rates or unchanged figures when comparing the years before and after 2005 [153-157].

One other explanation could be that bystanders and rescuers could have had the new 2010 recommendations in mind, whereas the multicentre trial was designed to adhere to the 2005 guidelines [158]. In the 2010 guidelines, the recommendation was to add 1 cm in depth of compression compared to those earlier guidelines. If this were true our results would indirectly confirm the findings in the study by Ruben and Johansen and Hellevuo et al. showing a correlation between increased depth of chest compressions and increased number of injuries [119, 120].

These possible explanations are merely speculations because of the fact that we were not able to measure the depth of chest compressions in any of our studies. Therefore we do not know if the intended depth of CPR by manual chest compressions or the LUCAS™ device was reached.

One interesting fact is that we have seen an increase in bystander CPR of approximately 21% in the L-CPR group and 8% in the M-CPR group when comparing the two studies. This increase might also have contributed to the increasing trend of injuries.

Efficacy of the LUCAS™ device

The results from Paper II show no difference between the two methods in terms of early survival and the numbers of patients hospitalised alive and still alive after one month were well in line with numbers from the Swedish national CPR registry of out-of-hospital cardiac arrests [27]. In experimental settings, the LUCAS™ device had proved to be beneficial in CPR but prior to our pilot study only Axelsson et al. had published results from a clinical setting. Axelsson et al. had higher numbers of patients hospitalised alive compared to our study but the exclusion of all unwitnessed cardiac arrests could probably explain this difference [60]. They also found no advantages in using the LUCAS™ device compared to manual chest compressions although in a two tier system with a median delay of 10 minutes from cardiac arrest to start of CPR by basic life support (BLS) units, a subsequent delay of about 2 minutes before start of CPR by advanced life support (ALS) units and another 6 minute delay before the start of the LUCAS™ device. This was to some extent a limitation and therefore our LUCAS pilot study looking at efficacy was designed with a first tier system and the LUCAS™ device was brought to all patients with suspected cardiac arrest, chest pain and breathing problems. Despite the change in design the time from cardiac arrest to start of CPR by ambulance personnel was in mean 10.4 minutes and it took almost 3 minutes before the start of the LUCAS™ device.

This trial was designed not only to evaluate mechanical chest compressions but also to evaluate a concept with mechanical chest compressions including defibrillation during on-going CPR compared to standard CPR.

In this pilot study we had no per protocol analysis and some of the patients in the study had been without circulation for a rather extended time period, which of course affected overall mortality in the study.

While conducting this feasibility study we learned that training and re-training of personnel was important, even though there had been studies showing that, despite similar training, the handling of mechanical devices could vary and that a learning curve could exist [60, 159-160].

We know that CPR is not without complications but the only way to avoid the complications is either to skip CPR entirely or to perform CPR in such a feeble way that it becomes worthless. Both of these alternatives would give the patient a zero chance of survival. Nevertheless, the desperate measures taken to save lives have the potential of harm.

Limitations

There are several limitations in this thesis but some of them are linked to the nature of the studies included. The first two studies were pilots and as feasibility studies they had a somewhat low inclusion number, which of course affected the power of these studies. To secure a sufficient number of patients in the autopsy pilot study we included in-hospital patients and this could be a limitation but this was done to secure a minimum number of patients.

The selection of patients is also a limitation as the majority of patients not surviving their cardiac arrest were not subjected to an autopsy. We were only able to randomize to the method of CPR and not on whom to perform an autopsy.

In the multicentre study there were a higher proportion of patients who had been treated with the LUCAS™ device. There are two possible explanations. Firstly, despite repeated information, there was a tendency among admitting physicians to think of the autopsy trial as a LUCAS autopsy trial. Secondly, it might be easier to remember to bring up the question of autopsy with relatives if there had been a mechanical device performing chest compressions when the patient arrived at the hospital.

In the autopsy studies it would have been interesting to be able to detect the frequency and depth of compressions. This thesis presents numbers of injuries due to modern CPR but in reality we do not know how the CPR was performed and whether there actually were any differences in the total numbers of compressions. As there are indications that there is a correlation between depth of compressions and number of rib fractures, it would also be interesting to see if we could have confirmed this.

Another limitation is that all patients received standard CPR prior to the start of LUCAS™ but we could not, ethically, defend a design where patients randomized to CPR with the LUCAS™ device would not receive CPR during the first 2 to 3 critical minutes of the resuscitation. We also know that in some cases bystander CPR was performed in suboptimal conditions (soft mattresses without stiff back plates) and this could also have influenced the incidence of injuries.

One other limitation was that the pathologists were not blinded. Due to skin marks and charts mentioning the mode of CPR it was impossible to blind them. There were a total of 40 different pathologists/forensic experts involved in the second autopsy study, which could also be considered a limitation, but in many cases at least two of them worked together to ensure the most thorough autopsy possible.

In Paper III we were not able to map the fractures found at autopsy and therefore we do not know whether the two methods found the same fractures.

Conclusions

There is no difference in early survival when comparing CPR with the LUCAS™ device, including defibrillations during on-going CPR, with manual chest compressions in out-of-hospital cardiac arrests.

In patients with unsuccessful CPR after out-of-hospital cardiac arrests, chest compression related injuries found at autopsy are frequent and were more common in patients after L-CPR. Rib fractures were found more often after L-CPR although no differences were found in the median number of rib fractures or number of sternal fractures and other less frequently observed injuries compared to the group treated with M-CPR. No CPR related injuries were considered life threatening by forensic experts.

CT and autopsy correlate closely in discriminating patients with any rib fractures from patients with no rib fractures. However, there is less concurrence in finding the same amount of rib fractures. Other injuries also do not have the same strong correlation.

Future perspectives

In the field of cardiopulmonary resuscitation there has been a shift in focus towards the importance of correct chest compression. Mechanical devices have the theoretical advantage of a defined number of compressions/minute. Automated mechanical devices like the LUCAS™ device are also designed to produce the same depth in every compression. This is certainly appealing but it is important to clarify whether the CPR given by the device is effective and safe for the patient. We have presented results that give us no indications of an increased risk of life threatening injuries with the LUCAS™ device. In combination with the results from the LINC trial, we will hopefully shed more light on the opportunity for the LUCAS™ device to be an effective and safe aid in modern CPR.

One could argue that it might be beneficial to conduct a CT scan to the head and trunk of all patients with ROSC prior to their admission to the ICU. The CT scan of the brain would reveal possible early negative prognostic factors and the investigation of the thorax and abdomen would reveal possible large bleedings that might require treatment. However, it would be a difficult task to handle these injuries as cooling the patients would also be a priority and we know that hypothermia affects the chances of effective coagulation. It would also be interesting to gather the results from the CT examinations in a large database were it might be possible to detect changes in the incidence of life threatening injuries after changes in CPR guidelines.

Due to the declining frequency of autopsies it has become more difficult to conduct studies to compare the incidence of injuries after unsuccessful CPR. We have presented results that tell us that CT alone cannot replace the autopsy but could be a valuable asset in finding rib fractures. It is important to try to understand the mechanisms behind injuries from CPR, and also to try to evaluate the clinical effect of the injuries: did the injuries lower the chances of a return of spontaneous circulation and long-term survival? The addition of CT and potentially also MRI to the autopsy could give extra information that might help us understand the dynamics of the injuries.

In the future it would be appropriate to conduct studies where we measure depth and the possible pauses of chest compressions and compare the LUCAS™ device with manual chest compressions in a clinical setting. This

could give us an indication whether the depth and/or the percentage of total time of chest compressions in cardiopulmonary resuscitation could be factors influencing efficacy and/or the degree of injuries. In connection to this it would also be interesting to try to locate where chest compressions have been performed on the chest in order to see how different positions might affect the efficacy and safety of CPR.

It would also be important to map the rib fractures during autopsy and compare them with results from CT to see if the two methods are detecting the same fractures.

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