Reporting and improving quality of cardiopulmonary resuscitation (CPR) during out of hospital cardiac arrest.

Thesis for the degree PhD for cand.med. Jo Kramer-Johansen

2007

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Ullevål University Hospital,
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Series of dissertations submitted to the
Faculty of Medicine, University of Oslo
No. 518

ISBN 978-82-8072-865-4

Cover: Inger Sandved Anfinsen.
Printed in Norway: AiT e-dit AS, Oslo, 2007.

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Til Jesper og Jørgen

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Acknowledgements

First, I like to thank my supervisors, Petter Andreas Steen and Lars Wik, who invited me into their unique collaboration and gave me the opportunity to experience a wonderful time at the Institute and really get absorbed in this exciting and clinically relevant field. In their very own way, both have supported me and been available for questions, opinions, and discussions at all times. Their enthusiasm is commendable and their network of contacts impressive – both these qualities are so valuable for anyone entering the field of science.

Over the last few years our group has expanded, and everyone has added their flavour and improved the stew. Elizabeth Dorph was here when I started, a great room-mate and inspiration. Kjetil Sunde soon came back to our group, filled with energy and new ideas. He deserves extra thanks for his supportive role when I first applied for my scholarship. Morten Pytte, my new room-mate, has an impressive capacity and is always a pleasant co-worker. Ann-Elin Tomlinson added her clinical touch to the group. Silje Ødegaard is only in the very start of her career, but with a very steep learning curve. Theresa Olasveengen, a brilliant researcher. Tonje Lorém and Trine Staff, both recent additions to our group, and already an integral part of our discussions.

I must also present my thanks to the staff at the Institute; the director Ole M. Sejersted and all the staff; scientific, administrative, technical, and in the animal department. Likewise, I would like to thank the heads of the dept. of anaesthesia (in rapid succession; Mariann Forsman, Johan Ræder, Terje Dybvik, and Kristin Sem Thagaard) for taking me in, training me, letting me have the time to finish this project, and hopefully, for taking me back in.

The Norwegian Air Ambulance Foundation is becoming the largest contributor in research in emergency medicine in Norway, and I am proud to be among their protégées. The efforts by Medical Director Jan Erik Nilsen to professionalize the medical part of the organisation combined with his generosity both personally and professionally are a great asset to the organisation.

Laerdal Medical has supported research in emergency medicine all over the world, and the personal commitment to improve survival after accidents and sudden death traces all the way to the top of the company; to Tore Lærdal and the Lærdal family. They have managed to recruit the best engineers in close competition with the petrochemical industry, based on this commitment. In the dept. of research and development, I have met these engineers. Without them, there would have been no project to present in this thesis. Helge

Myklebust has been the Laerdal connection in the work presented, but numerous talented people have sweated for this project.

Sweating is also what the paramedics and local coordinators in Akershus, Stockholm, and London have been doing. Without their efforts and good will, there would have been no data. During the last 5 years, I have also had the good fortune of working in the ambulance service in Oslo, and I will thank all the personnel for inspiring discussions and valuable experience. A special thank to medical director Anne-Cathrine Næss.

Last but not the least; I must thank my family for their patience and support. I hope they will remember the benefits of flexible hours and socially acceptable weekends and forget and forgive any frustrations and absentmindedness.

The present work was carried out at the Institute for Experimental Medical Research, Ullevål University Hospital, University of Oslo, Norway, during the years 2003-2007. A full time ph.d. scholarship and expenses were kindly provided by the Norwegian Air Ambulance Foundation.

Oslo, June 2007

Jo Kramer-Johansen

List of abbreviations

A	Asystole; electrical standstill of the heart, verified with an iso-electric ECG.
A-CPR	Advanced CPR; CPR with addition of drug administration, endotracheal intubation and defibrillation.
AED	Automatic external defibrillator; an externally applied defibrillator with software that automatically analyzes whether a shock is appropriate.
ALS	Advanced Life Support; A-CPR
B-CPR	Bystander CPR
BLS	Basic Life support; CPR with chest compressions and ventilation only.
CI	Confidence Interval; a measurement of the precision of the midpoint estimates; the 95 % CI of a mean marks the interval where a calculation of the mean from several samples of the population would be found 95 % of the times.
CPR	Cardiopulmonary resuscitation
D-CPR	Bystander or first responder CPR with the additional capacity of defibrillation using an AED.
EMS	Emergency Medical System; usually consists of a call centre (1-1-3 in Norway) with a dispatch unit and several first-responder units and ambulances, and even more advanced resources.
IHCA	In-hospital cardiac arrest
OOHCA	Out-of-hospital cardiac arrest
PEA	Pulseless Electrical Activity; organized rhythm visible on the ECG, but no palpable pulsations.
PCI	Percutaneous Coronary Intervention, the radiological procedure of visualisation of the coronary arteries and subsequent interventions to re-open these arteries.
ROSC	Return of spontaneous circulation
VAM	Voice Advisory Manikin; a manikin for CPR training that measures performance and provides automated feedback (verbal and visual) via an attached computer.

List of Papers

The thesis and the included original papers are based upon research at the Institute for Experimental Medical Research at Ullevål University Hospital, University of Oslo. The papers are referred to with roman numerals in the text:

I:

Quality of cardiopulmonary resuscitation during out-of-hospital cardiac arrest,
Wik,L.; Kramer-Johansen,J.; Myklebust,H.; Sørebø,H.; Svensson,L.; Fellows,B.; Steen,P.A. JAMA 2005;293:299-304.

II:

Quality of out-of-hospital cardiopulmonary resuscitation with real time automated feedback: Prospective interventional study,
Kramer-Johansen,J.; Myklebust,H.; Wik,L.; Fellows,B.; Svensson,L.; Sørebø,H.; Steen,P.A. Resuscitation 2006;71:283-92.

III:

Advanced cardiac life support before and after tracheal intubation-direct measurements of quality,
Kramer-Johansen,J.; Wik,L.; Steen,P.A. Resuscitation 2005;68:61-9.

IV:

Pauses in chest compression and inappropriate shocks; a comparison of manual and semi-automatic defibrillation attempts,
Kramer-Johansen,J.; Edelson,D.P; Abella,B.S.; Becker,L.B.; Wik,L.; Steen, P.A. Resuscitation 2007;73:212-20

Introduction

Background

Sustained life depends on circulation of oxygenated blood to the vital organs of the body. In daily life we rely on the heart to circulate blood, with sufficient oxygen transport capacity in the form of erythrocytes, and the lungs to provide gas exchange. In some circumstances and for limited periods of time, technical devices can replace one or more of these essential functions; e.g. during open heart surgery a heart-lung-machine temporarily oxygenates and circulates blood allowing the surgeons the luxury of operating on a motionless heart.

The Norwegian legal definition of death is described in relation to the Transplantation and Autopsy Act from 1977:

> *Certain signs of total destruction of the brain defined as complete and irreversible loss of function in Cerebrum, Cerebellum, and Medulla Oblongata.*

It is thus not the absence of heartbeat or breathing that defines death, although the permanent absences of these are the most commonly used criteria for death and if left untreated, these conditions invariably cause loss of all functions associated with life. Cardiopulmonary resuscitation (CPR) is the provision of circulation and ventilation by artificial efforts to postpone or avoid irreversible brain destruction. The cause of cardiopulmonary arrest can in some instances be reversed and to uphold oxygen transport to the vital organs in the meantime is decisive but not always sufficient to save lives.

The practical application of a combination of external chest compressions and artificial ventilation is attributed to the inspired collaboration of Kouwenhoven, Knickerboker and the legendary Peter Safar. They all admitted to have stood on the shoulders of others and records of resuscitation of victims of drowning and Chloroform anaesthesia go back for centuries. From the time of their first publications the recommendations of how to perform these tasks have been periodically published with increasing detail and scientific foundation. International collaboration to collect and evaluate scientific evidence and joint publications of guidelines for a uniform performance across the world was initiated in the 1970's and its latest effort is the present consensus on science and treatment recommendations.[1-3]

The international guidelines summarize the knowledge and give recommendations on how to perform the different skills of CPR:

- Chest compressions.
- Ventilations.
- Interventions such as defibrillation, intubation, *i.v.* access, and medication.
- The relationships between all these efforts, i.e. pattern.

We know from animal experiments and human experience that how we perform these tasks affects systemic and coronary blood flow and outcome. However, until recently we have not been able to control or monitor the performance of these skills during real episodes of cardiac arrest, and we have reason to believe that performance on manikins in a training environment is dramatically different from real life. The advent of new monitoring devices has been the directly initiating event for this project. Our resuscitation research group led by Prof. Petter Andreas Steen has been involved in this project for more than ten years and I too, recognise the shoulders on which this thesis stands; mainly those of Lars Wik, Kjetil Sunde and Elizabeth Dorph.

Outline of the thesis

In the present thesis I seek to understand how the guidelines for CPR are implemented clinically and if the quality of CPR can be improved by applying automated feedback on actual performance.

The first part of this thesis describes our experiences from monitoring the quality of CPR performance and how automated feedback influenced it in three ambulance services in Europe (clinical papers I-IV). In the second part I explore these findings and argue that monitoring and reporting quality of CPR must be standardized and included in any comparative study of resuscitation.

The progress of science is fast, and some recommendations that derive from the findings in our clinical papers are already implemented in current guidelines. At the time of our studies training and treatment protocols were based on the 2000 version of the guidelines.[4,5]

Summary of included papers

The following section summarizes the four papers included in the thesis and elaborates on some aspects of background, methods and results from these. Finally, a discussion of the implications of the current work is presented.

Background

Why does survival after cardiac arrest remain so poor? Numerous experimental and clinical studies indicate that quality of CPR influences hemodynamics and outcomes.[3] Additional predictors of outcome are peri-arrest events such as witnessed arrest, bystander CPR, response time, initial rhythm, and time to defibrillation.[6-8] Factors during in-hospital treatment after ROSC include protocols of systematic intensive care treatment with percutaneous coronary intervention (PCI) if indicated, and therapeutic hypothermia.[9-13]

Quality of bystander CPR is reported to influence survival.[14-16] The limitation of these studies was that quality of B-CPR was only assessed after arrival of the ambulance and only crudely scored by palpation of pulsations during chest compressions and observation of chest rise during inflations. During in-hospital resuscitation attempts with invasive blood pressure measurements a relationship between arterio-venous pressure gradient and short-term survival has been found.[17] Invasive monitoring is not feasible during routine out-of-hospital CPR and a non-invasive, robust, and objective tool to measure performance was needed.

Sunde *et al.* used the memory module of standard defibrillators and found some estimates of quality by examining the noise artefacts on the ECG tracings.[18] Their findings of long chest compression pauses and highly variable and often inadequate chest compression rates have been confirmed by other groups.[19,20] A prototype defibrillator was developed by Laerdal Medical. This defibrillator used an additional chest compression pad fitted with an accelerometer to characterize chest compressions and had an extra memory card to allow for downloading and reviewing the events electronically off-line.

In CPR performance studies on recording manikins automated feedback had impressive effects.[21-23] The number of compressions with target compression depth increased from 32 to 92 % with the introduction of automated feedback and even after 6 months reactivation of skills with automated feedback improved the same percentage from 46 to 81 %.[22]

We wanted to study the effects of similar automated feedback in a clinical setting. We hypothesized that such feedback would improve performance, and that the experience from

episodes with feedback could "spill over" with increased awareness of quality factors also in episodes without feedback. We therefore decided against randomization and for a sequential study design; first determining baseline quality of CPR without feedback (baseline phase) [I] followed by a period with automated feedback to the rescuers (feedback phase) [II].

The many tasks required during clinical advanced life support (ALS) add complexity to the situation and might divert attention from the performance of chest compressions and ventilations.[24,25] Most interventions should be performed at the start of a resuscitation episode, and we therefore planned to compare CPR quality the first five minutes to the remainder of the episode to assess whether interventions in general would jeopardize CPR quality. In addition, we studied the quality of CPR before and after intubation as a protected airway should allow continuous chest compressions without pauses for ventilations [III], and the effect of semi-automatic versus manual use of defibrillators [IV].

AEDs have made early defibrillation possible for lay-rescuers as well as professional first-responders and are also used by some during ALS. In animal studies[26] and retrospective analyses of human ECG data,[27] a longer delay from last chest compression decreases the chances for ROSC after a defibrillation. The pause induced by rhythm analysis and voice prompts by AEDs varies between different defibrillators,[28] whereas manual defibrillators should enable shorter pauses in chest compressions with a possible downside of more inaccurate ECG analysis.

These are certainly not the only conceivable factors influencing quality of CPR, and further investigations in our group will elaborate possible effects of attitudes and motivation, the effect of omitting administration of *i.v.* medications, and the effect of different policies towards end-of-treatment decisions.

Methods

Design and setting

All included papers are from a multi-centre intervention study conducted in the ambulance services of Akershus (Lørenskog, Asker and Bærum stations), Stockholm (Södermalm station), and London (NW sector, Fulham station). The collaboration also included in-hospital sites at Chicago University Hospitals in USA and at Allgemeine Krankenhaus, Medical University of Vienna, Austria. The collaboration was led by P.A. Steen in Oslo.

He was principal investigator for the out-of-hospital sites. L. B. Becker and F. Sterz were principle investigators for the in-hospital sites of Chicago and Vienna, respectively.

All patients with cardiac arrest that were treated with the experimental defibrillator in the three ambulance services were included. Patients younger than 18 years were excluded because the feedback system would not adjust for differences in size. No attempt to exclude patients with a non-cardiac or even a traumatic cause of cardiac arrest was made, as the primary endpoint was quality of CPR. Rates of ROSC and survival to hospital admittance and discharge were studied as secondary outcomes without power analysis as a standard requirement of CPR research.[29,30]

Six experimental defibrillators were deployed in each service and served as the primary defibrillator in ambulances dispatched to cardiac arrests. In Akershus and London a one tiered system responded to cardiac arrests with at least two ambulances. Each unit was manned with two persons of whom at least one was trained and certified in advanced life support including defibrillation, *i.v.* medications, and endotracheal intubation. In Stockholm the first tier consisted of two ambulance personnel with training in basic life support measures and a second tier with a nurse anaesthetist. The experimental defibrillator was dispatched with the first tier. The dispatch of the two tiers was simultaneous and they usually arrived at the same time. There were also differences in treatment protocols; in Akershus they were trained to provide three minutes of chest compressions before the first defibrillation attempt, and in London their standing orders were to transport the victims to the nearest hospital if initial resuscitation attempts were unsuccessful. The yearly demographics of the three ambulance services with regard to cardiac arrests are presented in table 1 of paper I.

We also collected data from in-hospital cardiac arrests that occurred outside the ICU and operating theatre at the University of Chicago Hospitals [IV]. The prototype defibrillator was dispatched along with the cardiac arrest team. The team leaders were residents of general internal medicine in a one-month cardiology rotation, and the rest of the team consisted of nurses, respiratory therapist and medical students, all trained and certified in advanced cardiac life support (ACLS) or basic life support (BLS) (nurses and medical students). The in-hospital teams and the ambulances in Akershus used the defibrillator in manual mode. In Stockholm and London the defibrillators default start-up mode was semi-automatic with the ECG-waveforms visible on the LCD-screen.

Technology and measurements

The common tool in these studies was the prototype defibrillator Heartstart 4000SP, developed by the section of Research and Development at Laerdal Medical in Stavanger in collaboration with Philips Medical (Andover, MA, USA) that provided the original defibrillators (Heartstart 4000). The work was led by Helge Myklebust. The automated feedback system was based on a manikin based feedback system developed at Laerdal Medical for research purposes. The defibrillators were approved for investigational use in Europe by DNV (CE-mark; 2002-OSL-MDD-0009) and in the US by FDA (IDE# G020121).

The original functions and specifications of the Heartstart 4000 biphasic defibrillator were left unchanged and included the possibility to choose manual or semi-automatic programs as the default start-up, and biphasic truncated exponential waveform with impedance-adjusted non-escalating energy output (150J).

The essential new feature of these research defibrillators was the addition of an extra chest compression pad to be placed between the rescuer's hands and the sternum of the patient. The chest sensors were fitted with an accelerometer (ADXL202e, Analog Devices, USA) and a pressure sensor (22PCCFBG6, Honeywell, USA). A similar accelerometer was mounted within the defibrillator housing to allow for cancelling out vertical movement of the supporting surface. This setup was validated in a manikin setup, and the error in depth estimation by double integration of the accelerometer signal was found to be less than ±1.6 mm.[31] The signal from the force transducer originally served as a trigger (2 kg force) to start and stop the integration process and to assure that decompression was complete so each new compression would start on a zero depth. In a third phase of the project the force transducers in all chest pads were replaced with more accurate ones (HBM DF2S-LAD, HBM, Darmstadt, Germany) to allow for calculation of the force-depth relationship.[32] The defibrillators were fitted with an extra LCD screen and storage capabilities to store not only ECG, defibrillator events and time-line in the standard storage memory card, but also additional information from the extra sensors in an extra memory card. The sampling rate was enhanced to 500Hz, and amplitude resolution for all channels was improved for the purpose of this research project.

The integrations were done on-line but the results were only revealed to the rescuers in the second phase of the project [II] through graphs on the extra LCD-panel and automated verbal feedback. When data were analysed in retrospect a second detection algorithm for chest compression depth was used when there was insufficient force or noisy signals from

the force sensor. This could be the case when the rescuers' hands were not placed directly over the compression pad, but rather on the rims of the pad.

The double integration resulted in a continuous curve of chest compression deflection with time. This allowed for detection of maximum depth for each compression which was averaged for each time period studied, detection of compression rate by determining the average of the reciprocal time interval between two distinct parts of the compression depth-time curve for intervals less than 1.5 s (as discussed on page 38), and the calculation of compression part of duty cycle as discussed on page 42 and Figure 11. A chest compression pad deflection of less than 8 mm was regarded as non-significant and not included in chest compression count or calculations.

Figure 1

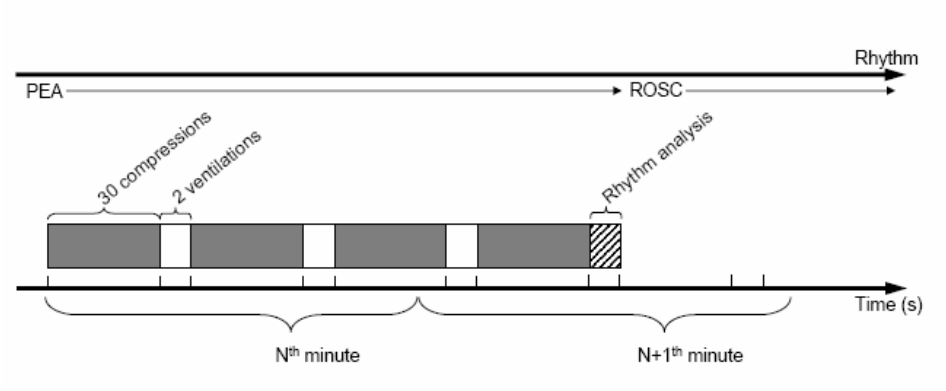

Figure 1 *shows an example of calculation of no-flow time. Time is represented along the X-axis and the upper line shows where the imagined change from a non-perfusing rhythm (PEA) changes to a pulse generating rhythm (ROSC). In the N^{th} minute we see 2 interruptions in chest compressions, for a total of ten seconds (NFT), resulting in a no-flow ratio (NFR) for this one-minute segment of 10s/60s=0.17. In the next minute ($N+1^{th}$) ROSC is detected after 40s, NFT is thus the time used for one ventilation pause (5s) and the rhythm check (5s) and NFR for this one-minute segment is 10s/40s=0.25. If the rhythm check is allowed according to the guidelines this time is subtracted for calculation of adjusted NFR (NFR_{adj}). This fraction is the potential for improvement of performance given the guidelines and defibrillators used. For the $N+1^{th}$ minute NFR_{adj} is 5s/40s=0.13. For the total two-minutes shown here the numbers will be:*
NFT = 20 s, NFR = 20s/100s = 0.20, NFT_{adj} = 15s, NFR_{adj} = 15s/100s = 0.15

The accumulated time without chest compressions in each episode was calculated by adding all intervals between two consecutive chest compressions longer than 1.5 s. Lack of

chest compressions is of course not a problem after ROSC. The available software did not allow for real-time detection of ROSC, and the rhythm and ROSC-status was evaluated retrospectively based on ambulance report forms and detection of QRS-related impedance changes.[33] The accumulated time without chest compressions when the cardiac rhythm was of a non-perfusing character (non-ROSC), was called no-flow time (NFT) to emphasize the consequences for the patient. This corresponds to the term hands-off time in manikin studies which emphasizes the rescuers potential for improving their performance. To facilitate comparison between episodes of different length, the NFT was divided by the total length of episode without ROSC and this ratio was called no-flow ratio (NFR). See Figure 1. During the feedback phase the LCD-panel showed the number of seconds since last chest compression and verbal prompts were given after specific numbers of seconds since the last chest compression.

Some NFT could be justified because of the needs for interventions such as rhythm analysis, defibrillation and pulse checks. To visualize the potential for rescuers' improvement we therefore calculated an adjusted NFT and NFR (NFT_{adj} and NFR_{adj}, respectively) where some time was deducted (from the numerator) for each intervention by a set of rules based on the guidelines recommendations, defibrillator specific times, and our own clinical experience with such required interventions.

Ventilation counts were estimated from typical changes in transthoracic impedance, as measured across the standard self-adhesive defibrillation pads by applying a near constant alternating current of 32 kHz. The impedance signal was further filtered by adaptive filtering. The information from the compression sensor (acceleration and force signals) was used to optimize the noise filtering.[34] The ventilations were automatically recognised and ventilation counts were reported for each time period studied. Maximum change in impedance and the inflation time as measured from the start of deflection to the maximum deflection were also registered. In the feedback phase the changes in transthoracic impedance were displayed on the LCD panel as a ventilation rate and a circle that was filled according to the magnitude of the impedance change. Automated verbal feedback was provided as described on page 15.

After collection of all raw data on a designated server, the data was electronically filtered, and downsampled from 500 to 50 Hz. The episodes could then be viewed and annotated in a custom-made computer program (SISTER studio, Laerdal Medical, Stavanger, Norway). All episodes were annotated automatically for chest compressions, pauses and ventilations, and then annotations for cardiac rhythm was added manually by

one of the medical researchers and one engineer with in-depth knowledge of the measurement technology. All annotations were checked for correctness and could be changed manually by one of the researchers before summary analysis of each episode.

The quality of CPR in each episode was summarized for the whole episode from the first recorded ECG-tracing (or first recorded chest compression) to the end of registrations or the end of active treatment. In cases without ROSC end of episode was defined as 10-20 s after the last recorded chest compression or defibrillation. In addition, CPR quality was summarized for the first five minutes of CPR, for the time before intubation, and the time after intubation if appropriate. Quality was also summarized for each one-minute segment of the episodes. Intubation was annotated in the episode based on written information from the rescuers and typical changes in compression:ventilation pattern.

In paper IV all defibrillation attempts were identified and classified as first, middle or last in a series of shocks, and the time intervals before, between and after shocks were registered. The human delay parts of these pauses were determined using the same rules as for NFT_{adj} described on page 14. (See also Figure 1, paper IV) In addition the pre-shock and post-shock rhythm were registered and the shocks were termed inappropriate if the pre-shock rhythm was not VF or VT, and successful if the rhythm 5 s after the shock was not VF or VT. Comparisons were made between manual and semi-automatic use of the defibrillators and secondarily between manual users in-hospital versus out-of-hospital.

Automated feedback

The rules for automated feedback were initially adapted from the "voice advisory manikin" (VAM)-software.[21] Additions and modifications were done to accommodate for differences in technology. Incomplete release was given a higher priority as this might not only be deleterious to the patient, but also jeopardize the depth measurements. (See on page 12). In addition, ventilation was measured based on changes in transthoracic impedance (in milliohms) and initially the grading of feedback on insufficient volumes was based on few experiments on healthy volunteers. The positive encouraging feedback, used during manikin practice, was removed from the software for fear that it would seem inappropriate during real resuscitation and for fear of feedback overload to the rescuers.

Partway into the feedback phase of the study, evaluation forms from the users and the results from the baseline phase [I] made us change the feedback software with more emphasis on no-flow time and less on ventilation volume grading. When originally designing the study, we had not realized that prolonged pauses not explained by guideline

required interventions would be a major problem, and feedback on this had been given low priority. Ventilation volume estimation was found to be too imprecise to be so heavily weighted in the feedback algorithm. The changes are summarized in table 1 in paper II.

During manikin practice, feedback had been given on pattern of compressions and ventilations based on whether endotracheal intubation was performed or not, and this feature was transferred into the defibrillators. The change in feedback rules was based on the pushing of the "intubation" button by the rescuers. However, this button was rarely used, and the consequences of leaving the feedback software in "unintubated" mode, was that only the first 15 compressions were evaluated until 2 ventilations were performed. This "error" was removed in the software revision so that all compressions and ventilations were available for real-time analysis and the feedback algorithm.

Figure 2

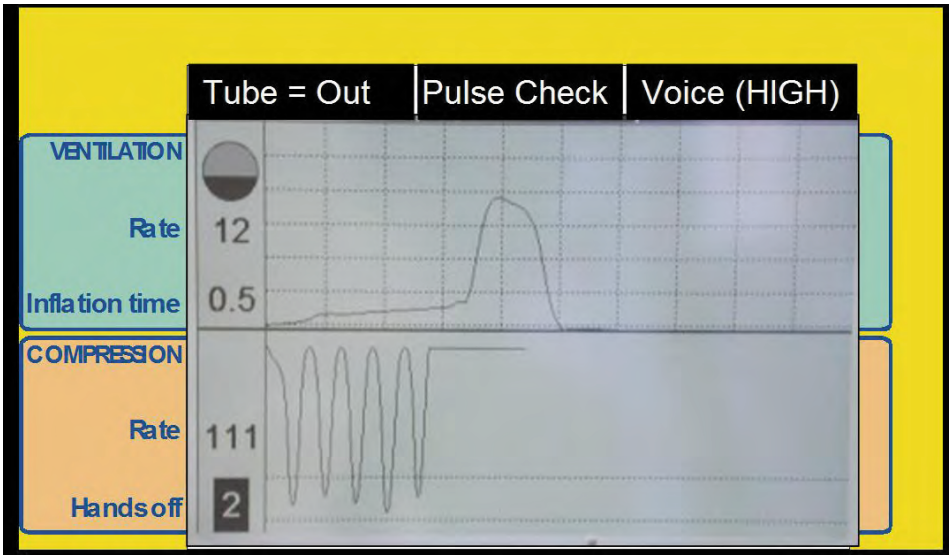

Figure 2 *shows a screenshot of the extra LCD-screen used for visual feedback which was activated during the second phase. The upper panel shows the impedance change tracing and the semi-filled circle according to a grading of the impedance change according to a target of 1.1 Ω (completely filled circle). The two numbers to the left are the ventilation rate determined form the last three ventilations (middle) and the inflation time for the last ventilation (bottom). The lower panel shows compression depth tracing, and to the left the current compression rate and the number of seconds from the last chest compression detected (highlighted).*

It is currently unknown what kind of feedback is needed to improve quality of clinical CPR. During manikin practice only verbal feedback was used, but during training of paramedics and medical students in CPR, many of the authors had also utilised the on-screen display of the VAM-software. To enable feedback regardless of background noise or if the user decided to silence the verbal feedback, this option was also included in the experimental defibrillators via an extra in-built LCD-panel. A screenshot of this panel is provided in Figure 2.

Statistics

The primary outcome in all the papers was quality of CPR. Secondarily, we analysed changes in outcome on an intention to treat basis in paper II, but the study was on purpose not powered to detect such changes. We also looked at adherence to guideline target values as an outcome [III].

Power analysis

Power analysis for the change in quality with introduction of automated feedback [II] was made with the software package Sample Power (ver. 2.0, SPSS Inc, Chicago, IL) based on effect of automated feedback in the manikin studies and the results from the baseline study. We wanted a power of more than 0.85 with an alpha of less than 0.05 to reject a null hypothesis of no difference if the real difference was less than 0.1 in no-flow-ratio or less than 4 mm chest compression depth. The baseline no-flow-ratio was 0.48 ± 0.18 and a reduction to 0.38 with similar variation would translate into a total of 211 patients (176 from baseline compared to 35 in the intervention group) and for an increase in chest compression depth from 34 ± 9 mm to within guidelines of 38 mm the power calculation prescribed a total of 246 (176 versus 70).

No power analysis was made for survival, but retrospectively to exclude a 50 % increase in survival to hospital admittance from 42/241 (17%) in the baseline period to 25% with a power of 0.85 and an alpha of 0.05 would have needed approximately 10 000 additional cases.

Statistical analysis

Data were collected and organized using a spreadsheet program (Excel 2003, Microsoft Corp., Redmond, WA) and statistical analyses were performed with SPSS for Windows (SPSS ver. 11.0 and 12.0, Chicago, IL).

For continuous data results are presented as mean with standard deviation (SD) or median with 25- and 75-percentiles depending on whether the data approximated a normal distribution. For comparisons mean differences with 95 % confidence intervals (CI) or medians with 95 % CI are presented. CI for medians are calculated using a normal approximation described by Altman.[35]

Testing for statistical significance was done with two-sided Student's t-test for independent samples or Mann-Whitney U-test as appropriate. When comparisons between quality in the first five minutes and the rest of the episode were done in paper I, and before and after intubation in paper III, each patient served as his/her own control and a paired t-test was applied. Proportions were tested with Chi-squares test with continuity correction or Fisher's exact test if expected number in any category was less than 5. Differences in proportions were also evaluated by univariate analysis with odds ratios (OR) with 95 % CI when possible.

Survival after cardiac arrest probably depends on several factors, summarized in the chain of survival[3] and described in retrospective analyses.[6-13] The factors described can be divided into;

- Patient factors such as age, gender, and co-morbidity.
- Peri-arrest factors such as cause, location, and initial rhythm.
- EMS/community factors such as bystander CPR, quality of bystander CPR, response intervals, and treatment algorithms.
- Post-resuscitation factors such as percutaneous coronary intervention (PCI) if appropriate, hypothermia, use of inotropes and circulation support, and intensive care in general.

There may be interdependence between several of these, such as bystander CPR and initial rhythm or response intervals and initial rhythm. To describe complex interactions on one outcome one can use a multiple regression, and when the outcome is dichotomous a logistic regression can be used to determine the relative importance between several determinants. It is important to notice that logistic regression is only descriptive and does not imply causality. It is however, a powerful tool to dig for relationships in data to find good questions for future studies.

We used a model of multiple logistic regressions in paper II where different measurements of CPR quality were entered into models of previously described predictors of short-time survival. Short-time survival was defined as admittance to hospital intensive

care unit or ward with spontaneous circulation. We used short-time survival as the dependent factor in this analysis, because we did not have information about in-hospital treatment which has been shown to influence on overall survival.[9,13]

Ethical issues

The studies were approved by the appropriate ethical boards at each site and registered as a clinical trail at http://www.clinicaltrials.gov/, (NCT00138996). The need for informed consent from each patient was waived in accordance with paragraph 26 of the Helsinki declaration for human medical research. The absolute condition for such research is that the subjects' physical/mental condition that prevents obtaining the informed consent is a necessary characteristic of the research population.[36] The ethical basis for this decision is firstly the assumption of altruism; an unselfish will to support research to improve future care for acute and serious illness of similar kind as the subject is currently suffering. Secondly, during acute and serious illness, the process of obtaining a fully informed consent is detrimental to the appropriate treatment and that during such circumstances the consent procedure could be considered as undue pressure to accept the investigation. The transfer of consent authority to relatives (if present) or bystanders is restricted by the same problem of undue pressure in addition to possible conflicting interests. There are inconsistent legal practices regarding representatives for adult patients under such circumstances in different countries.

In our study all patients were entered into the study based on these considerations. Informed consent cannot be obtained from a cardiac arrest victim before the interventions take place. In addition, the chance that the new interventions could be deleterious to the patients was remote; an extra chest pad fastened to the sternum with double adhesive tape, and, in the feedback phase [II and IV], the possibility that automated feedback could change performance of CPR. The possible (extra) emotional stress imposed on bystanders was not specifically addressed in the protocol, but the paramedics at the scene had the opportunity to turn the volume of verbal feedback down, switch to tonal feedback or to visual feedback on the LCD-panel only.

It could be critically argued that the patients were not the only study subjects, but also the involved ambulance personnel. It was their performance with and without automated feedback that was measured. The involved ambulance services decided on their participation on an organisational level which included discussions with the involved unions, but without formal consent process from each ambulance personnel. This may

influence data collection, as it is conceivable that an unwilling rescuer would be more reluctant to complete the process of collecting all necessary data. The cooperation of the ambulance personnel is indeed the crucial factor to succeed in this kind of research.

The publication of the first paper in JAMA [I], was extensively covered in news media internationally and in Norway. The coverage in the US media was based on the press release by JAMA/AP [37] and focused on the findings in the paper and the accompanying in-hospital study.[38] In contrast, the headline and ingress chosen by Aftenposten (major daily newspaper in Norway) was that inadequate CPR performed by paramedics killed 500 person per year in Norway.[39] Naturally, the paramedics involved in the study in Akershus (and elsewhere in Norway), were insulted and felt stabbed in the back. Quite a lot of work was required by the authors to regain the trust of the ambulance personnel to continue their participation in other on-going studies. A lesson learned for all about the dangers of popularisation of research findings.

Funding

The expenses for the development of research defibrillators and for the process of achieving CE-marking and FDA-approval for investigational purposes were covered by the two companies responsible for the development of the defibrillator; Laerdal Medical (Stavanger, Norway) and Philips Medical Systems (Andover, MA, USA). Furthermore, Laerdal Medical set up a data collection server, paid for additional training in the use of the custom defibrillators, and travel expenses.

The salaries for the researchers came from the Norwegian Air Ambulance Foundation (JKJ), Ullevål University Hospital, Division of Prehospital Emergency Medicine (PAS, HS and LW), University of Oslo (PAS) and the participating ambulance services (LS, RF). Helge Myklebust is a full-time employee of Laerdal Medical on a fixed salary. The American co-authors were paid by their respective hospitals. Furthermore, the projects were supported by unrestricted grants from the Regional Health Authorities East, Anders Jahre Foundation for Sciences and the Laerdal Foundation. None of the funding parties had any role in the interpretation of the data or the decision to publish.

Results

Paper I

In the baseline phase of the SISTER study 65/241 (27 %) episodes had insufficient data available for analysis of CPR quality. Two patients were wrongly included as they did not receive CPR. The main reasons for exclusion were failure to place the chest compression sensor (33/65) and technical problems (26/65). In addition, the technical quality precluded analysis of ventilation count in 13 episodes. The main result from the 176/241 (73 %) episodes was that CPR quality was generally poor, with long chest compression pauses between shallow chest compressions (Table 3, paper I). The only differences in quality between the first five minutes and the rest of the episode were a slightly longer No Flow Ratio when adjusted for required pauses (42 vs. 38 %) and fewer compressions actually given (60 vs. 64 per minute) during the first five minutes (Table 3, paper I).

Paper II

After introduction of automated visual and verbal feedback nine (8 %) of the 117 attempted resuscitated were excluded due to technical errors (5) and failure to attach the chest pad (4). The exclusion rate was significantly lower than in the first phase (OR for completeness of data 4.4 (95 % CI; 2.1, 9.2)). The number of episodes where ventilation count could be reliably estimated for the whole episode was similar (163/176 versus 98/108). Quality of CPR was improved for chest compression depth and rate, but NFR and NFR_{adj} was only marginally improved. Overall ventilation count per minute was similar in the baseline and feedback cohorts. This was as expected, since this measure had been close to target in the first phase. The fraction of one-minute segments with excessively high ventilation count was reduced from 10 % to 8 %. Though statistically significant, this slight improvement is unlikely to have a clinical impact.

When the two versions of feedback software were compared, we found an interesting improvement from version 1 to 2 for the more highly prioritized no flow time, apparently at the cost of poorer chest compression depth (Table 4, paper II).

Paper III

We were able to identify 119/176 episodes from the baseline cohort where we had reliable CPR quality recordings both before and after intubation. The reasons for exclusion were poor data quality (13), not intubated during the resuscitation (23) or intubated before

or within the first minute of chest compressions (17), and four cases of suspected unrecognized oesophageal intubation.

The quality increased after intubation when directly compared (Table 2, paper III), but not when CPR quality before and after intubation was compared to the target values of the international guidelines for unintubated and intubated patients (Table 1 and 3, paper III). After intubation, general quality was still too poor compared to what is needed to generate a good cardiac output.

We have repeated the analysis with the data from the feedback phase and the results are similar. Table 1 shows absolute measures of CPR quality and the figures shows frequency distributions of number of compressions per minute (Figure 3) and ventilations per minute (Figure 4) before and after intubation for one-minute segments.

An interesting observation was the possibility to detect failed intubation or misplaced endotracheal tubes by the absence of impedance changes (Figure 5, paper III). This could be of interest during out-of-hospital resuscitation as other methods of determining correct placement of an endotracheal tube are either very user dependent (visual inspection, auscultation), they require intended actions at several time points (rechecking tube placement after each repositioning of the patient), or they are based upon the level of CO_2 in exhaled air, which during low flow states such as during CPR, may be very low. Transthoracic impedance is on the other hand measured continuously by almost all defibrillators through the already present defibrillation pads.

Table 1

N=58	Before intubation	After intubation	Difference
Length of segment (s)	377 ± 245	1205 ± 540	
No flow time (s)	224 ± 176	401 ± 294	
NFR	0.57 ± 0.17	0.40 ± 0.17	-0.16 (-0.11, -0.21)*
Chest compressions			
Compressions per minute	48 ± 19	67 ± 20	19 (14, 25)*
Compression rate (min^{-1})	109 ± 13	111 ± 11	1 (-5, 2)
Compression depth (mm)	37 ± 7	38 ± 6	1 (-2, 1)
Ventilations per minute	6.3 ± 3.2	13 ± 3.7	6.5 (5.5, 7.6)*

Table 1 shows some summary CPR quality variables before and after intubation in the 58 episodes of the feedback phase where we had reliable quality registrations from at least one minute before intubation and after intubation. The asterisks (*) mark where a paired t-test for difference not equal to zero produced a $P<10^{-8}$.

Figure 3

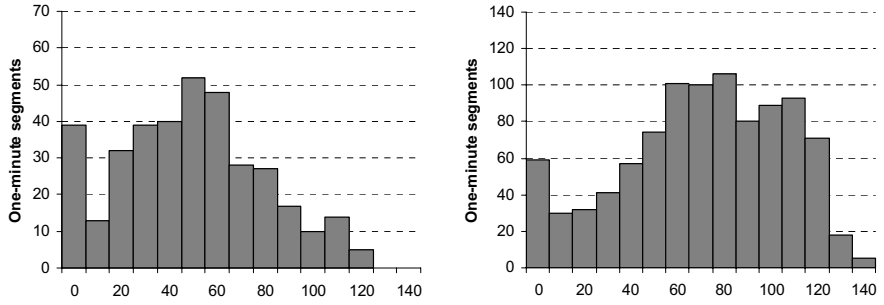

Figure 3 *shows the frequency distribution of number of compressions per one-minute segments before (left) and after (right) intubation in the 58 episodes where reliable quality registrations from both were available. The number of one-minute segments was 364 and 958, respectively.*

Figure 4

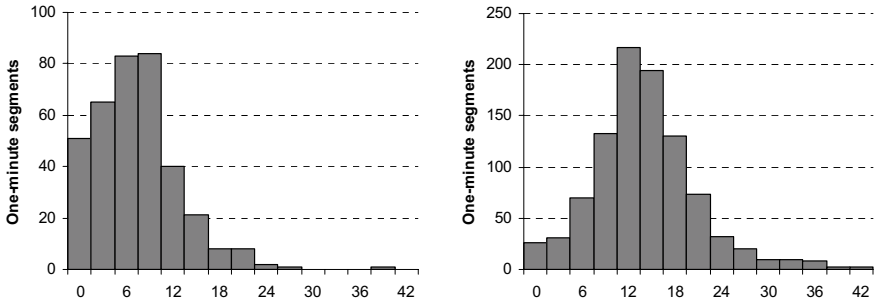

Figure 4 *shows the frequency distribution of number of ventilations per one-minute segments before (left) and after (right) intubation in the 58 episodes where reliable quality registrations from both were available. The number of one-minute segments was 364 and 958, respectively.*

Paper IV

We identified 1165 defibrillation attempts in a total of 223 episodes with at least one shock. There were 635 manual shocks and 530 AED-shocks, and the distribution of shocks per episode and the number of shocks given as first, middle or last in a series was similar in the two groups. Significantly more shocks were inappropriate in the Manual group with the highest rate in-hospital (Table 2, paper IV). In contrast, delays before, between, and after shocks were significantly shorter during manual use. Also the parts of the delays attributable to human factors were shorter in the manual group (Table 3, paper IV).

The successfulness of the shocks in the two groups was similar; in both groups VF/VT was terminated for more than 5 s after ~60 % of the shocks. However, there seemed to be a higher chance for more organized rhythms (PEA and ROSC) and a lower chance for asystole associated with manual defibrillation, OR for an organized rhythm after manual shock versus AED shock; 1.8 (95 % CI; 1.4, 2.4) (Table 2, paper IV).

Discussion

Together these four papers represent a first major effort to describe quality of CPR in detail with parallel papers from our collaborating partners from in-hospital resuscitation[38,40,41] and even CPR quality in a specialized emergency room environment[42] have been published. The data have been reused for secondary analysis of electrophysiology[43] and signal processing.[44,45] We have established a baseline dataset on how CPR is performed in the real world [I] and have tried to single out the effect of certain interventions both

practically [II] and theoretically [III and IV]. In addition, our understanding of the physics of chest compressions has improved,[32] and the importance of attitudes[46] and implementation have been highlighted.

I will first discuss some limitations of the current project and then some implications of the results. The final part of the discussion will be a recommendation including definitions to facilitate collection and reporting of CPR quality data for quality assurance purposes, for all clinical trials in resuscitation research, and for those of us who still think there is more knowledge to be gained by studying the relationship between specific quality measures and outcomes.

Limitations

The major concern when one wants to establish a cause effect relationship is the control group. The gold standard is the randomized study, where chance assigns subjects to intervention or control groups. Still, expectations of effect (or other subtle changes in behaviour) could influence both patients and researchers, and blinding is used to eliminate such bias. In double-blinded studies neither subjects studied nor the researcher(s) administering the intervention and evaluating the effect know whether the patient belong to the control or intervention group. Double-blinded randomized trials make determination of cause-effect relationships easier, as the two groups hopefully will be similar in all aspects other than the intervention. Such an approach was not possible in our project for several reasons. Firstly, feedback on quality of CPR to the rescuers was the intervention studied, and the rescuers could therefore not be blinded. The group assignment could have been kept from the researchers evaluating the collected data, but this would have delayed the results from the first phase by more than a year. Secondly, we have previously reported an extended effect of automated feedback to the next training sessions in manikin studies,[21-23] and in a randomized study, we feared a spill-over of skills into the control group.

We therefore chose a sequential approach. Prospectively planned studies with historical controls will not have the statistical strength of randomized studies, but all measures were taken to have the two cohorts as similar as possible, and by involving three different ambulance services the results should be more robust for generalization. The hypothesis of effect of automated feedback was prospectively determined, as were the sub analyses of the different interventions in paper III and IV. Any finding regarding CPR quality and the effect of automated feedback would have been potentially interesting to publish, and this

was also stated in the protocol. The study thus conformed with the requirements for studies without internal control described by Bailar.[47]

No-one in the ambulance services were informed about the results from the baseline phase before all data from the feedback phase had been collected. The awareness of being watched is by itself probably improving the quality,[48] and all involved personnel knew that we wanted to study quality of CPR from the start of phase one. However, the higher OR for completeness of data in phase two, predominantly due to higher adherence to protocol, *i.e.* placement of the extra chest pad, could either be due to increased familiarity with the equipment or indicate higher awareness of CPR quality in the second phase. The latter would be an indirect effect of the automated feedback in that the rescuers would want the feedback to be active, and not necessarily a confounding factor.

We cannot rule out the possibility that temporal trends influence the results. During the years 2002-2004 quality of CPR was not the hot topic it has since become, partly due to the present studies, and the ambulance services involved were operating with the same guidelines and local algorithms during the whole period.

A multi-centre study as this will also be vulnerable to changes in case-mix from the different sites. We found site-differences in quality and survival in the first phase and a relative change in proportions of episodes between the first and second phases. Site specific CPR quality data were not disclosed, and the changes were in the direction that the proportion of episodes from the site with better quality was smaller, underestimating the effect of automated feedback (Figure 5 and Figure 6). Some differences in CPR quality between sites may be due to different local protocols. Including sites with different protocols was an intention of the study, as this tends to make conclusions drawn from the results more general.

Figure 5

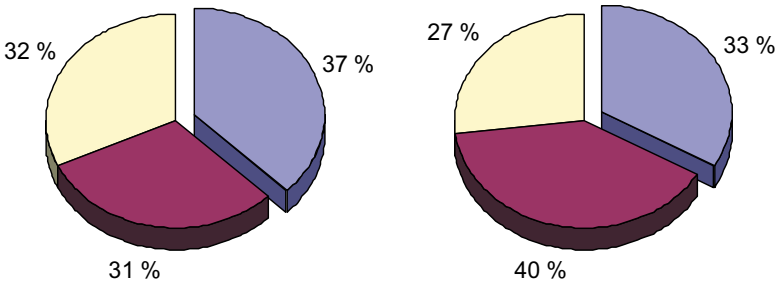

Figure 5 *shows the distribution of episodes included from each of the three sites in baseline phase (left) and feedback phase (right). The exploded slice of the pie represents the site with better quality during both baseline and feedback phase of the study. The change in distribution was not significant (P=0.3, Chi-square test).*

Figure 6

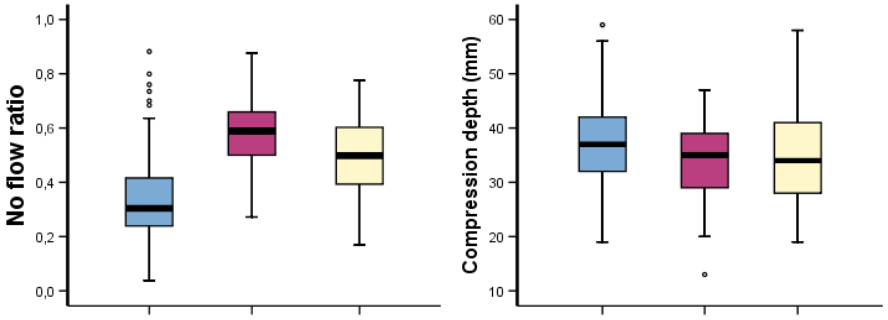

Figure 6 *shows overall quality of CPR during both phases for NFR (left) and Compression depth (right) for the three sites. The left site in both panels is the site with (slightly) better quality.*

CPR quality

We found overall poor quality of CPR. Pauses were long and frequent, and chest compressions were too shallow. Hyperventilation did not seem to be a major problem during out-of-hospital resuscitation in our material as has been reported by others.[38,49]

Chest compressions

Chest compression depth was less than guidelines recommendations, but improved significantly with automated feedback. In paper II the number of episodes with average compression depth within guidelines doubled. The increase in chest compression depth was lower after the second version of feedback software which gave higher priority to feedback on compression pauses was applied (Tables 3 and 4, paper II).

In addition, we found that chest compression depth whether expressed as average depth in the episode or as percentage of compressions within guidelines depth was associated with higher short term survival (Figure 1, paper II). To try to adjust for other known determinants of short time survival, we entered depth along with other CPR quality measures in a logistic regression model based on previous findings.[8] In this logistic regression approach we also found significantly increased odds for survival if the arrest was witnessed, in line with previous findings. In our model the other known factors such as response time, bystander CPR, and an initial rhythm of VF/VT did not achieve a level of significance, probably due to a limited number of cases or interactions. Interestingly, all these factors where found to be in the previously reported range in the unadjusted analysis, except for response time which in our analysis seemed unrelated to short time survival or even oppositely related. The explanation for this probably lays in site differences, where one site had shorter response times, but low rates of bystander CPR, poor quality of CPR and very low survival. The administration of adrenaline tended to be associated with poorer survival, similar to what was found in a large material from the Swedish cardiac arrest registry.[50] In this analysis we did not adjust for long episode duration which previously has been found to be associated with poorer survival and the number of medications given might be a surrogate for episode length.

There was no change in chest compression depth before and after intubation during the baseline period [III] or in the feedback material (Table 1 on page 23).

The chest compression rate was in the high acceptable range in the baseline phase [I], similar before and after intubation [III]. Automated feedback improved this quality measure to well within guideline targets [II]. Interestingly, the number of episodes with very high or very low chest compression rates was reduced, illustrated in the box plot in Figure 7.

Figure 7

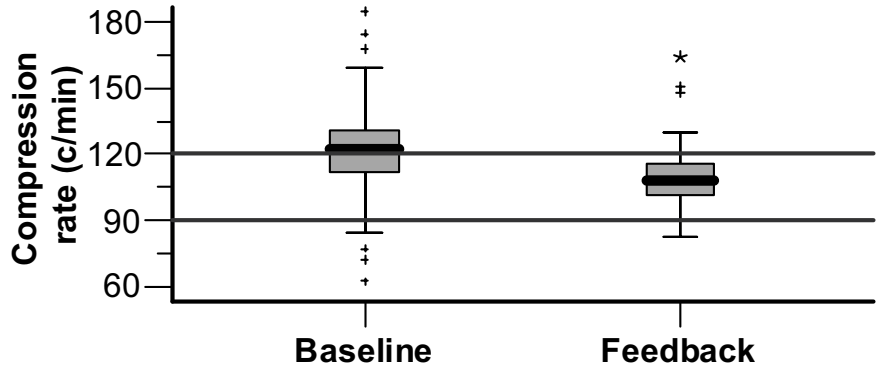

Figure 7 *shows a box plots of the distribution of average chest compression rates (min^{-1}) per episode in the baseline phase (left) and the feedback phase (right). The two horizontal lines show the limits for automated feedback (90 and 120 min^{-1}).*

The number of chest compressions actually delivered per minute did not change as this depends both on no flow ratio and compression rate which both were reduced.

Incomplete release was not a general problem in the baseline phase [I], and very little feedback was actually provided for such errors in the feedback phase [II], subsequently we did not find any changes in this measure. Only 277 (1.6 %) of more than 17 000 feedback prompts delivered during the 108 episodes of the second phase were for incomplete release even though this was the highest priority feedback for reasons of compression depth calculation (discussed on page 15). However, in some episodes incomplete release was a problem; 15/176 (9 %) in baseline phase and 7/108 (7 %) in the feedback phase had more than 10 % of the chest compressions with incomplete release (OR 0.7 (95 % CI; 0.3, 1.9), non-significant).

Similarly, chest compression duty cycle was remarkably constant, and did not change between the two phases. Only 97 (0.6 %) of more than 17 000 feedback prompts in phase two were for poor duty cycle. With the same technology duty cycle was 0.43 (95 % CI; 0.40, 0.45) during in-hospital CPR in Vienna[42] and 0.38 ± 0.07 in Chicago (D. Edelson, personal communication) even though the patients were compressed on a bed and not on the floor, a factor previously shown to reduce duty cycle during manikin practice.[51]

Ventilations

Overall, the number of ventilations per minute did not deviate from the recommendations [I], and after introduction of automated feedback the mean number of ventilations per

minute did not change [II]. Thus, we did not replicate the apparent finding of hyperventilation with a rate of 30 ± 3 per minute reported by Aufderheide *et al.*[49] They only reported the highest ventilation rate in a 16 s segment after intubation however, and such a short observation period may be misleading while the mean for the whole episode may disguise periods of hypo- or hyperventilation. When analysed by one-minute segments, we found a marked increase in mean ventilation rate after intubation, but the fraction of one-minute segments with ventilation rates above 20 min^{-1} were still only 20 % [II].

Figure 8

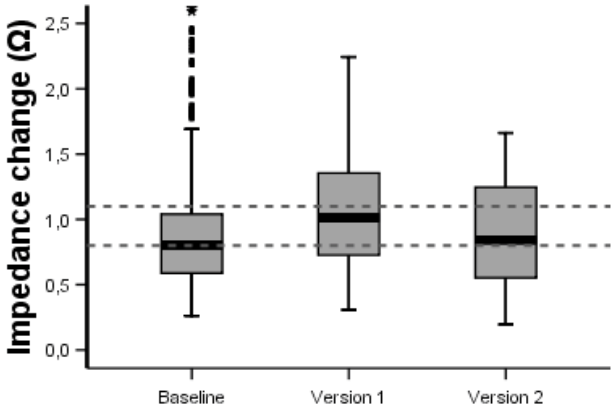

Figure 8 *shows the distribution of mean transthoracic impedance changes per ventilation in episodes from the baseline phase and from the feedback phase with the two versions of automated feedback (N=163, 61, and 37, respectively). The two dotted, horizontal lines mark the two levels of feedback used in version 1 (0.8 and 1.1 Ω). In version 2, feedback on ventilation volume was restricted to 0.8 Ω only.*

We were not able to analyse ventilation volumes and inspiration times reliably in all episodes, and as explained feedback was changed accordingly. Even so, we did find an increase in inspiration time from 0.8 ms ± 0.2 to 0.9 ms ± 0.2, $P<0.001$ from the baseline to the feedback phase. In contrast, impedance change as a surrogate for ventilation volume increased with the first version of feedback, but when feedback regarding ventilation was reduced from version 1 to 2 of the feedback software, the values changed back to baseline levels. (Figure 8) Longer inflation time and lower tidal volume have been associated with lower inspiratory airway pressure and less gastric inflation.[52]

Pauses and interventions

Without feedback there were no chest compressions nearly half the time when there was no spontaneous circulation, there were no chest compressions [I], and this fraction only improved when pauses were more aggressively addressed by changes in feedback software from only a tonal beep every 15 s without chest compressions to a tonal beep at 15 s followed by verbal prompts every 15 s thereafter [II].

Pauses in chest compressions that would be "necessary" according to the guidelines[5] for rhythm analyses, defibrillation attempts and possibly pulse checks could only explain a small fraction of the measured pauses. This "necessary" fraction of no-flow time was reduced in the feedback phase from median (25-, 75-percentiles) 0.08 (0.05, 0.12) to 0.06 (0.04, 0.09), P=0.02, Mann-Whitney U-test. Shorter mean episode length, slightly reduced fraction of episodes with VF as the initial rhythm, and fewer defibrillations per episode probably explains most of this difference.

Figure 9

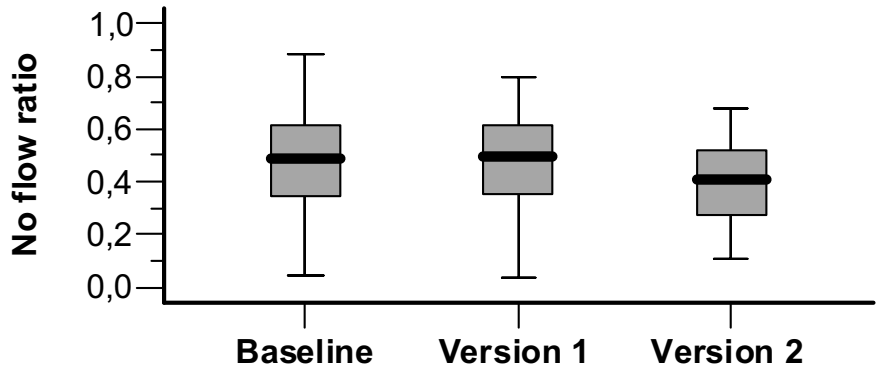

Figure 9 *shows the distribution of mean No-flow ratio in episodes from the baseline phase and from the feedback phase with the two versions of automated feedback (N=176, 69, and 39, respectively). Only the change from feedback version 1 to 2 was statistically significant (See table 4, paper II).*

Other interventions such as placement of *i.v.*-needle, medications and endotracheal intubation were thought to be most time consuming during the first minutes of resuscitation, but as described on page 21 the difference between no-flow ratio adjusted for rhythm analysis, defibrillation attempts and possibly pulse checks (NFR_{adj}) in the first 5 minutes and the rest of the episode was small [I]. This analysis was not published for the feedback material, but the differences were similar (Table 2). The reason for the small

differences in quality may be that the interventions we imagined should occur in the first 5 minutes actually did not occur until later in the episode, or that planned and intervention associated pauses in general only explains little of the poor quality observed. Supportive of the first explanation is the finding from paper III where less than half of the intubations occurred before five minutes.

Table 2

	First five minutes of CPR	Entire episode of CPR
No flow		
NFR	0.44 ± 0.19	0.44 ± 0.17
NFR_{adj}	0.38 ± 0.18	0.37 ± 16
Chest compressions		
Compressions per minute	64 ± 24	63 ± 21
Compression rate (min^{-1})	109 ± 14	109 ± 12
Compression depth (mm)	37 ± 7	37 ± 6
Ventilations per minute	9.3 ± 4.7	11 ± 4

Table 2 shows some quality measures for the first five minutes and the entire episode of CPR from the 108 episodes in the feedback phase. For ventilations the number of available episodes was 98. Numbers are presented as mean ± standard deviation. NFR; no-flow ratio, and NFR_{adj}; no-flow ratio adjusted for time "necessary" for rhythm analysis, defibrillation attempts, and pulse check, if appropriate. See text for explanations.

Before intubation we assumed that ventilations would generate much no flow time, as chest compressions are discontinued for two inflations with a bag-mask-valve device (or mouth-to-mouth/mask). In paper III we found a reduction of NFR of 0.20 from before intubation to after intubation, and similar findings are presented in Table 1 (on page 23) before and after intubation for the feedback cohort. If all this reduction in NFR was due to reduction in ventilation pauses, such pauses could be estimated to comprise one third of the mean 206 s of pause before intubation, or 69 s. The average length of episodes before intubation was 349 s, resulting in ~12 s per minute for ventilation pauses, not far from the recommended three ventilation pauses á 5 s. That leaves the remaining pause time of ~24 s per minute unexplained.

We were able to study the time delays associated with defibrillation attempts in two comparable groups using the same model of defibrillators in either manual or AED mode.

We found that manual mode resulted in shorter delays before, between and after the defibrillations and possibly a tendency towards more shocks resulting in an organized rhythm [IV]. This result was not adjusted for length of pre-shock pause which in another paper which studied only the first shock of every episode with manual defibrillation mode, was found to be inversely related to chance of VF termination.[40]

One fourth of the manual shocks were given without a shockable rhythm, and this fraction was even higher among residents during in-hospital resuscitation. Most inappropriate shocks were performed on an organized rhythm, mostly PEA, but luckily the resulting rhythm was the same after nearly 90 % of the inappropriate shocks, and there were no signs from circulation induced impedance changes that any inappropriate shock terminated a spontaneously circulating rhythm.

The results from this study support the changes in the current guidelines to give only single shocks, not up to three in a series.[1,2] If all shocks delivered as number two or more in a series were avoided, this would theoretically reduce the no-flow times associated with defibrillation by 70 % in episodes with VF as initial rhythm, and possibly reduce the number of inappropriate shocks by ~50 %. We showed that AEDs are better at recognising VF/VT than paramedics and even residents, and the risks of imposing more NFT and possibly electrically induced post-resuscitation myocardial dysfunction due to unnecessary shocks,[53,54] would favour a change to AED use in professional services as well. The pre shock pause of median 22 s (18, 28) induced by AEDs is not acceptable, however. Until the rhythm can be analysed during ongoing chest compressions, we suggest the use of an AED mode with chest compressions recommenced during defibrillator charging if this is allowed by the defibrillator and strict safety rules are applied.[55]

Further research

The major implications of our research are:

- We cannot trust CPR to be of uniform and good quality in any clinical trial.

On the contrary, we found CPR performance to be highly variable, and of such poor quality that in many instances it is likely that the blood flow generated was very small and inadequate to support the vital organs and to improve chances for a successful defibrillation. In an experimental study Pytte *et al.* showed no hemodynamic effects of peripherally administered adrenaline (epinephrine) when chest compressions depth was similar to the present findings and with compressions half the time.[56] A blood flow above a threshold may thus be needed to observe any effect of a drug.

This may indicate that most clinical drug trials should be redone with protocols that ensure uniform and good quality CPR which is adequately measured and reported.

- There is still more to learn from clinical studies of quality and outcomes, and this requires a reasonable consensus of definitions.
- Much research is needed to define an optimal automated feedback for use during clinical CPR. Different sites and settings may need different approaches.

Based on the present findings we hypothesise that the main reasons for no flow time during clinical CPR are not interventions or ventilations, but perhaps lack of understanding the priorities or just the overwhelming stress and difficult working conditions in the out-of-hospital cardiac arrest situation. To explore this further we probably need other methods than standard biomedical quantitative research methods. We need to explore why much scientific information is so poorly implemented, and for this we probably need to employ hermeneutic research tools and knowledge from quality improvement system strategies.

Mechanical chest compression devices

If the performance of professional rescuers is as poor as we have shown, why are not mechanical chest compression devices more successful than so far reported?[57-59] Even if chest compressions devices are considered an adjunct to manual CPR during out-of-hospital cardiac arrest, the situation where causal treatment cannot be provided on-scene occurs frequently. During transport and interventions in the radiology theatre (*i.e.* PCI), manual CPR may impose dangers to the rescuers and be ineffective for the victim.[60] Mechanical CPR may be a safer alternative to bridge pre-hospital and causal treatment.[57]

Currently no commercially available mechanical chest compression device possesses all the necessary qualities: The compressed air driven LUCAS® is easy to apply but noisy during operation. Questions have been raised about its safety for the rescuers due to the massive noise and the use of Oxygen as compressed gas source in most instances.[57] In the first clinical trial there was no survival benefit of the device.[61] More concerning, perhaps, is the reports of massive injuries seen in autopsy materials, even if the reports so far have serious methodological flaws.[62] On the other hand, AUTOPULSE® which works by the load-distributing band principle,[63] powered by internal batteries, proposes no apparent hazards to rescuers or patients, but two clinical trials seem inconclusive as to whether this device can replace manual chest compressions.[58,59] A potential problem with the AUTOPULSE® device has been its incompatibility with X-rays, but product development is expected to solve this to allow for continued CPR during PCI.

Manual chest compressions will always have to be the initial response to circulatory arrest and must be continued until a mechanical chest compression device can be operative. Lack of appreciation of this fact may be one reason for the conflicting results in the clinical trials so far.

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In the last part of the thesis, I will explore my views on the rationale for a uniform reporting of CPR quality and propose definitions for some of the quality variables.

Why measure and report quality of CPR

There are several good reasons to measure and report quality of CPR. Firstly, the process of debriefing, the retrospective critical review of an incident, is a powerful way of learning, and may be enhanced by accurate information. Any ambulance service or cardiac arrest team would like the opportunity to review their case, preferably shortly after. The efforts reported can be either a graphical representation of the episode, or a numeric presentation of key elements of quality. The focus must then be on variables with a documented impact on outcome, which are quantifiable, and, importantly, which can be improved by the team. This approach is not necessarily limited to professional rescuers, but also volunteers involved in a public AED programme or even the incidental bystander may want and profit from an objective review of the resuscitation efforts. The future availability of small stand-alone devices that measure quality of CPR and provide real time feedback can be extended to include recording and playback functionality. Using the same technology for training and real use would have some pedagogical benefits.

Secondly, the medical directors have a need for CPR quality reporting. The purposes can be; to be able to monitor the quality and the effects of any change in algorithms, standard operating procedures or devices, and to be able to compare the service to other providers.

Similarly, many clinical trials have recently failed to confirm promising results from experimental research. It can be speculated that if poor quality of CPR is the major determinant of survival in the studied cohorts, any differences from the studied pharmacological agent, intervention or device will be hard to demonstrate. Likewise, heterogeneous level of CPR quality between sites in multi-centre trials, differences in CPR

quality induced by the studied intervention in itself (*e.g.* prolonged no-flow time induced by a new intervention), or biased CPR performance that is dependent on the studied intervention in non-blinded trials (*e.g.* if the performers' beliefs in and attitudes to the intervention induce differences in other parts of the treatment), could severely confound any otherwise well designed trial. Quality of CPR must therefore be accounted for in any clinical trial, and differences between groups should be dealt with in logistic regression analyses, if possible. The variables needed for such reporting should therefore be supported by data on outcome, be quantifiable, and be possible to enter in a regression analysis as a co-variate. It must be an integral part of every research protocol to describe how quality of CPR is going to be monitored and reported.

Finally, the research community preoccupied with the study of the impact of CPR quality on outcome, needs precise definitions to be able to compare results across studies. The CPR research community have a long tradition of standardising reports from studies of CPR. Consensus papers based on scientific meetings at the Utstein Abbey outside Stavanger, have given definitions and recommendations on how to report a core set of information about the peri-arrest factors thought to influence outcome of out-of-hospital cardiac arrest.[29,30] The concept has been transferred to in-hospital cardiac arrest,[64] post-resuscitation care,[65] trauma research,[66] and animal laboratory CPR research.[67] These consensus papers have so far not been able to address quality of CPR, but recent technological advances, including, but not limited to, the technologies utilised in the current thesis, have made measuring and reporting CPR quality available for everyone. The commercially available devices have different methods to capture quality data. The researcher community needs to agree how **we** want to define and report on these variables, and make these definitions independent of manufacturer, devices, and currently available technology.

How to measure and report quality of CPR

In the following sections, I will propose definitions of each variable of CPR quality and discuss how these best can be reported for the different purposes outlined above. I believe that the next revision of the Utstein template for reporting on cardiac arrest will include some form of definitions and recommendation to report quality of CPR. Meanwhile, a collaboration group from Ullevål University Hospital, University Hospitals of Chicago and Allgemeines Krankenhaus Wien have a review paper on this topic with the present author as the lead author in press.[68]

Chest compressions

Chest compressions are the circulation generating part of the CPR sequence. In the earliest reports of external chest compressions on human victims of Chloroform anaesthesia it was noted that deep and rapid compressions were needed to produce palpable carotid pulsations and pupillary constriction:

> *„Man tritt an die linke Seite des Kranken, das Gesicht dem Kopf desselben zugewandt, und drückt mit raschen kräftigen Bewegungen die Herzgegend tief ein, indem der Daumenballen der geöffneten rechten Hand zwischen Stelle des Spitzenstosses und linken Sternalrand gesetzt wird. Die Häufigkeit der Compressionen beträgt 120 und mehr in der Minute.“* [69]

The effect of the chest compressions is to create pressure differences between segments of the vascular bed and thus make blood flow possible. The highest pressure differences are found during open chest cardiac massage, but the invasive nature of this intervention has so far limited its use outside the operating theatre.[3]

The different aspects of a chest compression must all be optimized to provide the best flow to the brain and the heart. Research into the different aspects of chest compressions have been conducted on animals, mostly dogs and pigs. Most of the studies have been performed with different mechanical chest compression devises that have allowed studies of each aspect of chest compression quality separately.

Chest compressions can be visible as electrical noise on ECG-printouts from the cardiac arrest. Sunde *et al.* used this method to be one of the first to report chest compression rates, pre shock pauses and delay from initiation of monitoring to the first chest compression.[18] Van Alem *et al.* used similar technology and had the advantage of additional sound recordings when she studied interruptions in CPR during first responder use of semiautomatic defibrillators.[19] The sound recordings add confidence about the presence of chest compressions when rescuers count out the compressions, and may add information of the reasons for pauses observed. Direct observations of chest compressions are also possible with a subjective rating of effectiveness by palpating pulsations [14,70,71] or only an assessment of number of compressions.[20] Evaluation of trans-thoracic impedance can be used to automatically detect chest compressions, and this method is utilised on registrations of out-of-hospital cardiac arrest in an ongoing study in the Oslo and Akershus EMS.[72]

To measure chest compressions more accurately additional devices are needed. In our projects we have used a chest compression sensor fitted with an accelerometer and a force

sensor. The chest compression sensor was placed between the heel of the rescuers' hands and the sternum and its movement considered equal to that of the sternum. The acceleration signal (m/s^2) can be integrated twice to obtain the distance (m), and the signal from both the accelerometer and the force sensors can be used to count the chest compressions. The CPREzy™ is a stand-alone device similarly placed that measures the force applied to sternum, but to my knowledge, without recording capability. In some studies the depth and force of manual chest compressions have been extracted with an external device with a linear potentiometer and a force transducer.[73]

Chest compression rate

International guidelines recommend chest compressions to be delivered at a rate of 100 min^{-1}.[1,2] Animal experiments showed increase in systemic flow and aortic systolic pressure with increasing chest compression rate.[74] When the coronary blood flow was measured in dogs chronically instrumented with electromagnetic flow probes on the circumflex artery, the shorter time in artificial diastole associated with higher chest compression rates resulted in decreasing values for coronary flow at rates above 120 min^{-1}.[75] As in normal physiology, the increase in rate in most experiments with mechanic chest compressions are due to a reduced decompression time, and this may explain why increasing the rate above a threshold can reduce venous return and cardiac filling and thus reduce cardiac output, however this effect was not found in dogs with a rate of 150 min^{-1}.[74,75] In a human study average end-tidal CO_2 ($ETCO_2$) increased from 1.7 to 2.0 kPa when manual chest compression rate was increased from 80 to 120 min^{-1}.[76]

The chest compression rate is defined as the reciprocal of the time interval between two identical parts of the compression curve, much in analogue to the calculation of heart rate from R-R intervals. (See Figure 10) In contrast to calculation of heart rate, the reporting of chest compression rate is complicated by frequent interruptions. The minimum chest compression rate (*i.e.* the maximum time between two adjacent chest compressions considered to be part of a series of chest compressions) must be defined. To evaluate chest compression rates down to 40 min^{-1} the interval between two identical parts of a compression curve (*e.g.* the maximum of each compression) must be less than 0.025 minute (which equals 1.5 s). Conversely, intervals longer than 1.5 s are regarded as pauses during which perfusion pressures and forward flow decline rapidly (see on page 46).

Figure 10

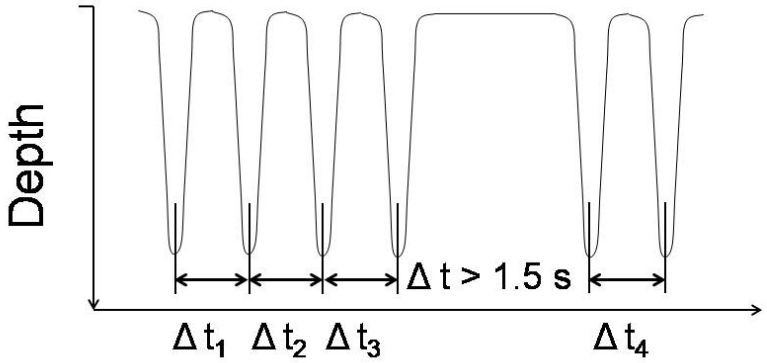

Figure 10 *shows time along the X-axis and the time differences (Δt_{1-4}) between corresponding points of the chest compression depth curve. The chest compression rate is then given by the formula:*

Chest compression rate = 1/Δt

The average chest compression rate is then the reciprocal of the average time interval for the whole episode, and this can be expressed for the purposes of immediate debriefing and research as a mean ± SD. It may also be possible to display graphically compression rate per one-minute segment during the episode to facilitate reflective learning in a quality improvement system. This number is also suitable as a summary for use in clinical trials. As discussed above, too low or too high compression rate is not good. The exact limits are not known for man but are assumed to be 100-120 min^{-1}. To be entered in a logistic regression chest compression rate should probably be transformed to a binominal measure representing within or outside any set target values.

While current resuscitation guidelines recommend a compression rate of 100 min^{-1}, the actual number of compressions delivered per minute reflects both the compression rate as well as the pauses in compressions. The number of chest compressions delivered per minute may be especially useful in quality improvement efforts and team debriefing. In the first paper we recorded compression rates of 121 ± 18 min^{-1}, but the mean number of compressions per minute was actually 64 ± 23 as a result of frequent interruptions [I]. Abella *et al.* found a correlation between number of registered chest compressions per minute and rate of short term survival during in-hospital resuscitation.[20]

Chest compression depth

Compression depth is defined as the maximum posterior deflection of the sternum prior to chest recoil. It is important to note that accurate determination of compression depth by measuring only sternal movement is not possible without a non-compressible surface beneath the patient such as the floor or a backboard.

I have described how we measured compression depth by the use of a combination of an accelerometer and a force sensor on page 12. In our study only vertical movement coincident with a force greater than ~2 kg on the force sensor and with a depth of more than 8 mm was considered to be a chest compression. These limits are such that very few intended compressions are excluded, and hardly any that would lead to generation of blood flow.

It is not known whether it is the depth *per se* or the force applied that is the main component in the generation of forward blood flow. The relationship between applied force and thoracic deformation has recently been evaluated in humans with the same equipment that was used for the papers included in this thesis.[32] The additional chest pad placed on the victims' sternum was fitted with a more accurate force sensor and this allowed for a retrospective analysis of the relationship. The results showed a wide variation among individuals in the force needed to reach a limit of 38 mm; 29.8±14.5 kg and 22.5±10.2 kg for males and females respectively, but 87/91 patients were compressed to 38 mm or more with the use of a force less than 50 kg. Previous studies of this relationship have been limited by the number of cases and the methods of force and depth measurements.[77,78]

Current guidelines recommend that a force necessary to produce chest compression depth of 4-5 cm (1.5 to 2.0 inches).[1,2] In animals both increased force up to 140 pounds (~63 kg)[79] and increasing depth between 1.5 and 2.5 inches[80] have been shown to improve systemic blood flow and systolic pressures. The thoracic cavities of four legged animals are keel-shaped whereas humans have broader chests with smaller anterior-posterior diameter. The compression depth noted in the animal papers equates to approximately one-fifth of the human chest diameter in a recent human radiographic observational study.[81]

Compression depth was one of the CPR aspects that could be modified by automated feedback in both manikins[21] and in our clinical trial [II]. In a quality improvement system chest compression depth would be one obvious measure to try to improve, and to report depth from clinical trials also seems reasonable.

For debriefing and improving quality the report should include the mean compression depth over an entire resuscitation episode and the fraction of the total minutes where mean compression depth was less than 38 mm, the lower end of guidelines recommendations. Adding a minute-to-minute analysis of mean depth allow rescuers to put quality measures into the context of the resuscitation event.

For research requiring accounting of CPR quality, mean overall compression depth with standard deviation would be the minimum requirement to show equivalence between two groups. However, such investigations could also report fractions of minutes with a depth of less than 38 mm, and both of these measures could be entered into a regression analysis.

We found an association between episodes with deeper chest compressions and short term survival in our study [II], but no prospective trial of compression depth have so far been conducted in humans, and based on the present data, one could argue that such a study would likely be unethical. Still, associations between chest compression depth and different outcome variables would be of interest and for all such research definitions would be useful.

Chest compression incomplete release

Complete release of pressure on the thorax in the decompression phase is believed to be essential to allow venous return and cardiac filling before the next compression. In a porcine model of cardiac arrest a residual compression depth of 1.2 cm increased mean intrathoracic pressure and reduced cerebral and coronary perfusion pressures.[82] In humans the exact residual force or intrathoracic pressure that would not compromise hemodynamics is not known.

We defined incomplete release as a residual vertical force of more than 4 kg on the chest pad between chest compressions. This was equivalent to the weight of the hands of one of the researchers. When the force sensor was replaced with a more accurate one for the third phases of the study, we found a mean residual force of 1.7 ± 1.0 kg.[32]

When this measure is reported the threshold value used must be reported. Incomplete release can be reported for each compression as a binary measure and the fraction of chest compressions can be summarized for the purpose of immediate debriefing. This fraction probably also should be reported from clinical trials, but more research is needed to associate this feature with changes in hemodynamics in humans.

Chest compression duty cycle

In laboratory research duty cycle was coined as term describing how long the pressure from the compression piston was allowed to deflect the sternum. It was the ratio of compression time to total cycle time (Figure 11 a). During manual chest compressions, the force registrations may be ambiguous. The decision on when the upstroke phase starts is not as straightforward as with mechanical chest compression devises. The definition of duty cycle was therefore modified to describe the amount of chest compression cycle with a downward position of the sternum. This is calculated as the ratio of the area under the time-displacement curve divided by the product of cycle time and maximum deflection (Figure 11 b). The two calculations give similar results, but the latter is computationally easier.

Figure 11

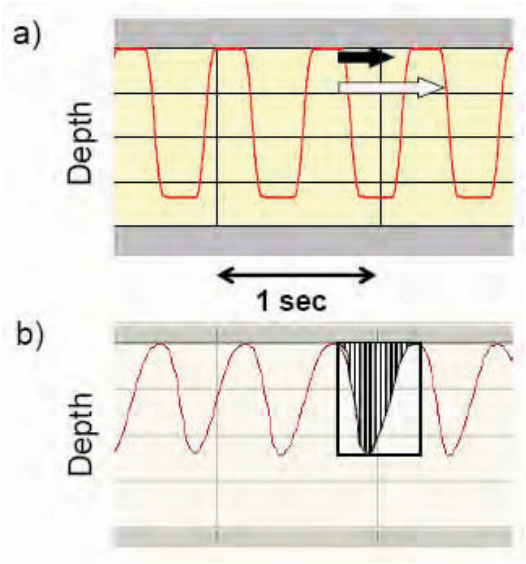

Figure 11 *shows time along the X-axis and sternal movement in the vertical direction on the Y-axis. The upper panel (a) shows calculation of duty cycle from mechanical chest compressions where the black arrow marks where force is applied and the white arrow the total length of the compression cycle. The lower panel (b) shows manual chest compressions where duty cycle is calculated as the area under the curve (hatched area) divided by the area of the deflection by cycle length square (thick lines).*

In some animal experiments with constant chest compression rate the optimal compression duty cycle have been found to be 40-50 %.[83,84] Others have found that a compression phase lasting 200-250 ms is necessary regardless of compression rate.[74,75]

This would translate to a 50 % DC when chest compression rates are 120-150 min^{-1}. No human studies have related this feature to survival, but higher arterial flow velocities were measured in 6 patients when increasing duty cycle from 30-40 % to 50-60 % with constant compression rate of 80 min^{-1}.[85]

The evidence so far suggests that duty cycle during manual chest compressions is fairly constant and hardly modifiable (see on page 28). However, as duty cycle may be an important feature of CPR quality, and that the height and nature of the surface might influence duty cycle,[51] it would be of interest in a systematic quality assurance program. For such purposes, a mean duty cycle for each episode would be sufficient and similarly mean and standard deviations would be needed in reports from clinical trials. For users of mechanical chest compression devices, it would be essential to describe the characteristics of the device used with regards to duty cycle and the method used to calculate this measure.

Other features of chest compressions

Many interventions and devices have been evaluated in the hope of improving the effect of chest compressions and survival. Examples include mechanical chest compression devices, active decompression CPR, the impedance valve and abdominal counter compressions or binding. It is beyond the scope of this review to go into details of all these and they have not been studied in the papers included in this thesis. However, their use should be registered and the effects they have on all aspects of quality and outcomes should be subject for quality improvement programs.

For clinical trials that study these adjuncts or principles, it would be essential to have thorough description of the effects these devices and techniques have on other aspects of CPR quality and on surrogate measures of outcome such as $ETCO_2$.

Ventilation

The concept of artificial ventilation may have been partly understood through centuries, but its use as a resuscitation measure is linked with the treatment of victims of drowning. The first society for the recovery of drowned persons was founded in Amsterdam, and the ample presence of canals made the society in 1793 claim 990 rescues during their first 25 years.[86]

During cardiac arrest the primary objective is to circulate blood and in the case of primary arrhythmias the arterial blood is fully saturated with oxygen until chest compressions are started. When chest compressions start to circulate the blood, it will return from the systemic circulation to the heart with very low oxygen content and as a function of cardiac output and time, arterial saturation will decrease in the absence of alveolar replenishment of oxygen. In a porcine model near complete arterial desaturation occurred within two minutes of chest compressions without passive or active ventilation.[87]

Positive pressure ventilation increases the intrathoracic pressure, which according to the discussion on page 41 should decrease venous return and cardiac output during low-flow states such as CPR.[88] As circulation ceases lower oesophageal pressure has been measured to drop rapidly from 20 cm H_2O to near zero.[89] This probably increases the risk of gastric inflation and subsequent regurgitation.[90] Thus, during one-rescuer CPR and CPR before the airways are secured, chest compressions are withheld to allow for ventilations. This results in frequent pauses, during which perfusion pressures drop and forward blood flow fades quickly.[91]

Concerns about the aesthetic issues of mouth-to-mouth ventilation and bystander willingness to initiate CPR,[92-94] and the detrimental effects of interruptions in chest compressions[91] have given the impetus to study the effect of omitting ventilation during the first minutes of resuscitation. Animal studies have shown improved survival and hemodynamics with continuous chest compression CPR compared to standard CPR with interposed ventilation in a 15:2 pattern.[91,95] Continuous chest compression CPR as the initial step during bystander and first responder CPR, has been evaluated and have been found to be easier to comprehend, shortening the delay to the first chest compression, in telephone-guided bystander CPR.[96-98] In one clinical trial survival was similar if not better, in the group that received instructions to start chest compressions only.[99]

From the discussion above we understand that both too many and no ventilations would be harmful during CPR, but the exact number of ventilations needed per minute is less well characterized. If adequate perfusion of the respiratory centres of the medulla oblongata is maintained with good quality chest compressions, spontaneous gasping can probably continue for many minutes after cardiac arrest and such agonal respiration has been linked to improved survival.[100]

Ventilation may be monitored during resuscitation by impedance penumography, capnography, and spirometry. Clinically, the monitoring device must be easy to apply, accurate, and preferably not include vulnerable or bulky equipment. A recent review

describes the different methods that can be used,[101] and I will discuss those most relevant for the main goal for clinical use; ability to provide real time information that can be used to modify therapy to the benefit of the victim.

Impedance pneumography is based on measured impedance across the thorax, which changes as the lungs inflate and deflate.[33] It is possible to filter out the impedance changes due to motion artefacts (mainly chest compressions) and the ventilation count and the impedance changes can be displayed on a screen in real time. The strengths of this technology are the applicability during all stages of resuscitation regardless of mode of ventilation (*e.g.* mouth-to-mouth/mask, bag-valve-mask, or via an endotracheal tube), it monitors changes in thorax volume continuously, possibly enabling detection of dislodged endotracheal tubes [III],[102] and it does not require any extra equipment other than standard self adhesive defibrillation pads. The problems are the inter-individual variability in the relationship between impedance changes and tidal volume,[103] and the vulnerability to movement artefacts caused by chest compressions.

Capnography is the registration of CO_2 in the exhaled air. It can be used either continuously or as a single use indicator to verify correct placement of endotracheal tubes, and capnography is considered an essential requirement for safe practice during intubation for anaesthesia.[104] During low-flow states such as cardiopulmonary resuscitation, the concentration of CO_2 in the exhaled air from the alveoli ($ETCO_2$) is more dependent on pulmonary blood flow (*i.e.* the cardiac output) and the delivery of CO_2 to the pulmonary capillaries, than the minute ventilation.[105] Very low values of $ETCO_2$ may therefore not unambiguously be interpreted as misplaced endotracheal tube under these circumstances.[106] However, the level of $ETCO_2$ may be used clinically as a non-invasive estimate of cardiac output.[107,108] The measured $ETCO_2$ have been related to short term survival, and ROSC can be detected by a marked increase in $ETCO_2$.[109,110] Measurements of $ETCO_2$ are not restricted to intubated patients, but the interpretation of low values is very difficult if the patient does not have a secured airway. Another problem is the equipment that introduces another device or connection to apply during resuscitation.

Spirometry can measure both airway pressures and volumes and can be attached to any secure airway or used in conjunction with a bag-valve-mask device. There are different technologies available, but so far, all requires bulky and/or vulnerable equipment. The measuring of airway pressures is appealing as this is a close estimate of intrathoracic pressure that may again be the culprit of decreased survival associated with increased ventilation rates.[49]

Ventilation rate is easy to measure with all three methods mentioned. High ventilation rates have been described in some in-hospital and out-of-hospital settings and is shown to be detrimental.[38,42,49] Lack of ventilation is probably also detrimental, especially after initiation of good quality chest compressions.[87] After attempted intubation, no registration of ventilation should prompt a check for misplaced or displaced tube which is associated with very low survival.[111] A report of number of ventilations per minute and a minute-by-minute summary of ventilations would be useful in post-event reviews. For clinical trials both a mean number of ventilations and a fraction of time with high and zero ventilation count would be interesting. From available literature the high limit for acceptable ventilation rate may be set at 20 min^{-1}.[49]

Other aspects of ventilation during cardiac arrest need further study, especially to elaborate how much ventilation that is really needed and the effects of changing tidal volumes, inflation rate (*i.e.* speed of inflation), and ventilation rate. How the different ventilation aspects are performed or changed may also serve as outcome in studies of airway interventions. For instance, the ability of the many alternative airway devices available to maintain adequate ventilation during continuous chest compressions have never been studied in humans, nor have the effects professional rescuers' ability to perform ventilations with bag-valve-mask device before intubation been studied during real cardiac arrests.

Pauses and interventions

When there are no chest compressions, the perfusion pressures fall rapidly and forward flow ceases.[91] Pauses will therefore add to the response time and decrease survival.[112] It may even be that each pause and each chest compression segment introduces a small, incremental ischemia-reperfusion injury to the brain and myocardium.

A plethora of interventions have been described and tried during CPR. The current guidelines focus on electrical defibrillation and medications in addition to chest compressions and ventilations. Each intervention may cause a pause in the delivery of chest compressions. The value of each intervention must be evaluated based on the "cost" of such interruptions and the "benefit" of the intervention when it comes to survival.

Defibrillation

It was the rising numbers of electrocuted linemen working for the power companies that sparked the sponsoring of Kouwenhoven and collaborators' work that resulted in first the

concept of open-chest internal defibrillation and later the closed chest defibrillator.[113] The first out-of-hospital "portable" defibrillator was used in the mobile intensive care unit in Belfast.[114]

The development of smaller defibrillators with automated ECG-analysis for detection of VF/VT has made defibrillators available nearly everywhere, and their use is no longer restricted to professional personnel. In cardiac arrest victims with an initial rhythm that can be defibrillated (*e.g.* VF/VT), the time delay to first defibrillation attempt has been found to correlate inversely with survival[115] with the highest reported survival reported from Las Vegas casinos where security officers managed to defibrillate most patients within 5 minutes.[116] Increased survival by adding defibrillating capacity and improving B-CPR skills to a fire brigade based EMS was shown in the OPALS study.[117]

Automated ECG-analysis to determine whether a rhythm is shockable requires a pause in chest compressions,[28] with the associated deleterious reduction in blood flow as discussed on page 46. Manual analysis may be quicker than the defibrillator software, but raises the question of analysis accuracy of man versus machine [IV].

Unsuccessful shocks still induce some no-flow time and each shock delivers electrical energy through the myocardium and possibly adds to the post-resuscitation cardiac dysfunction.[53,54] The best would be to avoid unsuccessful shocks by having some non-invasive method to assess CPP or myocardial metabolic status. Anecdotally, the coarseness of VF has been used during resuscitation as a predictor of defibrillation success. The best mathematical predictor currently seems to be based on wavelet analysis and have a specificity of ~60 % for a sensitivity of around 95 %, meaning that it will help avoid more than half of shocks that would not have resulted in ROSC.[118]

Medications

No drugs administered during out-of-hospital cardiac arrest have been shown to improve survival, and retrospective analysis from the Swedish Cardiac arrest registry even suggests a reduced survival when adrenaline was used.[50] There was no difference between adrenaline and vasopressin in a randomized, multi-centre study,[119] and no effect of iv buffer during out-of-hospital cardiac arrest.[120] Amiodarone was shown to improve short time survival when administered for persistent VF, but did not change survival to discharge.[121] Trombolysis during CPR showed promising results in pilot studies, but a randomized multi-centre study was prematurely stopped because of futility.[122]

Preceding the clinical trials, all these drugs have shown promising and spectacular effects in animal studies and pilot studies. The effect on surrogate measures such as coronary perfusion pressure has been very impressing for both adrenaline and vasopressin, how come they did not perform in the clinical environment?

Two main reasons are conceivable. Firstly, the pharmacological effects may be different in animals and man. While this may be true for many drugs, pilot studies and case reports have to be positive for a drug to enter clinical trials. However, it is likely that the drug effects in patients with advanced cardiovascular disease may be less or even different from those seen in piglets and rats. Secondly, the process of securing an *i.v.*-line, breaking of ampoules, and administering drugs may take time and concentration away from the circulation generating chest compressions. In a survey among paramedics in London and Akershus, 2/3 believed it to be very important to secure an *i.v.*-line and intubate the patients, and one out of five admitted that they stopped chest compressions to perform such tasks.[46] In randomized and blinded studies, this does not explain different outcomes between groups, but our findings of poor and highly variable quality of CPR [I and II] could indicate that CPR performed in these clinical trials does not circulate the drugs to their effect site[56] or just that poor quality CPR may be the major determinant of survival, obscuring the effect of any intervention.

Reporting pauses

Reporting of pauses during CPR would serve to identify opportunities for improvement in the case of immediate debriefing and real-time feedback. Here it would be helpful to associate pauses to each interventions and summarize which part could be attributed to rescuer delay and this could be a target for rehearsal and continued improvement programme.

In the case of reporting and comparing clinical trials, it is likely that accumulated no-flow time can influence on survival or neurological status and it should be reported as a mean absolute time of no-flow and as the mean fraction of no-flow time to time without spontaneous circulation. It must be acknowledged that our understanding of the detrimental effects of no-flow time is not complete, and further clinical studies would be needed.

VF-analysis has been shown to predict shock success,[118,123] and may non-invasively measure myocardial metabolic status. As such, it would be suitable as a surrogate end-point in studies of the effects of pauses associated with different interventions in patients with VF.

Target values and feedback

We used a hierarchical system of prioritized target values to provide verbal feedback to rescuers, originally based on the training software for voice assisted manikin.[21] The target values were found based on the current literature and international recommendations and are summarized in Table 1 in paper II. Current guidelines have changed with regards to recommended compression:ventilation ratio before intubation and regarding administration of shocks.[1,2] Table 3 gives current targets for the CPR quality variables we have studied.

Table 3

CPR variable	Target	Paper
No-flow time	as low as possible	
Before intubation	10 – 15 s per minute (i.e. NFR <0.25)	III
After intubation	5 s every 2 – 3 minute for rhythm checks (i.e. NFR <0.05)	III
Each rhythm check	5 s + possibly pulse check; 10 s	I, II
Each defibrillation attempt	rhythm analysis + shock; less than 10 s	IV
Compressions		
Compression rate	100 min^{-1}	I, II
Compressions per minute	Before intubation: 60 – 75	III
	After intubation: 90 – 110	III
Compression depth	4 – 5 cm	I, II
Compression duty cycle	40 – 50 %	I, II
Incomplete release	0 %	I, II
	unknown threshold	
Ventilations		
Ventilations per minute	Before intubation: 4 – 6	III
	After intubation: 10 (?)	III

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