DETECTION AND QUANTIFICATION OF GASPING IN OUT-OF-HOSPITAL CARDIAC ARREST AND RELATION TO OUTCOME

Martha WOLFSKEIL

Promotor: Prof. Dr. Said Hachimi-Idrissi
Co-promotor: Prof. Dr. Koen Monsieurs

Dissertation presented in the 2nd Master year in the programme of

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Preface

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ABSTRACT

INTRODUCTION

Gasing during cardiopulmonary resuscitation (CPR) is associated with increased cerebral perfusion, venous return and cardiac output; hence potentially increasing the chance of return of spontaneous circulation (ROSC).

The purpose of this study is to detect and quantify gasing during CPR and to investigate whether gasing is associated with improved short-term outcome.

MATERIALS AND METHODS

We conducted a retrospective observational study in patients who were resuscitated and orotracheally intubated by the mobile emergency group of Ghent University Hospital between March of 2009 and December of 2015. After intubation, a disposable kit existing of two catheters and connectors was inserted in the endotracheal tube (ETT). The catheters were connected to two pressure sensors and a logger in a registration device. The pressures were measured and registered proximal and distal in the ETT.

Pressure data were analysed with a specially designed application in LabVIEW (National Instruments, Austin, Texas, U.S.). Gasing volumes were calculated based on pressure differences between the catheters. Compression depth and rate were recorded using an accelerometer on a ZOLL X Series defibrillator (ZOLL, Chelmsford, U.S.). Endotracheal pressure data and compression data were analysed using SPSS Statistics 23 (IBM, Armonk, New York, U.S.). Data were expressed as mean values (standard deviation; range).

RESULTS

Data were collected in 296 patients with a mean age of 65 years (15.5; 18-89), 210 (71.2%) were male. The initial rhythm was asystole in 60.4%, ventricular fibrillation in 22.3%, pulseless electrical activity in 13.8% and ventricular tachycardia in 1.0%. Of 293 valid data (3 missing files), 36.6 % of the patients achieved ROSC. The mean chest compression depth was 4.9 cm (0.92; 2.0-8.5) and the mean chest compression rate was 115 per minute (12.7; 52-155).

In 84 patients (28.4%), the device registered gasing during CPR. The mean number of gasps per patient was 36 (57.8; 1-308). The mean gasing volume was 345 ml (208.8; 56-1280) with
a mean maximal gasping volume of 540 ml (318.7; 56-1576). The mean gasping rate was 5 gasps per minute (4.9; 0-18). The maximum gasping rate was 18 per minute. The most negative intratracheal pressure was on average -20 cmH₂O (13.7; -56.2 – -5.1).

In the group of gasping patients, 40.7% achieved ROSC, while 35.1% only of the patients in the non-gasping group achieved ROSC (P=0.37). The gasping rate was significantly higher in the ROSC group compared to the non-ROSC group (7.4 and 3.8 gasps per minute respectively (P=0.019)). The mean gasping volume in the non-ROSC group was 323 ml (166.7; 56-738) and 389 ml (266.5; 62-1280) in the ROSC group. Deeper negative pressures were associated with increased incidence of ROSC (P=0.022). Patients discharged from the hospital, had a significantly higher (P=0.032) mean gasping volume of 641 ml compared to those who died in the hospital (mean gasping volume of 329 ml).

**CONCLUSION**

The prevalence of gasping during CPR was high but there was no significant difference in ROSC between patients with gasping and those without. If gasping occurred, significant volumes were measured. There was wide variation between the gasping characteristics in and between patients. Increased gasping rate and deeper negative pressures were associated with increased incidence of ROSC. Furthermore, larger gasping volumes appeared to be associated with more hospital discharge. These findings need confirmation in a larger study.
INTRODUCTION

1. IN GENERAL

1.1. SUDDEN CARDIAC ARREST

Cardiovascular disease, in particular coronary artery disease, is the leading cause of death in Europe and accounts yearly for 4.1 million deaths. Approximately 37% of all deaths are patients younger than 75 years (1). In two thirds of the cases, sudden cardiac arrest occurs outside the hospital, a so called out-of-hospital cardiac arrest (OHCA) (2).

The yearly incidence of OHCA in Europe is 38 per 100 000 person-years (3). Each year, 350 000 people suffer from OHCA in Europe. Ten thousand of them occur in Belgium (4).

In the last years, a slight decrease in mortality is observed in most European countries, mainly because of increased prevention, changes in lifestyle and improved treatment strategies (2).

The overall survival of OHCA, however, remains disappointingly low, i.e. approximately 5-10% (5).

In the city of Ghent and its immediate surroundings, there are about 367 cardiac arrests treated yearly by medical services. The incidence is 39.29 per 100 000 person-years. The current survival rate is 8.5% and increases up to 20.6% if the first cardiac rhythm was ventricular fibrillation (VF) (6).

1.2. CHAIN OF SURVIVAL

The “chain of survival” (figure 1) refers to a series of actions that, when put into motion, reduce the mortality associated with cardiac arrest.

Figure 1. The chain of survival (7).
The first link represents the early recognition of an impending cardiac arrest and the early call to the emergency services. The two central links represent the most important components of resuscitation, being early initiation of CPR and early defibrillation (3).

If the cardiac rhythm is VF, rapid initiation of high quality CPR and defibrillation increases the chance of survival up to 49-75% (3).

This highlights the necessity to teach basic life support (BLS) to the general population.

The last link represents the importance of effective post-resuscitation care, which occurs at the hospital (3).

1.3. CARDIOPULMONARY RESUSCITATION

Cardiopulmonary resuscitation is the entire set of actions needed to maintain the vital functions of a patient with cardiac arrest and to achieve return of spontaneous circulation (ROSC).

The aim of BLS is to maintain a free airway and to support the respiration and the circulation, without using medical devices, except adjuncts, such as a pocket mask for personal safety and hygiene. BLS can be performed by lay people (8).

A free airway can be achieved by performing a head tilt and chin lift, to avoid obstruction of the airway by the tongue. Support of the circulation is performed by applying chest compressions on the lower half of the sternum. Thirty chest compressions should be alternated with two rescue breaths. The two rescue breaths can be given directly by mouth-to-mouth or with a pocket mask or face shield as protection against blood or vomit (8). BLS is taught in numerous first aid courses and should be applied by bystanders awaiting specialised medical help.

Good quality CPR is characterised by:

- good quality chest compressions at a rate of 100-120 per minute with a depth of 5-6 cm allowing recoiling of the chest between compressions with minimal interruption of the compressions (hands-off time) (9, 10).

A fundamental adjunct during BLS is the automated external defibrillator (AED), a device available in many public areas that can be used by lay people. Through two electrodes, adhering to the chest of the patient, it analyses the heart rhythm automatically and administers an electrical shock (semi)automatically (= defibrillation). The latter will only happen if the patient
has a shockable cardiac rhythm such as ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT). Non-shockable rhythms such as asystole and pulseless electrical activity (PEA) do not require an electrical shock (8).

During advanced life support (ALS), advanced medical equipment is used by trained health care providers.

In ALS, a stepwise approach in airway management is recommended. A free and safe airway can be achieved by orotracheally intubation, in which an endotracheal tube is inserted below the vocal cords. Trained medical rescuers perform this procedure, with an emphasis on minimal interruptions of chest compressions (11, 12). Other devices for maintaining a free airway are available such as supraglottic airway devices (12).

Continuous chest compressions should be performed at a rate of 100-120 per minute as soon as the airway is secured. The patient can be ventilated simultaneously at 10 ventilations per minute. The latter can be done manually with a ventilation bag or with a mechanical ventilator (12).

The ALS algorithm (figure 2) distinguishes between shockable and non-shockable rhythms (cfr. supra). If the patient is in a shockable rhythm, adrenaline 1 mg is injected intravenous (IV) every 3-5 minutes until ROSC is achieved. The initial dose of adrenaline is given after the third shock. A single dose of amiodarone 300 mg is indicated after the third shock. A further dose of 150 mg amiodarone can be considered after the fifth shock. If ROSC is not achieved after the third shock, the adrenaline may improve myocardial blood flow and increase the chance of successful defibrillation with the next shock. However, ALS interventions are of secondary importance to the interventions that contribute to improved survival after cardiac arrest: effective bystander BLS consisting of uninterrupted, high-quality chest compressions and early defibrillation in case of a shockable rhythm. Despite the widespread use of adrenaline during resuscitation, there is no placebo-controlled study showing that its routine use increases neurologically intact survival to hospital discharge (13). If the initial cardiac rhythm is non-shockable (PEA or asystole), 1 mg adrenaline is given as soon as venous (or intra-osseous) access is achieved. Repeated 1 mg adrenaline administration every 3-5 minutes is indicated if the patient has not yet achieved ROSC (13).
Figure 2. ALS algorithm (13).

Post-resuscitation care should be started immediately after the patient achieved ROSC to improve the neurological outcome of the patient. Figure 3 outlines the key interventions in post-resuscitation care.
Figure 3. Post-resuscitation care algorithm (14).
2. GASPING

2.1. DEFINITION
In 1973, the Glossary Committee of the International Union of Physiological Sciences has defined gasping as an abrupt, sudden and transient inspiratory effort (15). Inspiration and expiration are short and there is a longer expiratory pause of variable length (16, 17). It typically occurs within the first minute after cardiac arrest and follows then a crescendo-decrescendo pattern (18-24).
Gasping can also be referred to as agonal breathing. Gasping is a common mammalian phenomenon that occurs secondary to cerebral hypoxia. Previous research with animal models has shown that it occurs in cardiac arrest, mainly with ventricular fibrillation as cardiac rhythm (19). Gasping is more robust in immature animals and could be a protective reflex mechanism in the anoxic conditions of the birthing process (19).

2.2. PHYSIOLOGY
The physiological mechanisms and effects of gasping have been extensively studied in animal models of cardiac arrest. The “gasing centre” was first described in the brain stem of cats (16). Pigs were the first animals in which intrathoracic pressure, carotid artery blood flow and different pressures in heart and aorta were measured during gasping after induced VF (23). One study used pigs to calculate the stroke volume of the heart during gasping, utilizing echocardiography at the level of the aortic valve (20). In another study with pigs, intracranial pressure was measured by using a micromanometer-tipped epidural catheter (22).

All these studies have emphasized the beneficial effect of gasping on the physiological mechanisms in brain, the respiratory system and the circulatory system.

2.2.1. NEUROLOGICAL
In 1923, Lumsden et al. described the “gasing centre” as a centre localised in the brain stem, just below the acoustic striae. If the neurons located in the gasping centre are still working while the rest of the brain is disabled, these neurons are thought to cause gasping (16). St.-John et al. described the possibility that gasping is induced by a pacemaker mechanism in the medulla, more specifically in the “preBotzinger complex” in the rostral medulla. Respiration
is normal if the ponto-medullary circuit is intact. If this circuit is interrupted, gasping will occur if enough neurons in the area of this pacemaker are excited (25).

If gasping is induced by hypoxaemia, as it is usually during cardiac arrest, it can occur until the respiratory centre in the caudal part of the medulla oblongata does not function anymore (16). In induced apnea in a study environment, gasping occurred after approximately 2 minutes, when arterial oxygen pressure (PaO₂) dropped below 5 mmHg. Because of the gasping process, the oxygen pressure increased to over 30 mmHg, whereby spontaneous respiration could be restored (23).

Lumsden et al. speculated that gasping is a fundamental reflex that is associated to auto-resuscitation and that it is an evolutionary mechanism in many species (16, 26).

One study with pigs showed in 2006 that gasping also results in an immediate decrease of intracranial pressure, causing an increase of the cerebral perfusion pressure (22).

This primary reflex of the brain stem seems to be of great importance to temporarily sustain the functions of the vital organs in a setting cardiac arrest (23).

2.2.2. RESPIRATORY

Gasing enhances the entry of “fresh” air into the lungs, hence improving the gas exchange of oxygen (O₂) and carbon dioxide (CO₂). A study in pigs showed that spontaneous gasping can induce a ventilation flow up to 4 l/min (21), providing higher PaO₂ and lower PaCO₂ values (18).

2.2.3. HEMODYNAMICALLY

During the inspiratory phase of a gasp, there is an intrathoracic pressure drop, which causes a decrease in aortic and right atrium pressure (23). Corollary the venous return to the heart is increased and thus improving the cardiac output leading to a better cerebral perfusion (22).

The expiratory phase is characterised by an increase in intrathoracic pressure, with an increase in cardiac output, arterial blood pressure and coronary perfusion. During the expiratory phase of the gasp, even an increase of the stroke volume up to 60% in a healthy heart may be observed (20, 23).

Furthermore, gasping can enhance cerebral microcirculation, which could be the reason for the better neurological outcome in gasping patients (23, 27).

2.3. PREVALENCE DURING CARDIAC ARREST IN HUMANS
In 1991, an analysis was conducted on 445 sound recordings of emergency calls for OHCA. Agonal breathing was among others described as “barely breathing”, “heavily breathing”, “noisy breathing” or even was in 7% of the cases called “gasp” by the caller. Descriptions as gurgling or moaning were also used. Of all the witnessed cardiac arrests, 55% were associated with agonal breathing. In unwitnessed cardiac arrest, this was 20% (28).

In another study with 113 OHCA patients (witnessed and unwitnessed), gasping was seen in 39%. However, the same study showed that of all patients who had a cardiac arrest only after arrival of medical services, 33% showed gasping (29).

In a retrospective analysis of 283 cases of witnessed cardiac arrest, almost 60% of bystanders described that the patient displayed some kind of breathing. This way of breathing was described as “having trouble with breathing”, “weakly breathing” or snoring. In almost 22% of the cases, bystanders were not able to decide whether the breathing was normal or not. In approximately 40% of the cases, the patient wasn’t breathing at all (30).

2.4. Effects on outcome

As described before, gasping may create some beneficial physiological changes in the body during cardiac arrest, such as increased cardiac output, better coronary and cerebral perfusion and more efficient gas exchange in the lungs. This may increase the success rate of defibrillation or it could prevent, or at least reduce, neurological sequelae. Several animal studies have shown that gasping was associated with increased survival rate (20, 22, 23).

Also human observational studies with OHCA patients have shown that gasping patients are likely to have a greater chance of survival (28-30). Clark et al. found that 27% of patients with gasping were discharged alive from the hospital compared with 9% of those without gasping (28). In the study of Bobrow et al., 28.3% of gaspers survived and 7.8% of the non-gaspers survived (29).
3. RESEARCH PROJECT AND HYPOTHESIS

The current study is part of a larger research project evaluating the use of tracheal airway pressures during resuscitation. The purpose of this retrospective study is to detect the presence of gasping in OHCA patients and to determine the rate and the volume by means of in vivo tracheal pressure waveform analysis. Also the occurrence of gasping regarding the initial cardiac rhythm and quality of CPR will be determined and the effect of gasping on short outcome will be analysed.
MATERIALS AND METHODS

1. STUDY POPULATION

The study population consisted of adult patients (>18 years) with OHCA who were resuscitated and oro-tracheally intubated by the Mobile Emergency Team of Ghent University Hospital between March of 2009 and December of 2015.

The Ethics Committee gave approval to the research project and to this thesis.

If the patient achieved ROSC, informed consent to use the data was obtained from the patient or his family. If the patient deceased on the scene or during transport to the hospital, informed consent was waived by the Ethics Committee.

2. MATERIAL AND METHODS

2.1. EQUIPMENT

2.1.1. THE REGISTRATION DEVICE

After the patient was oro-tracheally intubated, the measuring of the intrathoracic pressures was started. We used two air-filled catheters to measure the pressure differences over the endotracheal tube (ETT). The catheters were inserted in the ETT and attached to its proximal end with a connector. The deepest catheter was positioned approximately 1 cm distally of the ETT and the second catheter was placed proximally at the connection point of the ETT. The disposable sets (figure 4) were assembled manually.

Figure 4. Disposable set.
The other endings of the catheters were connected to the registration device with two pressure sensors (BD Medical, New Jersey, U.S.), two amplifiers (Wheatstone bridge, type 132 B Sensor Amplifier, Datum Electronics, East Cowes, U.K.) and a logger (MSR145, MSR Electronics GmbH, Seuzach, Switzerland). The device was powered by two 9V batteries that were replaced each two to three weeks.

After use, the disposables were checked for the presence of blood or other secretions in the lumen which could interfere with a correct measurement.

Figure 5. Registration device with connected disposable set.

Figure 6. Registration device.

The data were transferred twice a week from the logger to a laptop, using an USB cable and the MSR software. The logger was then zeroed and formatted, ready for use.

Twice a year, the device was fully serviced and calibrated.
2.1.2. ZOLL X SERIES DEFIBRILLATOR

Upon arrival of the physician’s mobile emergency group, the patient was monitored with a Zoll X series defibrillator (ZOLL Medical Corporation, Chelmsford, U.S.). The cardiac rhythm was monitored using multifunctional defibrillation electrodes (CPR stat padz multifunction, ZOLL Medical Corporation).

Furthermore, an accelerometer – placed at the lower half of the sternum – was connected to the defibrillator. With this accelerometer, the quality of chest compression depth and rate were measured and registered.

Once resuscitation was terminated, the registrations were transferred to a laptop by using an USB-stick and the RescueNet™ Code Review software (Standard Edition 5.70, ZOLL Medical Corporation).

2.1.3. OXYLOG 3000

After orotracheal intubation, patients were ventilated manually by bag ventilation or mechanically with an Oxylog 3000 ventilator (Dräger, Lübeck, Germany). In the mechanically ventilated patients standard intermittent positive pressure ventilation (IPPV), with or without positive end-expiratory pressure (PEEP) was used at the physician’s discretion.

2.2. SOFTWARE “GVA – GASP VOLUME ANALYSER”

To analyse the intratracheal pressure measurements, we developed our own software. For this purpose, we received help from Mr. Samuël De Smet (Bachelor in electromechanics specialised in automatisation, with a special interest in medical applications.)

The program was written in LabVIEW (National Instruments, Austin, Texas, U.S.) and transformed into a user friendly application. By using this application, analysis was efficient and accurate.

The determination of the mathematic definitions and conditions to write the program was a very important and significant part of the study.

A pressure drop of 5 cmH₂O, in which the distally measured pressure had to be more negative than the proximally measured pressure, defined a gasp. This can be explained by the normal physiology of the respiration: during spontaneous inspiration, the distal intratracheal pressure is more negative than the more proximal pressure.
Without any respiratory effort, both pressures would ideally be zero cmH₂O. If 5 cmH₂O PEEP is used, they would both be 5 cmH₂O if no breathing or external interfering factors are present. The program detected a gasp as being a pressure that is smaller than -5 cmH₂O, so an extra option was added in case correction was needed when the patient was ventilated with PEEP. Furthermore, we took into account that any respiratory movement, whether bag/mechanically induced or whether it occurred spontaneously, could occur fragmented if chest compressions are done at the same time (figure 7, figure 8). The program was developed such that it would recognise those fragments, group them as one gasp and not counting every fragment as a gasp.

Figure 7. Print screen from GVA, showing a gasp during CPR, consisting of three fragments. The red line indicates the distal pressure, the green line indicates the proximal pressure.
Figure 8. Print screen from GVA, showing a gasp during CPR. The three fragments of the gasp are indicated by the three white arrows.

To determine the volume of one gasp, an empirical formula was used for the volume calculation based on pressure differences (“area between the curve”, figure 9). This formula was based on the relationship between pressure gradient and flow, given by the law of Darcy-Weisbach (31).

After repeated testing, debugging, comparison with manually analysed cases and various adjustments, the program became more and more accurate and sophisticated, resulting in a reliable and solid application.
In the current version of GVA v1.31, the following features are available:

- Automatic determination of deviations of the pressure sensors. Therefore, enough measured values at the beginning of the registration are needed when no chest compressions or ventilations are being performed. If there are insufficient values, one may correct the deviations manually by entering the offsets.
- Selection of a specific interval from the registration.
- Enter a PEEP value.
- Determination of:
  - number of gasps;
  - mean gasping volume in millilitres;
  - most negative pressure;
  - time to the most negative pressure (counting from the first gasp);
  - gasping rate, counting from the first gasp.
- Saving all variables and data from the pressure registration in an Excel file (Microsoft Office Excel).

Furthermore, the software visualises the pressure curves and one can use the zoom function, for example to study the graphical morphology of a gasp.

The volumes of the gasps are graphically visualised as well.

*Figure 10. Home screen GVA with analysed case.*
Figure 11. GVA with calculated gasping variables and graphical representation of the volumes of the individual gasps.

Figure 12. GVA with use of the zoom function. Two gasps during continuous chest compressions and IPPV are shown. The red pressure curve represents the distal intratracheal pressure; the green pressure curve represents the proximal pressure.

Each registration per patient was analysed in GVA and automatically exported to an Excel file. Afterwards, all patient data and analyses were entered in SPSS Statistics 23 (IBM, New York, U.S.) for further statistical analysis.

2.3. STATISTICAL ANALYSIS
All data were statistical analysed using SPSS Statistics 23 (IBM, Armonk, New York, U.S.). A significance level of $\alpha=0.05$ was used. Data are expressed as mean values (standard deviation; range).

**Relationship between gasping and ROSC.**

The hypothesis is that patients who gasp have a higher incidence of ROSC. Both gasping and achievement of ROSC are categorical variables, so a cross tabulation was formed and the Pearson Chi-Square test was performed. All the conditions for this test were met.

**Relationship between gasping and hospital discharge.**

The hypothesis is that patients who gasp have a higher incidence of discharge from the hospital and thus a lower short-term mortality. Both gasping and discharge from the hospital are categorical variables, so a cross tabulation was formed and the Fisher’s Exact Test was performed, because not all conditions for the Pearson Chi-Square test were met.

**Relationship between gasping and duration of hospital stay.**

To investigate if there is a difference in duration of hospital stay after ROSC between patients that showed gasping and patients that did not, the Mann-Whitney U Test was used, because the duration of hospital stay (in days) is a continuous variable without a Gaussian distribution and two unpaired groups were compared.

**Relationship between gasping characteristics and achievement of ROSC.**

All gasping characteristics (e.g. mean gasping volume, gasping rate, most negative pressure…) are continuous variables without Gaussian distribution. ROSC was used as grouping variable. To determine a statistical significance between each of the gasping characteristics and the achievement of ROSC, the Mann-Whitney U Test was used.

**Relationship between gasping characteristics and hospital discharge.**

Cfr. “Relationship between gasping characteristics and achievement of ROSC”. In this case, hospital discharge was used as grouping variable instead of ROSC.
Relationship between the occurrence of gasping and initial cardiac rhythm of the patient and quality of CPR.

The categorical variables of the context of the gasping were investigated with cross tabulations and the Pearson Chi-Square Test (if all conditions were met) or the Fisher’s Exact Test (if not all conditions for the Pearson Chi-Square Test were met).

For the continuous variables (which all had no Gaussian distribution), the Mann-Whitney U Test was used with the occurrence of gasping as grouping variable.

To study the relationship between the initial cardiac rhythm of the patient and the occurrence of gasping, the Fisher’s Exact Test was used, because not all conditions for the Chi-Square test were met.

Also for the chest compression rate and depth, the Fisher’s Exact Test was used, for the same reasons as explained before.

Relationship between the sex of the patient, the use of PEEP and the gasping characteristics.

These continuous variables without Gaussian distribution were statistically analysed with the gasping characteristics as grouping variables. The Kruskal-Wallis Test was used.

Sex of the patient and whether PEEP ventilation was used or not were investigated.
RESULTS

1. STUDY POPULATION

Of all patients included in the project, 714 had an OHCA and were resuscitated by the mobile emergency team. Since these pressure measurements were performed only in orotracheally-intubated patients, some registrations were only started after achievement of ROSC. For this reason, 140 patients were excluded.

Furthermore, we found that the registration was not fully reliable in 261 cases, e.g. because of the presence of secretions in the catheters.

Eight registrations were performed in patients <18 years and therefore excluded. We had insufficient data for nine patients.

![Figure 13. Patient selection flowchart.](image-url)
Data were collected in 296 patients with a mean age of 65 years (15.5; 18-89), 210 (71.2%) were male.

The occurrence of the initial cardiac rhythms upon arrival of the mobile emergency team is shown in figure 14.

PEEP was used during CPR in 57% of the resuscitated patients.

For 252 patients, we had valid CPR reports from the Zoll X series defibrillator. The mean chest compression depth was 4.9 cm (0.92; 2.0-8.5). The mean chest compression rate was 115 compressions per minute (12.7; 52-155).
Out of 293 valid data (3 missing files), 107 patients (36.6%) achieved ROSC and 186 patients (63.4%) deceased at the scene. Out of the patients who achieved ROSC, 86.0% deceased in the hospital and only 15 patients (14.0%) were discharged from the hospital.

![Figure 16. Short-term outcome of all patients.](image)

Patients who deceased in the hospital had a mean hospital stay of 5 days (9.0; 0-50). Patients who were discharged from the hospital, had a mean hospital stay of 34 days (40.5; 2-158). Of the discharged patients, 9 had a good neurological outcome, defined by the Modified Rankin Scale (mRS), 6 had a poor neurological outcome and for two patients we did not find any information about neurological outcome. The mRS is a scale from 0 to 6 measuring the degree of neurological disability or dependence in daily life activities. A 0 means good health without symptoms and 6 means that the patient is dead (32).
2. DETECTION AND QUANTIFICATION OF GASPING

We found on the pressure curves that 84 of 296 (28.4%) of the OHCA patients showed gasping during CPR.

![Occurrence of gasping during CPR](image)

*Figure 17. Occurrence of gasping during CPR.*

On average 36 gasps (57.8; 1-308) were recorded per patient.

In *table 1*, the characteristics of gasping are shown together with their descriptive characteristics. The number of valid cases used to determine the descriptive characteristics is given in the first column.

<table>
<thead>
<tr>
<th></th>
<th>Valid cases</th>
<th>Mean</th>
<th>Std. deviation</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Count</td>
<td>78</td>
<td>36</td>
<td>57.8</td>
<td>1</td>
<td>308</td>
</tr>
<tr>
<td>Mean gasping volume (ml)</td>
<td>78</td>
<td>345</td>
<td>208.8</td>
<td>56</td>
<td>1280</td>
</tr>
<tr>
<td>Gasping rate (gasps/minute)</td>
<td>62</td>
<td>5.2</td>
<td>4.86</td>
<td>0.3</td>
<td>18.2</td>
</tr>
<tr>
<td>Minimal gasping volume (ml)</td>
<td>78</td>
<td>165</td>
<td>153.9</td>
<td>9</td>
<td>892</td>
</tr>
<tr>
<td>Maximal gasping volume (ml)</td>
<td>78</td>
<td>540</td>
<td>318.7</td>
<td>56</td>
<td>1576</td>
</tr>
<tr>
<td>Duration of gasping (minutes:seconds)</td>
<td>59</td>
<td>10:09</td>
<td>09:35</td>
<td>00:12</td>
<td>40:16</td>
</tr>
<tr>
<td>Most negative pressure (cmH₂O)</td>
<td>78</td>
<td>-20</td>
<td>13.7</td>
<td>-56</td>
<td>-5</td>
</tr>
<tr>
<td>Time to most negative pressure (minutes:seconds)</td>
<td>57</td>
<td>06:59</td>
<td>08:36</td>
<td>00:00</td>
<td>35:30</td>
</tr>
</tbody>
</table>

26
The mean gasping volume was 345 ml (208.8; 56-1280). One patient had a mean gasping volume up to 1280 ml. The mean of all maximal gasps was 540 ml (318.7; 56-1576), with a highest absolute maximal gasp of 1576 ml.

![Boxplot of mean gasping volume.](image)

Figure 18. Boxplot of mean gasping volume.

The mean gasping rate, measured from the first to the last gasp, was 5 gasps per minute (4.9; 0-18). One patient had a mean gasping rate of 18 gasps per minute, which approached spontaneous breathing – and this during CPR.

The most negative intratracheal pressure observed in one patient was -56 cmH₂O. The mean most negative pressure of all patients was -20 cmH₂O (13.7; -56 – -5).
3. Relationship between gasping and short-term outcome

In the group of patients that showed gasping during CPR, 40.7% achieved ROSC. In the group of patients that did not show gasping, 35.1% achieved ROSC. This difference of 5.6% may be clinically relevant, but no statistical significance could be shown (P=0.37).

![Figure 19. Difference in achievement of ROSC between gasping and non-gasping patients.](image)

Of the gasping patients, 4.8% were discharged from the hospital however in non-gasping patients 5.2% were discharged. No further conclusions can be drawn because of the small sample size.

Different gasping characteristics (e.g. mean gasping volume, gasping rate, most negative pressure …) were examined in relationship to ROSC.

We found a clinically relevant and statistically significant relationship between the most negative intratracheal pressure that was measured in a patient and the achievement of ROSC (figure 20). The mean most negative pressure of all patients who did not achieve ROSC, was -17 cmH₂O. In the patients that did achieve ROSC, a mean most negative pressure of -24 cmH₂O was found (P=0.022).
Furthermore, there was a significant relationship found between the gasping rate and ROSC (figure 21): a mean gasping rate of 3.8 gasps per minute in patients who did not achieve ROSC vs. 7.4 gasps per minute in patients who did (P=0.019).

The mean gasping volume in the non-ROSC group was 323 ml (166.7; 56-738) and 389 ml (266.5; 62-1280) in the ROSC group, but the difference was not significant. No difference was
found for the number of gasps of each patient. None of the other gasping characteristics showed a difference between ROSC en non-ROSC patients.

In terms of hospital discharge, a significant difference (P=0.032) was found in mean gasping volume between patients who were discharged from the hospital and patients died in the hospital: the first group had a mean gasping volume of 642 ml (429.4; 349-1280), the latter had a mean gasping volume of 329 ml (182.6; 56-908).

There was no statistically significant relationship between the gasping rate and hospital discharge (P=0.15), but a gasping rate of 5 gasps per minute (4.8; 0-18) in deceased patients and a rate of 9 gasps per minute (4.9; 4-13) in discharged patients, may be clinically relevant.
4. GASPING AND ITS RELATION TO OTHER PARAMETERS

4.1. RELATIONSHIP BETWEEN THE OCCURRENCE OF GASPING AND THE SEX, AGE, PEEP, INITIAL CARDIAC RHYTHM AND CHEST COMPRESSIONS

Gasping occurred more in male patients (30.5%) than in female patients (23.3%), but the difference was not statistical significant (P=0.21).

We found no relationship between the age of the patients and the occurrence of gasping.

In the group of patients who were ventilated without PEEP, 26.9% showed gasping, whereas in the group who received PEEP ventilation, 30.2% showed gasping, but this difference was not statistically significant.

A clinical relevant and even statistical strongly significant relationship (P<0.001) was found between the initial cardiac rhythm of the patient and the presence of gasping.

![Occurrence of gasping by initial rhythm](image)

*Figure 22. Occurrence of gasping by initial cardiac rhythm.*

VF= ventricular fibrillation; PEA= pulseless electrical activity; ASY= asystole; VT= ventricular tachycardia.

Concerning the quality of CPR and the occurrence of gasping, there is trend in favour of a chest compression rate higher than 140 compressions per minute (P=0.05). Patients receiving chest compressions at a rate higher than 140 per minute showed in 62.5% of the cases gasping. For the recommended rate of 100 to 120 compressions per minute, that was in 22.6% of the cases.
Rates slower than 100 or rates between 120 and 140 displayed gasping in 33.3% and 33.8% respectively. There was no relationship found between the chest compression depth and the occurrence of gasping (P=0.53).

4.2. RELATIONSHIP BETWEEN THE SEX OF THE PATIENT AND THE USE OF PEEP AND THE GASPING CHARACTERISTICS

There were no significant differences found of the gasping characteristics between male and female patients, but there was a trend for male patients to have slightly greater mean gasping volumes and a greater maximal gasping volume (see Table 12 in the addendum).

PEEP appeared to influence the mean gasping volume (P=0.004). The mean gasping volume was smaller in patients that were ventilated with PEEP (294 vs. 411 ml). The gasping rate was higher in patients that were ventilated with PEEP but the difference was not significant.

No other relevant or significant relationships were found between the other context variables (e.g. chest compression rate and depth, initial cardiac rhythm…) and one or more of the gasping characteristics.


**DISCUSSION AND CONCLUSION**

This study is the first to quantify gasping in OHCA. All previous studies about gasping were based on experimental animal models and on observations by lay bystanders or by professional emergency care providers.

The purpose of this study was to develop in vivo detection and registration of gasping and to quantify the occurrence of gasping. Furthermore, we wanted to investigate the relationship between gasping and the outcome of the patient.

Occurrence and measurement of gasping in the prehospital setting were quite impossible because of the complexity of a resuscitation in the field, as it was not possible to measure gasping while performing CPR. A system as our device was needed to combine both research and adequate standard treatment of the patient without delaying resuscitative manoeuvres.

We found that 28.4% of the patients showed gasping during CPR. This is less than what was found by others, probably because of the later start of registration in our study. In our study, no time from the collapse to the start of the CPR was registered. This could imply an underestimation of gasping patients, because only in orotracheally and resuscitated patients, having the device in place and the registration started, we could detect gasping. Zuercher et al. found an occurrence of gasping in 55% of witnessed OHCA (27). Bobrow et al. found that 39% of all witnessed and unwitnessed OHCA patients gasped and that 33% of patients gasped who developed OHCA after EMS arrival (29). Clark et al. and Bang et al. found both that 40% of patients with witnessed or unwitnessed OHCA showed gasping (29).

We found a mean gasping rate of 5.2 gasps per minute. In 2006, Srinivasan et al. found in a pig model a remarkably similar mean gasping rate of 5.4 gasps per minute (22).

Also as published by Clark et al., we found that gasping mostly occurred in patients with VF as the initial rhythm (28). We found that 50% of patients with VF showed gasping. In the study of Clark et al., that was 56% of the patients. In a non-VF rhythm, only 34% of the patients in the
study of Clark et al. gasped (28). In our study, 44% of the patients in PEA and 19% of the patients in asystole had gasping.

Our study confirms what Zuercher et al. found in their animal model of gasping: a higher rate of gasping is associated with a higher incidence of survival (27). These findings are listed in Table 6 of the addendum.

Bobrow et al. found an overall survival to hospital discharge of 21.1% in the group of gasping patients and of 6.7% in the group of non-gasping patients (29). However, in our study, 40.7% of gasping patients achieved ROSC and 35.1% of the non-gasping patients achieved ROSC. We only found a hospital discharge of 4.8% in gasping patients and of 5.2% in non-gasping patients. The difference was not significant and only 15 patients were discharged from the hospital. Clark found that 27% of patients that gasped were discharged, were only 9% of the non-gasping patients were discharged (28). We found that a higher gasping rate and greater gasping volume were associated with more hospital discharge (see Table 7 in the addendum).

The limitations of animal models are that in the animal population all had a cardiac arrest with VF. It is known that gasping mostly occurs in this particular cardiac rhythm, but in our study only 22% of patients with OHCA had VF as the initial cardiac rhythm. Furthermore, animal studies are conducted on mostly healthy, young animals with induced cardiac arrest. Young animals are known to have more gasping and to have a more compliant chest. In our studied population, patients had comorbidities and a cardiac arrest in a real OHCA situation. Our patients of course had no induced cardiac arrest and they were not anesthetised before the onset of cardiac arrest.

LIMITATIONS

We used strict inclusion criteria for the analysis of gasping. Only those patients were included whose pressure registrations during CPR were of high quality and without doubt about the reliability of the registration. Sometimes registration was started after the achievement of ROSC, these patients were excluded. This could imply an underestimation of the occurrence of gasping in our study, because gasping is most frequent soon after the collapse and it decreases with time (29).
A previous study using an animal model showed that animals who started gasping at the beginning of cardiac arrest were more likely to continue gasping, even with higher frequencies than animals who did not show gasping at the beginning of the cardiac arrest (27). Similarly, this study showed that the time between the onset of cardiac arrest and the start of CPR influenced the gasping rate (27). In our study, no account was taken for the time until CPR was started. Neither was time to intubation (and hence time to registration upon onset of OHCA) registered. Again, this could imply an underestimation of gasping patients in our study. But even if the occurrence of gasping is underestimated, our study provides important new insights into the so-called “gasp...
gasping, sometimes the power of the statistical analysis was too small to achieve a significant statistical difference.

**FUTURE PERSPECTIVE**

These results emphasise the importance of further research with greater numbers of patients to determine the significance of the apparently clinically relevant and important findings.

A better understanding of gasping could not only have implications for the future approach to OHCA, but also for the development of new pre-hospital devices for resuscitation and to resuscitation training. It is yet unknown if some gasping patients generate sufficient ventilation in order to ensure adequate gas exchange in the lungs. If gasping could be induced by phrenic nerve stimulation as proposed by Xie et al., resuscitation protocols may be influenced significantly (20). That may also imply changes in pharmacological guidelines or recommendations during resuscitation and intubation: maybe it would be recommended not to use medication that depress the spontaneous ventilation of patients, and hence decrease gasping.

It is also of great importance to teach lay persons to recognise the occurrence of gasping as a sign of cardiac arrest, because there is a great risk that the start of CPR is delayed because of the incorrect presumption that the observed gasping is some sort of normal breathing and therefore delaying CPR.
REFERENCES

ADDENDUM

1. ADDITIONAL TABLES WITH RESULTS FROM THE STATISTICAL ANALYSIS

1.1. RELATIONSHIP BETWEEN GASPING AND ROSC

The hypothesis is that patients who gasp have a higher incidence of ROSC.
Both gasping and achievement of ROSC are categorical variables, so a cross tabulation was formed and the Pearson Chi-Square test was performed. All the conditions for this test were met.

<table>
<thead>
<tr>
<th>Gasping</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No gasping</td>
<td>137</td>
</tr>
<tr>
<td>Gaspng</td>
<td>48</td>
</tr>
<tr>
<td><strong>Count</strong></td>
<td>185</td>
</tr>
<tr>
<td><strong>% within gasping</strong></td>
<td>63.4%</td>
</tr>
<tr>
<td><strong>ROSC</strong></td>
<td>74</td>
</tr>
<tr>
<td><strong>No ROSC</strong></td>
<td>33</td>
</tr>
<tr>
<td><strong>Count</strong></td>
<td>107</td>
</tr>
<tr>
<td><strong>% within gasping</strong></td>
<td>36.6%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>211</td>
</tr>
<tr>
<td><strong>Count</strong></td>
<td>81</td>
</tr>
<tr>
<td><strong>% within gasping</strong></td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Table 2. Chi-Square tests for the relationship between gasping and ROSC.

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
<th>Asymptotic Significance (2-sided)</th>
<th>Exact Sig. (2-sided)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson Chi-Square</td>
<td>.810*</td>
<td>.368</td>
<td>0.416</td>
</tr>
<tr>
<td>Fisher's Exact Test</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N of Valid Cases</td>
<td>292</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 30.68.

1.2. RELATIONSHIP BETWEEN GASPING AND HOSPITAL DISCHARGE

The hypothesis is that patients who gasp have a higher incidence of discharge from the hospital and thus a lower short-term mortality.

Both gasping and discharge from the hospital are categorical variables, so a cross tabulation was formed and the Fisher’s Exact Test was performed, because not all conditions for the Pearson Chi-Square test were met.
**Table 3. Hospital discharge * Gasping cross tabulation.**

<table>
<thead>
<tr>
<th>Hospital discharge</th>
<th>No gasping</th>
<th>Gasping</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Count</td>
<td>201</td>
<td>80</td>
<td>281</td>
</tr>
<tr>
<td>% within Gasping</td>
<td>94.8%</td>
<td>95.2%</td>
<td>94.9%</td>
</tr>
<tr>
<td>Count</td>
<td>11</td>
<td>4</td>
<td>15</td>
</tr>
<tr>
<td>% within Gasping</td>
<td>5.2%</td>
<td>4.8%</td>
<td>5.1%</td>
</tr>
<tr>
<td>Total</td>
<td>212</td>
<td>84</td>
<td>296</td>
</tr>
<tr>
<td>% within Gasping</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

**Table 4. Fisher’s Exact Test for the relationship between gasping and hospital discharge.**

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
<th>Asymptotic Significance (2-sided)</th>
<th>Exact Sig. (2-sided)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson Chi-Square</td>
<td>0.023</td>
<td>0.880</td>
<td>0.572</td>
</tr>
<tr>
<td>Fisher's Exact Test</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N of Valid Cases</td>
<td>296</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*a. 1 cells (25.0%) have expected count less than 5. The minimum expected count is 4.26.*

**1.3. RELATIONSHIP BETWEEN GASPING AND DAYS OF HOSPITALISATION**

To investigate if there is a difference in duration of hospital stay after ROSC between patients that showed gasping and patients that did not, the Mann-Whitney U Test was used, because the duration of hospital stay (in days) is a continuous variable without a Gaussian distribution and there were two unpaired groups that were compared.

**Table 5. Descriptive statistics of hospital stay duration for patients who did not show gasping on registration and for patients who showed gasping.**

<table>
<thead>
<tr>
<th>Gasping</th>
<th>N</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean</th>
<th>Std. Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>No gasping</td>
<td>11</td>
<td>2</td>
<td>158</td>
<td>32.45</td>
<td>46.713</td>
</tr>
<tr>
<td>Gasping</td>
<td>4</td>
<td>16</td>
<td>61</td>
<td>38.50</td>
<td>18.412</td>
</tr>
</tbody>
</table>

There was no statistical significance (P=0.19).

**1.4. RELATIONSHIP BETWEEN SOME DIFFERENT GASPING CHARACTERISTIC AND ACHIEVEMENT OF ROSC**

All gasping characteristics (e.g. mean gasping volume, gasping rate, most negative pressure…) are continuous variables without Gaussian distribution. ROSC was used as grouping variable. To determine a statistical significance between each of the gasping characteristics and the achievement of ROSC, the Mann-Whitney U Test was used.
Table 6. Relationship between achievement of ROSC and some gasping characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Significance (P-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No ROSC</td>
<td>ROSC</td>
</tr>
<tr>
<td>Count</td>
<td>36</td>
<td>37</td>
</tr>
<tr>
<td>Mean gasping volume (ml)</td>
<td>323</td>
<td>389</td>
</tr>
<tr>
<td>Most negative pressure (cmH2O)</td>
<td>-17</td>
<td>-24</td>
</tr>
<tr>
<td>Gasping rate (min⁻¹)</td>
<td>3.8</td>
<td>7.4</td>
</tr>
</tbody>
</table>

1.5. Relationship between some different gasping characteristic and hospital discharge

Table 7. Relationship hospital discharge and some gasping characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Significance (P-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No hospital discharge</td>
<td>Hospital discharge</td>
</tr>
<tr>
<td>Mean gasping volume (ml)</td>
<td>329</td>
<td>641</td>
</tr>
<tr>
<td>Gasping rate (min⁻¹)</td>
<td>5.0</td>
<td>9.1</td>
</tr>
</tbody>
</table>

1.6. Relationship between the occurrence of gasping and the initial cardiac rhythm and the quality of CPR.

The categorical variables of the context of the gasping were investigated with cross tabulations and the Pearson Chi-Square Test (if all conditions were met) or the Fisher’s Exact Test (if not all conditions for the Pearson Chi-Square Test were met).

For the continuous variables (which all had no Gaussian distribution), the Mann-Whitney U Test was used with the occurrence of gasping as grouping variable.

To study the relationship between the initial cardiac rhythm of the patient and the occurrence of gasping, the Fisher’s Exact Test was used, because not all conditions for the Chi-Square test were met.

Table 8. Gasping * initial rhythm cross tabulation.

<table>
<thead>
<tr>
<th>Initial rhythm</th>
<th>Sinus</th>
<th>VF</th>
<th>PEA</th>
<th>ASY</th>
<th>VT</th>
</tr>
</thead>
<tbody>
<tr>
<td>No gasping</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Count</td>
<td>3</td>
<td>29</td>
<td>20</td>
<td>128</td>
<td>3</td>
</tr>
<tr>
<td>% within initial rhythm</td>
<td>100.0%</td>
<td>50.0%</td>
<td>55.6%</td>
<td>81.5%</td>
<td>100.0%</td>
</tr>
<tr>
<td>Gasping</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Count</td>
<td>0</td>
<td>29</td>
<td>16</td>
<td>29</td>
<td>0</td>
</tr>
<tr>
<td>% within initial rhythm</td>
<td>0.0%</td>
<td>50.0%</td>
<td>44.4%</td>
<td>18.5%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Count</td>
<td>3</td>
<td>58</td>
<td>36</td>
<td>157</td>
<td>3</td>
</tr>
<tr>
<td>% within initial rhythm</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>
Table 9. Fisher’s Exact Test for the relationship between the occurrence of gasping and the initial cardiac rhythm.

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
<th>Asymptotic Significance (2-sided)</th>
<th>Exact Sig. (2-sided)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson Chi-Square</td>
<td>28.420</td>
<td>.000</td>
<td>.000</td>
</tr>
<tr>
<td>Fisher's Exact Test</td>
<td>27.100</td>
<td></td>
<td>.000</td>
</tr>
<tr>
<td>N of Valid Cases</td>
<td>260</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a. 8 cells (57.1%) have expected count less than 5. The minimum expected count is .29.

Also for the chest compression rate and depth, the Fisher’s Exact Test was used, for the same reasons as explained before.

Table 10. Gasping * chest compression rate cross tabulation.

<table>
<thead>
<tr>
<th>Gasping</th>
<th>Chest compression rate (CCR) (min⁻¹)</th>
<th>&lt;80</th>
<th>80-100</th>
<th>100-120</th>
<th>120-140</th>
<th>&gt;140</th>
</tr>
</thead>
<tbody>
<tr>
<td>No gasping</td>
<td>Count</td>
<td>3</td>
<td>12</td>
<td>120</td>
<td>45</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>% within CCR</td>
<td>100.0%</td>
<td>66.7%</td>
<td>77.4%</td>
<td>66.2%</td>
<td>37.5%</td>
</tr>
<tr>
<td>Gasping</td>
<td>Count</td>
<td>0</td>
<td>6</td>
<td>35</td>
<td>23</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>% within CCR</td>
<td>0.0%</td>
<td>33.3%</td>
<td>22.6%</td>
<td>33.8%</td>
<td>62.5%</td>
</tr>
</tbody>
</table>

Table 11. Fisher’s Exact Test for the relationship between the occurrence of gasping and the chest compression rate.

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
<th>df</th>
<th>Asymptotic Significance (2-sided)</th>
<th>Exact Sig. (2-sided)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson Chi-Square</td>
<td>9.630*</td>
<td>4</td>
<td>.047</td>
<td>.046</td>
</tr>
<tr>
<td>Fisher's Exact Test</td>
<td>8.799</td>
<td></td>
<td></td>
<td>.050</td>
</tr>
</tbody>
</table>

a. 4 cells (40.0%) have expected count less than 5. The minimum expected count is .82.

1.7. Relationship between the sex of the patient and the use of PEEP and the gasping characteristics.

These continuous variables without Gaussian distribution were statistically analysed with the gasping characteristics as grouping variables. The Kruskal-Wallis Test was used.
1.7.1. SEX

Table 12. Relationship between sexes and some gasping characteristics.

<table>
<thead>
<tr>
<th>Comparison of gasping characteristics: male vs. female</th>
<th>Mean</th>
<th>Significance (P-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Mean volume</td>
<td>373</td>
<td>270</td>
</tr>
<tr>
<td>Most negative pressure</td>
<td>-21</td>
<td>-17</td>
</tr>
<tr>
<td>Gasping rate</td>
<td>4.4</td>
<td>7.2</td>
</tr>
<tr>
<td>Maximal gasping volume</td>
<td>1576</td>
<td>1085</td>
</tr>
</tbody>
</table>

1.7.2. PEEP

Table 13. Relationship between PEEP and some gasping characteristics.

<table>
<thead>
<tr>
<th>Comparison of gasping characteristics: PEEP vs. non-PEEP</th>
<th>Mean</th>
<th>Significance (P-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No PEEP</td>
<td>PEEP</td>
</tr>
<tr>
<td>Mean volume</td>
<td>411</td>
<td>294</td>
</tr>
<tr>
<td>Gasping rate</td>
<td>4.3</td>
<td>6.1</td>
</tr>
</tbody>
</table>
2. SUMMARY IN DUTCH

2.1. INLEIDING
Gasping dat optreedt tijdens cardiopulmonaire reanimatie (cardiopulmonary resuscitation, CPR) is geassocieerd met een verhoogde cerebrale perfusie, veneuze terugkeer en cardiale output. Op deze manier vergroot het de kans op terugkeer van spontane circulatie (return of spontaneous circulation, ROSC).

Deze studie is een deel van een groter project dat endotracheale drukken meet tijdens reanimeren bij patiënten met een hartstilstand buiten het ziekenhuis (out-of-hospital cardiac arrest, OHCA).

De bedoeling van dit onderzoek is om gasping tijdens CPR te detecteren en te kwantificeren, alsook om na te gaan of er een verband bestaat tussen gasping en de outcome van de patiënt.

2.2. MATERIALEN EN METHODE
Deze retrospectieve, observationele studie werd uitgevoerd met patiënten die gereanimeerd en orotracheaal geïntubeerd werden door de mobiele urgentiegroep (MUG) van het Universitair Ziekenhuis Gent tussen maart 2009 en december 2015.

Na intubatie werd een wegwerpset, die bestond uit twee met lucht gevulde katheters en connectoren, ingebracht in de endotracheale tube. De katheters waren verbonden met twee druksensoor en een logger in een registratietoestel. De drukken werden gemeten en geregistreerd proximaal en distaal in de endotracheale tube.


Reanimatiegegevens zoals compressiediepte en -snelheid werden geregistreerd met een accelerometer die verbonden was met de Zoll X series defibrillator (Zoll, Chelmsford, U.S.).

De endotracheale drukgegevens en reanimatiegegevens werden vervolgens geanalyseerd met SPSS Statistics 23 (IBM, New York, U.S.).

De resultaten worden weergegeven als gemiddelden (standaarddeviatie; range).

2.3. RESULTATEN
De gegevens van 296 patiënten konden worden verzameld en geanalyseerd. De gemiddelde leeftijd was 65 jaar (15,5;18-89). Onder hen waren 210 (71,2%) mannen. Het initiële hartritme
was asystolie bij 60,4% van de patiënten, ventriculaire fibrillatie bij 22,3%, polsloze elektrische activiteit bij 13,8% en ventriculaire tachycardie bij 1,0%.

Van 293 patiënten (de gegevens van 3 patiënten ontbraken), behaalden 36,6% ROSC.

De gemiddelde compressiediepte was 4,9 cm (0,92; 2,0-8,5) en de gemiddelde compressiesnelheid was 115 per minuut (12,7; 52-155).

Bij 84 van de 296 patiënten (28,4%) trad er gasping op tijdens de reanimatie die geregistreerd werd. Het gemiddeld aantal gasps was 36 per patiënt (57,8; 1-308). Het gemiddelde volume was 345 ml (208,8; 56-1280) met een gemiddeld maximaal volume van 540 ml (318,7; 56-1576). De gemiddelde gasping frequentie was 5 gasps per minuut (4,9; 0-18). De maximale frequentie lag bij 18 gasps per minuut. De meest negatieve intratracheale druk was gemiddeld -20 cmH₂O (13,7; -56 – -5).

In de groep van patiënten met gasping behaalden 40,7% ROSC, terwijl 35,1% ROSC behaalden in de groep van patiënten die niet gaspten. De gasping frequentie was significant hoger in de groep met ROSC vergeleken met de andere groep (respectievelijk 7,4 en 3,8 gasps per minuut).

Het gemiddelde volume in de non-ROSC-groep was 323 ml (166,7; 56-738) en 389 ml (266,5; 62-1280) in de ROSC-groep. Diepere negatieve drukken waren geassocieerd met een hogere incidentie ROSC.

Patiënten die overleefden tot aan het ontslag uit het ziekenhuis hadden tevens een significant hoger gasping volume dan patiënten die eerder overleden. De gasping frequentie was eveneens hoger in de groep patiënten die konden worden ontslagen uit het ziekenhuis.

2.4. CONCLUSIE

Er werd geen significant verschil gevonden in het behalen van ROSC tussen patiënten die gasping vertonen en patiënten die geen gasping vertonen. We vonden echter een hoge prevalentie van gasping tijdens CPR. Als er gasping optrad, werden significante volumes gemeten. Er was een grote variatie tussen de gasping karakteristieken in één patiënt en tussen verschillende patiënten.

Een hogere gasping frequentie en diepere negatieve drukken waren geassocieerd met toegenomen incidentie van ROSC. Verder kunnen we afleiden dat grotere gasping volumes geassocieerd waren met een grotere kans om levend uit het ziekenhuis te kunnen worden ontslagen.

Een grotere studie is nodig om deze bevindingen te kunnen bevestigen.
3. Copy of an informed consent form

TOESTEMMINGSFORMULIER

Naam van de studie: Onderzoek naar kwaliteit van beademing

Naam patiënt:
Datum van ondertekening:

Geachte,

U/Uw familieled werd behandeld door het medische interventieteam (MUG).

Tijdens de behandeling gebeurden er metingen van de drukken in de longen en van de uitgeademde lucht. De bedoeling van deze metingen is om de kwaliteit van de behandeling te bestuderen, met als uiteindelijke bedoeling om de kwaliteit van onze behandelingen te kunnen verbeteren. De metingen gebeurden met sensoren die geen enkel gevaar of extra tijdsverlies voor U/uw familieled inhielden. Er was ook geen enkele invloed op uw behandeling/de behandeling van uw familieled.

De gegevens zullen samen met gegevens van andere patiënten op een anonieme manier verwerkt worden (uw identiteitsgegevens/de identiteitsgegevens van uw familieled worden dus onherkenbaar gemaakt).

Om medische gegevens te kunnen bewaren en verder te gebruiken in het kader van onderzoek, vragen wij steeds schriftelijke toestemming aan de patiënt.

Gezien de omstandigheden was U/uw familieled niet in staat om zelf de goedkeuring te geven over het bewaren en verwerken van de gegevens. Daarom vragen wij u als meest nabije familieled om deze toestemming op dit moment schriftelijk te geven.


Indien u akkoord bent met het gebruik van de geregistreerde gegevens voor de studie, gelieve dan hieronder aan te duiden wat uw verwantschap tot de patiënt is. Hiermee bevestigt u dat eventueel hoger vermelde familieleden niet in de mogelijkheid verkeren om hun toestemming te geven omwille van de volgende reden:

Duid uw verwantschap aan aub:
1. samenlevende echtgeno(o)t(e) of samenwonende partner.
2. meerderjarig kind van de patiënt(e)
3. ouder van de patiënt(e)
4. broer of zus van de patiënt(e)
5. geen enkele van de hierboven vermelde familieleden

Naam van de vertegenwoordiger + handtekening,

Gelieve voor akkoord te willen ondertekenen met gelegen en goedgekeurd
en graad van verwantschap te willen vermelden

U ontvangt een kopie van dit formulier.
4. **Abstract and Poster from Our Pilot Study, Presented at the BeSEDIM Congress 2015.**

4.1. **Abstract**

**Measuring rate and volume of gasping during out-of-hospital cardiac arrest: a pilot study.**

Martha Wolfskeil¹, Maxim Vanwulpen¹, Christophe Duchatelet¹, Joline Goossens PhD¹-², Sophie Huybrechts³, Sabine Lemoyne MD², Koen Monsieurs MD, PhD¹-³, Said Hachimi-Idrissi MD, PhD, FCCM¹-².

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2. Department of Emergency Medicine, Ghent University Hospital, De Pintelaan 185, B-9000 Ghent, Belgium
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**Introduction**

Gasing during cardiopulmonary resuscitation (CPR) is associated with cerebral perfusion, and venous return, hence increases the chance of return of spontaneous circulation (ROSC) [1]. The current pilot study is part of a larger project measuring tracheal airway pressures during resuscitation in out-of-hospital cardiac arrest (OHCA). The purpose of this study was to develop a method to determine the rate and the volume of gasing in OHCA patients.

**Materials and methods**

Observational study of OHCA patients who were intubated and resuscitated by the Mobile Emergency Group. During CPR, an experimental device containing pressure sensors and a logger measured pressures at the distal and proximal end of the endotracheal tube. Pressure data were analysed with dedicated LabVIEW software. Spontaneous breathing was defined as a relative endotracheal pressure drop of 5 cm H₂O. The rate and the volume of each gasp were analysed. Volumes were calculated from the pressure differences between the catheters [2]. Compression data were recorded using an accelerometer on a Zoll X series defibrillator. All data are expressed as mean values (standard deviation; range).

**Results**

We analysed a convenience sample of 19 OHCA patients that showed gasing on the tracheal pressure waveforms. The mean age was 64 years (SD 11.9; range 47-87), 17 (89.5%) were male. In six (32%) patients ROSC was achieved. The initial rhythm was ventricular fibrillation in 42%, asystole in 26% and pulseless electric activity in 11%. During CPR, 10 patients (53%) received positive end expiratory pressure. The mean chest compression depth was 5.0 cm (SD 0.18; range 3.4-6.6) at a mean compression rate of 114 per minute (SD 16.4; range 83-146).

The mean gasing rate was 4.8 per minute (SD 1.35; range 0.4-23.1), the mean gasing volume was 572 ml (SD 225.0; range 243-1152).

**Conclusion**

Significant volumes were measured during gasing in OHCA patients, there was wide variation between the gapses of one patient, and between the gapses of different patients. Further analysis is needed to investigate if rate and volume of gasing are associated with outcome.
References
4.2. Poster

Measuring rate and volume of gasping during out-of-hospital cardiac arrest: a pilot study

Martha Wolskell1, Maxim Vanvuilen2, Christophe Duchateau1, Joline Goossens PhD1, Sofie Huybrechts2, Sabine Lemoyne MD2, Koen Monsieurs MD, PhD2,3, Saad Hachimi-Idrissi MD, PhD, FCCM1,2

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Keywords: gasping, cardiac arrest, tracheal pressure

Introduction

Gassing during CPR is associated with cerebral perfusion and various return, hence gasping increases the chance of return of spontaneous circulation (ROSC).

This pilot study is part of a larger project measuring tracheal airway pressures during CPR.

We developed a method to determine the rate and volume of gasping in out-of-hospital cardiac arrest (OHCA) patients.

Materials and methods

Observational study of OHCA patients who were intubated and resuscitated by the Mobile Emergency Group.

During CPR, an experimental device containing pressure sensors and a logger measured pressures at the distal and proximal end of the endotracheal tube.

Gassing was arbitrarily defined as a relative intrathoracic pressure drop of at least 5 cmH2O, since inspiration causes a pressure drop in the lungs and a subsequent pressure drop in the distal trachea.

We analysed rate and volume of the gasps.

Volumes were calculated from the pressure differences between the catheters, using dedicated LabVIEW software.

Results

We analysed 19 OHCA patients who showed gasping on the tracheal pressure waveforms.

![Figure 2: Proximal (green) and distal (red) pressure signal in the endotracheal tube during CPR. Volumes were calculated from the area between both curves.](image)

The mean age was 64 years (SD 11.9, range 47-77) and 17 (89.5%) were male.

In six patients ROSC was achieved.

The initial rhythm was ventricular fibrillation in 42%, asystole in 26% and pulses electrical activity in 11%.

During CPR, 10 patients (53%) received positive end expiratory pressure.

![Figure 3: Analyses of gasp characteristics of a patient in QVA (Gasp Volumes Analyzer).](image)

<table>
<thead>
<tr>
<th>Tabel 1: Analysed CPR characteristics</th>
<th>Mean</th>
<th>SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gassing rate (per minute)</td>
<td>4.8</td>
<td>1.35</td>
<td>0.4-23.1</td>
</tr>
<tr>
<td>Gassing volume (ml)</td>
<td>072</td>
<td>225.0</td>
<td>243-1152</td>
</tr>
<tr>
<td>Chest compression rate (per minute)</td>
<td>114</td>
<td>10.4</td>
<td>93-146</td>
</tr>
<tr>
<td>Chest compression depth (cm)</td>
<td>5.6</td>
<td>0.18</td>
<td>3.4-6.6</td>
</tr>
</tbody>
</table>

Conclusion

Significant volumes were measured during gasping in OHCA patients.

Wide variation in the volume of the gasps within the same patient were noticed as well as wide variation in gasp rate and volume between different patients.

Further analysis is needed to investigate if rate and volume of gasping are associated with outcome.

Contact: martha.wolskell@ugent.be

![Critical care](image)
5. **Abstract and Poster from Another Study Conducted Within the Progress, Presented at the BeSEDiM Congress 2016.**

5.1. **Award**

This abstract won the annual award “Best Appreciated Of BESedim Abstracts 2016” in the category “Studies”, handed out by the Scientific Committee of the Belgian Society of Emergency and Disaster Medicine (BeSEDiM) and the Belgian Resuscitation Council (BRC).

5.2. **Abstract**

**Effect of positive end-expiratory pressure during cardiopulmonary resuscitation on short-term survival.**

Martha Wolfskeil¹, Maxim Vanwulpen¹, Christophe Duchateau¹², Joline Goossens¹ PhD, Koenraad G. Monsieurs MD, PhD¹³, Said Hachimi-Idrissi MD, PhD, FCCM¹².

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². Department of Emergency Medicine, Ghent University Hospital, De Pintelaan 185, B-9000 Ghent, Belgium
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**Introduction**

The effect of positive end-expiratory pressure (PEEP) during intermittent positive pressure ventilation in patients undergoing cardiopulmonary resuscitation (CPR) on outcome is unknown. PEEP administration may increase cardiac output by reducing left ventricular afterload, reversing pulmonary atelectasis and hence lowering pulmonary vascular resistance (1). In a rodent model of cardiac arrest, the application of 5 cm H₂O of PEEP during and after CPR had beneficial effects on survival that were independent of oxygenation and without adverse cardiovascular effects (2). On the other hand, elevated positive pressures during CPR in humans increases intrathoracic pressure and may reduce cardiac output and organ perfusion by reducing venous return (3). The purpose of the current study is to evaluate the effect of PEEP on short-term survival in out-of-hospital cardiac arrest (OHCA) patients.

**Materials and methods**

Physician-staffed medical team resuscitated OHCA patients. They were intubated and ventilated using a bag with or without PEEP valve or with a mechanical ventilator with or without PEEP at the discretion of the attending physician. During ventilation, tracheal airway pressures were measured using two air-filled catheters connected to a custom-made portable external recording device consisting of two pressure sensors, two amplifiers and a logger. Compression data were recorded using an accelerometer on a Zoll X series defibrillator (Zoll, Chelmsford, US). Pressure and compression data were analysed with dedicated LabVIEW software (National Instruments, Austin, Texas, U.S.). Data were analysed using SPSS Statistics (IBM, Armonk, New York, U.S.). Data are expressed as mean values (standard deviation; range).

**Results**
Data were collected in 298 patients with a mean age of 65 years (15.6; 18-89), 211 (70.8%) were male. Of all patients, 36.9% achieved ROSC. The initial rhythm was asystole in 54.7%, ventricular fibrillation in 17.8%, pulseless electrical activity in 11.1% and ventricular tachycardia in 0.7%. The mean chest compression depth was 4.9 cm (0.91; 2.02-8.50) and the mean chest compression rate was 115 per minute (12.7; 52-155). Five cm H2O PEEP was used in 169 patients (56.7%). Patients ventilated with 5 cm H2O PEEP had significantly higher ROSC compared to patients without PEEP (48.2% vs. 22.2%, P<0.001).

**Conclusion**
The use of PEEP during CPR in OHCA patients was associated with higher ROSC. These results need to be confirmed in a multivariate analysis.

**References**
Effect of positive end-expiratory pressure during cardiopulmonary resuscitation on short-term survival

Martha Wolfskeil, Maxim Vanwulpen, Christophe Duchateau, Joline Goossens, PhD,
Koenraad G. Monsieurs MD, PhD, Said Hachimi-Ikriess MD, PhD, FCCM.

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Introduction
The effect of positive end-expiratory pressure (PEEP) ventilation in patients undergoing cardiopulmonary resuscitation (CPR) is unknown. It may increase cardiac output by reducing left ventricular afterload. However, it may also reduce cardiac output and organ perfusion by reducing venous return.

This study evaluated the effect of a limited level of PEEP on return of spontaneous circulation (ROSC) in out-of-hospital cardiac arrest (OHCA) patients.

Materials and methods
Physician-staffed medical team resuscitated OHCA patients. During CPR and after orotracheal intubation, physicians used whether bag valve ventilation or a ventilator with or without 5 cmH₂O PEEP at the discretion of the attending physician.

During CPR, tracheal airway pressures were measured using two air-filled catheters connected to a custom-made portable external recording device, consisting of two pressure sensors, two amplifiers and a logger.
Curves are viewed in the MSR-viewer (MSR Electronics GmbH, Seuzach, Switzerland).

Results
We analysed data from 298 OHCA patients. The mean age was 65 years (SD 15.6; range 19-89) and 211 (70.8%) were male.

The initial rhythm was asystole in 54.7%, ventricular fibrillation in 17.8%, pulseless electrical activity in 11.1% and ventricular tachycardia in 0.7%.

Out of 298 patients, 110 (36.9%) achieved ROSC.
In 169 patients (56.7%), 5 cmH₂O PEEP was used.

Patients ventilated with 5 cmH₂O PEEP achieved significantly (P<0.001) higher ROSC compared to patients ventilated without PEEP.

Conclusion
The use of limited PEEP during CPR in OHCA patients was associated with higher ROSC incidence.
These results need to be confirmed in a multivariate analysis.

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